Initiation of Disease-Modifying Antirheumatic Drug Therapy in Minority and Disadvantaged Patients with Rheumatoid Arthritis

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ABSTRACT. ***Objective.*** To evaluate disparities in time to initiation of disease modifying antirheumatic drugs (DMARD) in patients with rheumatoid arthritis (RA) receiving care in public or private healthcare settings.

Methods. We reviewed the records of patients with RA initially seen at one of 2 rheumatology clinics: a clinic in a public county hospital providing care primarily to minority, disadvantaged, or uninsured patients, and a private clinic providing care to patients with health insurance coverage. Both clinics were affiliated with the same medical school. We determined time to initiation of DMARD or steroid therapy using Kaplan-Meier analyses and Cox regression. Time to initiation of therapy was measured from onset of disease until a therapy was prescribed (event) or the patient was seen for the first time at one of the 2 clinics (censored at index visit). Independent variables were ethnicity and clinic setting (public or private).

Results. One hundred eighteen new patients with RA were seen in the public setting, 167 in the private setting; 83% of the patients in the public clinic and 18% in the private setting were non-White. Survival analysis (disease duration ≤ 10 yrs) showed that the median time to initiation of DMARD therapy was 6 years for the public clinic and 1.5 years for the private clinic ($p = 0.001$), and 7 years for non-White patients, compared to 1 year for White patients ($p < 0.0001$). For patients with disease duration ≤ 5 years, significant differences were observed for both clinic and ethnicity, with more patients in the private clinic (62%) than in the public clinic (32%) and more White (64%) than non-White (32%) patients having received treatment.

Conclusion. These findings suggest that ethnic minorities and uninsured patients are at risk of deleterious outcomes as a consequence of delayed therapeutic onset. (First Release Nov 1 2007; J Rheumatol 2007;34:2400–7)

Key Indexing Terms:
DISPARITIES RHEUMATOID ARTHRITIS STEROID ETHNICITY
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Disparities in access to healthcare services continue to exist although timely access to care is essential to the health and well-being of people in need of it. These disparities are not only limited to socioeconomic factors or health insurance coverage, but also include ethnicity, gender, geographic region, and comorbid conditions[1-13]. Studies have shown that disparities in access to care are associated with poor patient outcomes and increased healthcare costs[14-16]. Although access to health services has been studied extensively in other populations (e.g., patients with cardiovascular conditions)[17-26], this has not been the case with rheumatic diseases. The limited studies of patients with rheumatoid arthritis (RA) suggest that the lack of access to specialty services is associated with suboptimal treatment[27-30], and that patients who do not receive disease modifying antirheumatic drugs (DMARD) are at increased risk of joint damage[31,32]. A study evaluating very early RA therapy versus later RA therapy also found that those treated earlier did better with respect to disease activity, joint destruction, and functional outcome[33]. This finding is consis-

tent with current evidence that supports a more aggressive approach, with earlier use of DMARD[34-36], because it leads to improved disease outcomes, including retardation of radiological damage and increased work productivity[33,36-42].

Little is known about the onset of DMARD therapy in patients with RA who may be at a disadvantage when receiving care because of their socioeconomic status, their ethnicity, or their health insurance status. However, a potential delay in treatment in underserved and vulnerable populations may have dire health and economic consequences for patients and their families. The aim of this study was to determine time to initiation of therapy in patients with RA referred for rheumatology care to one of 2 different clinics (public and private) in the city of Houston, Texas.

MATERIALS AND METHODS

We conducted a retrospective cohort study and reviewed all medical records of new patients with a diagnosis of RA initially seen at 2 rheumatology clinics: a public clinic (n = 118) and a private clinic (n = 167). For the public clinic we reviewed all paper charts of new rheumatology consults of patients seen from 1995 to 2000. For the private patients we reviewed all billing records of patients with a diagnosis of RA between 1994 and 2000. Both clinics were affiliated with the same medical school (Baylor College of Medicine, Houston, Texas) and are considered tertiary-level settings. The first clinic is located in a public hospital that is part of the Harris County Hospital District and provides care primarily to minority, disadvantaged, and/or uninsured patients. The second clinic is located within 1 mile of the county hospital, is located in a private hospital, and provides care to patients with private health insurance coverage, most commonly through health maintenance organizations. The public clinic serves mostly uninsured ethnic minorities with low socioeconomic status, while the private clinic serves a broader spectrum of the population of Houston. Both clinics were staffed by Baylor rheumatology fellows and faculty. At the time of the study both clinics used paper medical records. Patients are usually referred to a rheumatology clinic by primary care physicians.

