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Use of Disease-Modifying Medications for Rheumatoid Arthritis by Race and Ethnicity in the National Ambulatory Medical Care Survey

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Abstract

Background—Disease-modifying anti-rheumatic drugs (DMARDs) are recommended for virtually all patients with rheumatoid arthritis (RA). We investigated the use of DMARDs in patients with RA in a nationally representative sample of visits to US physicians in the National Ambulatory Care Medical Survey (NAMCS).

Methods—We analyzed NAMCS visit data from 1996 through 2007 if the physician noted a diagnosis of RA. DMARD utilization was based on the medications listed by the physician. We used generalized linear models to examine the adjusted associations between DMARD use and potential predictors.

Results—Among 859 visits with a diagnosis code of RA were identified over the study period, 404 (47%, 95% confidence interval (CI) 44–50%) had an associated DMARD. The percentage of RA visits with DMARDs increased slightly over the twelve years ($p = 0.048$), with biologic DMARDs increasing to 20% of visits after their introduction (p for trend < 0.001). In fully adjusted models, Black race was associated with a 30% reduction in DMARD prescribing (risk ratio, RR, 0.70, 95% CI 0.48 – 1.00). A visit to a rheumatologist was the strongest correlate of DMARD prescribing (RR 2.33, 95% CI 1.89 – 2.86). Among visits to non-rheumatologists, Blacks were significantly less likely than Whites to receive a DMARD (RR 0.39, 95% CI 0.17–0.92), but not among visits with rheumatologists (RR 0.81, 95% CI 0.52–1.27).

Conclusions—In the NAMCS survey, most visits coded with RA did not have an associated DMARD prescription. Blacks were less likely to receive DMARDs than Whites, particularly when visiting non-rheumatologists.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory arthritis associated with pain, disability, and increased mortality. Disease modifying anti-rheumatic drugs (DMARDs) represent the standard of care for RA, with demonstrated ability to reduce pain

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and disability.¹ Whereas the traditional model of RA treatment had been a “pyramid” approach, beginning with nonsteroidal anti-inflammatory drugs (NSAIDs) and glucocorticoids for the first phase of treatment, the recommended strategy now includes immediate DMARD therapy.¹ These agents are recommended by the major rheumatologic societies and in rheumatic disease specialty practices, over 90% of patients with RA received DMARDs.¹⁻³ This approach has been widely embraced; in fact, US national care quality organizations have included DMARD treatment for RA as a performance standard.⁴

Since the 1990s, DMARD options have proliferated with increased numbers of both synthetic small molecules and biologic treatments, e.g., TNF inhibitors, B-cell depleting therapy, a co-stimulatory agonist, and an IL-6 antagonist.⁵ Despite the increased number of DMARD options and the agreement on their importance in RA, several studies suggest that many patients do not receive these therapies. A study using Medicare data from two US states from 1996-2004 showed that 30% of beneficiaries with RA filled a DMARD prescription during the 12 months after cohort entry.⁶ Data from British Columbia during 1996-2000 found only 43% of RA patients received DMARD treatment during 60 months of follow-up.⁷ Furthermore, a very recent study using data from Medicare Managed Care plans found that 59% of beneficiaries with RA used a DMARD in 2005 and 67% in 2008.⁸ These studies suggest that there may be widespread underuse of DMARDs for RA, but the reasons remain unclear. Prior studies identified older age, depression and lack of a rheumatology visit as correlates of not using a DMARD,⁶⁻⁸ suggesting potential disparities in DMARD use. However, these studies covered a short duration and focused on a relatively narrow range of patients, mostly older Medicare beneficiaries.

To overcome these limitations, we examined DMARD use for RA using nationally representative data on office visits with physicians from the National Ambulatory Medical Care Survey.⁹ Based on previous studies from other therapeutic areas suggesting the receipt of specific interventions often differs by race,¹⁰⁻¹³ we examined the effect of race, ethnicity and physician specialty on DMARD prescribing. The effects of race and ethnicity were first analyzed in the whole cohort. To examine whether access to rheumatology care modified a possible race and ethnicity effect, we also analyzed this relationship in samples stratified on whether the visit was with a rheumatologist.

METHODS

Study Sample

We studied data from NAMCS, an annual visit-based cross-sectional survey conducted in physicians’ offices. NAMCS includes a nationally representative probability sample of ambulatory physician practices across the US using a multi-stage cluster strategy, selecting physicians by geographic location and provider specialty. Physicians and their office staff are trained to complete the survey for all visits in a randomly sampled week. The purposeful sampling strategy and use of weights allows one to generalize to the approximately 650 million office visits made annually to physicians in the US. Physicians and patients are not sampled repetitively across years. Our study sample consisted of all visits recorded in NAMCS 1996-2007 with a diagnosis of RA listed among any of the diagnoses on the visit survey form.

