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Functional Improvement After RA Patients Start a New Disease Modifying Anti-rheumatic Drug Associated with Frequent Changes in DMARDs: CORRONA Database

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Abstract

Objective—Examine relationships of RA, disease duration(DD), number of previous DMARDs, and frequency of DMARD changes, to changes in function(mHAQ) after the start of a new DMARD in RA patients.

Methods—889 patients from the CORRONA database with active RA(patients included mHAQ>=0.5 and/or DAS28>=1.6) started a new DMARD(baseline) and had at least one follow-up (f/u) visit 6–12mos later. Change in mHAQ from baseline to f/u visit was modeled using univariate/ multivariate linear regression analysis. Due to colinearity, separate multivariate regression models were performed including/excluding the predictors: disease duration, number of prior DMARDs and frequency of DMARD changes.

Results—Baseline age, mHAQ, ESR, DAS28, and number of prior DMARDs differed across DD groups. The univariate linear regression model showed that higher baseline values of mHAQ, DAS28, SJC, TJC, CDAI, ESR, MD global, prednisone use, and subsequent addition/discontinuation of DMARDs associated with improvement of the mHAQ at f/u($p \leq 0.05$). The multivariate linear regression models demonstrated that mHAQ improvement associated with shorter DD, higher baseline mHAQ, addition of subsequent DMARD, and the DMARD frequency index(number of previous DMARDs divided by years of DD)($p<0.05$). Number of DMARDs patients previously used was not associated with mHAQ change in either model.

Conclusion—This study demonstrates that in clinical rheumatological practices, more frequent changes in DMARDs are associated with greater improvement in function(mHAQ). It does not support the idea that number of previous DMARDs used predicts response. Indirectly, these data support the concept that DMARDs should be changed if optimal responses are not achieved within a specified time.

Keywords

rheumatoid arthritis; outcome measures; disease modifying anti-rheumatic drugs

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Introduction

Rheumatoid arthritis (RA) is an inflammatory destructive arthritis of unclear etiology and affects approximately 1% of the general population. Although there is no cure for RA, disease modifying anti-rheumatic drugs (DMARDs) are the mainstay of therapy and are used to decrease the rate of joint destruction, reduce inflammation, and improve quality of life.

With the expanding repertoire of DMARDs available for the treatment of RA, it may be important to evaluate the impact of the DMARDs previously used on response to a new DMARD. Since the ultimate goal of RA treatment is to attain and sustain remission, rheumatologists are being encouraged to change DMARDs if the current therapy does not achieve pre-set goals for benefit within a pre-determined time, in order to reduce a patient's disease activity (1;2). The effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study) assessed an aggressive RA outpatient management strategy with a goal of DAS<2.4, and the BeSt study evaluated four common but different RA treatment strategies. The results of both studies demonstrated that aggressive management of RA is the optimal therapeutic approach, and stress the importance of changing a patient's treatment regimen if the response is not achieved.

Thus, the frequency or rate of DMARDs changed might be used to identify patients with aggressive DMARD management, which may result in less disease activity and better function (1;2). We hypothesize that the 'DMARD frequency index' (the ratio of the number of previous DMARDs used per disease duration in years) is associated with a better outcome.

There have been many efforts to identify important demographic and disease activity factors influencing physical function responses to the use of DMARDs. Meta-analyses of published reports of clinical trials suggest that patients with longer RA disease duration respond to DMARDs less well than those with shorter disease duration when evaluated with physical function measures (3–9). In addition, several papers have evaluated the use of previous DMARDs as a predictor of efficacy when a new DMARD was started (4;8;10–12). Some papers have suggested that inadequate response to previous DMARD was associated with decreased response to the next DMARD (4;8;10–12).

This study examines potential factors associated with mHAQ improvement, in a large cohort of community-based RA patients, with specific emphasis on disease duration, number of prior DMARDs used, and the rate of DMARD changes.

Patients and Methods

Patients

The CORRONA database was assembled for the purpose of facilitating cohort studies in rheumatologic diseases by accumulating longitudinal, 'real world' data representing community patients with rheumatic disease. This registry began in the spring of 2002 and continues to recruit and follow patients.

