Uptake and Clinical Utility of Multibiomarker Disease Activity Testing in the United States

Jeffrey R. Curtis, Fenglong Xie, Shuo Yang, Maria I. Danila, Justin K. Owensby, and Lang Chen

ABSTRACT. ***Objective.*** The clinical utility of the multibiomarker disease activity (MBDA) test for rheumatoid arthritis (RA) management in routine care in the United States has not been thoroughly studied.

Methods. Using 2011–2015 Medicare data, we linked each patient with RA to their MBDA test result. Initiation of a biologic or Janus kinase (JAK) inhibitor in the 6 months following MBDA testing was described. Multivariable adjustment evaluated the likelihood of adding or switching biologic/JAK inhibitor, controlling for potential confounders. For patients with high MBDA scores who added a new RA therapy and were subsequently retested, lack of improvement in the MBDA score was evaluated as a predictor of future RA medication failure, defined by the necessity to change RA medications again.

Results. Among 60,596 RA patients with MBDA testing, the proportion adding or switching biologics/JAK inhibitor among those not already taking a biologic/JAK inhibitor was 9.0% (low MBDA), 11.8% (moderate MBDA), and 19.7% (high MBDA, $p < 0.0001$). Similarly, among those already taking biologics/JAK inhibitor, the proportions were 5.2%, 8.3%, and 13.5% ($p < 0.0001$). After multivariable adjustment, referent to those with low disease MBDA scores, the likelihood of switching was 1.51-fold greater (95% CI 1.35–1.69) for patients with moderate MBDA scores, and 2.62 (2.26–3.05) for patients with high MBDA scores. Among those with high MBDA scores who subsequently added a biologic/JAK inhibitor and were retested, lack of improvement in the MBDA score category was associated with likelihood of future RA treatment failure (OR 1.61, 95% CI 1.27–2.03).

Conclusion. The MBDA score was associated with both biologic and JAK inhibitor medication addition/switching and subsequent treatment outcomes. (First Release November 15 2018; J Rheumatol 2019;46:237–44; doi:10.3899/jrheum.180071)

Key Indexing Terms:
RHEUMATOID ARTHRITIS BIOMARKER BIOLOGICS
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Management of patients with rheumatoid arthritis (RA) regarding changing treatments is routinely informed by clinical assessment through history-taking and physical examination. Composite disease activity indices, such as the Clinical Disease Activity Index (CDAI) or the Disease Activity Score in 28 joints (DAS28), are quantitative measurements that include tender and swollen joint counts and global assessments of disease activity from patients and/or clinicians[1]. Other composite disease activity indices, such as Routine Assessment of Patient Index Data 3, Patient Activity Scale (PAS), or PAS-II include only patient-reported data[1]. While the American College of Rheumatology recommends using composite measures to quantify RA disease activity[2], and their use is commonplace in RA clinical trials, these measures nevertheless have their limitations, owing to the interobserver variability in performing joint counts[3] and subjectivity inherent in patient's and physician's global assessments[4]. In addition, disease activity for some patients with RA may be difficult to assess because of concomitant comorbidities [e.g., fibromyalgia (FM), obesity][5,6] or because of the substantial deformity resultant from longstanding RA.

Laboratory-based assessment including C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR) may complement clinical assessments, but it likewise has limitations. For example, patients with clinically active disease

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based on clinical examination may have CRP and ESR values within the normal reference range[7]. Thus, other laboratory-based or new biomarkers (e.g., results of joint ultrasound) hold promise for informing RA management. However, the strategies by which these approaches should inform disease management in patients with RA are evolving. One such RA biomarker is the multibiomarker disease activity (MBDA) test, a 12-analyte test commercially available in the United States since 2012. The MBDA test, a prospectively validated measure of RA disease activity[8,9], has been shown to predict radiographic outcomes[10,11]. Unlike CRP or ESR, the MBDA test provides cutpoints that classify disease activity in RA as low (< 30), moderate (30–44), or high (> 44). However, the clinical utility of MBDA testing for patients with RA has not been studied in routine practice in the US. Thus, the goals of our study were to (1) describe the uptake of the MBDA testing by US rheumatologists and the pattern of its use in patients with RA enrolled in Medicare (medical insurance for the elderly), (2) evaluate the likelihood of RA treatment switching conditional on the MBDA score, and (3) examine improvement in the MBDA score as a predictor of future treatment response among patients who underwent repeat MBDA testing.

