Utility of administrative and clinical data to predict major change in medical treatment in US Veterans enrolled in the Veterans Affairs Rheumatoid Arthritis (VARA) registry

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Abstract

Objective

To examine factors associated with major therapeutic changes (MTC) among US Veterans with moderate/severe rheumatoid arthritis (RA) based on Disease Activity Score based on 28 joints (DAS28).

Methods

We used data from patients enrolled in the Veterans Affairs Rheumatoid Arthritis (VARA) registry from 1/1/2006 through 12/31/2014. The index date was a clinic visit with DAS28 >3.2 (moderate/severe disease) following an 18-month pre-index period that included ≥2 DAS28 measurements ≥60 days apart. The patients were followed for MTC from 7 days pre-index through 90 days post-index. Poisson multivariable regression models were used to identify associations with MTC. Chart review of a subset of randomly selected patients explored factors that impacted therapeutic decisions.

Results

Among 941 patients, 396 (42.1%) had MTC. Of these, 369 (39.2%) patients had worsening DAS28 at index, 118 (12.5%) had DAS28 improvements, and 454 (48.2%) patients had no change in DAS28 versus pre-index DAS28. Of the patients with worsening DAS28, no change in DAS28, and improved DAS28, respectively, 50.5%, 62.6%, and 70.3% had no MTC. Regression analyses showed index DAS28, oral steroid or non-biologic disease-modifying anti-rheumatic drug (nbDMARD) use in the previous year were associated with an increased likelihood of MTC; use of nbDMARDs in the previous 90 days was associated with a decreased likelihood of MTC. The most common reason for not modifying therapy despite DAS28 >3.2 was a judgement of mild disease.

Conclusion

Clinicians frequently do not institute major therapeutic changes despite DAS28 indicating moderate/severe disease activity; multiple factors are involved in real-world treatment decisions.

Key words

United States Department of Veterans Affairs, rheumatoid arthritis, Severity of Illness Index, clinical decision-making

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Introduction

The treat-to-target concept has been recommended in rheumatoid arthritis (RA) clinical guidelines after clinical trials showed that patients experienced better outcomes with intensive disease control (1-5). These initial studies employed conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs). The introduction of new biologic disease-modifying anti-rheumatic drugs (bDMARDs) provides an additional means to employ a treat-to-target strategy (6, 7). Treating to target requires focused management of disease activity, with changes in treatment (dose escalation, combination therapy, or switching to a different medication) directed by changes in disease activity (8-10).

To make treatment decisions based on disease activity, reliable disease activity measures that provide objective targets are required. The American College of Rheumatology (ACR) noted 6 disease activity measures for use in RA (8). The Disease Activity Score based on 28 joints (DAS28) is a composite measure of swollen and tender joint counts, a patient measure of general health, and erythrocyte sedimentation rate (ESR) as a measure of inflammation (DAS28-ESR); it does not, however, use physician global assessment, which is used in other composite measures of RA disease activity (11). The DAS28 has been validated against radiographic progression and physical function in patients with RA (12), and may be useful in both the clinical trial and clinical practice settings (13).

Real-world practices in the treatment of RA can be studied using clinical and administrative claims databases. Unfortunately, data as a byproduct of routine care rarely contain adequate information on disease activity or severity as the collection of core disease activity components is often not done explicitly and/or recorded in the medical notes in a way to support calculation of ACR-accepted disease activity measures. Information about disease status or treatment response is often relative rather than objective; for example, "the patient has improved after starting a new treatment." The lack of connection between treatment decisions and clinical outcomes in healthcare databases makes it difficult to determine the reason(s) why a patient may or may not have a change in therapy despite moderate to severe disease activity. The Veterans Affairs Rheumatoid Arthritis (VARA) database provides an ideal setting to determine the relationship between treatment changes and disease activity based on a validated disease activity measure that can be linked with administrative data. Patients enrolled in VARA undergo routine assessments by rheumatologists, which include the collection and documentation of core disease activity components that support calculation of multiple disease activity measures, including the DAS28 to determine the level of disease activity at each visit. This study was designed to explore the factors that influence and predict major changes in therapy among RA patients with moderate to severe disease activity.

The objectives of this study were to:

1. determine the number of RA patients with moderate/severe disease activity (DAS28 ≥3.2) who had a major change in RA therapy;
2. determine if a progressive, stable, or improving disease activity course influenced the decision to make a major change in therapy;
3. use multivariable regression techniques to evaluate whether other administrative and/or clinical factors were associated with a major change in therapy;
4. conduct a chart review to determine reasons for the decision to initiate or not initiate a change in therapy in patients with moderate/severe disease activity.

