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ORIGINAL RESEARCH

Continuity of Care Within a Single Patient Support Program for Patients with Rheumatoid Arthritis Prescribed Second or Later Line Advanced Therapy

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ABSTRACT

Introduction: Guidelines suggest patients with rheumatoid arthritis (RA) inadequately controlled by tumor-necrosis-factor-inhibitors (TNFis) may benefit from switching to Janus-kinase-inhibitors (JAKis); however, care coordination and access can be complicated. Disruptions in transitioning to JAKi treatment could lead to disease flares requiring hospitalization; however, transitioning between products within the same patient support program (PSP) services aimed at ensuring continuity of care may minimize disruptions.

Methods: A retrospective, longitudinal cohort study of adult patients with RA newly prescribed JAKi following TNFi treatment in the Symphony Health claims database. Patients with baseline TNFi use and ≥ 6 months of data before (baseline) and after (follow-up) the initial JAKi claim (approved or denied) were included. Cohorts were defined by transitions between products within the same PSP [adalimumab (ADA) and upadacitinib (UPA)] or not. Disruptions were defined as gap in care ≥ 15 days due to failure/delay in receiving coverage approval or picking up an approved prescription. Disruptions followed by JAKi dispense were considered temporary and those without permanent. Odds ratios (ORs) of disruption and hospitalization were estimated from logistic regressions controlling for patient characteristics and treatment history.

Results: A total of 2371 patients were included: 317 transitioning from ADA-UPA, 321 TNFi-UPA, 860 ADA-another JAKi, and 873 another TNFi-another JAKi. Temporary and permanent disruptions increased odds of hospitalization by 47% and 123% (both $p < 0.05$). Temporary disruption rates were lowest for ADA-UPA patients (19%) compared to other TNFi-UPA (25%; OR = 1.46), ADA-other JAKi (29%; OR = 1.59), and other TNFi-other JAKi (31%; OR = 1.74), all $p < 0.05$. For transitions to UPA, temporary disruptions were lower for patients using the PSP (17%) versus not (24%; OR = 1.45, $p < 0.05$). No differences were found for permanent disruptions.

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Conclusion: Disruptions for patients with RA transitioning from TNFi to JAKi treatment are associated with increased hospitalization rates. Transitioning between drugs within the same PSP could lower the risk of disruption.

Keywords: Continuity of care; Disruptions; Hospitalizations; Janus kinase inhibitors; Rheumatoid arthritis; Transitioning; Patient support program; Portfolio

Key Summary Points

Why carry out this study?

Many rheumatoid arthritis (RA) patients do not respond optimally to tumor-necrosis-factor-inhibitor (TNFi) therapy and could benefit from Janus-kinase-inhibitor (JAKi) treatment; however, transitioning can be complicated for patients potentially leading to disruptions in care, disease flares, and hospitalizations.

Transitioning between treatments within consistent benefit verification and care coordination services, and patient support program (PSP) participation could help patients better navigate access to treatment.

What was learned from the study?

Disruptions in care are common for RA patients transitioning from TNFi to JAKi treatment, primarily due to delays in coverage approval and increase the risk of hospitalization.

Patients transitioning between treatments within consistent access to support services have the lowest risk of experiencing a disruption.

PSP participation is associated with lower disruption rates when transitioning to JAKi treatment with upadacitinib.

INTRODUCTION

Efforts to curb wasteful healthcare spending have increasingly focused on encouraging the use of high-value care and limiting the use of low-value interventions, to help patients make cost-efficient use of healthcare resources while optimizing patient centered outcomes [1–3]. Avoiding preventable hospitalizations in particular could substantially lower the clinical and economic burden to the healthcare system [4, 5]. For pharmaceutical services, a value-based approach encourages increasing access to cost-effective treatments through care coordination and reduced cost-sharing to improve adherence and consequently reduce costly emergency room visits and hospitalizations [6–8]. Understanding that patients often require sequential therapies to manage chronic medical conditions, products are sometimes offered in the same disease area with different mechanisms of action (MOA) in the hope that targeted, clinically indicated treatment will cost-effectively improve outcomes. However, cost management strategies implemented by payers may complicate access to advanced therapies [9, 10]. To facilitate access to prescribed treatment and to minimize some of the largest contributors to wasteful spending, support services may be available that can help patients address administrative complexity (including lack of standardized forms and procedures), care coordination (including benefit verification and specialty pharmacy assignment), and non-adherence [through patient support programs (PSPs), medication reminders, and copay assistance] [11, 12]. Understanding the value of such services for patients transitioning between treatments with consistent support and their potential to reduce inefficiencies in the treatment of chronic diseases could inform efforts to cost-efficiently lower the burden to the healthcare system and increase patient response.

