Racial differences in treatment preferences among lupus patients: a two-site study

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Abstract

Objective

To identify the demographic, clinical and psychosocial characteristics associated with racial differences in willingness to receive cyclophosphamide (CYC) or participate in a research clinical trial (RCT) among patients with systemic lupus erythematosus (SLE).

Methods

Data from 163 African-American (AA) and 180 white (WH) SLE patients were evaluated. Structured interviews and chart reviews were conducted to determine treatment preferences in hypothetical situations and identify variables that may affect preferences. Logistic regression models were performed to evaluate the relationship between patient preferences and race, adjusted for patient characteristics.

Results

Among patients who had never received CYC (n=293), 62.9% AAs compared to 87.6% WHs were willing to receive the medication ($p<0.001$). This difference persisted (OR 0.37 [95% CI, 0.16-0.87]) after adjusting for socio-demographics, clinical characteristics, and perceptions about CYC and physicians. Income and higher perception of CYC effectiveness were other determinants of willingness to receive CYC.

Among patients who had never participated in an RCT (n=326), 64.9% AAs compared to 84.3% WHs were willing to do so ($p<0.001$). This difference persisted (OR 0.41 [95% CI, 0.20-0.83]) after adjusting for socio-demographics, clinical context and patients' perceptions of physicians. SLE damage score, number of immunosuppressive medications and higher trust in physicians were also independently associated with willingness to participate in an RCT.

Conclusion

Race remains an independent determinant of treatment preferences after adjustment for income, medications, medication efficacy expectations and trust in physicians. While some factors related to racial differences in preferences are relatively fixed, others that may alleviate these differences also exist, including medication beliefs and provider trust.

Key words

systemic lupus erythematosus, cyclophosphamide, clinical trial, treatment preferences.

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Introduction

Racial disparities in systemic lupus erythematosus (SLE) exist, with African-American (AA) patients experiencing more active disease, more organ system involvement and more psychological disturbances than white (WH) patients (1). In addition, several of these factors are associated with higher lupus damage score and greater disease activity over time (2, 3).

Cyclophosphamide (CYC) is a potent immunosuppressive agent that has been used extensively in the last three decades to treat severe organ manifestations of SLE (4, 5). Although very effective, CYC is associated with short-term and long-term toxicity, including malignancy, infertility and haemorrhagic cystitis. Nevertheless, the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have recommended its use in patients with moderate to severe lupus nephritis and those with significant neuropsychiatric involvement (4, 5). While novel drugs are being developed for SLE and are under investigation in clinical trials (6), AAs are often underrepresented in clinical trial studies (7). As SLE in AAs tends to be more severe than in WHs and may differ in pathophysiology (1), it is vital to recruit AAs into clinical trials to determine efficacy in this group.

Studies of multiple diseases have shown that AAs prefer less aggressive treatment than WHs. AAs are less willing than WHs to undergo invasive cardiac procedures (8, 9), carotid endarterectomy (10), or joint replacement surgery (11, 12). In our previous study of SLE patients, AAs were found to be less willing than WHs to receive CYC (13). The Institute of Medicine's model of health disparities acknowledges that patient treatment preferences may contribute to racial disparities in health among patients (14).

The purpose of the current study is to determine whether there are racial differences in willingness

i. to receive CYC when clinically indicated and physician recommended, or

ii. to participate in a research clinical trial (RCT) involving a novel, experimental medication among SLE patients from two different geographic recruitment sites. We also seek to determine which demographic, clinical and psychosocial characteristics may impact the racial differences in either measure of treatment preference. Patient attitudes and beliefs towards their disease, medications and physicians, and the associations of these patient-reported measures with treatment preferences will also be explored.

In comparison to our previous study of SLE patients' treatment preferences (13), the current study reflects preferences of a racially diverse group of patients recruited from two different geographic regions with twice the study sample size. Hence, we are able to assess a substantial range of variation in patient preferences and to elucidate possible explanations for the anticipated racial variation, including the perceptions of medication efficacy and risk, along with trust in medical providers.

