

# Rheumatoid Arthritis Medication Adherence in a Health System Specialty Pharmacy

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**R**heumatoid arthritis (RA) is a chronic progressive disease that causes pain and joint destruction, often leading to disability, low quality of life, and premature death.<sup>1</sup> RA can be treated with specialty medications that slow disease progression and induce remission.<sup>2,3</sup> However, rates of adherence to these medications are often suboptimal: Previous research has found adherence to RA therapy ranging from a medication possession ratio (MPR) of 0.44 to 0.83.<sup>4-7</sup> The Pharmacy Quality Alliance, a public-private cooperative founded to promote appropriate medication use, endorses an adherence threshold of greater than 80% for patients taking noninfused biologic medications used to treat RA.<sup>8</sup> Common patient barriers to RA treatment adherence include adverse drug effects, perceived treatment inefficacy, high out-of-pocket costs, and complexities of filling prescriptions and managing medications.<sup>4,5</sup> Nonadherence to antirheumatic medications is associated with worse clinical response as measured by Disease Activity Score 28 (DAS28), a validated measure of RA disease activity.<sup>9,10</sup>

Integrated health system specialty pharmacies (HSSPs) aim to overcome barriers to medication adherence by integrating clinical pharmacists and pharmacy technicians within specialty clinics.<sup>11</sup> The clinical pharmacist and pharmacy technician identify and address adverse effects, conduct proactive refill calls to avoid gaps in therapy, perform periodic assessments to optimize treatment, and help patients enroll for financial assistance. High rates of medication adherence have been reported among patients with malignancies, multiple sclerosis, and hepatitis C who receive care from an integrated HSSP.<sup>12-14</sup> However, adherence to RA therapy among patients at an integrated HSSP has not been previously reported.

The objective of this study was to evaluate adherence to specialty medication and identify characteristics associated with adherence in patients with RA at an integrated HSSP. The growing number of integrated HSSPs in the United States<sup>15</sup> are uniquely positioned to promote high medication adherence that optimizes patient outcomes on these expensive drugs.<sup>4,6</sup> Identifying patient characteristics associated with nonadherence may help practitioners develop best practices to improve patient adherence to RA therapy within specialty pharmacy.

## ABSTRACT

**OBJECTIVES:** To assess adherence to specialty medications for rheumatoid arthritis (RA) at an integrated health system specialty pharmacy (HSSP) and identify characteristics associated with adherence.

**STUDY DESIGN:** Single-center, retrospective cohort study.

**METHODS:** Study patients were adults with RA who filled at least 3 prescriptions for biologic disease-modifying antirheumatic drugs (bDMARDs) between July 1, 2016, and June 30, 2017, at an integrated HSSP. Data were collected from pharmacy claims and electronic health records. The primary outcome, adherence, was measured using proportion of days covered (PDC). Proportional odds logistic regression was used to test association between PDC and age, gender, race, insurance type, and out-of-pocket costs.

**RESULTS:** We included 675 patients: 77% were female, 90% were White, 29% were naive to treatment at initial dispensing, 60% held commercial insurance, and the median age was 56 years. Median (interquartile range [IQR]) patient out-of-pocket cost per fill was \$1.50 [\$0-\$5]. Median (IQR) PDC was 0.95 (0.84-1.00); 80% of patients achieved PDC of 0.80 or higher. Higher adherence was more likely in patients who were male [odds ratio [OR], 1.58; 95% CI, 1.15-2.18;  $P = .005$ ], naive to specialty medication treatment (OR, 3.04; 95% CI, 2.21-4.18;  $P < .001$ ), and older in age (per 10 years: OR, 1.17; 95% CI, 1.04-1.32;  $P = .008$ ), and adherence had a significant nonlinear association with average cost per fill ( $P = .006$ ); associations with race and insurance type were not significant.

**CONCLUSIONS:** At an integrated HSSP, patients with RA paid low out-of-pocket costs for bDMARD therapy and achieved high treatment adherence. Data suggest that integrated HSSPs assist patients in removing financial barriers to treatment.