The study protocol was approved by the Institutional Review Board of the Partners Healthcare System.

Rheumatoid Arthritis Treatment

Up to eight new or ongoing medications and up to three diagnoses were recorded for each visit in NAMCS. The primary outcome for these analyses was DMARD prescribing as

recorded on the visit survey form. We included both non-biologic DMARDs (azathioprine, cyclosporine, D-penicillamine, gold preparations, hydroxychloroquine, leflunomide, methotrexate, and sulfasalazine) and biologic DMARDs (abatacept, adalimumab, anakinra, etanercept, infliximab, and rituximab). A variable on the survey indicates whether the prescription is new or a continuation. Prescriptions for oral glucocorticoids, opioids, and NSAIDs (non-selective and selective) were also assessed.

Potential Correlates of DMARD Prescribing

The NAMCS visit survey includes a limited set of variables possibly related to DMARD prescribing. These include: sociodemographic variables concerning the presenting patient, such as age, gender, race (White, Black, and Other), ethnicity (Hispanic, non-Hispanic, and Unknown), health insurance coverage, and region of residence; the number of non-DMARD drugs prescribed; and the type of provider who conducted the visit. We categorized the types of providers as rheumatologists or non-rheumatologists.

Statistical Analyses

We assessed the percentage of RA visits associated with a DMARD prescription for each of the 12 study years. The variables were compared across visits with and without DMARDs and then risk ratios were estimated using Generalized Linear Models, accounting for the clustered nature of the visits and sampling weights. The unit of analysis is the visit coded for RA and not persons with RA; RA cases are not followed longitudinally over 12 years, since different RA individuals are sampled every year. The variables associated with DMARD use were examined in a series of models with an increasing number of covariates, testing whether the effect of race and/or ethnicity was diminished with increasing adjustment. Region of residence and health insurance status were not significant predictors in univariate or multivariate models and were removed from analyses. We added the rheumatologist covariate as the last variable to determine whether the effect of race and ethnicity were mediated by access to rheumatology care. Based on initial results, we further examined whether the effect of race and ethnicity were modified by rheumatology care by comparing risk ratios (RRs) in two sets of adjusted models – one for visits to rheumatologists and one for visits to non-rheumatologists. We also assessed the interaction effect of race and ethnicity by rheumatology care.

We used SUDAAN statistical software version 10.0.1 (Research Triangle Institute, Research Triangle Park, NC) to account for the complex survey design.

RESULTS

We identified 859 visits with a diagnosis of RA over the 12 year study period. When weighted to the US population, this total represents approximately 3.7 million visits over this period that included a diagnosis of RA. Characteristics of these 859 visits are described in **Table 1**. The majority of patients were 45 years and over and 76% were female. Most patients were White and non-Hispanic. None were pregnant or had HIV, two potential contraindications to the use of certain DMARDs.

Of the 859 visits associated with RA, 378 (44%) were associated with 3 or more non-DMARD drugs, 315 (37%) with 1 or 2, and 166 (19%) with none. About half of the visits were to a rheumatologist, with DMARD users much more likely to see a rheumatologist than non-users.

Of these 859 visits, 404 (47%, 95% confidence interval 44-50%) were associated with a prescription for a DMARD, representing approximately 1.9 million visits in the US. The

remaining 455 visits without an associated DMARD represent 1.8 million visits in the US. The percentage of visits with a DMARD prescription increased slightly over the study period (**Figure 1**). The percentage with a biologic DMARD gradually increased since they were introduced in 1999. In 2007, there were approximately 293,000 visits in the US associated with a DMARD and 110,000 were with a biologic DMARD. Of the 455 visits without an associated DMARD, 16 (3.5%) had eight medications listed on their NAMCS form (the maximum permitted) and 83 (1.2%) used oral glucocorticoids.