We selected all patients with a diagnosis of RA confirmed by a rheumatologist as determined by chart review. A diagnosis of RA was considered confirmed if the physician had noted in the chart that the patient had RA. Those patients whose diagnosis changed on followup or whose diagnosis of RA was doubtful according to physician chart notes were excluded. Only patients who had their first consult during the study inclusion dates were included (e.g., new patients). Data extraction included patient demographics, disease duration, and prior treatment with DMARD therapy or steroids at the time of the index visit to the rheumatology clinic. DMARD therapy included the following agents: methotrexate, leflunomide, sulfasalazine, hydroxychloroquine, chloroquine, azathioprine, penicillamine, gold salts, cyclosporine, minocycline, infliximab, and etanercept. These are agents commonly used by rheumatologists[43].

Statistical analysis was performed using t-tests and one-way analysis of variance for differences between means and chi-squared and Fisher's exact tests for comparisons between proportions. Nonparametric tests (i.e., Wilcoxon) were used for variables not normally distributed. Survival analysis was conducted by estimating time from the onset of disease (as specified in the medical record) to time to initiation of therapy (considered an event in the survival analyses). Because the medical records at both clinic sites were not precise, the data for disease and therapy onset were estimated in years, with a 6-month precision when possible, or assigning a midpoint interval to the year of onset. In 22 (8%) cases this information was not clearly presented in the medical records, for either disease duration or time to initiation of therapy (DMARD or steroids), and these cases were excluded from all analyses. Censoring occurred at the time the patient first presented to the clinic (index visit). This censoring point was chosen to see how much of a delay in therapeutic onset had occurred before the patient entered tertiary care in either rheumatology clinic. Independent variables included age, sex, ethnicity, clinic type, and year of visit. Clinic type served as a surrogate for the healthcare system where the patient was thought to primarily receive care previously. Therefore, patients seen at the public clinic were thought to have received care mostly through the county funded public health system prior to the index visit; patients at the private clinic were considered to have access to insured care prior to the index visit. Clinic type also served as a surrogate for socioeconomic status. Due to lack of reliable data in clinic charts we could not assess for socioeconomic status directly. Ethnicity was evaluated in 2 ways: (1) by comparing 4 groups (White, African American, Hispanic, Other), and (2) by dichotomizing patients into White and non-White. In general, no significant differences were observed with the 2 approaches. Therefore, most of the results are reported with ethnicity as a dichotomized variable. Initially, each independent variable was examined with Kaplan-Meier and Cox regression methods in a univariate fashion. Multivariate Cox regression was conducted using a stepwise approach with a p of 0.20 for variable inclusion and a p of 0.21 for variable exclusion. A closer inspection of the interquartile ranges for the survival results showed that some patients had a long duration of disease at the time of their index visit. Therefore, we conducted the analyses in 2 ways: (1) including all patients (n = 285); and (2) truncating the sample to those patients with 10 years' or less disease duration (n = 232). No significant differences were observed between the group of patients with ≤ 10 years' disease duration and the group with > 10 years' disease duration by sex and ethnicity. However, the group of patients with > 10 years' disease duration was slightly older (56 yrs) than the other group (52 yrs). All statistical analyses were performed with SPSS. Statistical significance was set at 0.05, 2-tailed. Institutional Review Board approval for the study was obtained from Baylor College of Medicine.

RESULTS

Patient characteristics are given in Table 1. One hundred eighteen new patients with RA were seen in the public clinic and 167 new patients with RA were seen in the private clinic. Eighty-three percent of the patients in the public clinic were non-White compared to 18% in the private clinic ($p < 0.0001$). Patients from the public clinic were also slightly younger than those from the private clinic ($p = 0.01$); they also had a shorter mean disease duration than those from the private clinic ($p = 0.007$). There were no statistically significant differences with respect to sex between patients attending the private versus the public clinic. By ethnicity, Hispanic and African American patients were younger and had shorter disease duration than White patients.

