Adherence to Subcutaneous Biologic Therapy Among Patients With Inflammatory Bowel Disease and Rheumatoid Arthritis: Impact of Therapy Management

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BACKGROUND

- Rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) are both chronic autoimmune diseases associated with significant morbidity, activity limitations, reduced quality of life, and financial burden[1,2]
- For patients with RA and IBD who are unable to manage their disease with conventional agents, biologic treatment has become the standard of care for management of moderate to severe disease activity[3,4]
- Evidence indicates that long-term use of biologics is challenging, and many factors complicate adherence to biologic treatment, including switching therapies, route of administration (injection or infusion), cost of treatment, new or worsening side effects, and loss of treatment effectiveness over time. Due to these issues, adherence estimates in both RA and IBD are suboptimal[5-6]
- Various clinical initiatives aim to identify risk factors for noncompliance to optimize adherence for patients on biologic therapy[6,7]
- This study aimed to identify factors related to adherence of subcutaneous biologic treatment for patients who were enrolled in a Therapy Management program

METHODS

Data Sources

- This was a retrospective claims analysis employing Fairview Health System Specialty Pharmacy Dispensary Data (12/1/2012-10/31/2017) and Therapy Management Program Databases (1/1/2016-10/31/2017)

Inclusion Criteria

- Diagnosis of RA or IBD (Crohn's disease or Ulcerative colitis)
- First evidence of receiving an eligible subcutaneous biologic therapy (adalimumab, abatacept, certolizumab pegol, etanercept, golimumab, tocilizumab, ustekinumab) during the Therapy Management enrollment period

Exclusion Criteria

- Diagnosis of >1 inflammatory disease state

Fairview Therapy Management Program

- Disease-specific therapy management programs aim to improve adherence by providing patients with knowledge about their disease and associated medications, minimizing side effects, and breaking down barriers to therapy continuation
- A clinical contact, or participation in the Therapy Management program, was defined as completion of ≥1 telephonic visit (≥1 contact) with a nurse or pharmacist
- Initial assessments involve counsel with a pharmacist to identify any drug-related problems
- Follow-up assessments take place with either a pharmacist or nurse who assesses side effects, pain, dose appropriateness, and evaluates medication adherence and persistence
- All patients, regardless of Therapy Management participation, are contacted before the initiation of a specialty pharmacy medication and before each refill. This study evaluated patients with clinical contacts, designated as "≥1 contact," and patients without clinical contacts, designated as "no contact"
  - Therapy Management Program Databases span from 1/1/2016 to 10/31/2017. Prior to March 2016, all clinical consults were documented on paper; thus, they were not retrievable and not counted as a contact

ANALYSES

Demographics

- Adherence was defined using proportion of days covered (PDC); patients indicating PDC ≥0.80 were defined as adherent, and the remainder were defined as nonadherent
- Biologic-naïve status was defined by a 6-month period prior to the initiation of Therapy Management with no evidence of pharmacy fills for study-eligible biologics
- Statistically significant differences were tested using either student's *t* test or chi-square analyses

Logistic Regressions

- Adherence served as the dependent variable in modeling, and predictor variables included patient age, sex, biologic experience status, disease state, and Therapy Management participation
- Therapy Management participation was dichotomized to those patients who had no clinical assessments (no contact) and those patients who had ≥1 clinical assessment (≥1 contact)
- An interaction term between biologic experience status (naïve vs experienced) and Therapy Management participation (no contact vs ≥1 contact) was entered into the final adherence model to better understand how adherence may vary between combinations of these groups (eg, biologic-naïve/no clinical contact vs biologic-naïve patients or no clinical contact patients)
- By including the interaction term, analyses allowed exploration of the distinct relationships that biologic-naïve or biologic-experienced status and Therapy Management participation have on adherence

RESULTS

Demographics (Table 1)

- The entire sample consisted of 3,248 patients: 2,116 with RA and 1,132 with IBD
- IBD patients were younger (40.7 vs 51.3 years; *P* <0.01) and more likely to be male (49.6% vs 26.8%; *P* <0.01)
- Patients primarily resided in the Midwest region of the United States