Patients and methods

Data source and study design

The VARA registry is a prospective, observational registry involving 11 Veterans Affairs (VA) medical centres (Birmingham, Alabama; Brooklyn, New York; Dallas, Texas; Denver, Colorado; Jackson, Mississippi; Iowa City, Iowa; Little Rock, Arkansas; Omaha, Nebraska; Philadelphia, Pennsylvania; Portland, Oregon; Salt Lake City, Utah and Washington, DC). Clinical disease activity measures (*i.e.* DAS28 and duration of disease) were obtained from the VARA registry, which has been described elsewhere (14, 15). A cohort

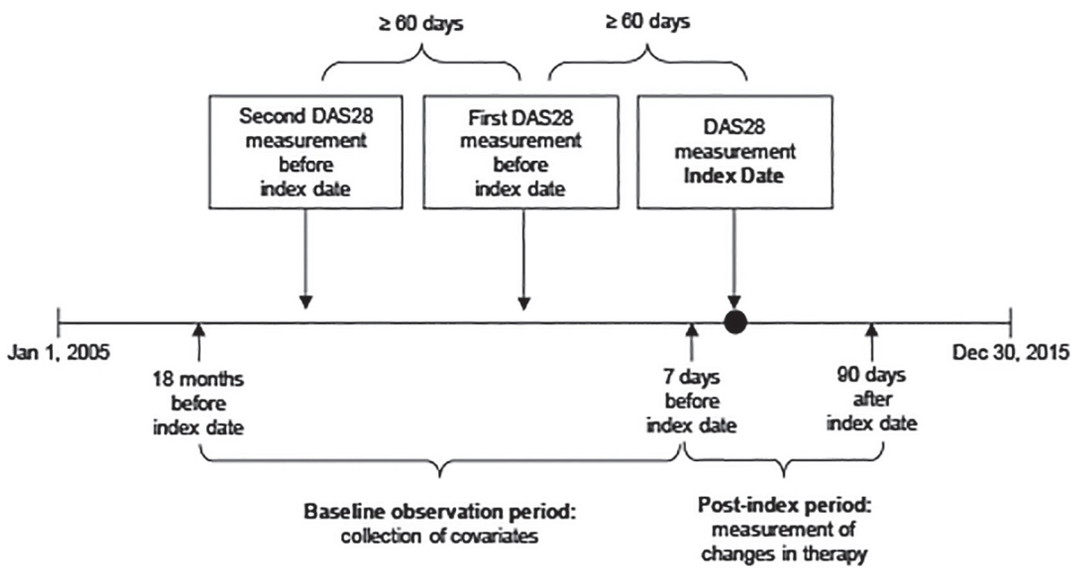

Fig. 1. Study schema.
DAS28: Disease Activity Score based on 28 joints.

study design was used on historical data available in the VARA registry and in the VA Informatics and Computing Infrastructure (VINCI), which houses the VA Corporate Data Warehouse (CDW). This study used VARA and VINCI data from January 1, 2006 through December 31, 2014. The index date was the first visit with a DAS28 measurement that fulfilled eligibility criteria (Fig. 1). An 18-month pre-index observation period was used to describe baseline disease activity leading up to index date for each patient. It was also used to describe covariate data. Patients were followed for 90 days after the index date to observe major changes in RA treatment.

This study was approved by the University of Utah Institutional Review Board, the VA Research Service, and the Scientific and Ethical Advisory Board of the VARA registry for analysis of VARA and VA administrative data. All patients provided written consent and authorisation for use of health information upon enrolment in the VARA registry.

Study population

To be included in the study, Veteran patients had to be enrolled in the VARA registry, be ≥18 years of age, have DAS28 ≥3.2 on index date (moderate to severe disease), and have ≥18 months of enrolment in the VA health care system prior to and ≥90 days after index date. Veteran patients were excluded if they met any of the following criteria because treatment for their RA could be modified based on these conditions: diagnosis of any active cancer, receipt of an organ transplant, or diagnosis of any other autoimmune disorder, including Sjögren's syndrome.

