

Association of Medication Beliefs, Self-efficacy, and Adherence in a Diverse Cohort of Adults with Rheumatoid Arthritis

Caroline McCulley, Patricia Katz, Laura Trupin, Edward H. Yelin, and Jennifer L. Barton

ABSTRACT. Objective. Rheumatoid arthritis (RA) patients' adherence to disease-modifying antirheumatic drugs (DMARD) is often suboptimal. We examined associations among medication beliefs, self-efficacy, and adherence to medications in RA.

Methods. Data were from a longitudinal observational cohort of persons with RA. Subjects completed telephone interviews on self-reported adherence, self-efficacy, demographics, and the Beliefs about Medicines Questionnaire (BMQ), which assesses beliefs in necessity and beliefs about taking medication. Bivariate and multivariate logistic regression identified correlates of poor adherence to synthetic DMARD and prednisone as well as to biologic therapy, including medication concerns and necessity.

Results. There were 362 patients who reported taking a synthetic DMARD and/or prednisone. Of these, 14% and 21% reported poor adherence to oral DMARD or prednisone, and biologics, respectively. There were 64% who reported concern about taking medicines, 81% about longterm effects, and 47% about becoming too dependent on medicines. In multivariate analyses, the BMQ necessity score was independently associated with better adherence to oral DMARD or prednisone (adjusted OR 0.61, 95% CI 0.41–0.91), while self-efficacy was associated with greater odds of poor adherence to oral medications (adjusted OR 1.23, 95% CI 1.01–1.59). Beliefs in medicines and self-efficacy were not associated with adherence to biologics.

Conclusion. In a diverse cohort of patients with RA, stronger beliefs in the necessity of medication were associated with better adherence to oral DMARD or prednisone, while higher self-efficacy was associated with poor adherence. Providers can play important roles in eliciting patient beliefs about medications to improve adherence and ultimately health outcomes. (J Rheumatol First Release September 15 2018; doi:10.3899/jrheum.171339)

Key Indexing Terms:

MEDICATION BELIEFS
RHEUMATOID ARTHRITIS

ADHERENCE
DISEASE-MODIFYING ANTIRHEUMATIC DRUGS

SELF-EFFICACY

Intentional nonadherence refers to a patient's decision not to take medications based on beliefs about the disease and its pharmacologic treatment¹. This decision to not take medica-

tions has far-reaching consequences, both on individual patient outcomes, as well as economic cost to society, which is estimated at US\$127 billion per year in related poor outcomes, inappropriate medication changes, wasted medications, absenteeism at work, and decreased productivity². Beliefs about medications may be both positive (medications will ease pain, prevent disease progression, cure) and negative (intolerable side effects, fear of becoming dependent on medications, longterm toxicity)³. A previous metaanalysis of 94 studies across multiple conditions, including 5 studies in rheumatoid arthritis (RA), showed a clear correlation of necessity and concerns about medication and adherence, with patients believing in the necessity of their medications being more likely to take the medications, and those with concerns related to the medications being less likely to take these medications⁴. While effect sizes were mostly small, this large metaanalysis confirmed that medication beliefs are important factors to consider when addressing adherence. Socio-economic status, education level, health literacy, sex, and age do not consistently predict nonadherence. Rather, patients make a deliberate cost/benefit analysis based on their beliefs

From the University of California, San Francisco, San Francisco, California; Oregon Health & Science University; VA Portland Health Care System, Portland, Oregon, USA.

P. Katz received funding from the US National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) Multidisciplinary Clinical Research Center [US National Institutes of Health (NIH): P60AR053308]. E.H. Yelin received funding from NIAMS Multidisciplinary Clinical Research Center (NIH: P60AR053308). J.L. Barton received funding from NIH/NIAMS (K23-AR-064372).

C. McCulley, MD, Rheumatology Fellow, Oregon Health & Science University; P. Katz, PhD, Professor, Division of Rheumatology, University of California, San Francisco; L. Trupin, MPH, Epidemiologist, Division of Rheumatology, University of California, San Francisco; E.H. Yelin, PhD, Professor Emeritus, Division of Rheumatology, University of California, San Francisco; J.L. Barton, MD, Associate Professor, Division of Rheumatology, Oregon Health & Science University, and VA Portland Health Care System.

Address correspondence to Dr. J.L. Barton, Oregon Health & Science University, Rheumatology, 3181 SW Sam Jackson Park Road, Mail Code: OP09, Portland, Oregon 97239, USA. E-mail: bartoje@ohsu.edu.