MATERIALS AND METHODS

Cohort selection. Patients with RA in the US Medicare program were identified using longitudinal 2011–2015 claims data obtained from the Center for Medicare and Medicaid Services (CMS). Patients with rheumatologist-diagnosed RA (International Classification of Diseases, 9th revision codes 714.0, 714.2, and 714.81) were linked to their MBDA test results (billed to Medicare as Healthcare Common Procedure Coding System codes 84999, 84179, and 84190) using methods previously described[12]. Briefly, the MBDA test results available from the centralized laboratory were linked to individual patients enrolled in Medicare based on patient's (1) full birth date and sex, (2) National Provider Identifier number of the ordering healthcare provider, and (3) MBDA test date. Although a minimum of a single RA diagnosis from a rheumatologist was required, the MBDA is approved for use only in patients with RA; thus, linkage to the laboratory test was expected to confer greater specificity to the identification of RA. The study was governed by a data use agreement from the CMS, and the University of Alabama at Birmingham Institutional Review Board for Human Use approved the analysis (IRB-121029003). Patient-level consent for data linkage was not required given that the data were already available and had been collected for purposes other than the present research study.

Uptake and patterns of use of the MBDA test. The cumulative number of patients with RA ever tested, and the cumulative number of rheumatologists (identified using Medicare specialty codes) who ordered the test were plotted over time to describe the uptake of the MBDA test in the Medicare RA population. An analysis was performed using only CMS data from 2015 to describe the proportion of all patients with RA in rheumatologists' care who underwent MBDA testing at least once that year. Rheumatologists were classified into 5 groups: those who did not order the MBDA test (group 0), and those who ordered the test, by quartiles of usage compared to their peers (groups 1, lowest usage through 4, highest usage). This analysis was restricted to clinicians with at least 10 patients with RA in their practice. The proportion of patients who added or switched biologics or Janus kinase (JAK) inhibitors then was quantified within each rheumatologist's practice that year to test the hypothesis that physicians with the highest usage of MBDA testing in that year were more likely to change RA treatments for their patients. This process was repeated each calendar year (2011–2014); MBDA use was thus updated for each physician annually. For physicians who used the MBDA and with at least 10 patients with RA in at least 2 consecutive years, we then identified the rheumatologists who increased their use of the MBDA substantially, which we defined as meeting 2 criteria: (1) a doubling in the proportion of patients tested in their practice compared to the prior year, and (2) testing of at least 15% of a rheumatologist's patients with RA in that calendar year. We then estimated the increase in biologic/JAK inhibitor add/switch behavior in each physician's practice in the year before versus after the year of MBDA increased use, compared to physicians who did not meet these criteria in that year.

Association between RA treatment switching and MBDA score. Initiation of RA biologics or tofacitinib was examined in relation to the MBDA score. New RA treatments were identified using a window of 4 and 183 days from the time of each MBDA testing. We assessed treatment switching in this wide time window because MBDA results become available about 3 days after testing but may not be used to motivate a treatment change decision until the next visit with the rheumatologist, and to allow for the necessary time to obtain prior authorization approval or conduct other procedures (e.g., tuberculosis testing) that may be required to initiate a new RA medication. Results were stratified by whether patients with RA were currently receiving a biologic or other targeted therapy (e.g., JAK inhibitor) in the 6 months prior to MBDA testing.

Change in MBDA as a predictor of future treatment response to an RA medication. MBDA testing can be used to monitor response to a new RA treatment. Patients who have higher MBDA levels (e.g., > 44) have the most inflammation and are at the greatest risk of radiographic progression[13]. Thus, these individuals may have poorer RA-related outcomes. Because improvements in CDAI or the DAS28 were not available, the primary outcome of our study was RA treatment failure, defined as the necessity to switch to a new RA biologic or JAK inhibitor. This approach has been used previously in RA studies as part of a claims-based effectiveness algorithm that was validated against change in the DAS28 over time[14].

We conducted an additional analysis among patients whose initial MBDA score was > 44, added a biologic or JAK inhibitor between 4 and 183 days later, and then were re-tested with the MBDA about 1–6 months later. We hypothesized that patients who had improvement in their MBDA score category (initially high, then improved to moderate/low) or who had the greatest numerical improvement (e.g., exceeding the minimal clinically important difference for the MBDA of an 8-unit change[14a]) after this treatment change would have the lowest risk of RA treatment failure.