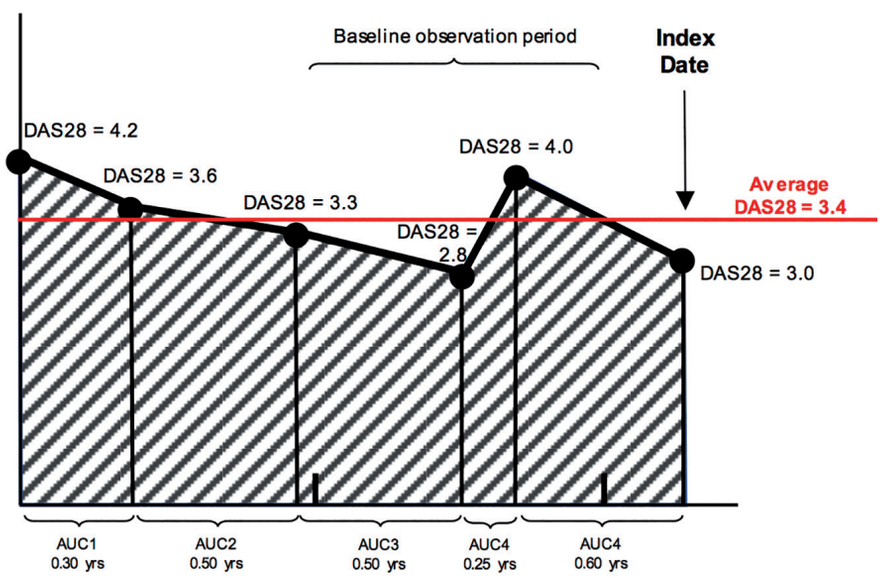

Fig. 2. Calculation of average DAS28 based on AUC.
AUC: area under the curve; DAS28: Disease Activity Score based on 28 joints.

To determine baseline disease activity, patients were also required to have ≥2 DAS28 measures separated by ≥60 days recorded in the VARA registry during the 18-month baseline observation period. DAS28 stability was calculated based on the area under the curve (AUC) for the observation period prior to the DAS28 index date using methods previously described by our group (Fig. 2) (16). EULAR response was defined by comparing the baseline DAS28 by the AUC calculation from the baseline period prior to index date to the DAS28 on the index date. EULAR response criteria have defined a 0.6 change in DAS28 as a significant response (17, 18). DAS28 worsening was defined as an index date DAS28 that was 0.6 higher than the average DAS28 based on AUC prior to index date, DAS28 improving was defined as 0.6 lower than average DAS28 prior to index date, and patients with DAS28 at index date that was not 0.6 higher or lower than average DAS28 were considered to have no change. A sensitivity analysis using a 1.2 change in DAS28 to define response was conducted.

Variables

• *Dependent variables*

During the 90-day follow-up period, patients were categorised as either undergoing a major change in RA therapy or not. A major change was defined as initiation of a new DMARD (or switch to a different DMARD of the same drug class), escalation of DMARD dose by >25% (except for loading dose protocols), initiation of prednisone, increase in average monthly prednisone dose by 25%, or ≥2 joint injections with corticosteroids. These changes have been shown in the VARA database to be associated with a failure to achieve clinical response as measured by DAS28, and thus are typical of changes made by treating providers in the VARA registry when patients are judged to not be experiencing clinical improvement (19).

• *Independent variables*

VARA and CDW data were linked to produce clinical and administrative variables used to explore the relationship among baseline disease activity trends (utilising pre-index DAS28 values), index DAS28 and index DAS28 individual components and major change in RA therapy, which were organised into demographic variables, VARA clinical variables, medications, procedures and comorbidity scores.

During the baseline observation period, administrative covariates to be analysed as potential predictors of major change in therapy were collected from the CDW. Covariates in the VARA database included sex, age, disease duration, tender joint counts, swollen joint counts, patient global assessment (20), physician global assessment (21), pain rated on a 10-cm visual analogue scale (VAS), patient-reported Health Assessment Questionnaire (HAQ) disability index (22), ESR (mm/hr), C-reactive protein (CRP; mg/L), rheumatoid factor (RF) status, anti-cyclic citrullinated peptide antibody (aCCP) status, and DAS28 values.

Chart abstraction

A subset of patients (n=403) was selected for a chart review, with stratification by disease activity, index date, and VA site to determine the reasons for continuing or changing therapy. The reason for continuation or change in therapy was recorded. The record was reviewed by clinical reviewer (JRS) for disease activity assessment reported by the patient and provider. If possible, a comprehensive provider judgment (CPJ) of disease activity by the provider was recorded as mild, moderate/severe, or undetermined disease severity.