Accepted for publication June 25, 2018.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2018. All rights reserved.

(accurate or not) before they decide whether to take a medication⁵. Studies have found that intentional non-adherence has the potential to be modifiable, specifically when related to patient medication beliefs^{6,7}.

Among patients with RA, adherence to disease-modifying antirheumatic drugs (DMARD) has been reported as low as 30%⁸. Previous literature suggests that patients with RA who have greater medication concerns are less likely to adhere to DMARD^{1,3,6,7,9,10}, while other studies suggest that patients will tolerate side effects if the perceived efficacy outweighs their concerns^{2,8,11}. Similarly, a cohort study identified a significant association between greater belief in the biologic medications and lower medication concerns with better adherence¹². However, other studies have demonstrated that adherence to biologics ranges from 11% to 88%¹³ and is likely affected by factors unique to biologic therapy, including different dosing regimens and frequency, needle phobia, and cost. One small study (n = 56) of a racially/ethnically diverse RA population in an urban setting showed that major medication concerns and low self-efficacy were both associated with poor adherence⁷. Self-efficacy is defined as an individual's belief in his or her ability to carry out certain behaviors to attain a goal, reflecting one's self-confidence in having control over motivations, behaviors, and environment¹⁴. This trait plays a role in patients' perceived ability to manage chronic disease, and could also be a modifiable factor in medication adherence.

Given reports of frequent suboptimal adherence to DMARD and biologics, the lack of consistent predictors of nonadherence in existing literature, and the role of medication beliefs in health behavior, the goal of our study was to investigate the association between medication beliefs, self-efficacy, and nonadherence among patients with RA. Because of the inherent difference in medication administration between subcutaneous or infusion biologic medication and oral DMARD, the adherence questions in the survey were asked in 2 ways: 1 regarding "RA pills" and 1 regarding RA injection or infusion in the past month. The objective of our study was to assess the association of medication beliefs and self-efficacy with adherence to oral synthetic DMARD and prednisone as well as to biologics in a diverse cohort of patients with RA.

MATERIALS AND METHODS

Study design and data collection. Data were derived from a longitudinal observational cohort study (RA Outcomes Study; RAOS) described previously¹⁵. RAOS includes participants from 1 of 3 prior RA cohorts: the RA Panel Study (first initiated in 1982), the University of California, San Francisco (UCSF) RA Cohort (initiated in 2006), and the RA Genetics Study (initiated in 2006). Enrollment in RAOS at the time of this telephone survey was 438 subjects. All RAOS participants were recruited from rheumatology practices and clinics in San Francisco, and all were diagnosed with RA by a physician. Interviews were conducted by trained interviewers in English or Spanish, according to participant preference, between 2012 and 2013. Interviewers queried RA symptoms and medications, other health conditions, functioning, psychological status, and sociodemographic characteristics.

Participants were excluded from the study if they did not speak English or Spanish, did not have a telephone, or were under 18 years of age. All procedures were approved by the UCSF Committee on Human Research (IRB No. 12-09845, reference no. 197998), and all participants provided verbal consent. For the purposes of this analysis, subjects were excluded if they did not report taking an oral DMARD, prednisone, or a biologic at the time of the survey. Oral DMARD included the following: methotrexate, hydroxychloroquine, leflunomide, sulfasalazine, azathioprine, or cyclosporine. Biologic therapies included etanercept, infliximab, adalimumab (ADA), anakinra, abatacept, certolizumab, golimumab, or tocilizumab.

Measures. The Beliefs about Medicines Questionnaire (BMQ) was used to elicit the participants' beliefs about medications^{16,17}. This measure includes 2 five-question subscales: a Necessity Scale and a Concerns Scale. Example BMQ questions include, "Sometimes I worry about the long-term effects of taking my medication" from the Concerns Scale, and "My life would be impossible without my medications" from the Necessity Scale. Higher scores in each scale reflect greater belief in the necessity of medication or a stronger concern about negative effects of taking medication, respectively. The BMQ has been validated in different populations with chronic diseases, including asthma, diabetes, and hypertension¹⁷.

Adherence was measured by self-report using a single-item questionnaire. Participants were asked, "How many times do you think you may have missed taking your pills in the last week?"^{18,19,20,21}. Among participants who answered "yes" to taking one of the biologics, adherence to biologic therapy was measured by self-report. Participants were asked, "How many times do you think you have missed your RA injection or infusion in the past month?" Given that rituximab is most frequently administered every 6 months, it was not included in the injection adherence question. Adherence was dichotomized into either poor adherence or good adherence, with poor adherence defined as missing ≥ 1 RA pills over the past week or ≥ 1 RA injections in the past month. A sensitivity analysis that dichotomized poor adherence as missing ≥ 2 oral medications was also conducted. An additional sensitivity analysis of adherence to biologics excluded the infusion therapies tocilizumab and infliximab, because different factors may be associated with adherence to self-injectables compared to infusions.