Table 1. Patient Demographics

	Full sample n = 3,248	RA n = 2,116	IBD n = 1,132	*P* value
Gender, n (%)				<0.01
Male	1,129 (34.8)	568 (26.8)	561 (49.6)	
Age, mean (SD)	47.6 (13.3)	51.3 (11.7)	40.7 (13.4)	<0.01
18-29 years, n (%)	441 (13.6)	132 (6.2)	309 (27.3)	
30-49 years, n (%)	1,153 (35.5)	657 (31.0)	496 (43.8)	
50-64 years, n (%)	1,483 (45.7)	1,187 (56.1)	296 (26.1)	
≥65 years, n (%)	171 (5.3)	140 (6.6)	31 (2.7)	
Region, n (%)				<0.01
Northeast	32 (1.0)	18 (0.9)	14 (1.2)	
Midwest	2,954 (90.9)	1,902 (89.9)	1,052 (92.9)	
South	91 (2.8)	65 (3.1)	26 (2.3)	
West	171 (5.3)	131 (6.2)	40 (3.5)	

SD, standard deviation.
Note: statistical comparisons were performed between the RA and IBD groups.

Clinical Factors (Table 2)

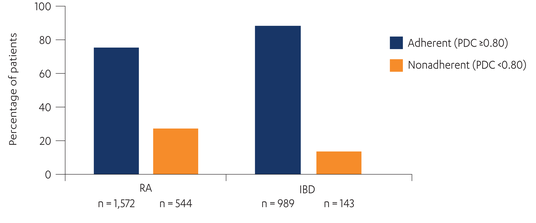
- Most patients (78.8%), regardless of disease state, were adherent (PDC ≥0.80) to biologic therapy
- While adherence was high for both groups, a higher percentage of IBD patients met the PDC ≥0.80 threshold compared to RA patients (87.4% vs 74.3%; *P* <0.01; **Figure 1**)
- A greater proportion of IBD patients were biologic-naïve compared to RA patients (66.3% vs 57.6%; *P* <0.01; **Figure 2**)
- Therapy Management participation was similar across both groups (**Figure 3**)

Table 2. Clinical Factors

	Full sample n = 3,248	RA n = 2,116	IBD n = 1,132	*P* value
Adherence, n (%)				<0.01
Adherent (PDC ≥0.80)	2,561 (78.8)	1,572 (74.3)	989 (87.4)	
Nonadherent (PDC <0.80)	687 (21.2)	544 (25.7)	143 (12.6)	
Biologic experience status, n (%)				<0.01
Biologic-naïve	1,970 (60.7)	1,219 (57.6)	751 (66.3)	
Biologic-experienced	1,278 (39.3)	897 (42.4)	381 (33.7)	
Fairview Therapy Management, n (%)				n.s.
No contact	1,510 (46.5)	960 (45.4)	550 (48.6)	
≥1 contact	1,738 (53.5)	1,156 (54.6)	582 (51.4)	

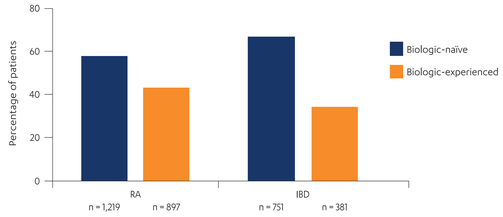
n.s., not statistically significant.
Note: Statistical comparisons were performed between the RA and IBD groups.

Figure 1. Adherence in RA and IBD patients.*



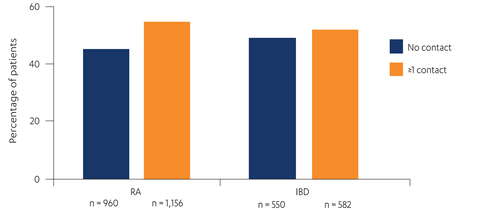
*P <0.01.

Figure 2. Biologic experience status in RA and IBD patients.*



*P <0.01.

Figure 3. Therapy Management participation in RA and IBD patients.*



*P = 0.08.