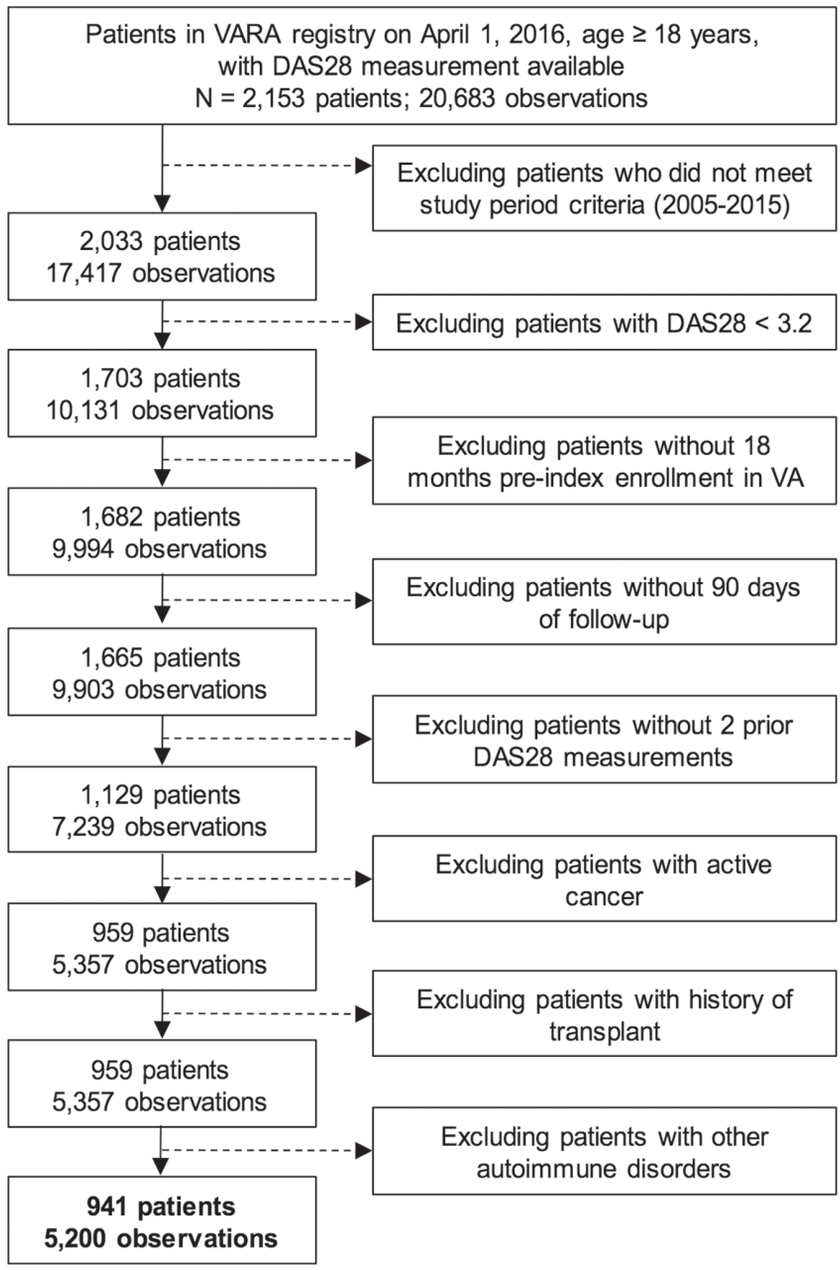

Fig. 3. Patient identification.
DAS28: Disease Activity Score based on 28 joints; VA: Veterans Affairs; VARA: Veterans Affairs Rheumatoid Arthritis registry.

Statistical considerations

Descriptive statistics were calculated with standard deviations (SD) or 95% confidence intervals (CI). Patients were categorised based on DAS28 stability during the baseline (pre-index) observation period. The relative risks (RR) with 95% CIs for baseline covariates were calculated for patients with a major change *versus* those with no major change. Poisson multivariable regression (23) with robust variance estimation (24) was used to estimate the ratio of incident proportions. The goal of the multivariable model was to de-

termine whether specific demographic characteristics, clinical characteristics, and/or treatment patterns influenced the decision to initiate a major change in therapy. Mean values with 95% CI for baseline covariates were compared between patients who were categorised as having mild RA *versus* moderate/severe RA among patients who were randomly selected for chart review.

Results

Patients

A total of 941 patients met eligibility criteria and were included in the analysis (Fig. 3); a subset of 403 patients was randomly selected for chart review. The population was predominantly male (88.9%) and the mean duration of RA was 13.5 years (Table I). Of the 941 patients included in the analysis, 369 (39.2%) patients had worsening DAS28, 118 (12.5%) had DAS28 improvements, and 454 (48.2%) patients had no change in DAS28 from the baseline observation period to index date. The sensitivity analysis using a 1.2 change in DAS28 as the cut point for change had no impact on these results.

Table I. Patient demographic and clinical characteristics.