We examined the correlates of any DMARD and biologic DMARD use in a series of multivariable models (**Table 2**). In Model 1 that includes the calendar year of the visit, race, and ethnicity, Black race was associated with a trend toward a reduced risk ratio of any DMARD use (RR 0.69, 95% CI 0.42 – 1.12). In Models 2 and 3, the effect of Black race was maintained and was statistically significant with increasing adjustment. The effect of race on the use of biologic DMARDs was qualitatively similar to any DMARD use, but it was not statistically significant (see **Table 2**). Furthermore, Black race was not significantly associated with a lower risk of any DMARD use (RR 0.81, 95% CI 0.52-1.27) in a fully adjusted model restricted to the 377 visits made to rheumatologists. When the same adjusted model was run for the 482 visits to nonrheumatologists, Black race had a stronger association with any DMARD non-use (RR 0.39, 95% CI 0.17-0.92) than among visits to rheumatologists (**Table 3**), however the p-value for interaction was 0.15.

Trends in the use of other drugs commonly used to manage pain and inflammation were also examined in the same 859 NAMCS visits (see **Figure 2**). During the 12 years of NAMCS studied, we found that 4-11% of the visits listed an opioid with an approximate doubling of use in recent years. Oral glucocorticoids and NSAIDs/coxibs were each used by one-quarter to one-third of subjects with RA without any clear time trends.

DISCUSSION

The early and aggressive use of disease modifying anti-rheumatic drugs (DMARDs) has improved the care and outcomes of RA.^{14, 15} However, several studies suggest that the potential benefits of DMARDs are not being reaped by many people suffering with RA because of under-use of these agents.⁶⁻⁸ To guide strategies to improve DMARD use, a better understanding of this problem and its determinants is required. We examined a US national survey over a 12-year time period, investigating whether race and/or ethnicity disparities exist in DMARD utilization.

Over the study period, we found that fewer than half of RA visits listed a DMARD, and the DMARD treatment rates improved only slightly over the 12 year study period. This was surprising as a substantial increase has been noted in several other studies.^{6, 8} It is unclear whether the relatively small increase that we observed in comparison to other studies was due to differences in the population or related to how DMARD use was measured. Black race was a significant correlate of DMARD non-use, with Blacks having a 30% reduced utilization of any DMARD compared to Whites; similar trends were observed for biologic DMARDs. Black race was noted to be a correlate of DMARD non-use in another US study among Medicare beneficiaries.⁶ As well, Black race has been found to be correlated with less frequent use of many health services, including total joint replacement, cardiac revascularization, and organ transplant.^{11, 13, 16, 17} Potential reasons for such treatment disparities include differences in access to care, attitudes and preferences of providers and patients, and differences in clinical presentation across different patient groups.¹⁸

It is noteworthy that in the entire sample of visits, the effect of Black race was attenuated when the rheumatologist indicator was added to the model. This suggests that lack of access

to a rheumatologist may be one mediator of the racial disparity. There was also evidence that the effect of Black race was modified by whether or not the visit was to a rheumatologist (**Table 3**). Health insurance status was not significantly associated with use of DMARDs.

While seeing a rheumatologist was strongly associated with DMARD use for all racial and ethnic groups, most persons with RA are not seen by rheumatologists, in the US or abroad.^{6, 7, 19, 20} Our data demonstrate that DMARD use has not increased over a period when (a) at least five new DMARDs were introduced, (b) scientific data clarified the important role of DMARDs,¹⁵ and (c) DMARDs for RA became a quality measure for health plans in the US. The lack of prescribing improvement speaks to the slow pace with which medical practice catches up to clinical evidence -- 17 years as estimated by the Institute of Medicine.²¹

This study has important limitations, mostly associated with NAMCS. The NAMCS survey does not allow one to confirm diagnoses. Thus, it is impossible to know the accuracy of the RA code. Based on the calculated national estimates compared with other data sources, it is likely that some visits coded with RA are inaccurate.²² Typically, this type of misclassification biases toward the null, making it more difficult to observe the effect of other variables, such as Black race. Moreover, the medication lists are not validated against prescription data, but prior work suggests that NAMCS data are acceptably accurate.²³ The scope of NAMCS is a great strength of this study. The purposeful sampling strategy used by NAMCS -- including urban and rural areas and patients of diverse racial and ethnic backgrounds -- allows one to generalize to the entire US. As well, we studied a relatively large group of visits sampled over a long period. Prior studies are typically restricted to specific patient groups or narrow geographic regions, while NAMCS represents a national sample. However, NAMCS does not include information about several sociodemographic variables of interest, including household income and education level. Health insurance status was not associated with DMARD use in these data, but future studies should also determine whether Black race is a surrogate for socioeconomic issues and/or limited access. While these variables may underlie some of the differences in DMARD treatment that we observed, the models presented herein point towards race as being an important patient characteristic that may serve as a useful target for further epidemiologic studies and interventions.