As of July 2006, 11,255 RA patients from 76 different sites and >200 rheumatologists in the United States had been enrolled in the CORRONA registry. At entry, patients fill out a patient enrollment questionnaire, including the modified health assessment questionnaire (mHAQ) (see below for details) (13). The patient enrollment questionnaire includes information regarding past medical history, past surgical history, family history, review of symptoms, and medication use. The patient entry and follow-up questionnaires include detailed information on DMARD therapy and corticosteroids. At subsequent patient visits, follow up questionnaires review symptoms over the last 8 weeks and current medication use. The physician review form

includes a list of current rheumatic diagnoses, recent hospitalizations, current clinical information, infections, co-morbidities, radiological reports, and laboratory findings (hematocrit, platelet count, etc). Clinical information includes: 28 tender joint count (TJC), 28 swollen joint count (SJC), physician global assessment (0–100 VAS scale), rheumatoid factor positivity, extra-articular manifestations, and acute phase reactants (ESR, CRP, as available). The patient completes the mHAQ in the office.

Methods

The mHAQ asks the patient one question from each of the 8 domains of the HAQ-DI(dressing, rising, eating, walking, hygiene, reach, grip, and usual activities). Each item is scored from 0–3, with '0' meaning that the patient is able to do the activity without any difficulty and '3' meaning that the patient is unable to do the task. The items are averaged so that the final mHAQ score is between 0–3. Because there are no validated, dichotomous cut-points to define patient clinical improvement or minimally clinically important differences for the mHAQ(14), we used the mHAQ as a continuous variable for our outcome measure to evaluate improvement. The change in mHAQ was calculated by subtracting baseline mHAQ from the f/u mHAQ at the last visit within the 6–12 months interval.

For our present analysis, the cohort was limited by predefined criteria to those RA patients who started a new DMARD and for whom the mHAQ was >=0.5 or DAS was >=1.6 at baseline. Clinical remission is considered the main therapeutic target in RA. However recent studies have shown that radiographic progression continues despite the satisfaction of remission criteria. Thus, the strictest definition of remission by DAS was used (i.e. <= 1.6). Baseline was considered the start of the new DMARD. Patients also were required to have at least one follow-up assessment within 6–12 months (889 patients). We also performed a similar analysis with a control cohort (data not shown). The control cohort consisted of RA patients who were stable on DMARDS/Biologics/Steroids (same dose) and had an interval of time between 6 and 12 months remaining on stable therapy. If a patient had more than one visit still on stable therapy and within 6 and 12 months, then we used the last visit in that time interval for analysis. The stable cohort was not analyzed in combination with the DMARD change cohort. In the analyses performed on the stable cohort we included the covariates of age, sex and disease activity in the models for mHAQ change.

The following clinical and laboratory factors were considered as potential predictors of treatment response, all at baseline: disease duration, age, gender, prednisone use, mHAQ, MD global assessment, swollen joint count, tender joint count, ESR, clinical disease activity index (CDAI), DAS28, RF positivity, number of prior DMARDs, number of DMARDs ever used, DMARD added after baseline, DMARD discontinued after baseline, ethnicity, and education. Patients were further sub-categorized by physician documented disease duration into <3 years, 3–5 years, and >5 years (Table 1). In addition, we developed a 'DMARD frequency index', which is number of DMARDs used previously divided by patients' disease duration (in years).

Statistical Analysis

We compared baseline characteristics of RA patients among the three disease duration groups (<3yrs, 3–5yrs, >5yrs) using one-way analysis of variance (ANOVA). ANOVA was also used to compare the change scores of study measures (baseline minus follow-up) among the disease duration groups. Univariate and multiple linear regression models were used to evaluate predictors of change of mHAQ in response to starting a new DMARD. Stepwise model selection was used to select variables for the multiple linear regression models. Disease duration and number of DMARD ever used were forced into these models even if not included by the model selection criterion. As an additional model, we included the 'DMARD frequency index' rather than disease duration and number of DMARD ever used. All three variables were

not used in the same model, as 'DMARD frequency index' is a direct function of disease duration and number of previous DMARDs.

Results

A total of 889 RA patients who were started on a new DMARD and had at least one follow-up assessment within 6–12 months were included in the cohort. Baseline characteristics for patients with disease duration <3 years, 3–5 years, and >5 years are described in Table 1. There was no difference among the 3 groups in ethnicity, education and RF positivity. However, baseline mHAQ scores, age, ESR, DAS28, and number of previous DMARDs, differed across the disease duration categories (p=0.005, <0.001, 0.037, 0.017, and <0.001 respectively). Change from baseline to follow-up time was evaluated across disease duration categories (Table 1). Decrease of prednisone dose and discontinuing prednisone were more likely in those with <3 years RA duration (p=0.016).