Patients and methods

Patients

Lupus patients were recruited from rheumatology clinics affiliated with either the University of Chicago or the University of Pittsburgh. Institutional Review Board approval from each university and participant informed consent were obtained. Only those who fulfilled the ACR SLE criteria were included. The exclusion criteria were: <18 years of age, race other than AA or WH, history of both taking CYC and participating in an interventional RCT involving a new medication, and severe cognitive dysfunction. Patients who were not successfully contacted or failed to answer the majority of the survey (>50% of questions) were excluded from analysis (Fig. 1). Data were obtained by structured telephone interviews and from medical record reviews. Each interview was conducted with exactly the same questions in the same order administered by a single physician (EV).

Study outcome variables

– Treatment preferences

After providing information regarding CYC and clinical trials, agreement with the following statements was measured: "If my lupus becomes more severe, se-

riously attacking my lung, heart, kidney or brain and if my doctor recommended it, then I would be willing to receive cyclophosphamide" and "If my lupus gets worse and if my doctor recommended it, then I would be willing to participate in a lupus research clinical trial that may involve the use of a new, experimental medication". Agreement with each statement was measured using a four-category ordinal response scale, and responses were dichotomised to 'willing' or 'unwilling' (13).

Primary predictor variable

Self-identified patient race was the primary predictor variable. Patients who self-identified as non-Hispanic AA or WH were eligible for enrollment.

Covariates

– Sociodemographic characteristic

Basic demographic characteristics examined included age, educational attainment, income, employment status, medical insurance and marital status.

– Clinical characteristics

Cumulative disease activity was assessed using the SLE Disease Activity Index (SLEDAI) (15). Accumulated organ damage from SLE was measured using the Systemic Lupus International Collaborating Clinics (SLICC) Damage Index (16). Medical comorbidity was assessed using the Charlson Comorbidity Index (17). Level of depression symptoms was measured using the Center for Epidemiologic Studies Depression (CES-D) scale (18).

– Medication-related questions

Current use of immunosuppressant medications was determined during chart abstraction. Measures of familiarity with CYC treatment (range: 0–3) as well as perceptions of risk (range: 3-15) and effectiveness of CYC treatment (range: 6–30) were determined using reliable and validated measures (13). Higher scores indicate better familiarity, higher perceived risk or higher perceived efficacy of treatment, respectively.

– Beliefs and attitudes

Patients' perceptions of the role of prayer in the management of SLE was based on a validated questionnaire which assesses how helpful patients consider prayer is for their lupus and how often they have used prayer to treat their lupus (range: 0–2 for efficacy, 0–3 for usage) (13, 19). Risk propensity was measured using the Domain-Specific Risk Attitude Scale's health and safety domain (range: 10–50; higher scores indicate higher likelihood of participation in risky behaviours) (20). Multidimensional Health Locus of Control (MHLC) was determined to measure the degree to which patients feel their own actions or other external factors (*i.e.* chance, powerful others) may affect their health. The score in each subscale indicates how strongly the individual believes in each dimension of control (range: 6–36) (21).

Participants were asked how important it was for them to see a rheumatologist of their own race, sex, or age using a five-category ordinal response scale (13). Patient perceived physician's participatory decision-making (PDM) Style (range: 0–100; higher scores indicate more participatory style) (22) and duration of physician-patient relationship were also measured. Hall's Trust in Physicians Scale, a measure used to assess interpersonal trust in a patient's individual physician, was determined (range: 11–55; higher score indicates greater trust). It is a measure with high validity and internal reliability (23). Patient perceived discrimination in the healthcare system was also assessed; higher values indicate more perceived racial discrimination (range: 4–20) (24).