In conclusion, we studied 12 years of data from a nationally representative sample of ambulatory visits in the US. Among visits identified with a diagnosis of RA, only 47% had a DMARD associated with them. DMARDs were prescribed much less often for Blacks than for Whites, especially among visits to non-rheumatologists. This finding suggests that part of the reason that Black race may be associated with reduced DMARD use is that Blacks have more limited access to rheumatologists. Interventions should be considered to improve DMARD prescribing, focusing particularly on patients who do not see rheumatologists and on Black patients who appear to have less access to rheumatologists. Health insurance status was not significantly associated with DMARD use in these data, but future studies should also determine whether Black race is a surrogate for socioeconomic issues and/or limited access. Expanding access to DMARDs will likely require improving collaborative care between generalists and specialists as well as learning more about patients' preferences and how they weight the potential benefits and risks of these agents.

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Bullet Points

- In a large US national survey of office visits to physicians, 47% of visits with a diagnosis of RA were associated with a DMARD.
- In fully adjusted models, Black race was associated with a 30% reduction in DMARD prescribing and a visit to a rheumatologist was the strongest correlate of DMARD prescribing, more than doubling the likelihood of receiving a DMARD.

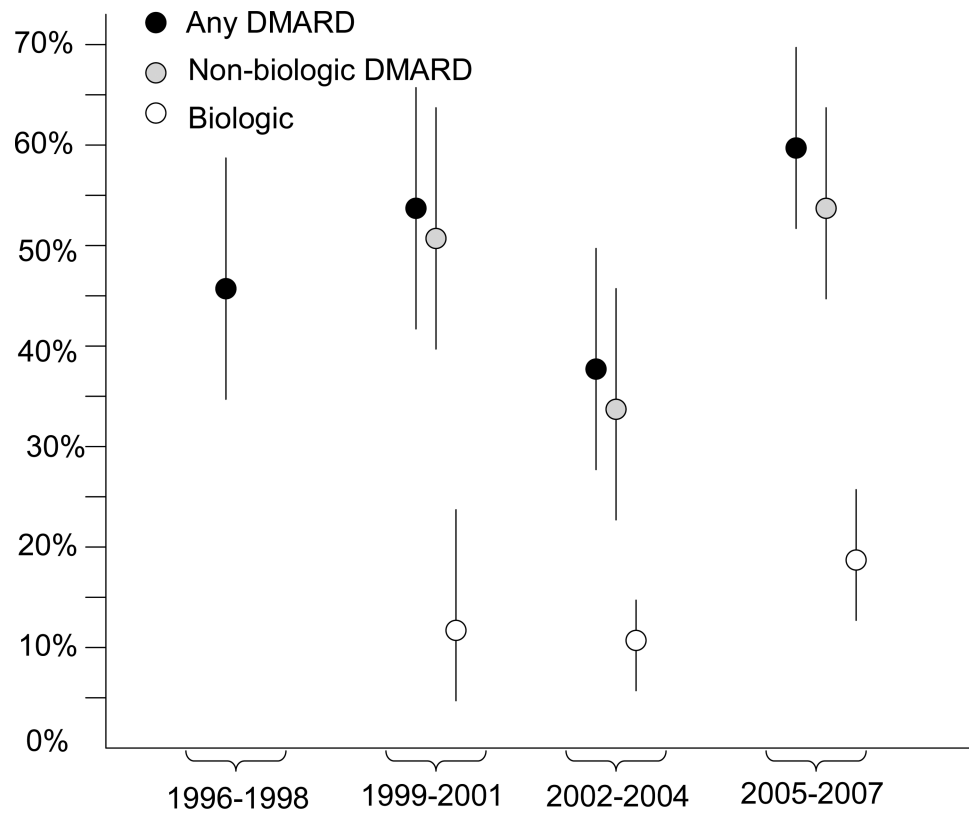


Figure 1.

The figure shows the percent of NAMCS visits with rheumatoid arthritis noted where a DMARD was listed. Data are graphed in three-year blocks across the 12 year study period, and are shown separately for any DMARD (black circles), non-biologic DMARDs (grey circles), and biologic DMARDs (white circles). There is only a black circle at the first time period (1996-1998) because all DMARDs were non-biologic. Over the period studied, there was a slight increase in any DMARD use (p for trend = 0.048), while there was an increase in biologic DMARD use (p for trend < 0.001).