The association of change in mHAQ with the number of previously used DMARDs per year of disease duration was evaluated (Table 2). There was a significant association between the 'DMARD frequency index' and the amount of improvement in the mHAQ, i.e. more frequent DMARD changes were associated with improvement in mHAQ (p=0.02).

The results of the univariate linear regression model showed that RA patients with higher baseline mHAQ, prednisone use, DAS28, SJC, TJC, ESR, CDAI, and MD global assessment was associated with mHAQ improvement during 6–12 month f/u (Table 2). The number of DMARDs ever used and disease duration did not correlate with change in mHAQ with the univariate analysis. However, the addition or discontinuation of a DMARD after baseline did correlate with improvement of mHAQ (p=0.012, 0.026).

The multivariate linear regression model for change in mHAQ as an outcome measure (without disease duration) demonstrated that baseline mHAQ score, 'DMARD frequency index' and addition of a new DMARD during follow-up were predictors of mHAQ response (overall model r^2=0.19) (Table 4). The multivariate regression model using disease duration the showed similar results (Table 3). The number of DMARDs ever used was not associated with change in mHAQ in any analysis.

A similar analysis was performed using a cohort of 1594 CORRONA RA patients who were stable on DMARDS/Biologics/Steroids (same dose) and had an interval of time between 6 and 12 months remaining on stable therapy (data not shown). The results show that the stable therapy cohort had a mean disease duration of 12.2 versus 11.9 years in the cohort starting a new DMARD. As expected, in this stable DMARD cohort mHAQ increased over time (worsened) (mean change +0.02, 95%CI: [.007, .033], p=0.002). In contrast, the mean change in mHAQ after initiation of a DMARD in the study cohort was −0.07 (a significant, although small, improvement).

Discussion

This study evaluates a large cohort of real-world RA patients who started a new DMARD while being followed by a large, representative sample of rheumatologists. The patients were evaluated for factors associated with functional improvement (measured by the mHAQ), using the prospective CORRONA database. This database is unique because of its overall size and its representation of data from >200 community rheumatologists throughout the United States. It represents a geographically diverse (northeast, southeast, midwest, northwest, and southwest of the USA) and generally representative sample of US clinical rheumatology practice. Our original hypothesis posited that patients with longer disease duration and those who had used more previous DMARDs, might be less responsive to the next DMARD and thus would not

improve their mHAQ (i.e. function), as much as those with RA exposed to fewer DMARDs and/or who had RA of shorter disease duration.

The univariate linear regression models showed that improvement in mHAQ generally was associated with baseline disease activity measures: DAS28, CDAI, SJC, TJC, and MD global assessment, i.e., those with higher baseline scores were more likely to decrease their scores. The univariate model did not show a relationship of change in mHAQ with disease duration or to the number of DMARDs a patient had previously used. However, the ratio of the number of DMARDs previously used divided by the disease duration (i.e. patients who switched DMARDs more frequently, DMARD Frequency Index) did show a relationship with change in mHAQ. The patients who changed DMARDs more frequently had more improvement in their mHAQ, suggesting that although the absolute number of previous DMARDs was not a factor in response to a new DMARD, the frequency with which DMARDs are changed is associated with a better clinical outcome. This is supported by the significant relationship between improvement in mHAQ and the addition or discontinuation of a DMARD during the 6–12 months following the introduction of a new DMARD.

Our multivariate linear regression models (not including the ratio of DMARDs previously used to disease duration) accounted for more variables and their inter-relationships. The DMARD frequency index, the addition of another DMARD during f/u, and higher baseline mHAQ predicted improvement of mHAQ. Repeating the model evaluating disease duration also showed similar results. Again, however, there was no relationship of mHAQ response to the number of DMARDs previously used.

Our study confirms the published clinical trial literature regarding the relationship of disease duration with response to the next DMARD in community dwelling patients across the country. In 2000, Anderson et al. performed a meta-analysis of 14 clinical trials (1985–1998) to evaluate factors predicting response to therapy in RA; 11 were methotrexate trials (4). There was a wide range of mean disease duration across the trials (0.5 years to 17.5 years). Tender/swollen joint count, ESR, patient severity, physician severity, HAQ-DI, and pain measures improved less in patients with longer duration of disease. Aletaha et al. in a meta-analysis using 36 clinical trials, found that HAQ-DI scores were higher with longer duration of RA, and suggested that less improvement in HAQ may be seen in patients with longer disease duration (3).