Statistical analysis. Descriptive statistics were used to evaluate the number of MBDA tests ordered, comparing patients by MBDA score category at the time of their initial testing. Multivariable-adjusted, alternating logistic regression[15] was used to examine the likelihood of RA treatment switch, conditional on the MBDA score and controlling for potential confounders including demographics (age, sex, race), disability as the reason for Medicare entitlement, use of a wheelchair or other assistive devices, low income status reflected by state buy-in for Medicare premiums, comorbidities (FM, chronic pulmonary disease, obesity, diabetes), Charlson comorbidity index, and measures of healthcare use (number of outpatient visits, recent hospitalizations). Multivariable-adjusted, alternating logistic regression also controlled for the clustering of RA patients within individual rheumatologists' practices, because RA treatment switching is motivated not only by patient factors, but also by physician-related behaviors and practice styles[16]. All analyses were conducted in SAS 9.4.

RESULTS

Between 2011 and 2015, more than 75,000 RA patients with fee-for-service Medicare coverage had at least 1 MBDA test, and more than 125,000 MBDA tests were performed (Figure 1). As shown in Table 1, patients categorized as having low disease activity by MBDA score were somewhat younger, more likely to be male and disabled, more likely to be taking

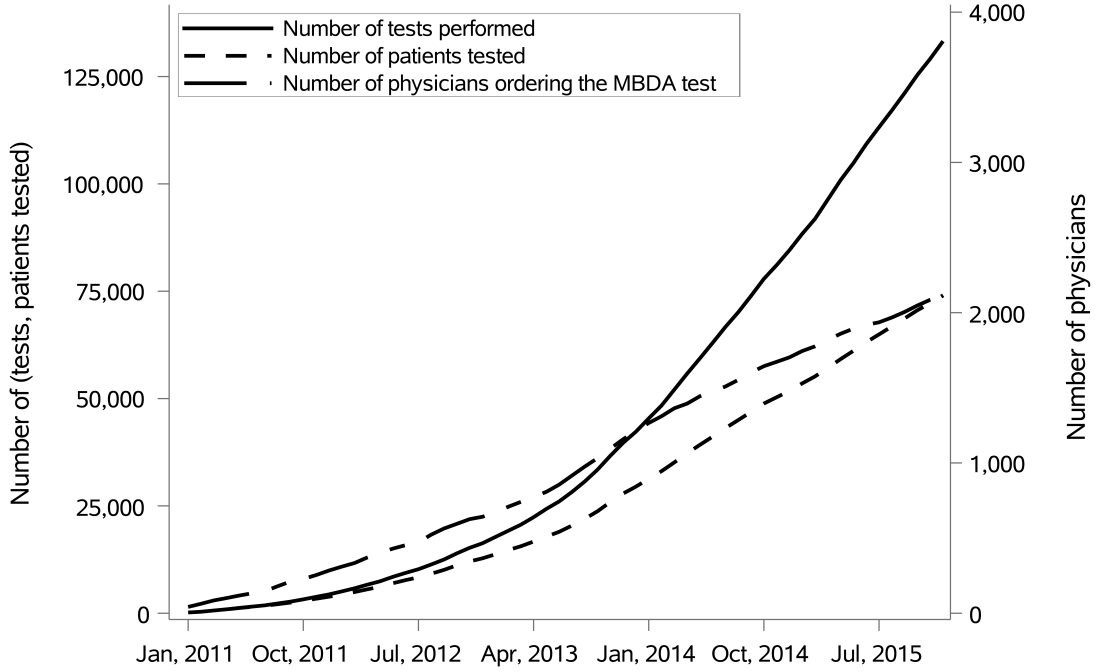

Figure 1. Use of MBDA testing and uptake by US rheumatologists among Medicare enrollees with RA. MBDA: multibiomarker disease activity; RA: rheumatoid arthritis.

Table 1. Descriptive characteristics of patients with RA tested with the MBDA, stratified by level of disease activity (N = 60,596).

	MBDA Score Category		
	Low, < 30	Moderate, 30–44	High, > 44
Demographics			
Age, yrs, mean ± SD	66.4 ± 11.3	69.4 ± 10.2	69.7 ± 10.5
Female, %	74.0	79.1	80.5
Low income, %	30.9	26.5	27.8
Disability (as reason for Medicare entitlement), %	40.4	35.5	38.8
Comorbidities, %			
Fibromyalgia	18.4	17.8	16.5
Diabetes	15.6	19.6	24.8
Chronic pulmonary disease	14.2	17.8	23.8
Obesity (as a diagnosis)	3.6	5.2	6.8
Charlson comorbidity index			
0	7.6	6.1	4.7
1	51.1	44.5	37.7
2	22.6	23.6	24.6
3+	18.7	25.8	33.0
Medication, %			
TNFi biologic	37.4	30.1	23.4
Non-TNFi biologic or JAK inhibitor	13.2	16.7	21.5
Methotrexate	49.1	51.0	48.2
HCQ, LEF, SSZ	36.5	36.4	36.0
Oral glucocorticoids	31.3	37.9	50.7
Health services use			
No. ambulatory visits (%)	8.0 (5.5)	8.5 (5.7)	9.4 (6.3)
Any hospitalization, %	6.2	8.5	14.1