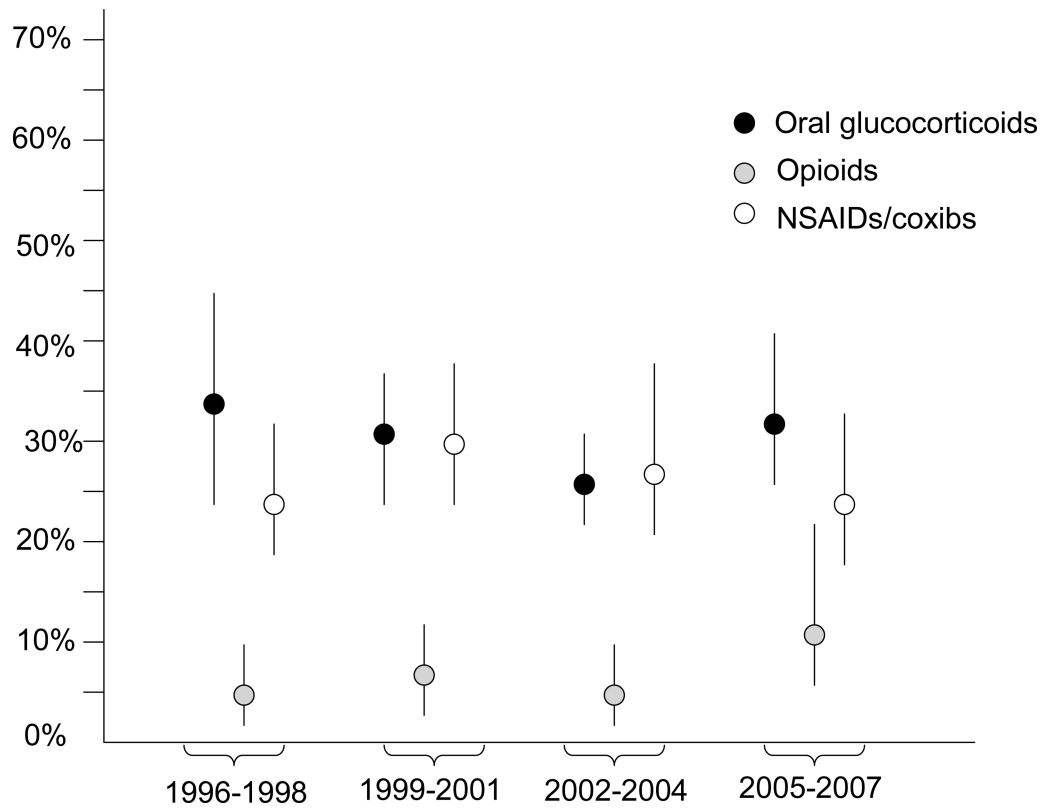


Figure 2.

The figure shows the percent of NAMCS visits with rheumatoid arthritis noted where a non-DMARD medication (oral glucocorticoid, opioid, or NSAID) was listed. Data are graphed across the 12 year study period in three-year blocks, and are shown separately for oral glucocorticoids (black circle), opioids (grey circle) and NSAIDs/coxibs (white circle).

Table 1

Characteristics of the patients seen for the visits associated with rheumatoid arthritis in NAMCS from 1996-2007, by DMARD use status

	DMARD use	No DMARD use	DMARD use	No DMARD use
	<i>N sample (%)</i>		<i>N weighted to all ambulatory US visits (%)</i>	
N	404	455	1,880,000	1,789,000
Age, years				
0-44	57 (14%)	69 (15%)	258,553 (14%)	259,392 (15%)
45-64	216 (53%)	186 (41%)	1,011,000 (54%)	745,247 (42%)
65 and over	131 (25%)	200 (44%)	610,784 (32%)	784,084 (44%)
Gender				
Female	305 (75%)	348 (76%)	1,429,000 (76%)	1,414,000 (79%)
Male	99 (25%)	107 (24%)	451,641 (24%)	375,124 (21%)
Race				
White	374 (93%)	405 (89%)	1,736,000 (92%)	1,570,000 (88%)
Black	21 (5%)	36 (8%)	103,480 (6%)	171,865 (10%)
Other	9 (2%)	14 (3%)	40,617 (2%)	47,207 (3%)
Ethnicity				
Hispanic	39 (10%)	29 (6%)	211,996 (11%)	148,308 (8%)
Non-hispanic	351 (87%)	402 (88%)	1,617,000 (86%)	1,528,000 (85%)
Unknown	14 (3%)	24 (5%)	51,097 (3%)	112,678 (6%)
Non-DMARD drugs				
0	38 (9%)	128 (28%)	182,568 (10%)	456,997 (26%)
1-2	146 (36%)	169 (37%)	712,700 (38%)	665,730 (37%)
3 or more	220 (54%)	158 (35%)	985,074 (52%)	665,997 (37%)
Rheumatology visit				
Yes	273 (68%)	104 (23%)	1,333,000 (71%)	477,041 (27%)
No	131 (32%)	351 (77%)	547,806 (29%)	1,312,000 (73%)

DMARD, disease modifying anti-rheumatic drug. See text for a list of these medications. Some column percentages may not equal 100% because of rounding.