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## METHODS

### Setting

This study was conducted at Vanderbilt University Medical Center (VUMC) in Nashville, Tennessee. At VUMC, a pharmacist and pharmacy technician are embedded in the outpatient clinic (Vanderbilt Rheumatology Clinic), and an integrated HSSP, Vanderbilt Specialty Pharmacy, dispenses medication to VUMC patients. With access to the electronic health records (EHRs), the clinic pharmacist assesses medication appropriateness, provides medication education, and ensures treatment optimization. The pharmacy technician facilitates insurance authorization and financial assistance enrollment to ensure that patients can access and afford therapy. Throughout treatment, the pharmacy technician screens for adverse effects and other barriers to adherence at medication refill phone calls; pharmacists intervene as necessary to address clinical and financial medication questions, help patients mitigate adverse effects, and determine whether dose adjustments or therapy changes are needed.

### Study Design

This was a single-center, retrospective cohort study of patients diagnosed with RA who filled specialty medications with Vanderbilt Specialty Pharmacy between July 1, 2016, and June 30, 2017. Data were collected from EHRs and pharmacy claims. This study was approved by the Vanderbilt University Institutional Review Board.

### Patient Eligibility

Participants included in the study were adults ( $\geq 18$  years), diagnosed with RA (*International Classification of Diseases, Tenth Revision, Clinical Modification* code M05 or M06), who filled 3 or more specialty medication prescriptions at Vanderbilt Specialty Pharmacy during the study period. Eligible specialty medications were abatacept (subcutaneous [SC]), adalimumab (SC), certolizumab (SC), etanercept (SC), tocilizumab (SC), and tofacitinib (oral). All included medications are either self-administered injectables or oral medications, both of which typically follow 28- to 30-day refill cycles. Patients were excluded if the medications were prescribed by a non-VUMC provider. We reviewed outliers based on proportion of days covered (PDC) less than 50% and excluded patients who had provider-directed extended gaps in therapy, as PDC for these patients does not accurately assess adherence to medication therapy. Reasons for appropriate gaps in therapy included pregnancy, infections lasting longer than 90 days, or an extended drug holiday. We also excluded patients who received sample medications for more than 3 months and patients with multiple overlapping specialty medication prescriptions.

## TAKEAWAY POINTS

In patients with rheumatoid arthritis treated with specialty medication, adherence and persistence to therapy are necessary to achieve optimal health outcomes. This study demonstrated high medication adherence rates and low patient out-of-pocket costs at an integrated health system specialty pharmacy.

- ▶ Adherence measured using median (interquartile range) proportion of days covered was 0.95 (0.84-1.00), and 80% of patients were adherent [proportion of days covered,  $\geq 0.80$ ].
- ▶ Rates of financial assistance were high; low out-of-pocket costs were associated with higher adherence.
- ▶ Odds of higher treatment adherence were greater in patients who were male, older in age, and naive to specialty medication.
- ▶ Further work should be done to identify patients at risk for nonadherence and remove barriers to adherence.

### Outcome Measures

From the EHR, we collected patient gender, race, and date of birth (to compute age at first fill). The pharmacy processing system was used to collect medication name, fill date, days' supply, insurance coverage/type, financial assistance use/type, and out-of-pocket cost for each fill. Patients were classified as treatment naive if they did not fill a prescription for a specialty medication included in the study within 6 months prior to the study period. Data were managed and stored in REDCap electronic data capture tools hosted at Vanderbilt University.<sup>16,17</sup>