	Full study cohort (n= 941)	Patients randomly selected for chart review (n=403)
Age, mean years (95% CI)	65.3 (64.6–66.0)	65.1 (64.0–66.1)
Sex, % male (95% CI)	88.9 (86.8–90.0)	86.8 (83.2–90.0)
Disease duration, mean years (95% CI)	13.5 (12.8–14.2)	14.1 (13.0–15.2)
RF positive, % (95% CI)	78.1 (75.3–80.7)	80.6 (76.4–84.4)
aCCP positive, % (95% CI)	67.5 (64.4–70.5)	63.8 (58.9–68.5)
Tender joints, mean count (95% CI)	5.7 (5.3–6.2)	4.8 (4.3–5.3)
Swollen joints, mean count (95% CI)	3.8 (3.6–4.1)	3.5 (3.2–4.0)
Patient global assessment, mean score, (95% CI)	49.0 (47.5–50.5)	48.8 (46.6–51.1)
Physician global assessment, mean score (95% CI)	31.5 (30.0–33.0)	30.7 (28.5–32.9)
Pain VAS, mean score (95% CI)	5.1 (5.0–5.3)	4.9 (4.6–5.2)
HAQ, mean score (95% CI)	1.06 (1.02–1.10)	0.97 (0.91–1.03)
ESR, mean mm/hr (95% CI)	31.7 (30.2–33.2)	32.7 (30.4–34.9)
CRP, mean mg/L (95% CI)	1.46 (1.32–1.60)	1.39 (1.17–1.60)
DAS28, mean (95% CI)		
Current value	4.4 (4.3–4.5)	4.4 (4.3–4.4)
AUC value	4.0 (4.3–4.4)	4.1 (4.0–4.2)

95% CI: 95% confidence interval; aCCP: anti-cyclic citrullinated peptide antibody; AUC: area under the curve; CRP: C-reactive protein; DAS28: Disease Activity Score based on 28 joints; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; RF: rheumatoid factor; VAS: visual analogue scale.

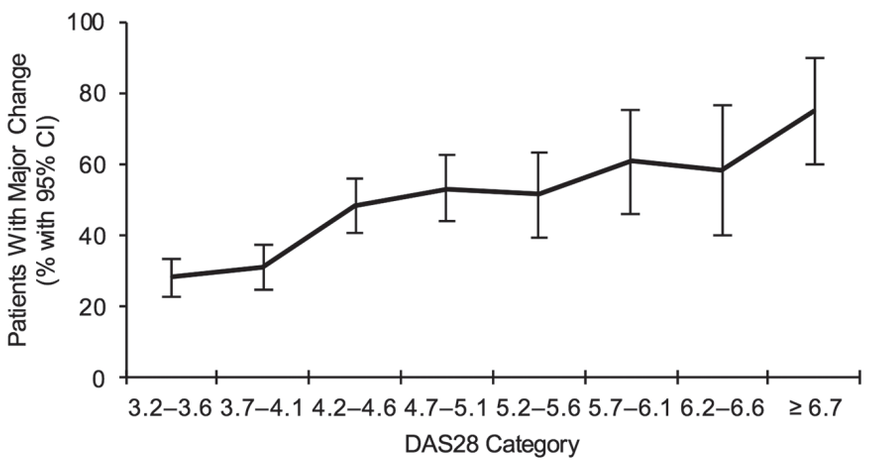

Fig. 4. Percentage of patients with major change in therapy based on DAS28 at index date. 95% CI: 95% confidence interval; DAS28: Disease Activity Score based on 28 joints.

Major changes in RA therapy

A major change in therapy was observed in 396 (42.1%) patients, including 50% of those patients with a worsening DAS28 during the baseline observation period. The rate of major change increased with increasing DAS28: among patients with DAS28 ≥4.2, more than 50% had a major change in therapy (Fig. 4). Multiple associations between administrative and clinical variables were noted in patients who had a major change in therapy and those who did not. For patients with worsening DAS28, these variables included baseline and index DAS28 values, tender and swollen joint counts, and pain measured on a VAS. For patients with no change in DAS28, associated variables included baseline and index DAS28 values, swollen joint counts, and patient global assessment and physician global assessment scores (Table II).

Predictors of major change in RA therapy

In the crude univariate analysis, patients with worsening DAS28 were 32% more likely to experience a major change compared to patients with stable DAS28 (RR: 1.32; 95% CI: 1.07–1.63), and those with DAS28 improvements were approximately 20% less likely to experience a major change compared to those with stable DAS28 (RR: 0.79; 95% CI: 0.55–1.14) (Table III). In multivariable models, patient demographic characteristics including age, sex, and Rheumatic Disease Comorbidity Index (RDCI) (25) were evaluated and were not found to contribute significantly to the model. Individual components of the DAS28 were not independently associated with a major therapeutic change (Table III). In the full multivariable model, current DAS28, oral steroid use in the past year, and use of non-biologic DMARDs (nbDMARDs) in the past year increased the likelihood of a major change; the use of nbDMARDs in the past 90 days decreased the likelihood of a major change (Table III).

Chart reviews

Similar to results for the overall cohort, 45% of patients included in the chart review experienced a major change in therapy. A CPJ that reported the patient had mild disease was the predominant reason for no major change in therapy

Table II. Clinical features of patients on index date with and without major changes in therapy.