Statistical analysis

Parametric and non-parametric tests were used to compare the demograph-

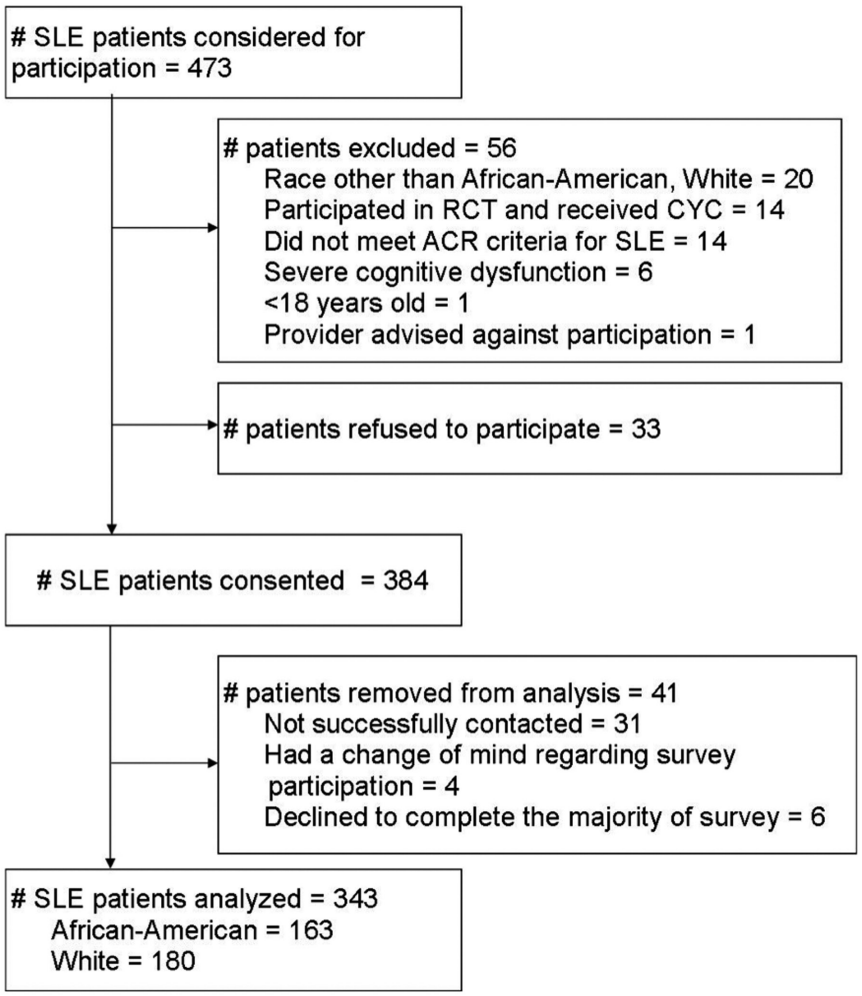

Fig. 1. SLE patients recruited for survey participation.

ic, psychosocial, and clinical characteristics of patients by race. Categorical variables were compared by χ^2 analysis and ordinal variables by Wilcoxon rank sum test. Continuous variables were compared by a two-sample *t*-test. In the same manner, these characteristics were then contrasted by willingness to receive CYC administration and by willingness to participate in a RCT.

Logistic regression models were performed to evaluate the relationship between patient preferences and race, adjusted for patient characteristics. Patients who had ever taken CYC were excluded from the willingness to take CYC analyses, and those who had been in a RCT were excluded from the willingness to participate in a RCT analyses. The initial model in these analyses included only race/ethnicity as the independent variable. Patient characteristics and beliefs that may mediate this relationship, based on bivariate analyses ($p \leq 0.05$) and theoretical models, were then added to subsequent models to determine whether these covariates may explain the difference between the racial groups' treatment preferences. A greater than 10% change in odds ratio (OR) after the addition of the potential mediating variable(s) suggests mediation (25, 26).

Results

Sample characteristics

A total of 384 patients were eligible and consented to participate in the study; a final cohort of 343 patients resulted (Fig. 1). AA patients, compared to WH patients, were more likely to be recruited from the University of Chicago than from the University of Pittsburgh ($p<0.001$) and were more likely to be younger ($p<0.001$). They were also less likely to have more than a HS graduate degree, have higher income and have private insurance (Table I).

Preferences for cyclophosphamide treatment

Among patients who had never received CYC (n=293), willingness to receive the medication was lower among AAs (62.9%) compared to WHs (87.6%) (crude OR, 0.24 [95% CI, 0.13–0.43]). AA SLE patients, compared to WH

Table I. Characteristics of SLE patients by race.