The primary outcome was medication adherence, which was measured using PDC. PDC was defined as the number of days that the patient had medication available within the observation window, divided by the length of the observation window. The observation window is patient-specific and measured as the number of days between the date of a patient's first fill of an included medication on or after July 1, 2016, and the date of the last fill before June 30, 2017. Each patient has a different denominator, up to a maximum of 12 months. The date of the last fill was used because, given the nature of the claims data, it can be impossible to tell the difference between a patient who is nonadherent and a patient who is lost to follow-up, is required to use an external pharmacy, or discontinues therapy. Commercial insurance plans often restrict the use of some specialty therapies to certain pharmacies, which limits the availability of complete patient data when calculated at the pharmacy level. Using the last-fill PDC method evaluates patient adherence behavior during the time they are known to be prescribed the medication and able to fill it at the internal pharmacy. Although this may bias PDC values high, the alternative method of using a fixed time period would likewise bias the PDC values low and confound with the concept of persistence by including time when a patient may no longer be on therapy or filling at the internal pharmacy. Because we are reporting PDC over a period when a patient is known to be receiving dispensations, we are avoiding making claims about PDC in the period when the bias would manifest. Of note, this bias is likely reduced when using a fixed interval PDC calculation for health plan data that requires

## CLINICAL

**TABLE 1.** Demographics, Out-of-Pocket Costs, and Adherence (N=675)

Characteristic	Mean (SD) or n (%)
Age in years as of 7/1/2016	55 (13)
Gender	
Male	154 (22.8%)
Female	521 (77.2%)
Race	
White	607 (89.9%)
Black or African American	49 (7.3%)
Other	8 (1.2%)
Unknown	10 (1.5%)
Treatment naivety*	
Naive	193 (28.6%)
Non-naive	482 (71.4%)
Insurance category	
Commercial	406 (60.1%)
Government	245 (36.3%)
Multiple	24 (3.6%)
Financial assistance	
No	177 (26.2%)
Yes	498 (73.8%)
Total out-of-pocket cost in \$	87.00 (555.00)
Total out-of-pocket cost in \$ by categories	
0.00	248 (36.7%)
0.01-25.00	180 (26.7%)
25.01-100.00	185 (27.4%)
100.01-8006.14	62 (9.2%)
Average out-of-pocket cost per fill in \$	11.00 (76.10)
Average out-of-pocket cost per fill in \$ by categories	
0.00	248 (36.7%)
0.01-5.00	222 (32.9%)
5.01-20.00	188 (27.9%)
20.01-1251.65	17 (2.5%)
PDC	0.89 (0.14)
PDC dichotomized	
< 80%	135 (20.0%)
≥ 80%	540 (80.0%)
PDC categories	
0.24-0.49	10 (1.5%)
0.50-0.79	125 (18.5%)
0.80-0.99	379 (56.1%)
1.000	161 (23.9%)

PDC, proportion of days covered.

\*Participants were considered naive to therapy if there were no pharmacy claims for any medications included in the study in the 6-month period prior to baseline.

continuous member enrollment and is capable of capturing claims from multiple pharmacies. Additionally, ending the PDC calculation at the date of the last fill limits patients from receiving an “extra” fill’s worth of covered days, potentially reducing the PDC.

Medication availability was based on the number of days’ supply at each fill, and any excess supply (from an earlier refill) was shifted forward such that the new fill began when the old fill was exhausted. The method fills in subsequent medication gaps, and any oversupply at the end of the study period was truncated so that the maximum PDC for each patient was 1.00.

PDC was calculated at the patient level, meaning medication switches contribute proportionally to PDC in accordance with how long the patient was on each medication. If a switch occurred while a patient still had medication in hand, the excess supply of the prior medication did not carry forward. We utilized raw PDC values for statistical analyses.

### Analysis

Descriptive statistics were calculated for the demographic and prescription data. Continuous variables were reported as medians, interquartile ranges (IQRs), means, and SDs. Categorical variables were reported as frequencies and proportions. We first performed univariate analysis using the proportional odds model to assess whether PDC was associated with age, gender, race, treatment naivety, medication costs, insurance type, or administration type. To avoid multicollinearity of similar variables (eg, total cost and average cost), the following covariates were selected for proportional odds logistic regression: age, gender, race, insurance category, average out-of-pocket cost, and treatment naivety. We examined nonlinear effects of age and average out-of-pocket cost on PDC using restricted cubic splines with 3 knots, but age was modeled as a linear effect in the final model because there was little evidence of a nonlinear effect of age. Multiple degree of freedom Wald tests were used to assess the significance of nonlinear effects. Odds ratios (ORs), 95% CIs, and *P* values were reported for regression results. All analyses were performed using the programming language R version 3.3.0.