Self-efficacy was measured using the validated 6-item "Self-efficacy in Chronic Disease Scale"²². Sample questions include, "How confident are you that you can keep the fatigue caused by your disease from interfering with the things you want to do?" and "How confident are you that you can do the different tasks and activities needed to manage your health condition so as to reduce your need to see a doctor?" Scores range from 1 to 10, with higher scores reflecting greater self-efficacy.

Health literacy was measured using a single, self-reported question developed by Morris and colleagues²³ and validated among English and Spanish-speaking populations in several prior studies^{24,25,26,27}. Participants were asked, "How often do you have someone like a family member, friend, hospital or clinic worker, or caregiver help you read health plan materials, such as written information about your health or care you are offered?" Answers included "always," "often," "sometimes," "occasionally," or "never." A response of "sometimes," "often," or "always" was considered limited health literacy^{23,28}.

Demographic information included race, ethnicity, age, sex, and education. Ethnicity was self-reported in response to the question, "Are you Latino or of Hispanic origin or descent?" Race was self-reported, with options of "white," "black or African-American," "Asian," "Native Hawaiian or other Pacific Islander," "American Indian or Alaska Native," or "other." Participants could indicate more than 1 category. The Patient Health Questionnaire (PHQ) was used to measure depressive symptoms. For a score ≥ 10 , this questionnaire has a sensitivity of 88% and specificity of 88% for major depression and predicting severity of depression²⁹. Functional limitations were measured with the Health Assessment Questionnaire³⁰, the most commonly used measure of function in RA. Scores range from 0 to 3 (from no difficulty to unable to do).

Statistical analysis. We used descriptive statistics to characterize differences

in patient demographics, disease duration, and depressive symptoms between adherent and nonadherent groups. Specifically, bivariable relationships between adherence and patient's age (continuous), sex, race/ethnicity, language, education level, health literacy level, disease duration (continuous), pain (continuous, 0–100 scale), function (continuous), and depressive symptoms (continuous) were assessed. We used Student t test for continuous variables and chi-square or Fisher's exact tests for categorical variables. We used a multivariable logistic regression analysis to measure the independent effects of patient demographics, disease duration, depressive symptoms, pain, function, and the BMQ necessity and concerns subscales on adherence to oral DMARD and prednisone. In the multivariate model, we included those covariates that were significant at $p < 0.20$ in the bivariate analysis. Sex was also included in the multivariable analysis. Separate bivariable and multivariable models for adherence to biologics were also conducted. All analyses were conducted using Stata/SE 13.1 (StataCorp).

RESULTS

Of the 438 eligible patients, 41 (9%) were not taking any RA medication, including DMARD, prednisone, or biologic therapy. Of the 397 remaining, 369 reported taking pills (DMARD and/or prednisone), and of these, 6 did not answer the adherence question and 3 did not complete the BMQ (Appendix 1). The total number of patients who reported either an oral DMARD or prednisone was 362. Characteristics of those taking oral DMARD or prednisone are displayed in Table 1: 88% were female, mean age was 61 (SD 13) years, 39% were non-white, and 20% were primary Spanish-language speakers. Mean disease duration was 23 (SD 12) years, nearly one-third (32%) of the study population had limited health literacy, and the mean PHQ score was 5.3 (SD 5.0). Overall, adequate adherence to oral DMARD or prednisone was 86%. In bivariate analyses of nonadherent versus adherent groups, younger age (55 vs 62 yrs, $p < 0.001$), Spanish language (36% vs 18%, $p = 0.004$), and higher PHQ scores (6.7 vs 5.1, $p = 0.04$) were associated with poor adherence.

Beliefs in medication. Regarding medication beliefs, the

mean BMQ Necessity score was 4.32 (SD 0.80), which indicates that patients somewhat agree or strongly agree with the necessity of their medications. The mean BMQ Concerns score was 2.98 (SD 1.1), which indicates weaker concerns about medications. The mean Necessity–Concerns differential⁴ was 1.34 (SD 1.15), which shows a benefit/risk ratio reflecting stronger beliefs in necessity than concerns. For proportions of patients who somewhat or strongly agreed with each item in the respective scales, see Table 2.