Characteristic	White (n=180)	African-American (n=163)	*p**
Demographic characteristics			
Number of subjects, n	180	163	n/a
Recruitment site, n(%)			<0.001
U Chicago	61 (33.9)	121 (74.2)	
U Pittsburgh	119 (66.1)	42 (25.8)	
Age, mean ± SD years	46.9 (12.8)	41.9 (13.0)	<0.001
Sex, n(%) F	168 (93.3)	153 (93.9)	0.841
Education, n(%)			0.004
Less than HS graduate	2 (1.1)	14 (8.6)	
HS graduate	35 (19.4)	40 (24.5)	
More than HS graduate	143 (79.4)	109 (66.9)	
Income, n(%)			<0.001
<$10000	15 (8.5)	53 (32.9)	
$10001-30000	26 (14.7)	47 (29.2)	
$30001-50000	25 (14.1)	31 (19.3)	
>$50000	106 (59.9)	30 (18.6)	
Employed, n(%)	95 (52.8)	64 (39.3)	0.024
Medical insurance, n(%)			<0.001
Without Private	26 (14.4)	101 (62.0)	
With Private	154 (85.6)	62 (38.0)	
Marital status, n(%)			<0.001
Married	117 (65.0)	45 (27.6)	
Other (Single, Divorced, Widowed)	63 (35.0)	118 (72.4)	
Clinical characteristics			
SLEDAI, mean ± SD	3.21 (2.8)	3.6 (3.7)	0.274
SLICC Damage Index, mean ± SD	1.5 (2.0)	2.1 (2.1)	0.010
Disease duration, mean ± SD months	151.1 (128.6)	135.3 (106.9)	0.221
#Immunosuppressants used in past, n(%)			0.040
0	96 (53.3)	62 (38.0)	
1	32 (17.8)	48 (29.5)	
2	27 (15.0)	31 (19.0)	
3	14 (7.8)	11 (6.8)	
≥4	11 (6.1)	11 (6.8)	
#Immunosuppressants currently being used, n(%)			0.400
0	12 (6.7)	9 (5.5)	
1	94 (52.2)	80 (49.1)	
≥2	74 (41.1)	74 (45.4)	
History of receiving CYC, n(%)			0.013
Current use	1 (0.6)	0 (0.0)	
Past use	17 (9.5)	31 (19.0)	
History of participating in a RCT, n(%)			0.430
Current	1 (0.6)	0 (0.0)	
Past	6 (3.4)	9 (5.5)	
Charlson Comorbidity Index, mean ± SD	1.9 (1.2)	2.4 (1.4)	0.005
CES-D, mean ± SD	15.9 (11.6)	20.2 (12.7)	0.001
Beliefs and attitudes			
Prayer efficacy, n(%)			<0.001
No help	24 (13.3)	8 (4.9)	
Some help	58 (32.2)	29 (17.8)	
Much help	59 (54.4)	126 (77.3)	
Prayer frequency, n(%)			<0.001
Never	31 (17.2)	13 (8.0)	
Monthly	28 (15.6)	22 (13.5)	
Weekly	44 (24.4)	25 (15.3)	
Daily	77 (42.8)	103 (63.2)	
DOSPERT, mean ± SD	16.7 (4.2)	16.9 (5.1)	0.611
Locus of control, mean ± SD			
Internal	24.0 (4.9)	25.6 (5.3)	0.004
Chance	17.6 (5.1)	19.0 (6.1)	0.024
Powerful others	24.2 (9.0)	24.9 (5.4)	0.381
Physician-patient relationship characteristics			
Relationship duration, mean ± SD years	4.3 (4.2)	6.2 (5.7)	<0.001
Duration of follow-up at clinic, mean ± SD years	7.7 (7.5)	8.0 (6.1)	0.603
Physician's PDM style, mean ± SD	75.4 (22.2)	66.1 (26.1)	<0.001
Trust in physicians, mean ± SD	38.5 (8.5)	38.9 (7.8)	0.690
Perceived discrimination, mean ± SD	8.9 (3.2)	10.8 (3.4)	<0.001

*Significance level of the χ^2 statistic (or Wilcoxon's rank sum test) for categorical variables and 2-tailed *t*-test for continuous variables.

CES-D: Center for Epidemiologic Studies Depression Scale; CYC: Cyclophosphamide; DOSPERT: Domain-specific risk attitude scale; HS: High School; PDM: Participatory decision-making; RCT: research clinical trial; SLEDAI: Sytemic Lupus Erythematosus Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics.

Table II. SLE patients' treatment preferences and perceptions.