## RESULTS

### Sample Characteristics

We included 675 patients, whose demographic characteristics and treatment outcomes are summarized in **Table 1**. Most patients were female (77%), White (90%), non-naive to treatment (71%), and held commercial insurance (60%). Some patients (10%) switched medication within the study period, resulting in a total of 753 prescriptions dispensed. Patients were most frequently prescribed etanercept (34.5%) or adalimumab (34.1%), followed by tofacitinib (12.4%), abatacept (11.2%), certolizumab pegol (4.9%), and tocilizumab (2.7%). Self-injectable medications administered at home comprised 87.6% of prescriptions dispensed. Most (81%) patients had at least 6 fills within the study period. Further, most received financial assistance (74%), and the median (IQR) for patients’ average out-of-pocket cost per fill was \$1.50 (\$0-\$5). The median (IQR) number of fills per patient was 9 (6-12). For the primary outcome, mean (SD) PDC was 0.89 (0.14) and median (IQR) PDC was 0.95 (0.84-1.00). Eighty

percent of patients achieved a PDC greater than or equal to 0.80. The distribution of patients' PDC is displayed in **Figure 1**, and **Figure 2** presents medians and IQRs of PDC stratified by baseline patient characteristics of age, gender, race, treatment naivety, insurance type, and average out-of-pocket cost category; both figures show skewed distribution of PDC.

**Regression Analyses**

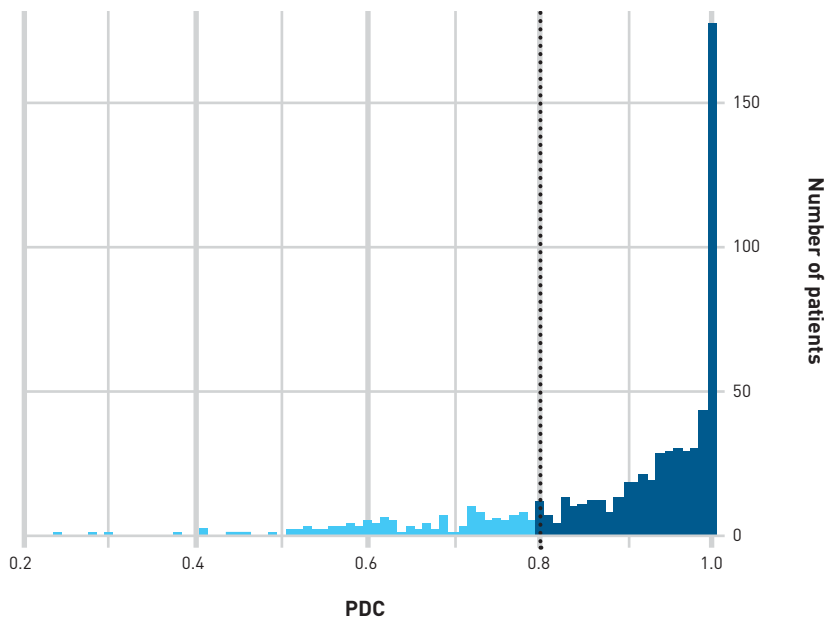
Univariate analyses showed that higher PDC was significantly associated with older age ( $P < .001$ ), male compared with female gender ( $P = .008$ ), government compared with commercial insurance ( $P = .002$ ), and naivety compared with previous treatment ( $P < .001$ ). No association was found between PDC and race, when comparing White patients with non-White patients, or between PDC and route of administration, when comparing injectable with oral drugs.