Adherence to oral DMARD and prednisone. In unadjusted analyses, BMQ Necessity subscale was not significantly associated with adherence to oral RA medications, while BMQ Concerns subscale was associated with greater odds of poor adherence (unadjusted OR 1.34, 95% CI 1.02–1.77). In multivariate analyses (Table 3), higher BMQ Necessity scores were associated with better adherence to oral DMARD or prednisone [adjusted OR (AOR) 0.61, 95% CI 0.41–0.91], whereas the relationship of the BMQ Concerns subscale to adherence was attenuated (AOR 1.09, 95% CI 0.74–1.59). Higher self-efficacy was independently associated with greater odds of poor adherence in multivariate analysis (AOR 1.23, 95% CI 1.01–1.50). In addition, older age was associated with better adherence to oral agents (AOR 0.96, 95% CI 0.93–0.99).

Adherence to biologic therapy. Over the prior 12 months, 218 subjects reported taking a biologic (Table 4); 168 (77%) were also taking an oral DMARD, 110 (50%) were taking prednisone, and 30 (14%) were taking biologic monotherapy. Of those taking biologic therapy, 21% reported poor adherence to biologics. The BMQ subscales and self-efficacy were not associated with poor adherence to a biologic in either bivariable or multivariable analyses (Table 5). However, low income (defined as $< 125\%$ of federal poverty level, accounting for household size) with an AOR of 0.19

Table 1. Characteristics of 362 patients with RA by adherence to oral DMARD or prednisone.

Characteristics	Total, n = 362	Nonadherent, n = 50	Adherent, n = 312	p
Age, yrs	61 ± 13	55 ± 15	62 ± 12	< 0.001
Female	319 (88)	46 (92)	273 (88)	0.48
Non-white	141 (39)	24 (48)	117 (38)	0.16
High school or less	120 (33)	20 (40)	100 (32)	0.33
Spanish-speaking	73 (20)	18 (36)	55 (18)	0.004
Limited health literacy	117 (32)	19 (38)	98 (31)	0.42
Disease duration, yrs	23 ± 12	21 ± 13	24 ± 12	0.11
Biologic use	176 (49)	23 (46)	153 (49)	0.76
PHQ score	5.3 ± 5.0	6.7 ± 5.9	5.1 ± 4.8	0.04
Function, HAQ	1.2 ± 0.75	1.2 ± 0.84	1.2 ± 0.74	0.82
Self-efficacy score, range 1–10	6.7 ± 2.0	7.0 ± 2.2	6.7 ± 1.9	0.28
High self-efficacy (score ≥ 7)	189 (52)	31 (62)	158 (51)	0.17
“Considering all the ways that your arthritis affects you, rate how well you are doing.” (0–100)	65 ± 27	65 ± 28	65 ± 26	0.85

Values are mean ± SD or n (%). Values in bold face are statistically significant. RA: rheumatoid arthritis; DMARD: disease-modifying antirheumatic drugs; PHQ: Patient Health Questionnaire; HAQ: Health Assessment Questionnaire.

Table 2. Percentage of patients with RA who agree or strongly agree with each of the items from the BMQ Necessity and Concerns subscales.

BMQ Items	Agree or Strongly Agree, %
Necessity scale	
My health, at present, depends on my medicines	92
My life would be impossible without my medicines	80
Without my medicines I would be very ill	85
My health in the future will depend on my medicines	90
My medicines will protect me from becoming worse	93
Concerns scale	
Having to take medicines worries me	64
I sometimes worry about the longterm effects of my medicines	81
My medicines are a mystery to me	34
My medicines disrupt my life	30
I sometimes worry about becoming too dependent on my medicines	47

RA: rheumatoid arthritis; BMQ: Beliefs about Medicines Questionnaire.

Table 3. Unadjusted and adjusted OR of poor self-reported adherence to oral DMARD or prednisone by BMQ subscale scores and self-efficacy.

Variables	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Age	0.96 (0.94–0.98)	0.96 (0.93–0.99)
Spanish language	2.63 (1.38–5.02)	2.33 (0.97–5.60)
BMQ Necessity	0.89 (0.62–1.27)	0.61 (0.41–0.91)
BMQ Concerns	1.34 (1.02–1.77)	1.09 (0.74–1.59)
Self-efficacy	1.58 (0.86–2.92)	1.23 (1.01–1.50)

* Adjusted for sex, race, disease duration, PHQ score, HAQ, poverty, and the variables listed in this table. Values in bold face are statistically significant. DMARD: disease-modifying antirheumatic drugs; BMQ: Beliefs about Medicines Questionnaire; PHQ: Patient Health Questionnaire; HAQ: Health Assessment Questionnaire.