All differences are significant at $p < 0.0001$ except for the comparison of HCQ/LEF/SSZ, which was not significant. RA: rheumatoid arthritis; MBDA: multibiomarker disease activity; TNFi: tumor necrosis factor inhibitor; JAK: Janus kinase; HCQ: hydroxychloroquine; SSZ: sulfasalazine; LEF: leflunomide.

a tumor necrosis factor (TNF) inhibitor, and less likely to be taking systemic glucocorticoids. They also had a higher prevalence of FM and a lower prevalence of other comorbidities.

Using data specifically for 2015, we observed wide variability in patterns of MBDA testing among US rheumatologists. A total of 1426 rheumatologists (25% of the total of 5639 rheumatologists identified in the Medicare data who cared for at least 1 patient with RA) ordered the MBDA test for at least 1 patient with RA. There was a weak correlation ($r = 0.14$, $p < 0.0001$) between the number of patients with RA seen by the physician and the proportion who underwent MBDA testing. Among clinicians who tested at least 1 RA patient with the MBDA and who had at least 10 patients with RA in 2015, the proportion of patients tested at least once is shown in Figure 2. At the 50th percentile, 11% of the rheumatologists' patients with RA were tested, and at the 75th percentile, 30% of patients with RA were tested.

Restricting the sample of rheumatologists to those with at least 10 patients with RA yielded about 3708 rheumatologists (Appendix 1). Grouping them each calendar year based on their frequency of MBDA test use in that year (rank 0, non-user; to rank 4, highest user), we plotted the proportion of patients with RA who added or switched biologics or JAK inhibitors. In the practices of rheumatologists who did not use the MBDA at all (rank 0, n = 2447, 66% of all rheumatologists in 2015) or minimally (rank 1), about 9% of patients with RA added or switched to a biologic or JAK inhibitor each year, compared to about 14% for patients of rheumatologists in the highest category of use. There was not a significant interaction between category of MBDA use and the likelihood of switching treatment ($p = 0.55$). However, comparing rheumatologists' rate of treatment switching in the calendar year before versus after they substantially increased their use of the MBDA test, there was a small (about 1%) but significant ($p = 0.02$) increase in the likelihood of adding or switching biologics or JAK inhibitor therapy in the year following a rheumatologists' greater use of the MBDA test compared to the prior year, versus physicians who did not meet this definition, among whom there was no change.

The pattern of RA treatment switching after MBDA testing is shown in Figure 3. A total of 60,596 patients with RA were analyzed, of whom 7970 (13.2%) added (n = 5196) or switched (n = 2774) to a biologic or JAK inhibitor. Of