Table 2

Correlates of disease modifying anti-rheumatic drugs use in NAMCS

	Any DMARD use, risk ratio (95% confidence interval)			Biologic DMARD use, risk ratio (95% confidence interval)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Age, years						
0-44	...	1.27 (1.02-1.58)	1.12 (0.90-1.37)	...	3.76 (1.62-8.75)	3.30 (1.40-7.80)
45-64	...	1.30 (1.11-1.54)	1.29 (0.98-1.30)	...	2.44 (1.11-5.38)	2.12 (0.92-4.88)
65+	...	1.00	1.00	...	1.00	1.00
Race/ethnicity						
Black, non-hispanic	0.69 (0.42-1.12)	0.63 (0.40-1.00)	0.70 (0.48-1.00)	0.61 (0.18-2.15)	0.51 (0.16-1.61)	0.57 (0.20-1.63)
Hispanic	1.11 (0.86-1.42)	1.09 (0.84-1.42)	1.15 (0.96-1.37)	1.15 (0.53-2.51)	1.12 (0.51-2.48)	1.20 (0.56-2.58)
Other	0.85 (0.48-1.52)	0.83 (0.50-1.37)	1.17 (0.85-1.59)	2.01 (0.87-4.62)	1.85 (0.86-3.96)	2.52 (1.35-4.70)
White	1.00	1.00	1.00	1.00	1.00	1.00
Gender						
Female	...	0.94 (0.79-1.12)	0.94 (0.79-1.11)	...	0.70 (0.46-1.09)	0.96 (0.79-1.16)
Male	...	1.00	1.00	...	1.00	1.00
Medication number [*]						
3 or more	...	1.95 (1.40-2.70)	1.80 (1.37-2.36)	...	3.63 (1.41-9.35)	3.53 (1.44-8.65)
1-2	...	1.64 (1.18-2.28)	1.44 (1.10-1.87)	...	4.02 (1.57-10.28)	3.62 (1.43-9.15)
None	...	1.00	1.00	...	1.00	1.00
Rheumatologist						
No	1.00	1.00
Yes	2.33 (1.89-2.86)	2.32 (1.19-4.54)

All models include calendar year of NAMCS survey. In addition, Model 1 includes race/ethnicity. Model 2 adds age, gender, and medication number. Model 3 adds rheumatologist. The ellipses (...) denote variable not included in a given model. The first set of models with any DMARD use as the dependent variable are based on data from 1996-2007. However, the models with biologic DMARD use as the dependent variable are based on data since the marketing of these agents in 1999.

Abbreviation: DMARD, disease-modifying antirheumatic drug.

* Medication number does not include disease-modifying antirheumatic drugs.

Table 3

Multivariable correlates of disease modifying anti-rheumatic drugs use in NAMCS among visits to rheumatologists and non-rheumatologists, 1996-2007

	Rheumatology visits (n = 377)	Non-Rheumatology visits (n = 482)
Any DMARD use, risk ratio (95% confidence interval)		
Age, years		
0-44	1.05 (0.84-1.31)	1.27 (0.78-2.08)
45-64	1.08 (0.95-1.22)	1.25 (0.89-1.78)
65+	1.00	1.00
Race/ethnicity		
Black, non-Hispanic	0.81 (0.52-1.27)	0.39 (0.17-0.92)
Hispanic	1.18 (1.02-1.37)	1.05 (0.73-1.52)
Other	1.20 (0.92-1.56)	1.25 (0.68-2.30)
White	1.00	1.00
Gender		
Female	0.96 (0.78-1.17)	0.92 (0.65 – 1.30)
Male	1.00	1.00
Medication number*		
3 or more	1.43 (1.08-1.91)	4.12 (2.01 – 8.41)
1-2	1.40 (1.03-1.92)	2.09 (1.07 – 4.06)
none	1.00	1.00

Notes: All variables were adjusted for in each model.