Table 2 shows the proportions of patients who received previous DMARD or steroid therapies before the index visit as well as median disease duration at the time of initial therapy. Statistically significant differences were observed between clinics, with more patients in the private clinic having received previous treatment than in the public clinic (72% vs 50% for DMARD therapy, $p < 0.0001$; and 79% vs 46% for steroid therapy, $p < 0.0001$). Median disease duration for initiation of either DMARD or steroid therapy in the public clinic was 1.5 years versus 0.5 years in the private setting ($p = 0.02$).

Table 3 shows median times to initiation of RA therapies in years by ethnicity and clinic type. A depiction of these values is shown in Figures 1 and 2. Survival analysis by clinic type in patients with disease duration of 10 years or less showed

Table 1. Patient characteristics at index visit by clinic type and by ethnicity.

	All, N = 285	Clinic Type Public Setting, N = 118	Private Setting, N = 167	p	Ethnicity† White. N = 142	AA, N = 37	Hispanic, N = 72	Other, N = 16	p
Age, yrs (SD)	52.7 (13.7)	50.2 (13.1)	54.4 (14.0)	0.010	56.1 (12.4)	50.8 (16.3)	48.7 (13.2)	47.8 (15.9)	0.001
Sex, %									
Male	16	13	18	0.24	15	31	8	25	0.019
Female	84	87	82		85	69	92	75	
Ethnicity, %									
White	53	17	82	< 0.0001	—	—	—	—	—
AA	14	24	6						
Hispanic	27	52	7						
Other	6	7	5						
Mean disease duration, yrs (SD)	8.5 (9.0)	6.7 (8.2)	9.7 (9.3)	0.007	10.9 (10.1)	6.1 (6.5)	6.7 (8.2)	3.9 (3.5)	< 0.0001
Clinic type, %									
Public	—	—	—	—	14	76	86	50	< 0.0001
Private					86	24	14	50	

† Ethnicity established in 267 patients. AA: African American.

Table 2. Prior therapy with DMARD or steroid by clinic type.

	All, N = 285	Public Setting, N = 118	Private Setting, N = 167	p
Prior DMARD therapy, n (%)	180 (63)	59 (50)	121 (72)	0.0001
Median disease duration at the time of initial DMARD, yrs, mean (IQR)*	1.0 (0, 5.8)	1.5 (0, 6.5)	0.5 (0, 5.0)	0.19
Prior steroid therapy,n (%)	186 (65)	54 (46)	132 (79)	< 0.0001
Median disease duration at the time of initial steroid treatment, yrs, mean (IQR)*	0.0 (0, 3.0)	0.2 (0, 3.0)	0 (0, 3.0)	0.93
Prior DMARD or steroid therapy, n (%)	234 (82)	84 (71)	150 (90)	< 0.0001
Median disease duration at the time of initial DMARD or steroid treatment, yrs, mean (IQR)*	0.5 (0.5, 5.0)	1.5 (0.5, 7.0)	0.5 (0.5, 3.5)	0.02

* Median disease duration to therapy. Statistical significance $p < 0.05$; Fisher's exact test (discrete values) or Wilcoxon (continuous values).

that the median time to initiation of DMARD therapy was 6 years for patients seen at the public clinic, and 1.5 years for patients seen at the private clinic ($p = 0.001$). Similarly, the median time to onset of steroid therapy was 6 years for the public clinic and 0.5 year for the private clinic ($p < 0.0001$). Considering the median time to onset of DMARD or steroid therapy, patients at the private clinic had a shorter median time than patients at the public clinic (median 6 mo vs 2 yrs; $p = 0.001$). Survival analyses results also showed that there were racial differences in the initiation of RA therapies, with White patients receiving DMARD earlier than non-Whites (1 vs 7 yrs; $p < 0.0001$) and White patients receiving steroids earlier than non-White patients (6 mo vs 3 yrs; $p = 0.004$). The direction of the association remained unchanged when the results were repeated with all patients included.

We also conducted a multivariate Cox regression analysis to evaluate the effects of ethnicity and health setting after controlling for patients' age and sex and year of index visit, and also to evaluate which of the 2 factors, ethnicity or clinic setting, appeared to be more important, given that both were highly correlated. Table 4 shows the univariate and multivariate hazard ratios. Results are shown for non-Whites grouped together, because no differences were observed between Hispanics and African Americans. Multivariate analysis showed that non-Whites were less than half as likely to have received a DMARD as White patients (HR 0.41, 95% CI 0.28–0.62) and 30% less likely to have received either DMARD or steroids (HR 0.70, 95% CI 0.51–0.96). For steroids alone, the effect of clinic setting dominated ethnicity, with patients in the public setting being less likely to have

Table 3. Median times to initiation of RA therapies [in years, with (25%–75%) interquartile range].