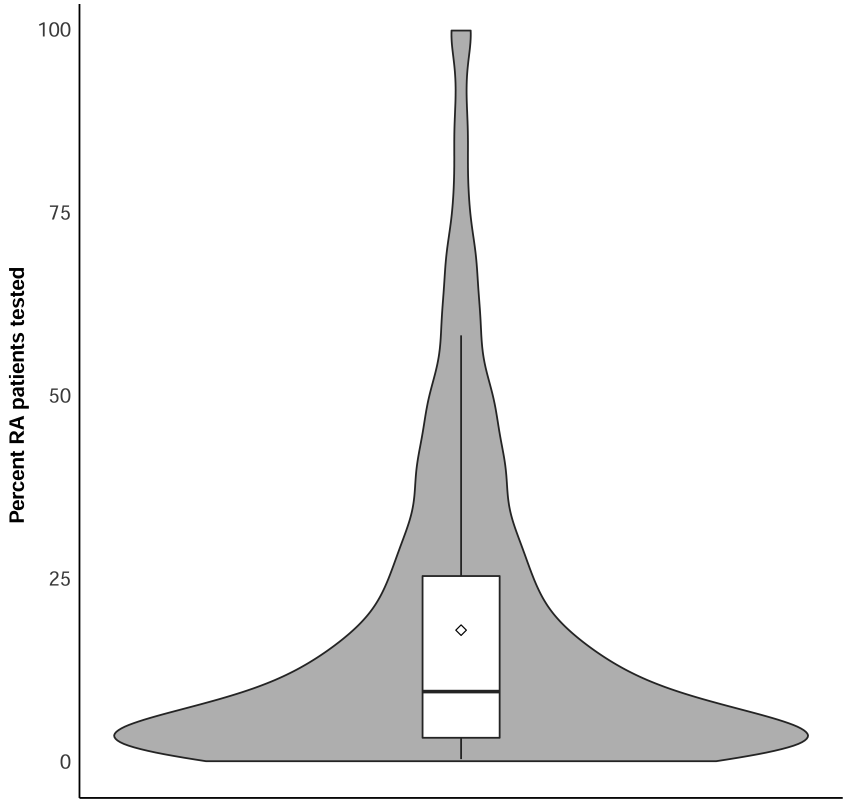

Figure 2. Distribution of the proportion of patients with RA tested at least once with the MBDA within the practice of each rheumatologist who had at least 10 patients with RA in 2015 (n = 1426). The solid black horizontal line refers to the proportion of patients tested in the median physician's practice, and the diamond represents the mean proportion tested. MBDA: multibiomarker disease activity; RA: rheumatoid arthritis.

these, 61% were subsequently re-tested (ever) with the MBDA. There was a strong association between the MBDA score and the likelihood of initiating a biologic or JAK inhibitor. Among patients not receiving biologics/JAK inhibitors at baseline (Figure 3, left panel), the likelihood of initiating a biologic or JAK inhibitor was highest (19.7%) for those with high MBDA scores (about half of those tested), compared to the likelihood of initiating a biologic/JAK inhibitor among patients with a moderate MBDA score (11.8%) or a low MBDA score (9.0%). Trends were similar and significant among those already taking one of these medications at the time of MBDA testing (Figure 3, right panel). For patients with high MBDA scores, the median [interquartile range (IQR)] time to switch to a new RA therapy was 36 (IQR 22–70) days, and 60 (IQR 28–110) days to add a therapy. Results were minimally different in the time to add or switch for patients with low or moderate MBDA scores.

Among the 60,596 analyzed, and after adjusting for potential confounders, the odds of adding or switching to a biologic or JAK inhibitor were highest among those with high MBDA scores compared to patients with low MBDA scores (OR 2.62, 95% CI 2.26–3.05; Table 2). Patients with MBDA scores in the moderate range (30–44) were also more likely to add or switch biologics/JAK inhibitors (OR 1.51, 95% 1.35–1.69). Older patients, men, and African Americans were less likely to add or switch biologics/JAK inhibitors. Higher comorbidity scores and recent hospitalization were associated with an increased likelihood to change RA medications. Current treatment with a TNF inhibitor or non-TNF inhibitor biologic was associated with a lower likelihood of treatment change, whereas use of methotrexate and oral glucocorticoids was associated with a greater likelihood of treatment change.

A total of 1517 patients with RA who had high MBDA scores at baseline subsequently added a new RA medication and were included in the analysis examining lack of improvement in MBDA score upon re-testing as a predictor for failure of the recently initiated RA treatment. Over a median (IQR) followup time of 14.0 months (8.0, 22.0), 28.4% of patients whose MBDA scores remained high (> 44) upon re-testing subsequently changed RA treatments, compared to 20.3% of patients whose MBDA scores had decreased to moderate or low disease activity (p = 0.0007). After adjusting for confounding factors, the likelihood of subsequent RA treatment failure for patients who retained a high MBDA score was 1.61-fold greater (95% CI 1.27–2.03) compared to patients whose MBDA score category improved to low or moderate (≤ 44). Analyzing the change in MBDA as a continuous variable, and compared to patients with the most improvement in their MBDA score (> 16-unit improvement, referent group), those with some improvement (> 8- and ≤ 16-unit improvement) were 1.50-times (95% CI 1.03–2.19) more likely to change treatments. Those with minimal or no improvement (< 8-unit improvement) were 2.47-times (95% CI 1.79–3.40) more likely to add or switch to a new RA biologic or JAK inhibitor (Table 3). Older age was associated with patients being less likely to add/switch