Rheumatoid arthritis (RA), one of the most common chronic autoimmune diseases, incurs substantial burden, including increased hospitalization rates, especially for non-responders to first-line treatment [13–16]. Although targeted immunomodulator therapies (TIMs) are

effective in treating patients with RA, 30–40% of patients have an inadequate response to first-line treatment [typically tumor-necrosis-factor-inhibitor (TNFi) therapy], and patients who initially respond to first-line treatment may experience a loss of response over time [17–22]. For patients with inadequately controlled disease, guidelines recommend transitioning to a TIM with a different MOA, such as Janus-kinase-inhibitors (JAKis) for patients on TNFis, to improve their likelihood of achieving a response [23–25]. When a patient and provider make the shared decision that a change in treatment is appropriate, the transition can be complicated for patients, including navigating access to coverage, understanding financial implications, and logistics of initiating the new therapy, which can lead to treatment disruptions [26–30]. Evidence suggests utilization of support services can help patients initiate a new TIM faster and more successfully [27, 31].

AbbVie (North Chicago, IL, USA) offers both a TNFi [adalimumab (ADA)] and JAKi [upadacitinib (UPA)] in the treatment of RA, and provides support services across products, including benefit verification resources, education materials on both treatment and financial assistance options, and nurse ambassadors to provide individualized support in achieving treatment goals [32, 33]. As these services aim to minimize the burden of treatment transition, comparing the disruption rate when transitioning between ADA and UPA to that when transitioning between other TNFis and JAKis could provide insight into the value of such services in maintaining access to care for patients with RA undergoing a change in treatment.

The purpose of this study is to examine treatment disruption rates for patients with RA transitioning from TNFi to JAKi therapy, and the impact of (1) switching between products within the same support services where administrative complexity should be minimized and (2) participating in a PSP for patients transitioning to UPA (where enrollment data were available). To understand the importance of avoiding disruptions from a value-based care perspective, the study further evaluates the relationship between treatment disruptions around the time of transition and subsequent healthcare resource use (HRU), such as hospitalizations.

METHODS

Study Design and Data Sources

A retrospective, longitudinal cohort study was conducted using patient-level data from the Symphony Health (SH) administrative claims database from January 2018 through December 2020. The SH database collects information on medical and pharmacy claims from a geographically-diverse set of commercial and government (Medicare and Medicaid) electronic claims processors across the United States, including International Classification of Diseases, Tenth Revision diagnosis codes, dates of service, setting of care, National Drug Code numbers, and charge amounts. For a subset of patients, the SH database provides pharmacy claim lifecycle information, allowing for the observation of rejected and reversed claims, along with reasons for rejection. For ADA and UPA patients, SH claims have been linked with PSP enrollment records, details of which have been described previously [34]. Any risk associated with linked data content was evaluated by an external Health Insurance Portability and Accountability Act of 1996 statistician who certified patient anonymity of the resulting files. Because deidentification was conducted before providing claims to SH and PSP records to researchers, and no identifiable protected health information was included in the data used, Institutional Review Board approval was not required.

Study Population

Eligibility Criteria

Patients were included if they had their initial approved or denied JAKi claim (index date) on or after the UPA U.S. Food and Drug Administration approval date (August 16, 2019), had a medical claim with a diagnosis code for RA before or on the index date, had a dispensed

claim for TNFi treatment in the 6 months prior to the index date, and were at least 18 years old as of their index date [35]. Patients were also required to have at least one medical and pharmacy claim both 6 months before (baseline period) and after (follow-up period) the index date to proxy for eligibility coverage in the absence of an enrollment file.

Cohort Assignment

Patients who met the eligibility criteria were categorized into four mutually exclusive cohorts according to their TNFi and JAKi treatment type: ADA-UPA; other TNFi-UPA; ADA-other JAKi; and other TNFi-other JAKi. TNFis included ADA, certolizumab, etanercept, golimumab, and infliximab. JAKis included baricitinib, tofacitinib, and UPA. In a subgroup analysis of patients transitioning to UPA, cohorts were constructed based on PSP participation, defined as at least two interactions with a nurse ambassador within 30 days of the initial UPA claim.

Outcomes

Treatment disruption was defined as a gap of at least 15 days when transitioning from TNFi to JAKi treatment, where the start of the gap was the end of TNFi treatment (based on the date and days' supply of the last dispense), and the end of a gap was a successful JAKi dispense. Gaps could be due to failure to receive coverage approval, delay in receiving coverage approval, and/or failure to pick up an approved prescription. A 30-day window around the index date was used to evaluate gaps to assess disruptions specific to transitioning therapies, as opposed to, for example, a voluntary drug holiday. Temporary disruption was defined as a disruption with a subsequent JAKi dispensing during the 180-day follow-up period. Patients without a JAKi dispense during the follow-up period were considered to have a permanent disruption in transitioning to JAKi treatment. For patients with a temporary or no disruption, days from last TNFi use to JAKi initiation were calculated. For patients with a permanent disruption, the proportion returning to their original TNFi or transitioning to another TIM were descriptively summarized. For patients with data available on the index JAK claim, reasons for rejection were also descriptively summarized. HRU during the 180-day follow-up period was evaluated as the proportion of patients with a hospitalization, emergency visit, and outpatient visit, identified based on the location of service reported on medical claims.