	White	African-American	*p**
Willing to receive CYC, n(%)†	141 (87.6)	83 (62.9)	<0.001
Familiarity with CYC, mean ± SD†	0.5 (0.7)	0.3 (0.6)	0.017
Perception of effectiveness of CYC, mean ± SD†	21.7 (3.5)	20.7 (4.3)	0.013
Perception of risk of CYC, mean ± SD†	10.5 (2.4)	10.8 (2.3)	0.009
Willing to participate in a RCT, involving a new medication, n(%)‡	145 (84.3)	100 (64.9)	<0.001

*Significance level of the χ^2 statistic (or Wilcoxon's rank sum test) for categorical variables and 2-tailed *t*-test for continuous variables.
†Among patients who had never received CYC (n=293, 132 AA and 161 WH).
‡Among patients who had never participated in a RCT, involving a new medication (n=326, 154 AA and 172 WH).
CYC: Cyclophosphamide; RCT: research clinical trial.

SLE patients, were also less likely to be familiar with CYC and more likely to believe that the medication has low efficacy and is associated with high risk (Table II). Willingness to receive CYC was also associated with having high income, having private insurance and being married (Supplementary table I). Perceiving CYC to be highly efficacious ($p<0.001$) or associated with low risk ($p<0.001$) were also associated with willingness to receive the medication. Finally, higher trust in physicians ($p=0.003$) and lower perceived discrimination ($p=0.005$) were also significantly associated with willingness to receive CYC.

Multivariate associations between race and willingness to receive CYC among those who had never received the medication are presented in Table III. After adjustment for income, private medical insurance and marital status, the OR of willingness to receive CYC was attenuated but remained significant (Model 2; adjusted OR, 0.30 [95% CI, 0.15–0.59]). After further adjustment with SLICC damage index score, familiarity with CYC, perception of effectiveness of CYC and perception of risk of CYC, this OR was further lowered (Model 4; adjusted OR, 0.39 [95% CI, 0.17–0.85]). This OR did not appreciably

Table III. Logistic regression of willingness to receive CYC, with serial addition of sociodemographics, clinical context, and perceptions about CYC and clinicians*.

Variable, OR (95% CI)	Model 1	Model 2	Model 3	Model 4	Model 5
Race/ethnicity					
White	1.00	1.00	1.00	1.00	1.00
African-American	0.24 (0.13-0.43)†	0.30 (0.15-0.59)†	0.29 (0.14-0.58)†	0.39 (0.17-0.85)†	0.37 (0.16-0.87)†
Income					
<$10000		1.00	1.00	1.00	1.00
$10001-30000		1.15 (0.51-2.58)	1.17 (0.51-2.65)	1.51 (0.57-4.01)	1.49 (0.56-3.97)
$30001-50000		2.71 (0.92-7.97)	2.98 (1.00-8.92)†	3.61 (1.05-12.43)†	4.07 (1.15-14.33)†
>$50000		3.19 (1.10-9.23)†	3.12 (1.08-9.04)†	4.07 (1.15-14.35)†	4.45 (1.24-15.97)†
Medical insurance					
Without private		1.00	1.00	1.00	1.00
With private		0.56 (0.25-1.29)	0.56 (0.24-1.29)	0.63 (0.25-1.59)	0.60 (0.24-1.52)
Marital status					
Not married		1.00	1.00	1.00	1.00
Married		1.58 (0.78-3.22)	1.70 (0.83-3.51)	1.33 (0.57-3.12)	1.32 (0.55-3.14)
SLICC damage					
0			1.00	1.00	1.00
1			1.65 (0.73-3.75)	1.34 (0.53-3.39)	1.30 (0.51-3.28)
2			1.30 (0.53-3.24)	1.38 (0.47-4.08)	1.37 (0.46-4.11)
3			1.17 (0.42-3.23)	1.17 (0.37-3.70)	1.18 (0.37-3.78)
4			0.68 (0.21-2.19)	1.25 (0.31-4.98)	1.16 (0.28-4.73)
≥5			1.13 (0.30-4.28)	1.13 (0.24-5.34)	1.02 (0.21-4.85)
CYC familiarity					
0				1.00	1.00
1				1.25 (0.50-3.13)	1.23 (0.49-3.09)
2-3				2.61 (0.46-14.81)	2.25 (0.40-12.81)
CYC effectiveness				1.42 (1.26-1.60)†	1.41 (1.25-1.59)†
CYC risk				0.96 (0.80-1.14)	0.97 (0.80-1.16)
Trust in physicians					1.04 (0.98-1.10)
Perceived discrimination					1.00 (0.87-1.15)

*Among patients with no history of taking CYC (n=293, 132 African-American and 161 White).
†$p<0.05$.
CYC: Cyclophosphamide; SLICC: Systemic Lupus International Collaborative Clinics.

change when further adjusted for trust in physicians and perceived discrimination (Model 5). Race (p=0.023), income ($30001-50000 *vs*. <$10000, p=0.029; >$50000 *vs*. <$10000, p=0.022) and perception of effectiveness of CYC (p<0.001) were all significantly associated with willingness to receive CYC in the final model (Model 5).