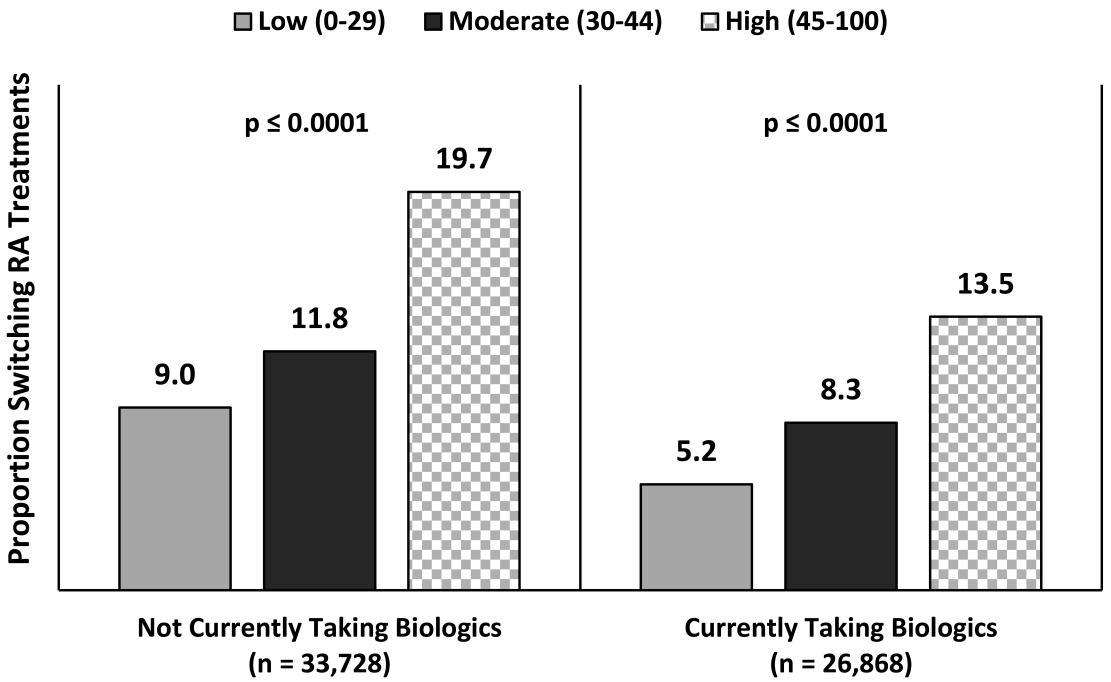

Figure 3. Patterns of adding or switching biologics or JAK inhibitors*, according to MBDA score (N = 60,596). *Addition or switching between days 4 and 183 after the MBDA test. JAK: Janus kinase; MBDA: multibiomarker disease activity; RA: rheumatoid arthritis.

Table 2. Factors associated with RA biologic or JAK inhibitor treatment switch (N = 60,596 patients analyzed).

	Adjusted* OR (95% CI)
MBDA score	
Low (referent)	1.0
Moderate, 30–44	1.51 (1.35–1.69)
High, > 44	2.62 (2.26–3.05)
Age (5-yr increments)	0.91 (0.89–0.92)
Male sex (female referent)	0.85 (0.79–0.91)
Low income**	1.16 (1.07–1.25)
Race (white referent)	
Black	0.76 (0.69–0.84)
Other	0.93 (0.86–1.01)
Fibromyalgia	1.13 (1.05–1.21)
Charlson comorbidity index	
0	1.0 (referent)
1	1.24 (1.10–1.40)
2	1.25 (1.10–1.42)
3+	1.38 (1.12–1.47)
Recent hospitalization	1.18 (1.10–1.28)
RA medications	
TNFi biologic	0.60 (0.52–0.68)
Non-TNFi biologic	0.57 (0.47–0.68)
MTX	1.09 (1.02–1.16)
HCQ/SSZ/LEF	1.01 (0.95–1.08)
Glucocorticoid	1.40 (1.33–1.48)

* Also adjusted for diabetes, chronic pulmonary disease, obesity, and being disabled, none of which were significant, and for physician clustering (OR 1.19, 95% CI 1.06–1.34). ** Reflected by state buy-in for Medicare premiums. RA: rheumatoid arthritis; JAK: Janus kinase; MBDA: multibiomarker disease activity; TNFi: tumor necrosis factor inhibitor; MTX: methotrexate; HCQ: hydroxychloroquine; SSZ: sulfasalazine; LEF: leflunomide.

to a new biologic, and already taking a biologic was associated with a greater likelihood.

DISCUSSION

We found that in Medicare enrollees with RA, use of the MBDA test increased rapidly from the time of its commercial introduction through 2015. We observed that treatment switching to biologics or JAK inhibitors was more likely for patients who had high MBDA scores, as expected. For patients who were tested, found to have high MBDA scores, initiated a biologic or JAK inhibitor, and then were re-tested for monitoring purposes, lack of improvement in MBDA score or MBDA score category was a significant predictor of subsequent RA treatment failure. RA treatment failure led to the need to switch to a new targeted RA therapy, an outcome that has been used previously in RA studies and validated against longitudinal change in RA disease activity[14].