Clinical variables from VARA registry, mean value (SD)	Patients with major change	Patients with no major change	RR (95% CI)	*p*-value
Patients with worsening DAS28 (n=369), n	**183**	**186**		
Baseline DAS28*	3.7 (1.0)	3.3 (0.9)	1.20 (1.05–1.37)	0.009
Index date DAS28	5.1 (1.1)	4.5 (1.0)	1.25 (1.11–1.42)	< 0.001
Swollen joint count	5.6 (5.4)	4.0 (4.8)	1.03 (1.00–1.04)	0.031
Tender joint count	8.8 (7.1)	6.5 (7.1)	1.02 (1.00–1.04)	0.027
HAQ score	1.1 (0.6)	1.0 (0.6)	1.08 (0.87–1.37)	0.051
Pain VAS score	5.7 (2.7)	4.8 (2.7)	1.07 (1.01–1.13)	0.028
Patient global assessment score	54.7 (24.2)	48.8 (23.5)	1.01 (1.00–1.01)	0.093
Physician global assessment score	26.2 (18.9)	24.3 (17.1)	1.00 (0.99–1.01)	0.474
ESR mm/hr	36.4 (28.8)	29.5 (23.1)	1.01 (1.00–1.01)	0.073
CRP mg/L	2.2 (3.3)	1.5 (2.0)	1.04 (1.00–1.08)	0.056
Patients with no change in DAS28 (n=454), n	**170**	**284**		
Baseline DAS28*	4.3 (1.0)	4.0 (0.8)	1.27 (1.09–1.47)	0.002
Index date DAS28	4.4 (1.0)	4.1 (0.8)	1.30 (1.12–1.51)	0.001
Swollen joint count	4.1 (4.2)	2.8 (3.4)	1.05 (1.01–1.08)	0.006
Tender joint count	5.2 (2.8)	4.8 (6.0)	1.01 (0.98–1.03)	0.530
HAQ score	1.0 (0.6)	1.0 (0.6)	1.03 (0.81–1.31)	0.743
Pain VAS score	5.3 (2.8)	4.8 (2.6)	1.04 (0.99–1.10)	0.145
Patient global assessment score	52.0 (20.8)	45.3 (22.3)	1.01 (1.00–1.02)	0.014
Physician global assessment score	34.6 (18.4)	27.6 (17.1)	1.01 (1.00–1.02)	0.002
ESR mm/hr	30.5 (22.2)	29.0 (21.0)	1.00 (1.00–1.01)	0.582
CRP mg/L	1.4 (1.7)	1.0 (1.3)	1.08 (1.00–1.17)	0.990
Patients with improved DAS28 (n=118), n	**35**	**83**		
Baseline DAS28*	5.2 (0.9)	4.9 (0.7)	1.27 (0.86–1.87)	0.219
Index date DAS28	4.1 (0.8)	3.9 (0.7)	1.23 (0.82–1.82)	0.318
Swollen joint count	4.4 (5.3)	2.5 (3.9)	1.06 (0.99–1.12)	0.070
Tender joint count	2.6 (3.3)	3.1 (5.0)	0.98 (0.91–1.07)	0.671
HAQ score	1.2 (0.5)	1.2 (0.6)	0.90 (0.50–1.61)	0.722
Pain VAS score	4.8 (2.5)	5.5 (2.8)	0.93 (0.83–1.05)	0.257
Patient global assessment score	42.9 (19.8)	46.2 (24.4)	1.00 (0.98–1.01)	0.560
Physician global assessment score	40.9 (24.4)	36.8 (20.1)	1.01 (0.99–1.02)	0.402
ESR mm/hr	37.2 (20.0)	34.8 (21.2)	1.00 (0.99–1.02)	0.630
CRP mg/L	1.7 (2.1)	1.3 (1.4)	1.08 (0.92–1.28)	0.344

*Baseline DAS28 refers to the DAS28 values collected during the 18-month pre-index observation period; however, all clinical covariates were collected at the index date.
95% CI: 95% confidence interval; CRP: C-reactive protein; DAS28: Disease Activity Score based on 28 joints; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; RR: relative risk; SD: standard deviation; VARA: Veterans Affairs Rheumatoid Arthritis registry; VAS: visual analogue scale.

Table III. Predicting a major change with clinical and administrative data.

Comparison, RR (95% CI)	Crude model	Demographic-adjusted model	Demographic + DAS28 and components-adjusted model	Full model*
Worse *vs*. stable DAS28	1.32 (1.07–1.63)	1.31 (1.06–1.61)	1.08 (0.80–1.45)	1.10 (0.82–1.48)
Improved *vs*. stable DAS28	0.79 (0.55–1.14)	0.80 (0.55–1.15)	0.87 (0.56–1.32)	0.85 (0.55–1.30)
Index DAS28			1.49 (1.13–1.97)	1.42 (1.07–1.89)
Oral steroid use in past year				1.42 (1.07–1.89)
nbDMARD use in past year				1.68 (1.08–2.63)
nbDMARD use in past 90 days				0.67 (0.49–0.92)

*Data represent only statistically significant variables from the series of models after inclusion of disease stability measures.
CI: confidence interval; DAS28: Disease Activity Score based on 28 joints; nbDMARD: non-biologic disease-modifying anti-rheumatic drug; RR: risk ratio.