Results of the multivariate analysis are reported in **Table 2**. Older age, male gender, and treatment naivety were associated with higher PDC; associations with race and insurance type were not significant. For every 10-year increase in age, a patient's odds of higher adherence increased by 17% (OR, 1.17; 95% CI, 1.04-1.32). Men were 58% more likely to achieve higher PDC than women (OR, 1.58; 95% CI, 1.15-2.18). Treatment-naive patients were about 3 times more likely to achieve higher PDC than non-naive patients (OR, 3.04; 95% CI, 2.21-4.18). We also found a significant nonlinear association with average out-of-pocket cost per fill; the odds of higher adherence are greatest for patients with \$0 cost per fill, and decrease until roughly \$6, around which the odds of higher adherence level off.

**DISCUSSION**

In our study of adult patients with RA who filled specialty medications from Vanderbilt Specialty Pharmacy, we found high adherence to medication as measured by PDC. In previous research, integrated HSSPs have demonstrated beneficial patient outcomes, including lower risk of relapse and higher rates of adherence in patients with multiple sclerosis<sup>12,13,18</sup> and lower total costs and higher rates of adherence in oncology.<sup>14</sup> Our study is among the

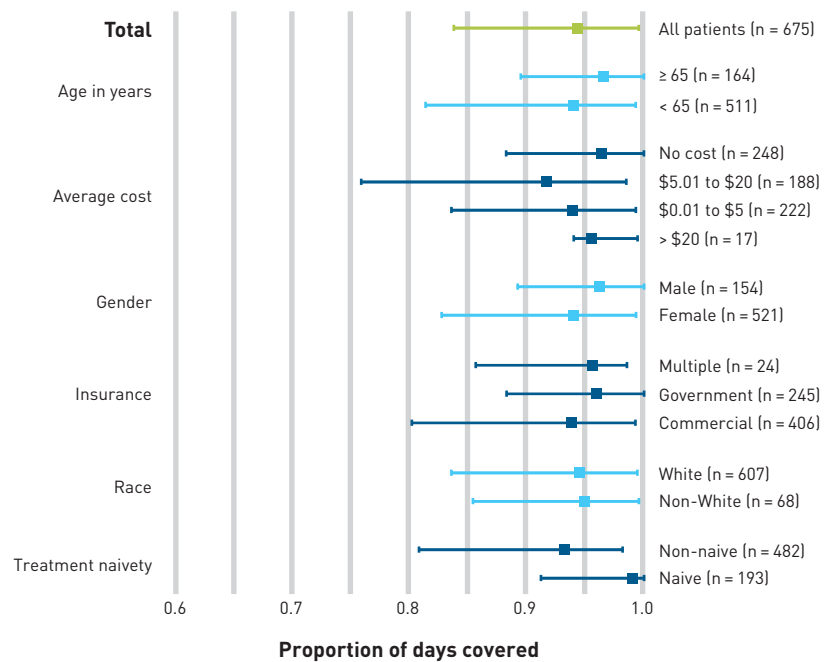
**FIGURE 1.** Distribution of PDC\*



PDC, proportion of days covered.

\*Mean [SD] PDC is 0.89 [0.14], and median PDC is 0.95. Eighty percent of the population met or exceeded the threshold for medication adherence above which a reasonable clinical benefit can be expected (PDC ≥ 0.80).

**FIGURE 2.** Median and Interquartile Range of Proportion of Days Covered by Participant Characteristics\*



\*Patient characteristics were determined at the beginning of the study period, and average cost was determined per fill.

**TABLE 2.** Proportional Odds Logistic Regression Analysis

Variable	Odds ratio <sup>a</sup>	95% CI	P
Age			
Per 10 years	1.17	1.04-1.32	.008
Gender			
Male vs female	1.58	1.15-2.18	.005
Race			
White vs non-White <sup>b</sup>	0.91	0.57-1.46	.692
Insurance category			
Government vs commercial	0.99	0.70-1.41	.972
Multiple vs commercial	1.13	0.55-2.29	.744
Treatment naivety <sup>c</sup>			
Naive vs non-naive	3.04	2.21-4.18	<.001

<sup>a</sup>Odds ratios are presented for categorical and continuous predictors modeled linearly.