Type of RA Therapy	By Clinic Type: Patients with 10 Years or Less Disease Duration			All Patients		
	Public Clinic	Private Clinic	p	Public Clinic	Private Clinic	p
DMARD	6.0 (1.5–∞)	1.5 (0.5–7)	0.001	7.0 (1.5–23)	3.0 (0.5–12)	0.003
Steroid	6.0 (1.0–∞)	0.5 (0.5–4)	< 0.0001	23.0 (1.5–∞)	1.0 (0.5–11)	< 0.0001
Either	2.0 (0.5–7)	0.5 (0.5–3)	0.003	3.0 (0.5–8)	0.5 (0.5–6)	0.003

Type of RA Therapy	By Ethnicity (dichotomized): Patients with 10 Years or Less Disease Duration			All Patients		
	White Subjects	Non-White Subjects*	p	White Subjects	Non-White Subjects	p
DMARD	1.0 (0.5–6)	7.0 (1.5–∞)	< 0.0001	3.0 (0.5–12)	7.0 (1.5–23)	0.001
Steroid	0.5 (0.5–5)	3.0 (0.5–8)	0.004	2.0 (0.5–14)	7.0 (0.5–23)	0.14
Either	0.5 (0.5–3)	2.0 (0.5–7)	0.003	0.5 (0.5–8)	3.0 (0.5–8)	0.24

Type of RA Therapy	By Ethnicity†: Patients with 10 Years or Less Disease Duration				All Patients			
	White	AA	Hispanic	p	White	AA	Hispanic	p
DMARD	1.0 (0.5–6.0)	7.0 (1.5–∞)	6.0 (1.5–∞)	< 0.0001	3.0 (0.5–12)	7.0 (1.5–∞)	7.0 (2.0–23.0)	0.01
Steroid	0.5 (0.5–5)	2.0 (0.5–8)	3 (0.5–9)	0.032	2.0 (0.5–14.0)	7.0 (0.5–12.0)	6.0 (0.5–23.0)	0.46
Either	0.5 (0.5–3)	2.0 (0.5–7.0)	1.5 (0.5–6)	0.026	0.5 (0.5–8.0)	5.0 (0.5–8)	2.0 (0.5–8.0)	0.67

† Ethnicity category "other" was not included in the table. *Non-Whites comprised mostly African-Americans and Latino patients. Statistical significance $p < 0.05$ (log-rank test).

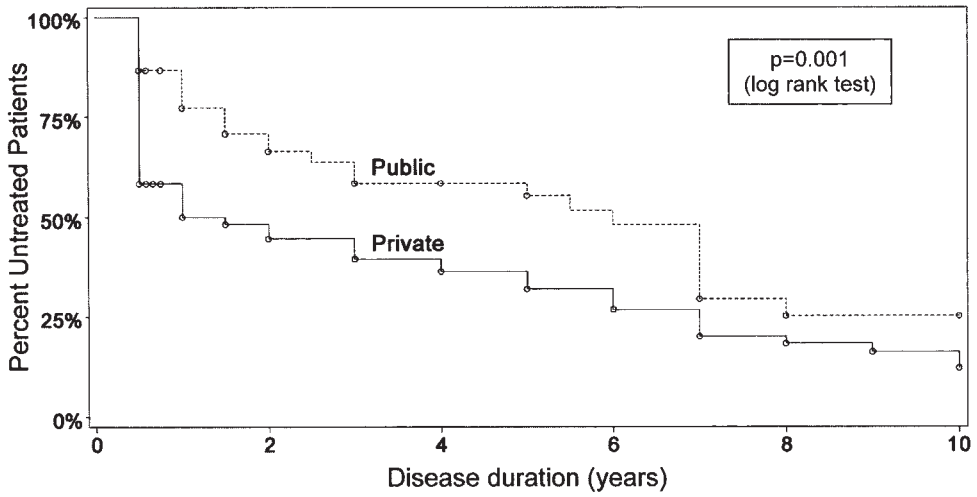

Figure 1. Kaplan-Meier survival curve: time to initiation of DMARD therapy by clinic type.

received steroids than those in the private setting (HR 0.47, 95% CI 0.30–0.71). No statistically significant differences were observed in sex, age, or year of index visit. Additionally, although highly correlated, no significant interaction was observed between ethnicity and clinic type.