(Table IV). Patients who were considered to have mild disease based on CPJ had lower tender and swollen joint counts and lower physician global assessment scores compared to patients who were considered to have moderate/severe disease. A lower overall DAS28 was observed in patients with mild disease by CPJ, but was still clinically significant at 3.9. A CPJ designating mild disease activity was not associated with other variables, including patient global assessment, ESR or CRP levels, or the HAQ (Table V).

Discussion

This study was developed to explore factors that drive major changes in RA therapy in VA patients with moderate or severe disease activity based on DAS28. The results demonstrated that a significant number (more than half) of

Table IV. Reasons for not instituting a major change.

Reason for continuing therapy without a change, n (%)	Patients randomly selected for chart review without a major change in therapy (n=220)
Clinician comprehensive judgement of RA as mild/remission	149 (68.0)
Provider recommended continuing current therapy with anticipation of improvement	13 (5.9)
Patient with low adherence to prescribed therapy	13 (5.9)
Patient disagreed with provider recommendation for major change	7 (3.0)
Symptoms explained by non-RA musculoskeletal disease activity	6 (3.0)
No change in therapy recommended because of pending procedure	2 (0.9)
Patient requested additional time to consider therapy change before accepting change	2 (0.9)
Provider waiting for imaging or laboratory results to decide on therapy changes	2 (0.9)
Active hepatitis C	1 (0.5)
Change of medication by non-VA provider	1 (0.5)
Reason could not be determined by chart review	24 (10.9)

RA: rheumatoid arthritis; VA: Veterans Affairs.

VA patients with RA did not receive a major change in therapy despite moderate or severe disease activity, including those patients with worsening disease as indicated by DAS28. We looked at individual clinical and administrative variables as well as multivariable regression models to try to understand what influenced major therapeutic change decisions. We found that while several individual variables were associated with a major change in therapy, any attempt to place this data set into a multivariable regression model did not result in clinically useful models that provided a deeper understanding of how clinicians are making decisions to escalate therapy. The most informative variable in the model was the index DAS28 score, with the likelihood of a major therapeutic change increasing by approximately 40% with each additional DAS28 unit. Further investigation involving chart review of a randomised sample of these patients suggested that many clinicians are not employing the DAS28 as part of their decision-making process and are relying on CPJ despite a documented DAS28 >3.2. This assessment did not appear to be associated with any particular clinical or administrative variable as documented in the patient charts; however, CPJ determinations did appear to correlate with disease activity measures and clinical variables such as swollen and tender joint counts and the physician global assessment.

This study is consistent with prior work that has demonstrated challenges with implementing RA treatment guidelines (5). Baseline data from the TRACTION trial showed that 64% of RA patient visits did not have any documentation to show that providers were employing a treat-to-target strategy (26). While some data were collected at some visits, it was evident that in these real-world practices a treat-to-target strategy was rarely employed before a focused educational intervention. With the TRACTION intervention, the rate improved to 57% (27); however, this result would imply that almost half of patients still did not have full guideline implementation. The analysis by Harrold *et al*. using the Consortium of Rheumatology Researchers of North America (Corrona) registry showed no change in treatment with the publication of the 2008 ACR treatment guidelines (28). In this analysis, approximately 50–60% of patients with moderate or severe disease activity were not receiving an escalation of therapy as recommended by the guidelines. This percentage of patients without a change in therapy was similar to that seen in our study.

Table V. Comparison of CPJ chart review with administrative and clinical data for patients with no major change.

Baseline characteristics, mean value or % (95% CI)	Patients randomly selected for chart review without a major change in therapy (n=220)	CPJ from chart review	
		Categorised as mild RA based on CPJ (n=149)	Categorised as moderate RA based on CPJ (n=71)
Age, years	66.6 (65.3–67.9)	67.1 (65.6–68.7)	65.4 (63.1–67.8)
Male, %	88.2 (83.9–92.5)	89.3 (84.2–94.3)	85.9 (77.6–94.2)
Disease duration, years	14.8 (13.2–16.4)	14.7 (12.8–16.5)	15.2 (12.0–18.4)
Tender joint count	4.0 (3.2–4.7)	3.3 (2.5–4.1)	5.4 (4.0–6.7)
Swollen joint count	2.6 (2.2–3.1)	1.8 (1.4–2.2)	4.4 (3.3–5.4)
Patient global assessment score	46.6 (43.4–49.8)	45.6 (41.7–49.5)	48.7 (42.8–54.7)
Physician global assessment score	28.4 (25.6–31.3)	24.6 (21.4–27.8)	36.5 (30.9–42.0)
Pain VAS score	5.0 (4.6–5.3)	4.7 (4.3–5.2)	5.4 (4.8–6.1)
HAQ score	1.0 (1.0–1.1)	1.0 (0.9–1.1)	1.1 (1.0–1.2)
ESR, mm/hr	31.0 (28.2–33.7)	31.0 (27.6–34.4)	30.6 (26.0–35.3)
CRP, mg/L	1.1 (1.0–1.4)	1.1 (0.8–1.3)	1.3 (0.9–1.7)
DAS28			
Current value	4.1 (4.0–4.2)	3.9 (3.8–4.0)	4.5 (4.2–4.7)
AUC value	3.9 (3.8–4.0)	3.8 (3.6–3.9)	4.2 (3.9–4.4)