The following interaction terms were separately added to Model 5: race*income and race*perception of effectiveness of CYC. None of the interactions were found to be statistically significant, and the inclusion of each interaction term did not improve model fit. Hence, they were removed from the final model.

Preferences for clinical trial participation

Among patients who had never participated in a RCT involving a new, experimental medication (n=326), 64.9% of AAs, compared to 84.3% of WHs were willing to do so (crude OR, 0.34 [95% CI, 0.20-0.58]). Willingness to participate in a RCT was also associated with being employed, having private insurance and being married (Supplementary table II). Taking more than one immunosuppressive medication was also associated with RCT participation willingness (p=0.034). In addition, believing that having a racially concordant physician is very unimportant

Table IV. Logistic regression of willingness to participate in a RCT, with serial addition of sociodemographic variables, clinical context and patients' perceptions of clinicians*.

Variable, OR (95% CI)	Model 1	Model 2	Model 3	Model 4
Race/ethnicity				
White	1.00	1.00	1.00	1.00
African-American	0.34 (0.20-0.58)†	0.41 (0.21-0.78)†	0.39 (0.20-0.77)†	0.41 (0.20-0.83)†
Income				
<$10000		1.00	1.00	1.00
$10001-30000		1.12 (0.52-2.45)	1.05 (0.45-2.42)	1.05 (0.44-2.53)
$30001-50000		0.81 (0.31-2.11)	0.95 (0.33-2.67)	1.24 (0.42-3.72)
>$50000		0.81 (0.30-2.23)	0.75 (0.26-2.18)	0.89 (0.29-2.71)
Employment				
Not currently employed		1.00	1.00	1.00
Currently employed		1.28 (0.69-2.38)	1.21 (0.61-2.40)	1.18 (0.58-2.38)
Medical insurance				
Without private		1.00	1.00	1.00
With private		1.37 (0.62-3.02)	1.32 (0.56-3.16)	1.26 (0.51-3.09)
Marital status				
Not married		1.00	1.00	1.00
Married		1.46 (0.76-2.82)	1.61 (0.81-3.19)	1.65 (0.81-3.35)
SLICC Damage Index				
0			1.00	1.00
1			0.94 (0.42-2.11)	0.89 (0.39-2.03)
2			0.89 (0.34-2.33)	0.81 (0.30-2.17)
3			0.62 (0.22-1.77)	0.64 (0.22-1.87)
4			0.26 (0.08-0.83)†	0.23 (0.07-0.74)†
≥5			0.81 (0.25-2.59)	0.67 (0.20-2.24)
Charlson Comorbidity Index				
1			1.00	1.00
2			0.88 (0.40-1.93)	0.86 (0.38-1.93)
3			0.92 (0.37-2.28)	0.94 (0.37-2.39)
4			1.23 (0.40-3.73)	1.35 (0.43-4.24)
≥5			1.42 (0.38-5.30)	1.85 (0.48-7.12)
#Immunosuppressive medications, currently				
0			1.00	1.00
1			3.67 (1.19-11.31)†	3.65 (1.14-11.73)†
≥2			5.65 (1.76-18.21)†	5.45 (1.62-18.30)†
Physician's PDM style				1.00 (0.99-1.02)
Prefer seeing a physician of own race				
Very unimportant				1.00
Unimportant				0.47 (0.25-0.89)†
Neutral, important or very important				0.57 (0.24-1.34)
Trust in physicians				1.04 (1.00-1.08)†

*Among patients with no history of participating in a RCT (n=326, 154 African-American and 174 White).
†p<0.05.
RCT: Research clinical trial; PDM: Participatory decision-making; SLICC: Systemic Lupus International Collaborative Clinics.

(p=0.014) and having a higher trust in physicians score (p=0.023) were also related to preference for RCT participation.