(95% CI 0.04–0.92), and greater pain (AOR 0.98, 95% CI 0.97–0.99) were independently associated with better adherence to biologics. Sensitivity analyses that removed subjects who reported infusion biologic therapies did not change the main results.

DISCUSSION

In a diverse population of adults with RA, stronger beliefs in the necessity of medication were independently associated with better medication adherence to oral DMARD and prednisone, consistent with results demonstrated in other studies across multiple conditions, including RA⁴. Somewhat surprisingly, however, higher self-efficacy was independently associated with greater odds of poor adherence to oral DMARD or prednisone, a finding that is contrary to prior published studies^{1,31}. Concerns about medications were not independently associated with adherence in our present study.

Gadallah and colleagues³² demonstrated that greater adherence is associated with positive beliefs about medications and consequently less RA disease activity among patients attending an outpatient rheumatology clinic in Egypt. Likewise, Morgan and colleagues found an association between increased beliefs in medication necessity (and decreased concern) and increased adherence to biologic therapy among patients with RA in the United Kingdom, although the effect of beliefs in medications decreased over time¹². Parallel to the unadjusted findings in our study, several studies found poorer adherence among patients who reported higher levels of concern, specifically related to pain, fatigue, and previous adverse effects^{3,9,10}. The same study that noted increased concern based on pain and fatigue also paradoxically noted higher necessity scores for these same reasons³. A study conducted in a largely African American non-RA population at an inner-city hospital pharmacy found

Table 4. Characteristics of 218 patients with RA by adherence to injectable biologic therapy.

Characteristics	Total, n = 218	Nonadherent, n = 45	Adherent, n = 173	p
Age, yrs	58 ± 12	58 ± 12	56 ± 12	0.84
Female	196 (90)	43 (96)	153 (88)	0.26
Low income	27 (12)	2 (4)	25 (15)	0.08
Non-white	91 (42)	21 (47)	70 (40)	0.5
High school or less	65 (30)	11 (24)	54 (31)	0.47
Spanish-speaking	39 (18)	6 (13)	33 (19)	0.51
Limited health literacy	55 (25)	11 (24)	44 (25)	1
Disease duration, yrs	22 ± 12	23 ± 12	22 ± 13	0.55
DMARD use	168 (77)	37 (82)	131 (76)	0.43
PHQ score	5.2 ± 4.8	6.2 ± 5.2	4.9 ± 4.7	0.13
Self-efficacy score (range 1–10)	6.9 ± 2.0	6.6 ± 1.6	6.9 ± 2.1	0.36
High self-efficacy (score ≥ 7)	119 (55)	20 (44)	99 (58)	0.13
“Considering all the ways that your arthritis affects you, rate how well you are doing.” (0–100)	64 ± 28	64 ± 28	65 ± 29	0.9
Pain, 0–100	34 ± 30	28 ± 23	36 ± 31	0.14
HAQ, 0–3	1.1 ± 0.7	1.1 ± 0.7	1.2 ± 0.8	0.68

Values are mean ± SD or n (%). RA: rheumatoid arthritis; DMARD: disease-modifying antirheumatic drugs; PHQ: Patient Health Questionnaire; HAQ: Health Assessment Questionnaire.

Table 5. Unadjusted and adjusted OR of poor self-reported adherence to injectable biologics by the Beliefs about Medicine Questionnaire.

Variables	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
BMQ Necessity	1.06 (0.68–1.63)	0.98 (0.60–1.58)
BMQ Concerns	1.05 (0.77–1.45)	1.02 (0.70–1.48)
Self-efficacy	0.93 (0.79–1.09)	0.97 (0.79–1.20)
PHQ-9 (for every 1-point increase)	1.05 (0.99–1.12)	1.10 (1.00–1.20)
Low income	0.28 (0.06–1.21)	0.19 (0.04–0.92)
Pain	0.99 (0.98–1.00)	0.98 (0.97–0.99)

* Adjusted for age, sex, race, oral DMARD, and the variables listed in this table. Values in bold face are statistically significant. BMQ: Beliefs about Medicines Questionnaire; PHQ-9: Patient Health Questionnaire 9; DMARD: disease-modifying antirheumatic drugs.

that more negative medication beliefs were associated with 2.1-times greater odds of poor adherence⁹. Health literacy level was not associated with medication adherence, as in our current study.