Statistical Analyses

Demographics, comorbidities, corticosteroid and methotrexate use, and medical charges were evaluated in the baseline period and summarized using descriptive statistics [36]. TIM treatment history was assessed using all available data back to January 2018. Outcomes were evaluated using means, proportions, odds ratios (ORs), 95% confidence intervals (CIs) and p values where appropriate, with $p < 0.05$ considered statistically significant. Multivariable logistic models were used to estimate the odds of a disruption and hospitalization, controlling for baseline demographics, payer type, comorbidities, and RA treatment history. To evaluate the effect of PSP participation on odds of treatment disruption when transitioning to UPA, a logistic model with propensity score weighting was used to control for differences in baseline covariates [37]. All analyses were conducted using SAS software v.9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Sample Baseline Characteristics and Treatment History

The sample included 2371 patients transitioning from TNFi to JAKi: 317 from ADA to UPA, 321 from another TNFi to UPA, 860 from ADA to another JAKi, and 873 from another TNFi to another JAKi (Fig. 1). Among patients transitioning to UPA, 190 participated in the PSP and 448 did not. The cohorts were 78–85% female and had mean ages of 54–57 years old at the time of treatment transition (Table 1).

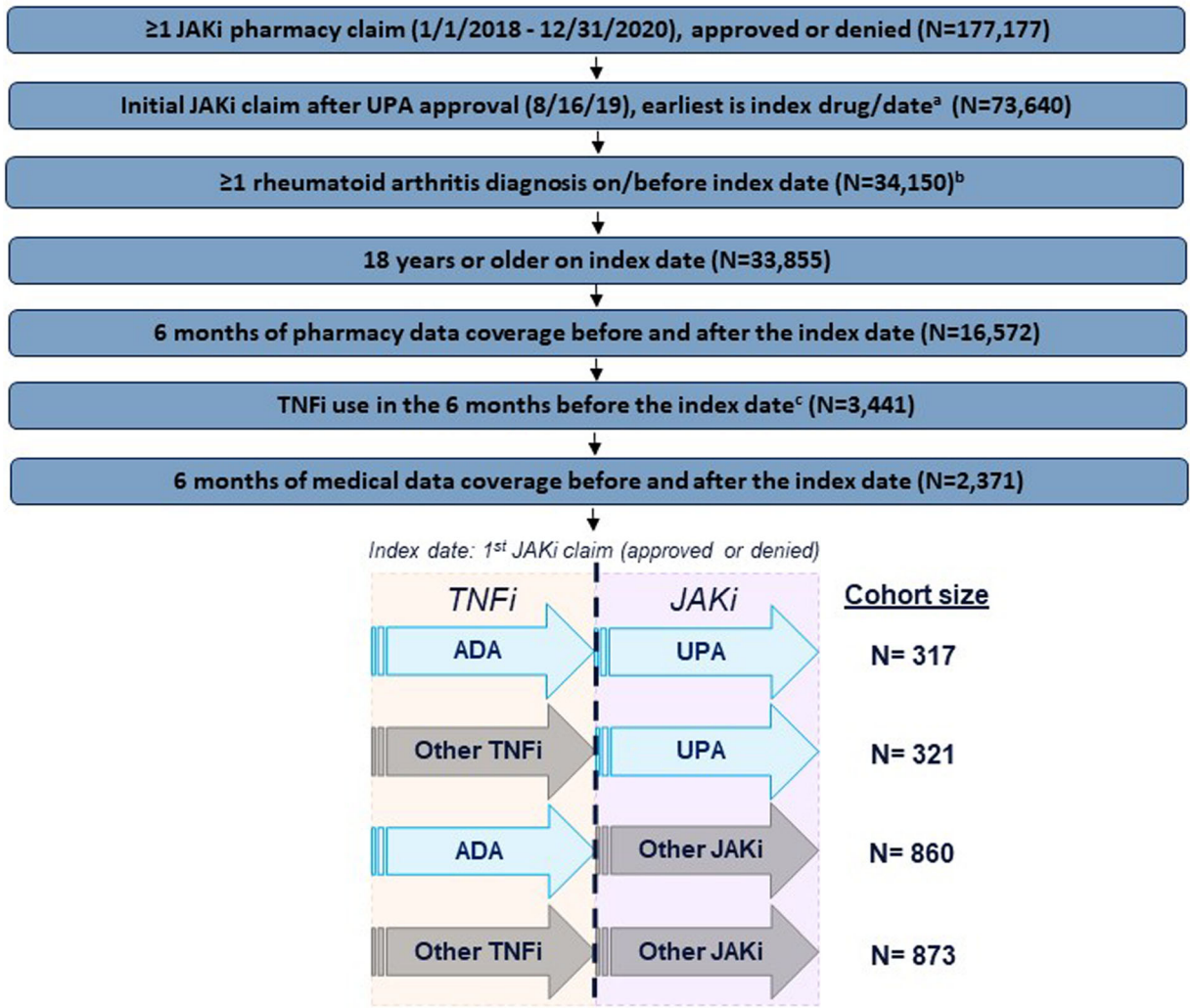


Fig. 1 Sample selection. [a]JAKis include baricitinib, tofacitinib, and UPA. Patients with claims for multiple JAKis on their index date are excluded ($n = 82$). [b]Excludes patients with no prior medical claim ($\sim$ 13 k) or who are taking a JAKi for a condition other than RA (e.g., tofacitinib for psoriatic arthritis or ulcerative colitis). [c]Not necessarily 1st line use, as patients may be naïve or experienced prior to baseline TNFi use. TNFis include ADA, certolizumab, etanercept, golimumab, and infliximab. Patients with claims for multiple targeted immunomodulator therapies during the baseline period are excluded ($n = 597$). *ADA* adalimumab, *JAKi* Janus-kinase inhibitor, *RA* rheumatoid arthritis, *TNFi* tumor-necrosis-factor inhibitor, *UPA* upadacitinib