Multivariate associations between race and willingness to participate in a RCT among those without RCT experience are presented in Table IV. After adjustment for income, employment, private medical insurance and marital status, the OR of willingness to participate in the RCT was attenuated but remained significant (Model 2; adjusted OR, 0.41 [95% CI, 0.21–0.78]). Further adjustment for SLICC damage index score, comorbidity index and current number of immunosuppressive medications did not appreciably change this OR (Model 3). Further controlling for perceived physician's PDM style, physician race preference and trust in physicians also did not appreciably change this value (Model 4). In the final model (Model 4), race (p=0.013), SLICC damage index score (4 *vs*. 0, p=0.014), current number of immunosuppressive medications (1 *vs*. 0, p=0.029; ≥2 *vs*. 0, p=0.006) and trust in physicians (p=0.031) were among the variables significantly associated with willingness to participate in a RCT.

The following interaction terms were individually added to Model 4: race* SLICC score, race*number of current immunosuppressives, race*physician race preference, and race*trust in physicians. None were found to be statistically significant, and the addition of each did not improve model fit. They were all subsequently removed from the final model.

Potential recruitment site effects

There was no statistically significant association between recruitment site and either measure of SLE treatment preference (Supplementary tables I & II). To examine recruitment site effects, sensitivity analyses were conducted. When recruitment site and the interaction between race and recruitment site were added in the final model of willingness to receive CYC, neither independent variable was found to be significantly associated with the dependent variable. Findings were similar when both recruitment site and the interaction between race and recruitment site were also added in the final model of willingness to participate in a RCT.

Discussion

In this study, SLE patients were given hypothetical situations regarding their disease course. We found that, compared to WH SLE patients, AA SLE patients were less likely to accept provider-recommended CYC as treatment even if their disease worsened. In the same scenario, AAs were also less willing than WHs to participate in a lupus clinical trial. These differences in preference remained after controlling for sociodemographic variables, clinical factors and patient attitudes towards medications and providers. Besides race/ethnicity, perception of medication effectiveness and household income appear to also be important determinants of preference for CYC treatment. Moreover, number of current immunosuppressive medications and trust in physicians were associated with preference for clinical trial participation.

Patient preferences may contribute to racial and ethnic health care and outcome disparities although the pathways of this phenomenon are not fully known (14). Some evidence suggests race differences in patient preferences may influence race-associated differences in provider treatment recommendations, which may lead to race differences in treatment utilisation (27). Although AAs experience a higher incidence of SLE, as well as higher mortality and morbidity rates due to the disease, underutilisation of necessary rheumatologic care continues in this population (28). In previous studies of women with lupus nephritis, a substantial minority deferred CYC treatment, although it has been shown to confer improved kidney survival advantage over a less potent immunosuppressive medication (29, 30). Medication efficacy and risk of infection were found to have the greatest impact on medication preference among these patients, who were primarily WH (>80%) females (29). Our previous study of SLE patients found that AA patients were less willing than WH patients to accept CYC (13). This particular study was limited as it included only patients recruited from a single academic medical centre.

Besides confirming a previous report that AA patients are less inclined to receive CYC treatment for SLE than WH patients (13), our two-site study extends the generalisability of this finding. This result has important implications as patient and renal survival tend to be poorer in AA than in WH SLE patients (31, 32), and clinical trials have demonstrated the benefits of CYC among patients with renal, neurologic and other internal organ manifestations of SLE (4, 5, 33). Recent evidence has shown that AAs with lupus nephritis may respond less well to CYC than WHs and that mycophenolate mofetil may be an equally effective alternative treatment (4, 34). Nonetheless, SLE treatment guidelines have continued to recommend the use of CYC (4, 5).

Similarly, reluctance of AA patients to participate in lupus clinical trials has significant implications. Over the past decade, there have been clinical trials evaluating agents that target SLE; agents include anti-cytokine therapies, B-cell depleting drugs and therapies that interact with T-cell activation (6). Yet, the underrepresentation of racial minorities in clinical research is a common problem, and failure to enrol AAs in clinical trials limits study generalisability and may result in unrecognised effects of the study treatment (7). Differences in the physiologic response of AAs compared with WHs exist, and AAs in clinical research should be sufficient in number to elucidate potential variations in response compared with WHs (7).