Because RA treatment appears to be more effective in patients with early disease, we dichotomized patients into those who had disease duration at the time of the index visit of ≤ 5 years and those with > 5 years. Of the 135 patients who had a disease duration ≤ 5 years at the time of the index visit, 32% in the public setting and 62% in the private setting had been treated with DMARD (p = 0.0001); 43% in the public setting and 74% in the private setting had been treated with steroids (p = 0.0001). Additionally, 64% of Whites, 35% African Americans, 26% of Hispanics, and 50% of "Others" had received DMARD prior to the index visit (p = 0.02).

DISCUSSION

We conducted this retrospective cohort study to evaluate potential disparities in the onset of DMARD or steroid therapy in RA patients with differential access to healthcare. Studies on patients with RA suggest that the lack of access to specialty services is associated with suboptimal treatment of this condition[27-29,44], and that lack of access to therapies is

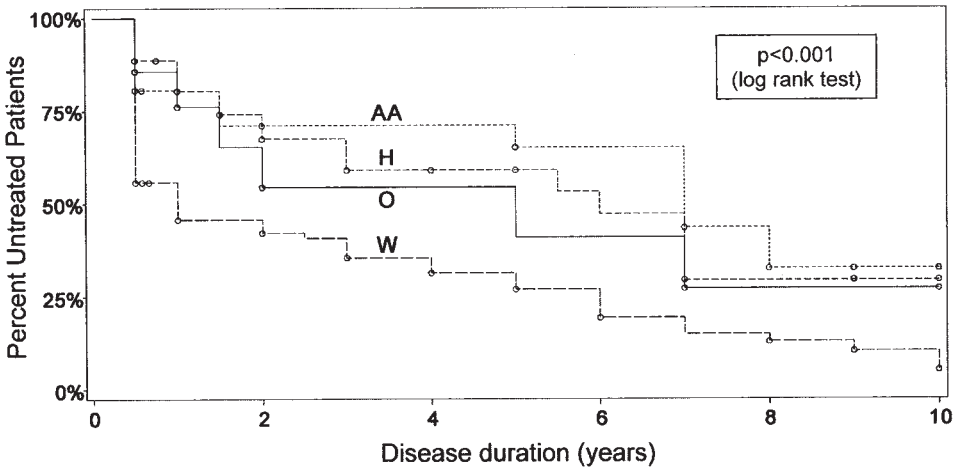

Figure 2. Kaplan-Meier survival curve: time to initiation of DMARD therapy by ethnicity. AA: African-American, H: Hispanic, O: Other, W: White.

associated with joint damage[31]. Indeed, studies have shown that RA patients from low socioeconomic strata are at particular risk for poor disease outcomes, comorbidity, and mortality[45-48]. One study showed that patients with RA and low socioeconomic status were less likely to use allied healthcare services than patients from higher socioeconomic strata[48]. A second study also showed that years of education was associated with delay to onset of DMARD[49].

Our study revealed disparities in the initiation of DMARD and steroid therapy, with a greater proportion of White patients and patients in the private setting having been prescribed therapy before referral to the tertiary center than was the case for the ethnic minority and public clinic patients. The reasons for these disparities are not clear, but could be related to system factors (e.g., access to care), physician factors (e.g., practice patterns or bias), or patient factors (e.g., financial status, education). Most patients in the private clinic were White, and most patients in the public clinic were non-White. Yet in the multivariate model only ethnicity persisted as a significant independent predictor for DMARD initiation, suggesting that the differences are more likely to be caused by individual patient or physician determinants related to ethnicity than health system factors.

Houston is the fourth largest city in the US, and it only has 2 rheumatology clinics in the Harris County Hospital District: one is affiliated with Baylor College of Medicine and the other with University of Texas; both are located in tertiary hospitals. The Baylor-affiliated clinic operates twice a week, and the University of Texas clinic once a week. This study was conducted at the Baylor clinic, so conceivably at least half of the patients with RA referred to public Harris County rheumatology clinics were being referred to Baylor from a broad geographic base. The private clinic was also affiliated with Baylor and located in a private tertiary hospital. Given this broad referral base, we believe that these findings represent community utilization patterns before referral to tertiary setting clinics, and that it is unlikely that they reflect merely the practice patterns of a few physicians, or the experience of selected patient groups in our city.