Approximately two-thirds of patients had commercial insurance coverage, a quarter were covered by Medicare and roughly 10% had Medicaid insurance on their initial JAK claim. Mean baseline medical charges and the proportions of patients with baseline corticosteroid and methotrexate use were similar across cohorts, although no statistical testing was conducted.

Disruptions in Transitioning from TNFi to JAKi Treatment

One in three patients (33%) transitioning from TNFi to JAKi treatment experienced any disruption in treatment; 28% with a temporary disruption and 6% with a permanent disruption (Fig. 2). Patients with a temporary disruption had a median time to JAKi initiation of 27 days,

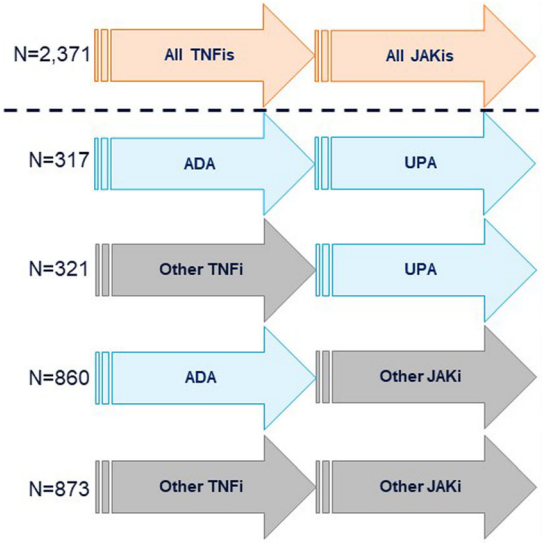
Table 1 Baseline characteristics

Characteristic, *n* (%)	ADA → UPA	Other anti-TNF → UPA	ADA → Other JAK	Other anti-TNF → other JAK
n	317 (13%)	321 (14%)	860 (36%)	873 (37%)
Demographics				
Age (mean)	56.9	57.0	53.9	55.1
Sex				
F	254 (80%)	274 (85%)	670 (78%)	707 (81%)
M	63 (20%)	47 (15%)	190 (22%)	166 (19%)
Year of index claim				
2019	106 (33%)	90 (28%)	452 (53%)	473 (54%)
2020	211 (67%)	231 (72%)	408 (47%)	400 (46%)
Primary payer				
Assistance program	5 (2%)	2 (1%)	16 (2%)	5 (1%)
Cash	1 (0%)	0 (0%)	1 (0%)	1 (0%)
Commercial	209 (66%)	202 (63%)	568 (66%)	557 (64%)
Medicaid	27 (9%)	23 (7%)	108 (13%)	115 (13%)
Medicare	75 (24%)	94 (29%)	167 (19%)	195 (22%)
Treatment and health history				
Months from 1st RA TIM claim (mean)	15.2	18.7	14.2	15.5
Minimum number of prior TIMs for RA				
1	256 (81%)	214 (67%)	687 (80%)	636 (73%)
2	54 (17%)	75 (23%)	161 (19%)	203 (23%)
3+	7 (2%)	32 (10%)	12 (1%)	34 (4%)
Other prior treatments for RA				
Corticosteroid use	199 (63%)	199 (62%)	511 (59%)	534 (61%)
Methotrexate use	125 (39%)	116 (36%)	343 (40%)	316 (36%)
Charlson Comorbidity Index (mean)	1.44	1.30	1.32	1.31
Total medical charges (mean)	$12,010	$12,324	$12,236	$11,428