95% CI: 95% confidence interval; AUC: area under the curve; CPJ: comprehensive provider judgement; CRP: C-reactive protein; DAS28: Disease Activity Score based on 28 joints; ESR: erythrocyte sedimentation rate, HAQ: Health Assessment Questionnaire; RA: rheumatoid arthritis; VAS: visual analogue scale.

The decision to change RA therapy is complex. A study by Shaw *et al*. showed that despite evidence of persistent moderate to severe disease activity, 40% of rheumatologists delayed DMARD adjustment for at least 3 months (29). They showed that approximately one-third (32.3%) of these patients did not receive DMARD adjustment for greater than 6 months. This delay in treatment change was associated with bDMARD use, lower disease activity at baseline, longer disease duration, and elderly status. The RADIUS study showed that the decision to change therapy was based more on physician-specific assessments (*e.g*. joint swelling and physician global assessment) rather than on patient-reported measures (*e.g*. joint tenderness and patient global assessment) (30). Van Hulst *et al*. reported similar results, with joint swelling and physician global assessment having a much greater impact on decisions to change therapy (31). Aletaha *et al*. also reported similar findings (32). In contrast, patients were more likely to consider changes in therapy on the basis of physical function and mobility, and joint pain (31). Curtis *et al*. (33) and Kalkan *et al*. (34) reported that a physician preference or practice pattern is an important independent factor in the decision to initiate biologic DMARDS, independent of disease activity. In general, our data support this prior work showing that providers are more likely to change therapy on the basis of joint swelling and provider assessment of disease activity, rather than the use of a formal disease activity measure. The reliance of providers on physician-based rather than patient-based disease outcome measures in treatment decisions may not be practical in clinical practice (35).

A strength of our study was the rheumatologist-confirmed diagnosis of RA. Additionally, the VA system has a wide geographic distribution of patients across the US, can collect baseline and post-treatment disease severity information using the DAS28, and has standardised medical records and administrative databases across all participating sites. Veterans enrolled in VA care have access to DMARD therapy as needed. Additionally, the VA does not have specific utilisation management criteria, formulary guidelines, or regulations that would require selection of a specific DMARD or prevent switching if deemed appropriate by the treating physician. Limitations of the study included a predominance of men with RA of long-term duration reflecting the US Veteran population, which may limit generalisability of study findings. Also, it is worth mentioning that while the treat-to-target strategy is well known and validated, it is considerably difficult to define and report an individual patient target. This could further limit the generalisability of this study. There is a potential for bias toward patients with more active disease given the requirement for at least 2 DAS28 scores recorded during the 18-month pre-index period based on the assumption that patients with more active disease may attend more clinical visits than patients with mild disease; however, the inclusion of multiple visits prior to the index date allowed for evaluation of disease trajectory. The potential exists for patients to have received DMARD therapy outside the VA, which would not be captured by this analysis; however, in our experience, US Veterans rarely seek DMARD therapy from other sources while receiving their care through the VA. The federally negotiated cost for DMARD therapy in the VA system may be less than costs in the community, which may limit comparisons with other healthcare systems. Our study did not identify the reasons for switching or interrupting DMARD therapy, including for safety concerns; such factors could confound the observed results. However, switching for safety concerns did not appear to be common reason for change, occurring in only 5 of the 403 patients (1.2%) evaluated by chart review.

In summary, our work demonstrates that providers do not consistently or regularly use disease activity measures in real-world clinical practice in the decision to escalate therapy for patients with moderate or severe RA. While many factors may influence the decision to change therapy, as noted in our work and the literature, physician assessment is a major factor in these decisions. These observations are in the context of established evidence-based observations and guidelines that recommend a treat-to-target strategy. The observation that physicians in real-world practice do not regularly employ a treat-to-target strategy in the face of this evidence suggests that a system needs to be developed and tested to see if a real-world treat-to-target strategy can be implemented and impact outcomes in RA care. This challenge represents a tremendous opportunity for the development of practical and applicable disease activity monitors and systems for the real-time use of these data in improving the care of RA patients.

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