Our results are consistent with prior analyses evaluating the MBDA score as a catalyst for changing RA treatments[17]. In 1 analysis, 18% of patients made a change in their biologic treatment after receiving information about the MBDA score. The MBDA test has been found to be

Table 3. Factors associated with subsequent RA treatment failure* for patients with RA who added or switched treatments, conditional on MBDA score improvement (n = 1517).

	Adjusted** HR (95% CI)
MBDA score change at time of re-assessment	
Most improvement (> 16 units)	1.0 (referent)
Some improvement (> 8–16 units)	1.50 (1.03–2.19)
Minimal to no improvement (< 8 units)	2.47 (1.79–3.40)
Age (5-yr increments)	0.88 (0.83–0.93)
Female sex (male referent)	1.27 (0.94–1.70)
Low income***	0.95 (0.74–1.24)
Race (white referent)	
Black	0.93 (0.63–1.38)
Other	1.26 (0.98–1.63)
Fibromyalgia	1.33 (1.05–1.70)
RA medications	
TNFi biologic	1.49 (1.08–2.04)
Non-TNFi biologic	1.50 (0.87–2.56)
MTX	0.87 (0.70–1.09)
HCQ/SSZ/LEF	1.03 (0.83–1.28)
Glucocorticoid	1.22 (0.99–1.51)

* Leading to subsequently adding or switching to a new biologic or Janus kinase inhibitor. ** Adjusted for diabetes, chronic pulmonary disease, obesity, low income, disability, inpatient hospitalization, no. ambulatory visits, and Charlson comorbidity index, none of which were significant. *** Reflected by state buy-in for Medicare premiums. HCQ: hydroxychloroquine; LEF: leflunomide; MBDA: multibiomarker disease activity; MTX: methotrexate; RA: rheumatoid arthritis; SSZ: sulfasalazine; TNFi: tumor necrosis factor inhibitor.

cost-effective in a comprehensive RA management program in which clinical decisions were informed by MBDA testing[18]. In our analysis, we found that patients with RA who had higher MBDA scores were more likely to add (or switch) biologics or JAK inhibitors compared to patients who were tested and had lower MBDA scores. While we cannot provide certainty that the main reason that clinicians switched therapies was the MBDA test result, we note that the median time to add or switch to a new RA treatment was 1–2 months after testing, lending plausibility to the MBDA test being influential in this decision. Moreover, we were able to compare the overall likelihood of treatment switching within the practices of physicians not ordering the test, or who ordered it infrequently. We found (Appendix 1) that rheumatologists who used the test most frequently had a small but significant increase over time in the likelihood of switching their patients' RA medications. While this ecologic association does not imply causality, it nevertheless lends evidence to physicians being more confident in switching therapies based on the results of and access to MBDA testing.

Strengths of our study include a large-scale evaluation of uptake, practice variability, and the switching of medication associated with use of MBDA testing. In evaluating RA treatment switching, we also were able to control for factors associated with RA treatment failure (e.g., comorbidities).

Despite these strengths, our findings need to be interpreted in light of several limitations. Because of the observational study design, clinicians were not randomized regarding access to the MBDA test, and those clinicians who ordered the test may have different practice styles from those who did not order the test. We lacked information regarding why the test was ordered or associated clinical disease activity measures (e.g., DAS28, CDAI), making it difficult to assess the incremental value of the information provided by testing above and beyond clinical measurement, or to know whether the treatment changes were appropriate (based on longterm outcome data). Additionally, although we evaluated MBDA testing regarding adding or switching to a new RA medication, it is likely that the test was ordered for reasons that were not studied (e.g., to confirm that a patient's RA was quiescent with minimal subclinical inflammation). The diversity of clinical scenarios that may motivate testing may in part explain the overall relatively low likelihood of treatment switching following MBDA testing and also likely affected the distribution of MBDA disease activity categories (low/moderate/high) observed in this cohort. We also note that the minimally important difference of the MBDA has been made available to the rheumatology community only recently, and so clinicians were likely unaware of what change in the MBDA score might be considered actionable. Additionally, treatment switching was confined to examination of biologic and JAK inhibitor addition or switching. We did not study dose changes of medications the patients were already taking, because of imprecision in the data source to quantify such dose changes. For both these reasons, our estimates regarding the likelihood of medication changes made regarding MBDA testing likely represent a conservative underestimate.