Demographics assessed using the most recently available data as of the index date. Only birth year available for calculating age. Treatment history evaluated prior to the index date (i.e., initial JAKi claim) back to Jan. 2018; comorbidities and charges during the 6-month baseline period

JAKis include baricitinib, tofacitinib, and UPA. TNFis include ADA, certolizumab, etanercept, golimumab, and infliximab

ADA adalimumab, *JAKi* Janus-kinase inhibitor, *RA* rheumatoid arthritis, *TIM* targeted immunomodulator therapy, *TNFi* tumor-necrosis-factor inhibitor, *UPA* upadacitinib



	Temporary disruption in transition to JAKi			Permanent disruption in transition to JAKi		
	%	Odds ratio	95% CI	%	Odds ratio	95% CI
All TNFis → All JAKis	28%	-	-	6%	-	-
ADA → UPA	19%	*Ref.*	*Ref.*	6%	*Ref.*	*Ref.*
Other TNFi → UPA	25%	1.46*	1.00–2.15	7%	1.10	0.58–2.12
ADA → Other JAKi	29%	1.59*	1.16–2.20	5%	0.79	0.45–1.42
Other TNFi → Other JAKi	31%	1.74*	1.27–2.40	6%	0.87	0.50–1.55

Fig. 2 Temporary and permanent disruptions in transitions to JAKi[a,b]. [a]Disruptions were defined as a gap in care ≥ 15 days due to failure/delay in receiving coverage approval or picking up an approved prescription. Disruptions followed by JAKi dispense were considered temporary and those without permanent. [b]JAKis include baricitinib, tofacitinib, and UPA. TNFis include ADA, certolizumab, etanercept, golimumab, and infliximab. *$p < 0.05$ from a logistic multivariate regression controlling for patient demographics, payer type, baseline comorbidities, and treatment history. *ADA* adalimumab, *CI* confidence interval, *JAKi* Janus-kinase inhibitor, *TNFi* tumor-necrosis-factor inhibitor, *UPA* upadacitinib

compared with 9 days for patients without a disruption. For patients with a permanent disruption in transitioning to JAKi treatment, 25% returned to their original TNFi treatment, 31% transitioned to another TIM, and 42% had no TIM treatment. Disruptions were most common for patients with Medicaid coverage (40%), followed by patients with Medicare (32%) and those commercially-insured (31%) (Supplementary Material Fig. S1). For patients with data available on reasons for denial ($n = 95$), 92% had JAKi coverage rejected due to formulary restrictions, most commonly for prior authorization requirements (Supplementary Material Fig. S2).

Patients transitioning treatments within the same support services experienced the lowest rate of temporary disruptions (19% for ADA-UPA vs. 25% for other TNFi-UPA, 29% for ADA-other JAKi, and 31% for other TNFi-other JAKi), while the permanent disruption rate was similar across cohorts (Fig. 2). Adjusting for baseline characteristics, payer type, comorbidities, and treatment history, odds of a temporary disruption were 46% (OR = 1.46; 95% CI = 1.00–2.15; $p < 0.05$), 59% (OR = 1.59; 95% CI 1.16–2.20; $p < 0.05$), and 74% (OR = 1.74; 95% CI 1.27–2.40; $p < 0.05$) higher for other TNFi-UPA, ADA-other JAKi, and other TNFi-other JAKi, respectively, relative to ADA-UPA. No significant differences were found across cohorts in the odds of a permanent disruption in transitioning to JAKi treatment.

In the subgroup analysis of patients transitioning to UPA (where PSP data were available), participation in the PSP was associated with reductions in the disruption rate when transitioning. Rates of temporary and permanent disruptions were lowest for patients engaged with the PSP relative to those transitioning without PSP support (17% vs. 24% for temporary; 5% vs. 7% for permanent) (Fig. 3). After