Regarding the effect of prior DMARDs on the response to subsequent DMARDs, Hurst et al. and Fries et al. state that the order in which DMARDs are received by the patient is important in determining response (8;11). Aletaha et al. showed that the first DMARD employed was continued longer by patients and was more effective, compared to subsequent drugs used (10). Kapral et al. showed that 86 patients re-challenged with low dose MTX improved and continued the medication, but others having used other DMARDs did not improve when re-challenged with those other DMARD (12). These data, while interesting, do not directly address the question of lesser responses as more DMARDs are used. Evaluating the relationship of rate of change of DMARDs (ratio of number of previous DMARDs to disease duration in years) with mHAQ response has not been reported in the literature. Our finding regarding the rate of change of DMARDs in real-life RA patients supports the view that DMARDs should be changed frequently if response is not achieved and support the evolving concept of goal-oriented DMARD management, in which DMARD treatment is changed if the patient has not reached a targeted response (e.g. DAS<2.6) by a certain time (e.g. 3–4 months). We did not perform extensive subgroup analyses, thus it is possible that the DFI is not predictive of mHAQ improvement in all types of patient subgroups. This result requires further validation, but the rate of DMARD change may provide a marker of treatment intensity.

Our study showed no effect of the number of previously used DMARDs on subsequent response. Our results may differ from datasets that used data derived from clinical trials, which represent a more selected patient group. Our data represent a large number of patients in real-world, clinical practice, and probably more closely describes the general USA RA population.

This study has some limitations. The prospective observational CORRONA database was not specifically designed for the purpose of this study. Patients in the CORRONA database have lower disease activity compared to other databases (low baseline mHAQ) and this may contribute to a floor effect, where the 0.3–0.4 lower baseline mHAQ scores (inherent in the instrument compared to the scores using HAQ-DI (15)) leaves less room for improvement. Residual joint damage can be associated with higher mHAQ score that may not be amenable to changes in DMARDs. However, clinical trials have shown that mHAQ can detect change when evaluating the data (16), thus mHAQ was selected as an adequate measure of quality of life in the CORRONA database. In addition, the database did not collect data on reasons for previous DMARD withdrawl, which may have been another covariate in the model for mHAQ response.

In conclusion, this study shows that in the CORRONA database, higher baseline mHAQ, shorter disease duration, addition of another DMARD during follow-up and the frequency of DMARD changes are associated with improvement in mHAQ when evaluating the response to a new DMARD. However, the total number of DMARDs ever used does not predict improvement of the mHAQ. The frequency of change of DMARDs during patients' disease duration is a relatively new way of evaluating how rapidly patients, physicians change DMARDs. These results support the view that rheumatologists should change patients' DMARDs when needed to improve RA disease activity.

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Reference List

1. Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Allaart CF, Van ZD, Kerstens PJ, Hazes JM, et al. Clinical and radiographic outcomes of four different treatment strategies in patients with early rheumatoid arthritis (the BeSt study): a randomized, controlled trial. Arthritis Rheum 2005;52(11): 3381–3390. [PubMed: 16258899]
2. Grigor C, Capell H, Stirling A, McMahon AD, Lock P, Vallance R, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. Lancet 2004;364(9430):263–269. [PubMed: 15262104]
3. Aletaha D, Ward MM. Duration of rheumatoid arthritis influences the degree of functional improvement in clinical trials. Ann Rheum Dis 2006;65(2):227–233. [PubMed: 15975967]
4. Anderson JJ, Wells G, Verhoeven AC, Felson DT. Factors predicting response to treatment in rheumatoid arthritis: the importance of disease duration. Arthritis Rheum 2000;43(1):22–29. [PubMed: 10643696]
5. Baumgartner SW, Fleischmann RM, Moreland LW, Schiff MH, Markenson J, Whitmore JB. Etanercept (Enbrel) in patients with rheumatoid arthritis with recent onset versus established disease: improvement in disability. J Rheumatol 2004;31(8):1532–1537. [PubMed: 15290731]
6. Capell HA, Porter DR, Madhok R, Hunter JA. Second line (disease modifying) treatment in rheumatoid arthritis: which drug for which patient? Ann Rheum Dis 1993;52(6):423–428. [PubMed: 8100702]
7. Drossaers-Bakker KW, de BM, Van ZD, Zwinderman AH, Breedveld FC, Hazes JM. Long-term course and outcome of functional capacity in rheumatoid arthritis: the effect of disease activity and radiologic damage over time. Arthritis Rheum 1999;42(9):1854–1860. [PubMed: 10513799]