The other main finding in our observational cohort study was the association between a higher level of self-efficacy and poor adherence to oral DMARD and prednisone. Previous studies in RA demonstrate the opposite: greater self-efficacy is associated with greater adherence to a medication regimen^{8,33}. It is unclear why the results of our study differ from those of prior studies and therefore more investigation is warranted of the association between medication beliefs and adherence among diverse populations with RA. However, if this finding remains consistent, the association between increased self-efficacy and poorer adherence may be explained by patients having, or believing that they have, better self-management skills and thus choosing not to take their medications regularly. It is also possible that the current results reflect the effect of confounding variables given that self-efficacy was not significant in the unadjusted results but became significant in the multivariable analysis.

Medication adherence has a substantial effect on both the cost of healthcare and individual patient outcomes. The socioeconomic burden of medication nonadherence is estimated to be between US\$100 billion and US\$127 billion annually^{2,6}. When patients do not take prescribed, often very expensive, medications, these unused medications and the subsequent increase in disability and missed work add up to significant costs to society. Further, patient outcomes worsen, with increased disease progression and disease activity³², and decreased functionality. Additionally, nonadherence may also lead to inappropriate changing of medication regimens owing to their perceived ineffectiveness by the prescribing clinician.

Medication beliefs are complex and dynamic, formed by a patient's belief about his or her condition and medications³⁴ and past experiences with similar medications¹⁰. Patients perform a risk-benefit analysis, weighing the perceived efficacy (symptom relief, prevention of deterioration, quality

of life)³⁵, benefits, and risks (becoming dependent on medications, adverse side effects)^{3,8,9,11}. Because there are well-recognized modifiable factors in a patient's deliberations and up to 20% of adherence is attributed to medication beliefs^{9,12}, clinicians play an important role regarding beliefs and adherence. Specifically, clinicians should elicit patients' perception of medication necessity and concerns early in the disease course and repeat this assessment over time¹². Clinicians can help inform patient beliefs and perceptions regarding effectiveness and promote realistic risk-benefit assessments. Further, clinicians and care teams should spend more time exploring fears about longterm effects and dependency; 1 study among patients with RA found that negative beliefs outweighed positive necessity beliefs in the decision-making model³.

Our study has several limitations. First, the adherence measurement was by self-report only, with inherent potential for decreased recall and response bias in the phone interview. Additionally, we dichotomized poor adherence as missing 1 or more pills per week, whereas other studies define poor adherence as taking < 80% of medications. Of note, a sensitivity analysis that used a stricter cutoff of missing RA pills ≥ 2 times in the past week yielded results similar to the main findings. Because of the wording of the adherence-to-pills question, we were unable to separate adherence to oral DMARD from adherence to prednisone. Another weakness is the cross-sectional design and inability to show causality. Additionally, the majority of the study population was female, with a 9:1 female/male ratio, which is greater than the 3–4:1 female/male ratio of real-world RA disease prevalence, and thus may limit generalizability. However, this is less likely a source of bias, because sex was not associated with different patterns of adherence in our study. It should also be noted that the patients with RA in our study had a relatively long RA disease duration, which may reflect the higher rates of adherence identified in this cohort compared to the patients in other studies. The association of higher self-efficacy with poorer adherence to oral therapies may have been due to improved outcomes with biologics; however, we were unable to determine this based on our data and consider it a potential area of investigation in future studies.

Conversely, our study has several notable strengths. First, a diverse population completed the study, including a significant number of Latino patients and patients with limited health literacy. Further, depressed mood was included as a covariate, and was associated with poorer adherence to biologic therapy. Depressive symptom severity has been shown to be an independent predictor of adherence difficulties among patients with systemic lupus erythematosus³⁶ as well as with adherence to synthetic DMARD among Chinese patients with RA³⁷ and among ethnically diverse and economically disadvantaged patients with RA in the United States³⁸. However, no significant association of depressed

mood with poorer adherence to biologic therapy among diverse populations with RA has been shown (Morgan, *et al* evaluated depression and anxiety but neither was predictive of adherence to ADA¹²). Interestingly, low income was significantly associated with better adherence to biologic therapy. While cost-related medication nonadherence has been reported in patients with RA, the literature has not demonstrated an association of low income with greater adherence to biologics; however, higher out-of-pocket costs for biologic therapies have been associated with poorer adherence³⁹. Another strength was the study sample size, which was relatively large compared to many other studies, increasing the validity of the findings. The findings in our study are the first steps needed to better understand and inform patient beliefs and adherence across diverse populations with RA.