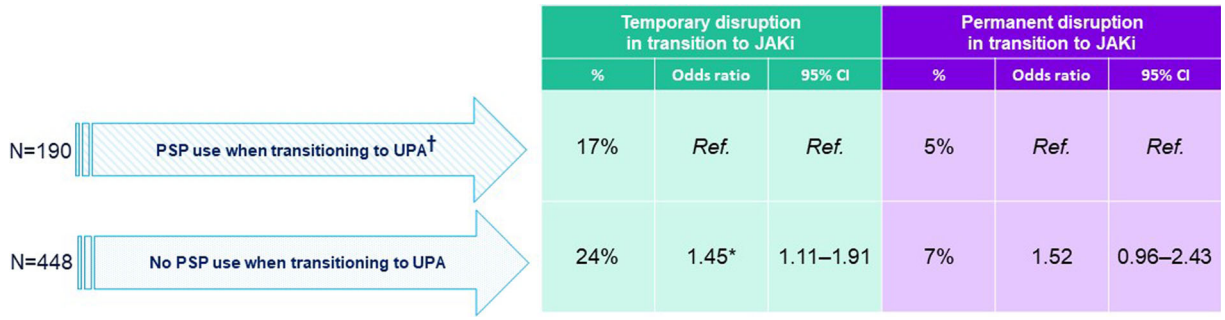


Fig. 3 Subgroup analysis of transitions to UPA; temporary and permanent disruptions based on PSP participation[a,b]. [a]Disruptions were defined as a gap in care ≥ 15 days due to failure/delay in receiving coverage approval or picking up an approved prescription. Disruptions followed by JAKi dispense were considered temporary and those without permanent. [b]Includes the subgroup of patients transitioning to UPA from any TNFi; data on PSP participation were not available for other JAKIs. †PSP defined as ≥ 2 engagements with a Nurse Ambassador within 30 days of the initial UPA claim. *$p < 0.05$ from a logistic regression with inverse-probability-of-treatment-weighting, in which propensity scores are generated using patient demographics, payer type, baseline comorbidities, treatment history, and prior TNFi. *CI* confidence interval, *JAKi* Janus-kinase inhibitor, *PSP* patient support program, *TNFi* tumor-necrosis-factor inhibitor, *UPA* upadacitinib

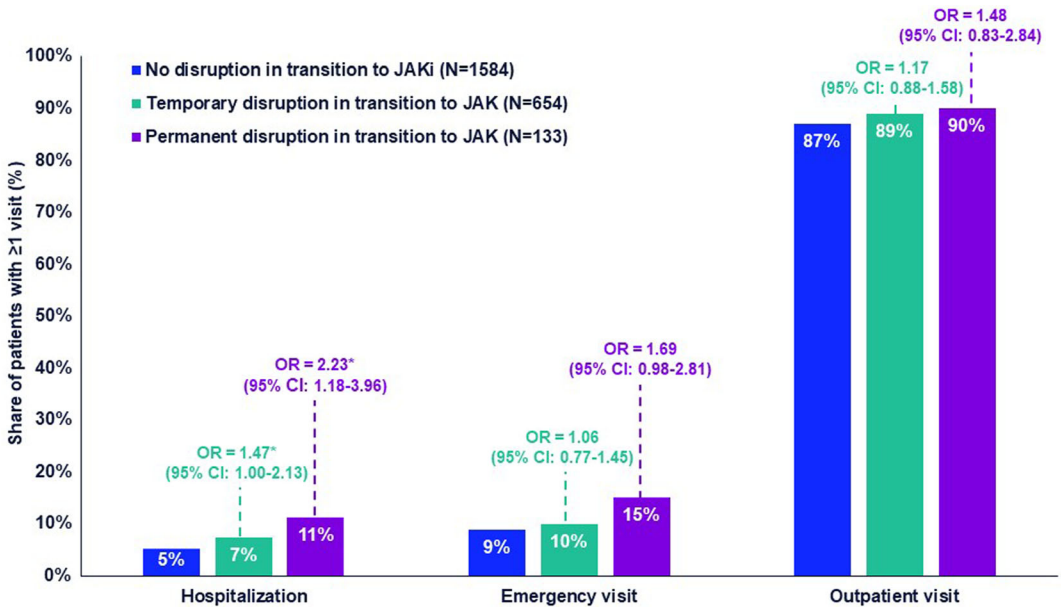


Fig. 4 Healthcare resource use[a,b]. [a]Disruptions were defined as a gap in care ≥ 15 days due to failure/delay in receiving coverage approval or picking up an approved prescription. Disruptions followed by JAKi dispense were considered temporary and those without permanent. [b]Odds ratio estimates from a logistic multivariate regression controlling for patient demographics, payer type, comorbidities, and treatment history. *$p < 0.05$ in two-sample *t* tests or chi-squared tests, and from multivariable regressions where noted, with no disruption as the reference group. *CI* confidence interval, *JAKi* Janus-kinase inhibitor

adjustment, transitioning to UPA without PSP support significantly increased the odds of temporary disruption by 45% (OR = 1.45; 95% CI = 1.11–1.91; $p < 0.05$) and numerically (but not statistically significantly) increased the odds of permanent disruption by 52% (OR = 1.52; 95% CI = 0.96–2.43; $p > 0.05$).