8. Hurst S, Kallan MJ, Wolfe FJ, Fries JF, Albert DA. Methotrexate, hydroxychloroquine, and intramuscular gold in rheumatoid arthritis: relative area under the curve effectiveness and sequence effects. J Rheumatol 2002;29(8):1639–1645. [PubMed: 12180722]

9. Situnayake RD, McConkey B. Clinical and laboratory effects of prolonged therapy with sulfasalazine, gold or penicillamine: the effects of disease duration on treatment response. J Rheumatol 1990;17(10): 1268–1273. [PubMed: 1979349]

10. Aletaha D, Smolen JS. The rheumatoid arthritis patient in the clinic: comparing more than 1,300 consecutive DMARD courses. Rheumatology (Oxford) 2002;41(12):1367–1374. [PubMed: 12468815]

11. Fries JF, Williams CA, Singh G, Ramey DR. Response to therapy in rheumatoid arthritis is influenced by immediately prior therapy. J Rheumatol 1997;24(5):838–844. [PubMed: 9150069]

12. Kapral T, Stamm T, Machold KP, Montag K, Smolen JS, Aletaha D. Methotrexate in rheumatoid arthritis is frequently effective, even if re-employed after a previous failure. Arthritis Res Ther 2006;8 (2):R46. [PubMed: 16507172]

13. Pincus T, Summey JA, Soraci SA Jr, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. Arthritis Rheum 1983;26(11):1346–1353. [PubMed: 6639693]

14. Wells GA, Tugwell P, Kraag GR, Baker PR, Groh J, Redelmeier DA. Minimum important difference between patients with rheumatoid arthritis: the patient's perspective. J Rheumatol 1993;20(3):557–560. [PubMed: 8478873]

15. Wolfe F. Which HAQ is best? A comparison of the HAQ, MHAQ and RA-HAQ, a difficult 8 item HAQ (DHAQ), and a rescored 20 item HAQ (HAQ20): analyses in 2,491 rheumatoid arthritis patients following leflunomide initiation. J Rheumatol 2001;28(5):982–989. [PubMed: 11361226]

16. Strand V, Scott DL, Emery P, Kalden JR, Smolen JS, Cannon GW, et al. Physical function and health related quality of life: analysis of 2-year data from randomized, controlled studies of leflunomide, sulfasalazine, or methotrexate in patients with active rheumatoid arthritis. J Rheumatol 2005;32(4): 590–601. [PubMed: 15801012]

TABLE 1

BASELINE CHARACTERISTICS				
Duration of RA	<3yrs	3–5 yrs	>5yrs	p-value
Number Patients	150	155	584	
Age (years), (SD)	56 (14.6)	56 (13.7)	60 (12.0)	<0.001
White %	82	84	84	NS
College Education	44	48	43	NS
Female %	77	75	77	NS
RF+ ever %	75	76	77	NS
Prednisone Dose (mg/day), (SD) [of patients using]	5.6 (2.9) N=64	6.0 (2.9) N=54	5.6 (2.9) N=247	NS
mHAQ (0–3), (SD)	0.57 (0.5)	0.47 (0.4)	0.61 (0.5)	0.005
SJC (28), (SD)	6.0 (6.3)	6.8 (6.3)	6.5 (6.0)	NS
TJC (28), (SD)	5.8 (6.9)	5.8 (6.4)	5.8 (6.2)	NS
ESR (mm/hr), (SD)	23 (18.4)	25 (19.7)	28 (22.8)	0.037
DAS28, (SD)	3.9 (1.5)	4.0 (1.3)	4.3 (1.4)	0.017
CDAI (0–76), (SD)	18 (13.9)	18 (12.6)	20 (12.9)	NS
# DMARDs Ever, (SD)	1.08 (0.9)	1.9 (1.5)	2.55 (1.9)	<0.001
DMARD Frequency Index* (SD)	0.80 (0.7)	0.51 (0.4)	0.19 (0.2)	<0.001
CHANGE FROM BASELINE TO FOLLOW-UP 6–12 MONTHS LATER				
Duration of RA	<3yrs	3–5 yrs	>5yrs	p-value
Months from Initiation of new DMARD, at baseline (SD)	9.2 (1.8)	9.3 (1.7)	9.3 (1.7)	NS
Number Patients	150	155	584	
Change in Prednisone Dose (mg/day), (SD)	−0.7 (2.6)	−0.3 (2.7)	0.01 (2.8)	0.016
Discontinued Prednisone (%)	15	5	6	0.001
mHAQ (0–3), (SD)	−0.13 (0.5)	−0.03 (0.4)	−0.07 (0.4)	NS
SJC (28), (SD)	−1.4 (6.6)	−1.8 (5.8)	−1.6 (5.7)	NS
TJC (28), (SD)	−1.6 (7.8)	−1.0 (6.6)	−1.4 (6.8)	NS
ESR (mm/hr), (SD)	−1.6 (12.3)	−1.1 (16.8)	−2.3 (16.4)	NS
DAS28, (SD)	−0.29 (1.4)	−0.39 (1.4)	−0.46 (1.4)	NS
CDAI (0–76), (SD)	−4.3 (16.4)	−3.4 (13.6)	−4.6 (13.7)	NS
DMARD Added % of Patients	8.0	5.2	5.8	NS
DMARD Discontinued % of Patients	10.7	14.2	9.8	NS