In this study, we found other factors that independently influence SLE patients' treatment preferences. Lower income was found to be independently associated with reduced willingness to receive CYC treatment but not with willingness to participate in a RCT. This is not surprising given the costs associated with intravenous CYC infusion, including those related to the medication, intravenous equipment, nursing care, and physician supervision (35). In contrast, subjects are often paid for participating in a clinical trial.

Lupus disease activity and organ damage from the disease were minimally

associated with either measure of treatment preference. This is consistent with a prior finding that disease severity is not a significant determinant of preference for knee replacement surgery among minority osteoarthritis patients (12). However, higher number of immunosuppressive medication use seems to be strongly linked to increased willingness to participate in an RCT. This may be a case of past behaviour predicting future behaviour, as noted by social psychologists (37).

Higher perception of CYC effectiveness was also found to be associated with increased likelihood of accepting CYC treatment. Indeed, in a study of primarily WH SLE patients' preferences using adaptive conjoint analysis, perceived medication efficacy and risk for infection had the greatest impact on preference (29). In studies of osteoarthritis patients' treatment preferences, racial variations in willingness to undergo joint replacement surgery were found to be attributable to patient expectations about effectiveness of and familiarity with the procedure (11, 12). Finally, higher trust in physicians was an independent determinant of preference for lupus clinical trial participation. In a study of cardiac patients, level of medical mistrust was an independent predictor of patient satisfaction (24). In turn, other studies have established links between patient satisfaction, patient compliance, and utilisation of health services (14). Moreover, in a study of 198 Hispanic, AA, and WH patients with osteoarthritis, physician trust played an important role in patient consideration for joint replacement (12).

This study shows that variations in patient treatment preferences are associated with income, medication history, expectations of medication efficacy and trust in physicians. After adjusting for these variables, race remains an independent determinant of lupus patients' willingness to receive CYC and participate in a RCT. There are a few potential explanations. Our study may be subject to residual confounding. For example, other patient-level variables that may affect the association between race and either measure of lupus treatment preference, such as health literacy and self-efficacy, were not assessed, and may contribute to the differences noted. In addition, previous medication experiences (*e.g.* limited efficacy, affordability) and social support may differ by race and determine or impede willingness to receive treatment but these factors were also not measured. Alternatively, AAs may be more likely to be skeptical than WHs; such personality trait may make patients less willing to try new medications.

Regardless, this study identified factors, including perceived treatment efficacy and trust in providers, that can be addressed to increase the odds that both AA and WH SLE patients receive a potentially life-saving immunosuppressive medication when necessary and participate in clinical trials. In a conceptual model by House (36), relatively fixed factors such as socioeconomic position and race/ethnicity shape individuals' experience of environmental and biomedical risk factors that help explain the magnitude and persistence of disparities in health care. However, other factors, such as those we found, may interact with fixed factors and help attenuate disparities in lupus care and outcomes (28, 36).

Perception of medication efficacy and trust in physicians are major determinants of lupus patients' treatment preferences, and both are potentially modifiable. For example, patient beliefs and attitudes can be changed through interventions in health communications and by improving interactions and relationships between physicians and patients (37). Subsequently, providers who treat SLE may be able to effectively implement shared decision-making in which both physicians and patients choose the best course of treatment for each patient. Likewise, clinical researchers may be more successful in enrolling AA subjects in clinical trials for SLE treatment.

Our study was not without limitations. First, selection bias may be present; we were unable to evaluate specific clinical and psychosocial differences between participants and non-participants. However, the observed racial distribution of participants and non-participants was similar (data not shown).Second, we chose not to include Hispanics and Asian-Americans in this study, and our findings may not be generalisable to other racial/ethnic minority lupus patients. Third, although the evidence is minimal, provider knowledge and attitudes may also contribute to racial disparities in treatment utilisation. This study, though, was designed to assess potential contribution of only patient-level factors to racial disparities in treatment use.

Knowledge accumulated over the years on SLE genetics, serology, hormonal and environmental influences permits us to better classify the various manifestations of the disease and provide more targeted and personalised therapies (38). In addition, a consensus now exists that patient perspectives regarding their disease and treatments should be taken into account when treating SLE patients (39). Future studies should focus on patient preferences and the factors which underlie them as these preferences not only influence treatment but are also potentially modifiable.

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