Healthcare Resource Use

Relative to patients without a disruption, patients with a temporary disruption in transitioning from TNFi to JAKi treatment had higher follow-up HRU on all measures, which were further increased for patients with a permanent disruption (Fig. 4). A greater proportion of patients with a temporary or permanent versus no disruption had a hospitalization (7.3% and 11.3% vs. 5.3%) and an emergency visit (9.9% and 15.0% vs. 8.8%) during the follow-up period. After adjustment, the odds of hospitalization were 47% higher (OR = 1.47; 95% CI = 1.00–2.13; $p < 0.05$) for a temporary disruption and 123% higher (OR = 2.23; 95% CI = 1.18–3.96; $p < 0.05$) for permanent disruption relative to no disruption. Odds of an emergency visit (OR = 1.06; 95% CI = 0.77–1.45; $p > 0.05$ for temporary disruption; OR = 1.69; 95% CI = 0.98–2.81; $p > 0.05$ for permanent disruption) and outpatient visit (OR = 1.17; 95% CI = 0.88–1.58; $p > 0.05$ for temporary disruption; OR = 1.48; 95% CI = 0.83–2.84; $p > 0.05$ for permanent disruption) were not statistically significantly different from experiencing no disruption.

DISCUSSION

Summary of Findings

Extensive evidence supports the clinical benefits of transitioning to a TIM with a different MOA for patients with uncontrolled RA; however, research is limited on heterogeneity in the transitioning experience regarding the time to and rate of successful initiation of the new advanced therapy [21, 23]. The findings presented here provide novel evidence on the frequency and consequences of disruptions in treatment when transitioning from TNFi to JAKi therapies. In addition, with the recent approval of UPA in RA, this study examined for the first time the impact of transitioning between products within consistent support services and of UPA PSP participation.

The results of this analysis demonstrate that disruptions are common, and are most often temporary, resulting in delayed receipt of JAKi treatment as patients await coverage approval. Transitioning between products within consistent support services is associated with a lower disruption rate, as is PSP participation. Both temporary and permanent disruptions in transitioning from TNFi to JAKi treatment were associated with higher risk of hospitalization. These findings inform the potential benefits of multiple MOA options within consistent support services in maintaining continuity of care when transitioning treatments for RA.

Disruptions and Associated Burden

Studies on adherence to RA TIM treatment often focus on measures of primary (i.e., abandonment) and secondary adherence (i.e., persistence on treatment); however, disruptions in care when transitioning treatments due to failure to receive coverage approval, delay in receiving coverage approval, and/or failure to pick up an approved prescription, can also affect disease management and patient outcomes [29, 30, 38]. The results presented here demonstrate that such disruptions are common when transitioning from TNFi to JAKi treatment, and add burden to the healthcare system by increasing odds of hospitalization by 47% and 123% following temporary and permanent disruptions, respectively.

Most disruptions were temporary, indicating that patients received the JAKi treatment, but after a median delay of 27 days from when the prescription was written, during which time disease symptoms could worsen and require hospitalization. Prior research showed that disruptions in RA treatment of even two weeks correlate with increases in joint stiffness and pain, but subsequent HRU was not examined

[39]. A recent study on treatment interruptions during the COVID-19 pandemic for patients with rheumatic conditions found that a gap in treatment (for non-COVID-19 patients) increased the odds of hospitalization in the following 90 days by 20% [40]. Although reasons for rejection were only available for a small subset of the sample in this analysis, the finding that coverage restrictions are causing unnecessary delays in JAKi treatment initiation is consistent with what has been observed for other high-cost drugs [9].

Multiple MOAs Within Consistent PSP Services as High-Value Care

It has long been recognized that adherence to treatments for RA, and other chronic diseases is suboptimal and leads to increased HRU, especially emergency visits and hospitalizations [41–43]. A value-based care approach to pharmaceutical treatments encourages innovative interventions that improve access and adherence to advanced therapies [6–8]. Despite guidelines recommending that patients with inadequately controlled RA on TNFis may benefit from switching to JAKis [23–25], studies have found that more than 60% of patients cycle through TNFis instead of transitioning to an advanced therapy with a different MOA [44–46]. This is concerning from a value-based care perspective, as patients who do transition to a different MOA have longer persistence, better disease control, and lower healthcare costs than TNFi cyclers, suggesting that initiatives to facilitate transitions between TNFi and JAKi treatment could improve outcomes for patients and payers [44–47].