*DMARD Frequency Index= Number of DMARDs ever used divided by disease duration in years. For 877 observations (12 missing because duration was “0”); mean = 0.35 (SD 0.42), median = 0.2, range = 0–3.33

TABLE 2

Univariate Linear Regression Analysis, change in mHAQ during 6–12 months follow-up

	Estimate(Δ in mHAQ)	Confidence Interval	p-value
Duration (per 10yrs)	0.01	(−0.01, 0.04)	NS
Duration Groups			
<3yrs	Referent		
3–5yrs	0.096	(−0.00, 0.19)	0.040
>5yrs	0.060	(−0.01, 0.13)	NS
*DMARD Groups			
Group A	Referent		
Group B	−0.030	(−0.09, 0.03)	NS
Group C	0.040	(−0.08, 0.16)	NS
# DMARD Ever Used			
0 DMARDs	Referent		
1 DMARDs	−0.02	(−0.11, 0.07)	NS
2 DMARDs	−0.02	(−0.11, 0.07)	NS
3 DMARDs	−0.06	(−0.16, 0.04)	NS
>=4 DMARDs	−0.07	(−0.17, 0.03)	NS
Age (per 10yrs)	0.02	(0.00, 0.04)	0.084
Female	−0.03	(−0.09, 0.04)	NS
White	0.02	(−0.05, 0.09)	NS
College Education	0.01	(−0.04, 0.07)	NS
Prednisone Use	−0.06	(−0.12, −0.01)	0.028
DMARD Frequency Index+	−0.075	(−0.14, −0.01)	0.020
DMARD Added	−0.14	(−0.26, 0.03)	0.012
DMARD Discontinued	−0.10	(−0.19, −0.01)	0.026
Baseline Variables			
mHAQ	−0.302	(−0.35, −0.25)	<0.001
DAS28	−0.50	(−0.72, −0.28)	<0.001
SJC	−0.07	(−0.11, −0.03)	0.002
TJC	−0.08	(−0.12, −0.04)	<0.001
ESR	−0.02	(−0.04, −0.01)	0.001
CDAI	−0.06	(−0.08, −0.04)	<0.001
MD Global	−0.03	(−0.04, −0.02)	<0.001
RF+	−0.02	(−0.10, 0.05)	NS
#DMARD Prior Used	−0.01	(−0.03, 0.00)	NS

*DMARD Groups: A) TNF inhibitors or if the patient was started on more than one DMARD at baseline, B) Methotrexate, Arava, Sulfasalazine, immuran, or cyclosporine started, C) Hydroxychloroquine or minocycline started.

+DMARD Frequency Index is the ratio of number of previous DMARDs divided by disease duration in years.

TABLE 3

Multiple Linear Regression, Change in mHAQ versus Baseline Values

	6–12 Months Follow-Up N=863		
Covariates	**Estimate(Δ in mHAQ)**	**Confidence Interval**	**p-value**
DiseaseDuration (per 10 years)	0.027	(0.002, 0.052)	0.036
# DMARDs Prior	−0.001	(−0.016, 0.013)	NS
MHAQ	−0.315	(−0.37, −0.26)	<0.001
DMARD added	−0.131	(−0.30, −0.09)	<0.001

TABLE 4

Multiple Linear Regression, Change in mHAQ versus Baseline Values (including the frequency of DMARD changes variable)

	6–12 Months Follow-Up N=851		
Covariates	**Estimate(Δ in mHAQ)**	**Confidence Interval**	**p-value**
DMARD Frequency Index[+]	−0.064	(−0.123, −0.005)	0.034
MHAQ	−0.299	(−0.35, −0.25)	<0.001
DMARD added	−0.196	(−0.30, −0.09)	<0.001

[+] DMARD Frequency Index is the ratio of number of previous DMARDs divided by disease duration in years.