<sup>b</sup>Includes African American patients, patients of other races, and those with no specified race.

<sup>c</sup>Participants were considered naive to therapy if there were no pharmacy claims for any medications included in the study in the 6-month period prior to baseline.

first to examine adherence to RA therapy at an integrated HSSP. Eighty percent of patients achieved PDC greater than or equal to 0.80, a commonly used benchmark threshold that represents “a reasonable likelihood of achieving the most clinical benefit” and was set by the Pharmacy Quality Alliance.<sup>8</sup> Average PDC in our sample (0.89) exceeds previously reported rates of adherence to specialty medications for RA in patients receiving medication from traditional, nonintegrated pharmacies, which ranged from 0.44 to 0.70.<sup>4,6,19</sup> We also found that higher adherence was associated with lower out-of-pocket medication costs, treatment naivety, male gender, and older age. These findings extend the growing body of literature on integrated HSSPs’ ability to promote high access and adherence to specialty medication.

Patients’ out-of-pocket medication costs were low during the 1-year study period, and higher costs were associated with lower adherence. Specialty medications for RA are expensive, with average wholesale prices per dose for etanercept and adalimumab of \$1552.22 and \$3104.46, respectively.<sup>20</sup> Previous research has demonstrated a negative association between medication cost and adherence in patients with RA.<sup>5,21</sup> One retrospective study of 85,812 patients with commercial insurance receiving specialty medications for RA found that out-of-pocket costs of more than \$50 per week significantly reduced treatment persistence over 1 year and an increase in weekly out-of-pocket costs of even \$5.50 could reduce adherence levels, based on MPR.<sup>5</sup> In our study, patients paid an average of \$11 per medication fill, whereas the median of patients’ average out-of-pocket cost per fill was \$1.50. On average, patients paid a total of \$87 over the course of the 1-year study period. This is considerably less than the \$400 in annual out-of-pocket costs when filling prescriptions from nonintegrated pharmacies in a commercially insured population and likely contributes to the high rates of adherence seen in our population.<sup>5</sup>

Vanderbilt Specialty Pharmacy team members pursue insurance approval and enroll patients in financial assistance programs as needed when therapy is initiated and during medication refills. Financial assistance programs—which are available through manufacturer co-pay cards, charitable foundation grants, or a medication assistance program funded by the health system—reduce or eliminate patients’ medication co-payment. Although these programs are accessible to the public, they require time and expertise to identify and enroll patients. Enrolling patients in financial assistance programs is an important role of integrated HSSPs, and higher rates of financial assistance use for oral anticancer medications following integrated HSSP involvement have been demonstrated compared with no specialty pharmacy integration.<sup>22</sup> Three-quarters of patients in our study received financial assistance, and more than one-third did not incur any out-of-pocket medication expenses during the 1-year study period. Furthermore, patients with government-provided insurance (36.3% of our population) do not qualify for manufacturer financial assistance programs.<sup>23</sup> In our study, high rates of adherence were seen in patients with commercial and government-provided insurance.

Patients naive to specialty medications for RA were more likely to be adherent than non-naive patients in our study. This finding contrasts with the previous literature showing that naive users of etanercept and adalimumab were adherent to therapy 42% and 41% of the time, respectively, whereas existing users were adherent 51% and 47% of the time.<sup>24</sup> Similarly, 3 studies have demonstrated that patients taking oral disease-modifying antirheumatic drugs before initiating specialty medication were more likely to be adherent.<sup>5,25,26</sup> It is unclear why patients naive to treatment in our sample have higher adherence than non-naive patients, and future work is warranted to explore potential characteristics that might explain this association. For example, patients who are not naive to treatment may have higher disease severity, which has previously been associated with decreased persistence<sup>27</sup> and may have influenced adherence in our study.