Greater beliefs in medication necessity are associated with better adherence to oral DMARD and prednisone in a diverse cohort of patients with RA. Higher self-efficacy is associated with higher odds of poor adherence, regardless of beliefs. More research is needed to better understand these associations and the role of medication beliefs in adherence over time, and how clinicians may play a role in eliciting beliefs among diverse patients with RA.

ACKNOWLEDGMENT

The authors thank the patients who participated in this longitudinal study. They also thank the telephone interviewers who obtained information from the study participants. Finally, they thank the University of California San Francisco, Oregon Health & Science University, and the VA Portland Health Care System for supporting this work.

REFERENCES

- van den Bemt BJ, Zwikker HE, van den Ende CH. Medication adherence in patients with rheumatoid arthritis: A critical appraisal of the existing literature. *Expert Rev Clin Immunol* 2012;8:337-51.
- Elliott RA, Barber N, Clifford S, Horne R, Hartley E. The cost effectiveness of a telephone-based pharmacy advisory service to improve adherence to newly prescribed medicines. *Pharm World Sci* 2008;30:17-23.
- Neame R, Hammond A. Beliefs about medications: a questionnaire survey of people with rheumatoid arthritis. *Rheumatology* 2005;44:762-7.
- Foot H, La Caze A, Gujral G, Cottrell N. The necessity-concerns framework predicts adherence to medication in multiple illness conditions: A meta-analysis. *Patient Educ Couns* 2016;99:706-17.
- Schuz B, Marx C, Wurm S, Warner LM, Ziegelmann JP, Schwarzer R, et al. Medication beliefs predict medication adherence in older adults with multiple illnesses. *J Psychosom Res* 2011;70:179-87.
- Phatak HM, Thomas J 3rd. Relationships between beliefs about medications and nonadherence to prescribed chronic medications. *Ann Pharmacother* 2006;40:1737-42.
- Spruill TM, Ogedegbe G, Harrold LR, Potter J, Scher JU, Rosenthal PB, et al. Association of medication beliefs and self-efficacy with adherence in urban Hispanic and African American rheumatoid arthritis patients. *Ann Rheum Dis* 2014;73:317-8.
- Salt E, Frazier SK. Adherence to disease-modifying antirheumatic drugs in patients with rheumatoid arthritis: A narrative review of the literature. *Orthop Nurs* 2010;29:260-75.
- Gatti ME, Jacobson KL, Gazmararian JA, Schmotzer B, Kripalani S. Relationships between beliefs about medications and adherence. *Am J Health Syst Pharm* 2009;66:657-64.
- Shiyanbola OO, Farris KB, Chrischilles E. Concern beliefs in medications: Changes over time and medication use factors related to a change in beliefs. *Res Social Adm Pharm* 2013;9:446-57.
- Berry D, Bradlow A, Bersellini E. Perceptions of the risks and benefits of medicines in patients with rheumatoid arthritis and other painful musculoskeletal conditions. *Rheumatology* 2004;43:901-5.
- Morgan C, McBeth J, Cordingley L, Watson K, Hyrich KL, Symmons DP, et al. The influence of behavioural and psychological factors on medication adherence over time in rheumatoid arthritis patients: A study in the biologics era. *Rheumatology* 2015; 54:1780-91.
- Bhoi P, Bessette L, Bell MJ, Tkaczyk C, Nantel F, Maslova K. Adherence and dosing interval of subcutaneous antitumour necrosis factor biologics among patients with inflammatory arthritis: Analysis from a Canadian administrative database. *BMJ Open* 2017;7:e015872.
- Bandura A. Self-efficacy: Toward a unifying theory of behavioral change. *Psychol Rev* 1977;84:191-215.
- Katz PP, Barton J, Trupin L, Schmajuk G, Yazdany J, Ruiz PJ, et al. Poverty, depression, or lost in translation? Ethnic and language variation in patient-reported outcomes in rheumatoid arthritis. *Arthritis Care Res* 2016;68:621-8.
- Horne R. Patients' beliefs about treatment: The hidden determinant of treatment outcome? *J Psychosom Res* 1999;47:491-5.
- Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999;47:555-67.
- Haynes RB, McDonald HP, Garg AX. Helping patients follow prescribed treatment: Clinical applications. *JAMA* 2002; 288:2880-3.
- Jerant A, DiMatteo R, Arnsten J, Moore-Hill M, Franks P. Self-report adherence measures in chronic illness: Retest reliability and predictive validity. *Med Care* 2008;46:1134-9.
- Mullan RJ, Montori VM, Shah ND, Christianson TJ, Bryant SC, Guyatt GH, et al. The diabetes mellitus medication choice decision aid: A randomized trial. *Arch Intern Med* 2009;169:1560-8.
- Stephenson BJ, Rowe BH, Haynes RB, Macharia WM, Leon G. The rational clinical examination. Is this patient taking the treatment as prescribed? *JAMA* 1993;269:2779-81.
- Lorig KR, Sobel DS, Ritter PL, Laurent D, Hobbs M. Effect of a self-management program on patients with chronic disease. *Eff Clin Pract* 2001;4:256-62.
- Morris NS, MacLean CD, Chew LD, Littenberg B. The single item literacy screener: Evaluation of a brief instrument to identify limited reading ability. *BMC Fam Pract* 2006;7:21.
- Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. *Fam Med* 2004;36:588-94.
- Chew LD, Griffin JM, Partin MR, Noorbaloochi S, Grill JP, Snyder A, et al. Validation of screening questions for limited health literacy in a large VA outpatient population. *J Gen Intern Med* 2008; 23:561-6.
- Miller MJ, Allison JJ, Schmitt MR, Ray MN, Funkhouser EM, Coughlin DJ, et al. Using single-item health literacy screening questions to identify patients who read written nonsteroidal anti-inflammatory medicine information provided at pharmacies. *J Health Commun* 2010;15:413-27.
- Wallace LS, Rogers ES, Roskos SE, Holiday DB, Weiss BD. Brief report: Screening items to identify patients with limited health literacy skills. *J Gen Intern Med* 2006;21:874-7.
- Al Sayah F, Williams B, Johnson JA. Measuring health literacy in individuals with diabetes: a systematic review and evaluation of available measures. *Health Educ Behav* 2013;40:42-55.
- Kroenke K, Spitzer RL, Williams JB. The phq-9: Validity of a brief