Multiple MOAs provide a variety of options to prescribers for treatment management, which is of particular importance in RA, where the majority of patients do not achieve their treatment goals on first-line TIM therapy, yet transitioning to a new MOA can be challenging. Benefits of transitioning between products within the same support services may include familiarity with the specialty pharmacy network, benefit verification resources, and financial assistance options. PSP services can provide additional support to help patients access and initiate their prescribed treatment. Comprehensive PSPs can help patients navigate insurance coverage requirements and assist with appealing denied coverage. Prior research has shown that participation in a PSP reduces both the abandonment rate and the time to initiation of ADA for patients with RA [27, 31]. The PSP studied here has previously been shown in TIM-naïve populations to improve access to care, reduce abandonment, and increase adherence and persistence; the last of which in particular is associated with a reduced risk of hospitalizations [27, 31, 34, 48]. The results of the current study provide novel evidence on the benefits of transitioning between products within consistent support services, and of PSP participation during treatment transition when the risk of a disruption is particularly high for a TIM-experienced population.

Strengths and Limitations

Strengths of this study include the use of a large, all-payer database that, in addition to providing longitudinal patient-level claims for observing treatment history and patterns, allows for insights into denied and abandoned prescriptions often not available in claims databases. Additional strengths include leveraging a novel database linking effort to directly examine the role that PSP participation plays in improving patient outcomes and providing the first evidence on treatment transitions between products within the same support services given the recency of UPA approval. As with all retrospective studies, limitations of the data sources and study design should be noted, many of which have been previously reported, including the lack of an enrollment or eligibility file for the SH database [34]. Being an observational study, statistical analyses can examine associations between cohorts and outcomes of interest, but true causality may not be established. Furthermore, an important limitation of any cohort study is the potential for selection bias (i.e., patients prescribed a particular treatment and/or participating in the PSP may differ from others on characteristics not observable in the data, but related to the outcomes assessed). To address this

concern, multivariate models of treatment disruptions and hospitalizations controlled for an extensive list of patient characteristics and treatment history, but bias could remain. In addition, propensity-score weighting was used to balance covariates that could be predictive of PSP enrollment, with weighted standardized differences well within acceptable limits (< 0.1); however, adverse selection is still a concern (Supplementary Material Table S1) [49]. Similarly, there may be heterogeneity in the benefits of both switching between products within consistent support services and participating in the PSP, which the current sample was too limited to examine; however, whether efforts to improve continuity of care could help vulnerable and difficult-to-treat subpopulations in particular should be an area of further research. Additionally, limited data were available to assess HRU outcomes stratified by treatment cohort, which should be topics of further research as data accrue. Another limitation was the definition of treatment disruption. While there is no single threshold of disruption that has been established as clinically meaningful in RA, prior studies have found that (1) disruptions in the regular course of RA treatment typically last 2 weeks or less but are correlated with increases in joint stiffness and pain, (2) patients initiating ADA without PSP support took 2 weeks on average to fill, and (3) 15-day gaps are predictive of risk of hospitalization in other chronic diseases [31, 39, 50, 51]. No other TNFi and JAKi pair in RA had consistent services across products to provide a benchmark for the results seen for ADA to UPA patients, and information on PSP participation and specialty pharmacy use for patients treated with other products was not available, though this should be examined pending future approvals. Lastly, findings may not be generalizable to other support services, disease areas, or treatment transitions other than the TNFi to JAKi transition for patients with RA.

CONCLUSIONS

Guidance recommends transitioning TNFi patients with uncontrolled RA to JAKi therapy; however, the frequency and consequences of disruptions during transition have not been well characterized. This study provides novel evidence that disruptions are common and are associated with substantial increases in hospitalizations. The recent approval of UPA provides the first opportunity to examine how outcomes differ when transitioning between treatments within consistent support services, where administrative complexity and access hurdles may be minimized. The results show that patients transitioning from ADA to UPA have the lowest disruption rate among all TNFi to JAKi transitions. Participation in a PSP that can help patients navigate coverage requirements to initiate prescribed treatment sooner and more successfully was also associated with lower disruption rates for transitions to UPA. These findings provide new evidence on the hurdles patients with RA face when transitioning treatments, and the potential benefits of transitioning between products within consistent support services in reducing disruptions and subsequent HRU. Future research should examine specific aspects of support services associated with improved outcomes and the benefits of consistent support services across different MOAs and PSPs in additional treatment areas.

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Compliance with Ethics Guidelines. This article does not contain any studies with human participants or animals performed by any of the authors. Database permission was obtained via a license from the provider; however, the database is otherwise not publicly available. Any risk associated with linked data content was evaluated by an external Health Insurance Portability and Accountability Act of 1996 statistician who certified patient anonymity of the resulting files. Because deidentification was conducted before providing claims to SH and PSP records to researchers, and no identifiable protected health information was included in data used, Institutional Review Board approval was not required.

Data Availability. The claims data used in this study may be licensed from Symphony Health. The datasets analyzed in the current study that linked claims data with patient support program records are not publicly available as patient support program participation records are proprietary and confidential.

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