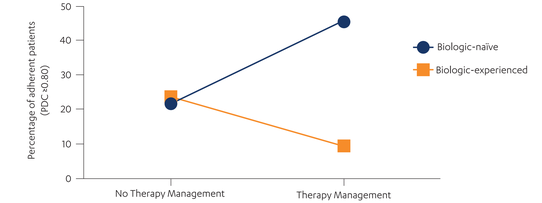
Logistic Regression Results

- In the logistic regression model, factors significantly associated with adherence (PDC ≥0.80) included IBD diagnosis (odds ratio [OR]: 2.9), age (50-64 years, OR: 2.0; ≥65 years, OR: 3.2), and biologic-naïve status (OR: 2.3; all *P* <0.01; **Table 3**)
- The interaction between biologic experience status and Therapy Management participation indicates that biologic-naïve patients with ≥1 clinical Therapy Management contact were 2.6 times more adherent than biologic experienced patients with ≥1 clinical Therapy Management contact (OR: 2.6; *P* <0.001; **Table 3**; **Figure 4**)

Table 3. Results of the Logistic Regression Model

Variable	OR	95% confidence limits
Gender (female vs male)	0.865	0.709, 1.054
Biologic experience status (naïve vs experienced)	2.254	1.731, 2.953
Therapy Management (no contact vs ≥1 contact)	0.686	0.520, 0.907
Age (18-29 years) vs		
Age (30-49 years)	1.084	0.809, 1.447
Age (50-64 years)	2.017	1.491, 2.720
Age (≥65 years)	3.200	1.904, 5.570
Diagnosis (IBD vs RA)	2.883	2.298, 3.640
Interaction (level of biologic experience × level of Therapy Management)	2.645	1.818, 3.843

Figure 4. Effect of Therapy Management and biologic experience status among adherent RA and IBD patients (n = 2,561).



- In the subsample of adherent patients (PDC ≥0.80), Therapy Management clinical contact had a profound effect on adherence in biologic-naïve patients compared to biologic-experienced patients, overall and in both disease states (*P* <0.01 in **Table 4**; **Figure 4**)

Table 4. Effect of Therapy Management and Biologic Experience Status in Adherent Patients (PDC ≥0.80)

	Full sample n = 2,561	RA n = 1,572	IBD n = 989	*P* value
No Therapy Management, n (%)				
Naïve	556 (21.7)	289 (18.4)	267 (27.0)	n.s.
Experienced	602 (23.5)	386 (24.6)	216 (21.8)	
Therapy Management, n (%)				
Naïve	1,162 (45.4)	755 (48.0)	407 (41.2)	<0.01
Experienced	241 (9.4)	142 (9.0)	99 (10.0)	

Limitations

- The study data only include self-administered subcutaneous biologic medications. Some patients may have received intravenous (ustekinumab, vedolizumab, infliximab) or oral (tofacitinib) therapy, which could affect PDC calculations
- The study data did not include a patient eligibility file; eligibility was estimated using a proxy
- The study did not include clinical factors likely to impact adherence, such as duration of illness, severity of illness, comorbidities, and surgeries
- Analyses were restricted to patients within the Fairview Pharmacy System; therefore, results may not be generalizable to all RA or IBD patients participating in similar Therapy Management programs

CONCLUSIONS

- **Regardless of Therapy Management participation, a high percentage of RA and IBD patients was adherent (79% of patients overall) to subcutaneous biologic therapy. High adherence across disease states may be influenced by the standard, nonclinical, Fairview Specialty Pharmacy contact that occurs for all patients before the initiation of a specialty pharmacy medication and before each drug refill**
- **Disease state, age, prior biologic use, and Therapy Management participation were all significant predictors of adherence in this population**
- **The significant interaction term suggests that Therapy Management participation was associated with improved adherence for those patients who were biologic-naïve compared to biologic-experienced (Table 3; Figure 4). Lower adherence in biologic-experienced patients could be due to drug holiday–related life events, such as surgeries, infections, and pregnancies**
- **Additional studies are necessary to understand the association of lower adherence with biologic-experienced patients in the Therapy Management program. It is possible that these patients have higher disease activity/severity, more life events, or other factors that affect adherence, and that these patients seek out therapy management in an effort to better control their disease severity**

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CONFLICTS OF INTEREST

TD, AA, JNL, and CR are employees of Health Analytics, LLC. JP and WB are employees of Janssen Scientific Affairs, LLC. HB, AM, and MS are employees of Fairview Pharmacy Services.

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