Men showed higher adherence than women in our sample. The association between gender and adherence has been explored, with mixed findings: Some studies have found higher adherence in men with RA compared with women,<sup>5,7,28</sup> whereas others have reported nonsignificant differences in adherence between men and women.<sup>6,26</sup> The association that we found between gender and adherence could be attributed to patient characteristics that we did not measure, such as differences in socioeconomic status, disease severity, or presence of comorbidities. In a large, observational study of adults with prescription drug benefits, women were more often prescribed multiple medications than men but were less adherent and less likely to receive treatment recommended by evidence-based guidelines for chronic conditions.<sup>29</sup> Gender, familial, or cultural differences—such as spousal or family support and communication with health care providers—might also contribute to medication-taking behavior. As RA is more prevalent in women than men, future studies could explore sociodemographic and clinical predictors of



adherence to specialty medications to ensure that women with RA achieve positive health outcomes.

Age is another demographic characteristic we found to be associated with adherence: For each 10-year increase in age, a patient's odds of higher adherence increased by 17%. Other studies have also found higher adherence in older patients,<sup>7,26,28</sup> but this association has been inconsistent.<sup>25</sup> Because our findings suggest that younger patients may be at higher risk of nonadherence, it is worth exploring potential barriers to adherence in younger patients with RA and identifying interventions. For example, some have suggested that younger patients may be good candidates for interventions that use technology and alternative forms of communication, such as a multicomponent smartphone app,<sup>30</sup> secure messaging service, or interactive voice response.<sup>31</sup>

Controlling for other variables, adherence did not differ between patients with government and commercial insurance types. Insurance type influences patients' eligibility for financial assistance: Patients with government-funded insurance (eg, Medicare, Medicaid) are ineligible for manufacturer co-pay cards and must rely on grant assistance from foundations, which could influence a patient's out-of-pocket costs and thus medication-taking behavior. No known research has compared adherence between government and commercially insured patients, but previous studies have reported suboptimal adherence in patients with commercial and government insurance. In 2 studies of Medicaid populations, 58% of patients were adherent<sup>19</sup> and mean PDC was 0.66 to anti-tumor necrosis factor medications (commonly used in RA).<sup>27</sup> In populations with commercial insurance, a study of adherence to RA medications reported that 44.4% of patients achieved PDC greater than or equal to 0.80.<sup>32</sup> Two other studies of commercially insured patients reported adherence rates of 0.61<sup>4</sup> and 0.79<sup>6</sup> by MPR, a similar but less conservative adherence measurement than PDC. In our sample, patients with government and commercial insurance achieved higher adherence than in previous studies, suggesting that pharmacists in our integrated health system were successful in facilitating affordable treatment regardless of insurance status.

Literature has shown that high adherence is associated with clinical and financial outcomes, such as higher treatment success and lower total medical costs, whereas nonadherence to medications for chronic conditions overall has been associated with 30% to 50% of treatment failures.<sup>33</sup> Adults with higher adherence are more likely to have lower RA disease activity and are less likely to experience disease flares.<sup>10,34</sup> Moreover, among commercially insured adults with RA, patients with PDC of 0.80 or greater incurred lower net health care costs (excluding RA biologic medication costs) than patients with PDC less than 0.80.<sup>32</sup> Health systems and payers may be incentivized to participate in an integrated HSSP model given the evidence that high adherence to specialty medications for RA reduces nonpharmacy health care costs. Future research is warranted to explore the long-term impact of medication adherence on clinical and financial outcomes within an integrated HSSP.

Other barriers to medication adherence in patients with RA include disease and symptom severity, adverse effects, and negative perceptions about the medication.<sup>35</sup> Within our integrated HSSP, clinical pharmacists are essential members of the health care team and pharmacists can help patients overcome adherence barriers by providing them with comprehensive education, realistic expectations for treatment, and strategies to manage and mitigate adverse effects. Pharmacists can intervene during monthly refill calls and notify physicians of adherence problems through the EHR, streamlining the delivery of care and ensuring that patients are prescribed the best therapy and dosage to optimize treatment outcomes. This high-touch model, in which frequent patient interaction is emphasized, has previously been associated with high rates of medication adherence<sup>36,37</sup> and might have contributed to the high adherence seen in our sample.