Our findings are concerning because early treatment with DMARD delays joint damage and improves productivity[33,36-42]; moreover, joint damage occurs early in the course of RA[50,51]. Our study also showed a delay in initiation of steroids, which has also been found to retard radiological progression when administered early in the course of the disease[52,53]. This delay is of particular concern in patients from low socioeconomic strata, who are often employed in manual labor, and may be most vulnerable because their livelihood and employability are closely linked to their physical function.

Our study has limitations. Clinic type may also not be an accurate surrogate for socioeconomic hardship or type of care received prior to the index visit; some patients may have become unemployed as a result of disease activity or progression by the time they presented to the index visit and may not have been able to afford the more expensive private insurance any longer. Generalizability is limited to patients referred to tertiary settings, but this is of concern because these patients are likely to have greater disease severity than nonreferred patients. Our results are also prone to bias in the recall of dates, such as dates for disease duration and dates on time to initiation of therapy. Moreover, we had no information on how many patients had seen a rheumatologist prior to their index visit, nor did we have information on disease severity or on patients' patterns of health services utilization with respect to their disease. We also recognize that other determinants of healthcare utilization, such as comorbidity and health literacy, can be confounding factors, but we were unable to assess them given the retrospective design of the study. Finally, our sample size may not have been large enough to adequately assess for the interaction between ethnicity and clinic setting.

Our study showed concerning ethnic and healthcare setting disparities in the initiation of effective RA therapy. The poten-

Table 4. Multivariate model of factors associated with receipt of RA therapies.

	DMARD					
	Univariate Model			Multivariate Model*		
Variable	HR	CI	p	HR	CI	p
Hospital (private = reference)						
Public	0.56	0.37–0.82	0.004			
Sex (female = reference)						
Male	1.14	0.72–1.81	0.58			
Ethnicity (white = reference)						
Non-White	0.45	0.31–0.67	< 0.0001	0.41	0.28–0.62	< 0.0001
Year (1994 = reference)						
1995	1.61	0.55–4.73	0.38			
1996	1.38	0.53–3.63	0.51			
1997	1.32	0.51–3.47	0.57			
1998	1.22	0.47–3.20	0.68			
1999	1.34	0.52–3.46	0.55			
2000	1.36	0.48–3.86	0.57			
Age (continuous)	1.01	0.99–1.02	0.37			

	Steroids					
	Univariate Model			Multivariate Model*		
Variable	HR	CI	p	HR	CI	p
Hospital (private = reference)						
Public	0.51	0.34–0.77	0.001	0.47	0.30–0.71	< 0.0001
Sex (female = reference)						
Male	1.18	0.74–1.90	0.49			
Ethnicity (white = reference)						
Non-White	0.57	0.39–0.84	0.005			
Year (1994 = reference)						
1995	2.78	0.62–12.46	0.18			
1996	2.63	0.61–11.29	0.19			
1997	2.23	0.53–9.41	0.28			
1998	2.43	0.57–10.3	0.23			
1999	2.24	0.53–9.55	0.28			
2000	2.12	0.47–9.58	0.33			
Age (continuous)	1	0.99–1.02	0.56			

	Either Agent					
	Univariate Model			Multivariate Model*		
Variable	HR	CI	p	HR	CI	p
Hospital (private = reference)						
Public	0.51	0.35–0.74	< 0.0001			
Sex (female = reference)						
Male	0.92	0.59–1.44	0.72			
Ethnicity (white = reference)						
Non-White	0.49	0.34–0.70	< 0.0001	0.7	0.51–0.96	0.02
Year (1994 = reference)						
1995	1.64	0.58–4.67	0.35			
1996	1.48	0.56–3.88	0.42			
1997	1.51	0.58–3.92	0.4			
1998	1.44	0.55–3.75	0.46			
1999	1.75	0.68–4.52	0.25			
2000	1.36	0.48–3.86	0.57			
Age (continuous)	1.01	1.00–1.02	0.29			

* Stepwise model included the following variables: hospital, sex, age, race, and year of entry into cohort. Statistical significance $p < 0.05$.

tial effects of these disparities on longterm outcomes are unclear, but could be very detrimental in light of the evidence supporting early onset of DMARD therapy for most patients. Larger studies involving ethnically and socioeconomically diverse populations are needed to assess why these disparities occur, and to establish effective programs that can ensure equitable access to effective therapies for all patients with RA.

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