- depression severity measure. *J Gen Intern Med* 2001;16:606-13.
30. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980;23:137-45.
 31. Brus H, van de Laar M, Taal E, Rasker J, Wiegman O. Determinants of compliance with medication in patients with rheumatoid arthritis: the importance of self-efficacy expectations. *Patient Educ Couns* 1999;36:57-64.
 32. Gadallah MA, Boulos DN, Gebrel A, Dewedar S, Morisky DE. Assessment of rheumatoid arthritis patients' adherence to treatment. *Am J Med Sci* 2015;349:151-6.
 33. de Achaval S, Suarez-Almazor ME. Treatment adherence to disease-modifying antirheumatic drugs in patients with rheumatoid arthritis and systemic lupus erythematosus. *Int J Clin Rheumatol* 2010;5:313-26.
 34. Leventhal H, Diefenbach M, Leventhal EA. Illness cognition: using common sense to understand treatment adherence and affect cognition interactions. *Cogn Ther Res* 1992;16:143-63.
 35. Goodacre LJ, Goodacre JA. Factors influencing the beliefs of patients with rheumatoid arthritis regarding disease-modifying medication. *Rheumatology* 2004;43:583-6.
 36. Julian LJ, Yelin E, Yazdany J, Panopalis P, Trupin L, Criswell LA, et al. Depression, medication adherence, and service utilization in systemic lupus erythematosus. *Arthritis Rheum* 2009;61:240-6.
 37. Xia Y, Yin R, Fu T, Zhang L, Zhang Q, Guo G, et al. Treatment adherence to disease-modifying antirheumatic drugs in chinese patients with rheumatoid arthritis. *Patient Prefer Adherence* 2016;10:735-42.
 38. Waimann CA, Marengo MF, de Achaval S, Cox VL, Garcia-Gonzalez A, Reveille JD, et al. Electronic monitoring of oral therapies in ethnically diverse and economically disadvantaged patients with rheumatoid arthritis: Consequences of low adherence. *Arthritis Rheum* 2013;65:1421-9.
 39. Barton JL. Patient preferences and satisfaction in the treatment of rheumatoid arthritis with biologic therapy. *Patient Prefer Adherence* 2009;3:335-44.

APPENDIX 1. Subjects receiving RA medications, by type (biologic therapies, DMARD, prednisone, or none) and combinations.

Medication Types	N (%)
Biologic + prednisone	17 (4)
Prednisone alone	23 (5)
Biologic alone	28 (6)
No RA medication	41 (9)
DMARD + prednisone	73 (17)
DMARD + biologic	74 (17)
DMARD + prednisone + biologic	88 (20)
DMARD alone	94 (21)
Total	438

RA: rheumatoid arthritis; DMARD: disease-modifying antirheumatic drugs.