Our study adds to existing literature by demonstrating rates of adherence and potential risk factors for nonadherence within an integrated HSSP. The high rates of adherence seen in our study contribute to the growing evidence of the benefit of the high-touch integrated HSSP model, which now accounts for 25% of all<sup>38,39</sup> accredited specialty pharmacies.<sup>4,11,13,40,41</sup> High adherence rates within the integrated HSSP model demonstrated in our study, and other disease states, are likely a result of many factors. These factors include persistent efforts to remove barriers to medication access and adherence; proactive monitoring for efficacy and adverse effects through frequent telephone follow-up and clinic visits; extensive patient education that may occur in person in the clinic or by audio and visual telehealth communications within our population; and seamless communication with providers within the EHR regarding completion of monitoring parameters needed for insurance medication approval, longitudinal assessment of patient response to therapy, and the need for treatment adjustments that optimize therapy.

### Limitations

Our study has limitations. As with all studies using claims data to measure medication adherence, medication fill history might not reflect a patient's medication-taking behavior, nor does it account for clinically relevant reasons for gaps in therapy. This study did not address primary nonadherence (how frequently a medication is prescribed and not filled) or medication persistence (the duration of continuous therapy following initiation), which are important outcomes to understand patient behavior regarding therapy initiation and discontinuation. Reasons for primary nonadherence, secondary nonadherence, and discontinuation may vary significantly. In this study, we used secondary nonadherence to evaluate patients' ability to administer prescribed therapy that had been deemed safe and appropriate by a prescriber. As a measure of adherence, we defined PDC using the observation window to the date of the last fill during which patients fill the prescriptions at the interval pharmacy. We note, however, that depending on PDC calculation methods, the results could be different. For example, if PDC had been defined

with a fixed interval by extending the observation window to the end of the study period, another commonly used method, mean PDC would be 0.85 and median (IQR) PDC would be 0.93 (0.75-1.00). As this method forces us to include an extended time period in the denominator (ie, larger denominator in the calculation), even though some patients were no longer able to fill at the internal pharmacy, it yields lower PDC values compared with those calculated with the last fill date as we defined it for this study. Because the time period when patients filled the prescriptions at the internal pharmacy is the only time period we know about patients' adherence behavior, the PDC with a fixed interval—which extends the observation period beyond the time a patient fills prescriptions with us—would not be an appropriate method of PDC calculation for our study; this method also brings the concept of persistence into the mix. Studies evaluating persistence are more likely to shed light on reasons a patient may no longer have fill data due to transitioning to external pharmacies or stopping therapy when it is no longer safe, appropriate, or feasible for the patient. The cross-sectional, retrospective cohort design does not allow us to interpret causality between patient services and medication outcomes. Also, clinical characteristics, such as disease severity scores (eg, DAS28), were not readily available for data extraction at the time of study. Therefore, clinical or sociodemographic characteristics beyond age and gender were not collected, although we expect that patients' disease severity and comorbid conditions might influence their adherence to specialty medications for RA. Implementing and quantifying the impact of interventions such as pharmacist verification and monitoring, medication education, insurance authorization and navigation, financial assistance enrollment, identifying and addressing barriers to adherence, and mitigation of adverse effects on adherence is an interesting consideration for future research.

## CONCLUSIONS

We found high rates of medication adherence and low out-of-pocket costs in patients with RA receiving care through an integrated HSSP, and adherence was higher in male patients, treatment-naïve patients, older patients, and patients with lower out-of-pocket costs. In a disease that can be effectively managed with specialty therapy, integrated specialty pharmacists prevent and address barriers to medication adherence through medication education and financial assistance support. Further work is needed to identify and support patients at risk of treatment nonadherence. ■

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