Clinical inertia continues to exist within RA care, and several studies have repeatedly shown failure to advance treatment for patients with active disease[19,20,21,22]. Even for patients who might seem to be in low disease activity based on clinical assessment, a high MBDA score has been shown to predict increased risk for radiographic progression[10,13]. As a necessary first step to evaluating patients with RA and facilitating a treat-to-target management style, quantitative clinical disease activity assessment is key, yet remains underused in the US[23]. The MBDA test can be used to complement clinical assessment and can categorize patients as being in low, moderate, or high disease activity; something that ESR, CRP, or advanced joint imaging does not allow. Ongoing clinical trials (NCT02832297) and forthcoming data (e.g., MBDA to refine the patient-specific predicted risk of future radiographic damage) will be useful to further define the optimal role for the MBDA test in clinical practice to optimize longer-term outcomes. At present, physician judgment remains key in interpreting the test result for an individual patient and acting upon it accordingly to provide personalized care.

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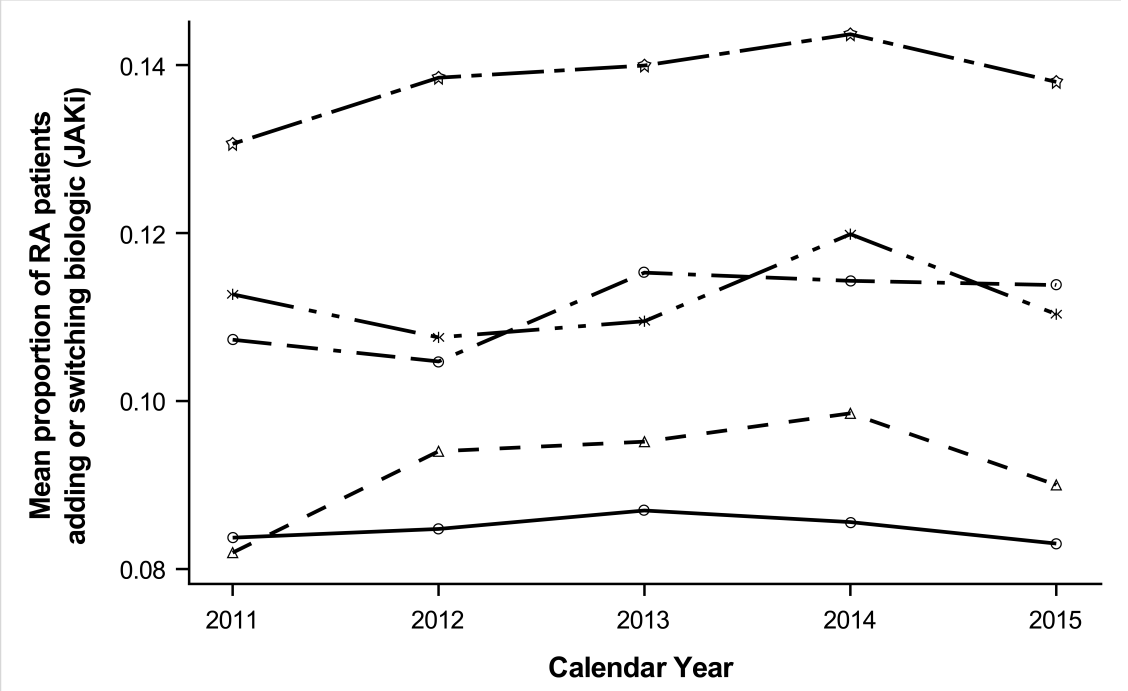
APPENDIX 1. Annualized rate of biologic or JAKi addition/switching, by MBDA test score use (n = 3953 eligible rheumatologists). Rank 0 refers to physicians who did not order the MBDA test for an RA patient with fee-for-service Medicare in that year. Ranks 1–4 correspond to the first (lowest) to the fourth (highest) quartiles of MBDA test use in the practices of clinicians who ordered the test at least once in that year. Analysis was restricted to rheumatologists who cared for at least 10 patients with RA in each pairwise year comparison. The p value for test for interaction between year and rank is 0.55. JAKi: Janus kinase inhibitor; MBDA: multi-biomarker disease activity; RA: rheumatoid arthritis.



Number of Rheumatologists (Median proportion of Patients tested for MBDA) by rank and Year

0	2775(0.0)	2717(0.0)	2532(0.0)	2453(0.0)	2447(0.0)
1	52(0.7)	106(0.8)	198(1.1)	271(1.4)	315(1.3)
2	53(1.9)	106(3.0)	199(4.0)	270(5.3)	314(5.1)
3	53(5.7)	107(8.9)	199(12.3)	271(15.5)	317(14.3)
4	52(18.0)	105(26.4)	198(40.6)	271(44.2)	315(42.2)