

Predictors of Non-Adherence with Anti-Rheumatic Medication in Rheumatoid Arthritis Patients: Results from the Ontario Best Practices Research Initiative

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Background: Despite the availability of safe and effective treatments and the establishment of treatment guidelines, real-world effectiveness remains suboptimal largely due to low patient adherence with prescribed treatment. The purpose of this study was to systematically evaluate sociodemographic, health insurance, and disease-related factors associated with non-adherence with anti-rheumatic medications (ARM) in a large observational cohort of RA patients followed in Canadian routine clinical care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) clinical registry and had at least two years of follow-up were included in the analysis. Non-adherence with treatment was defined as ARM discontinuation due to the patient non-adherence. Independent predictors of non-adherence with ARM were evaluated with multivariate cox-regression using both time-fixed and time-dependent variables. Factors considered included patient sociodemographics (age, gender, race, education status, annual income, smoking history), health insurance information (private vs. non-private, % coverage), disease parameters (RA duration, presence of erosion, RF positivity, DAS28, physician global, HAQ-DI, number of comorbidities), types of medications used, and physician characteristics (gender, academic position, urban vs. rural, distance from patient's residence).

Results: A total of 1,762 patients were included in the analysis with a mean (SD) age of 57.4 years and disease duration of 8.5 (9.3) at the time of enrolment to the registry (baseline). At baseline, the majority of patients were female (77.7%), Caucasian (85.1%), had post-secondary education (55.3%), and had private insurance (67.2%). In terms of disease severity, 54.5% had a prior erosion, 69.5% were RF positive, and mean (SD) DAS28 was 4.5 (1.5).

Table 1 shows the association between all factors considered in the analysis and non-adherence with ARM. In multivariate analysis, unmarried status, RF positivity and higher number of comorbidities were identified as significant predictors of increased adherence while higher physician global score, NSAID use, and polypharmacy were associated with non-adherence.

Conclusion: In this systematic approach to identify factors associated with patient non-adherence with ARM, a variety of factors encompassing sociodemographic, disease, and medication characteristics, were identified as significant independent predictors of non-adherence. These results should be taken into consideration when developing patient adherence support programs and in the choice of treatment regimens.

Table 1: Independent Predictors of Patient Non-Adherence with ARM

	HR (95% CI), p-value		
	Univariate analysis	Multivariate saturated analysis	Backward stepwise regression analysis
<u>Sociodemographics</u>			
Age	0.99 (0.98-0.99), 0.03	1.24 (1.02-1.51), 0.03	-
Female gender, n (%)	1.09 (0.85-1.38), 0.50	-	-
Marital status, n (%)			
- Married	Ref	Ref	Ref
- Single/widowed/divorced	0.82 (0.67-1.00), 0.05	0.72 (0.55-0.95), 0.02	0.73 (0.56-0.96), 0.02
Race, n (%)			
- Caucasian (white)	Ref	-	-
- Non-Caucasian	1.04 (0.75-1.43), 0.83		
Education status, n (%)			
- High school or less	Ref	Ref	-
- Post-secondary	1.20 (0.98-1.46), 0.07	1.10 (0.85-1.43), 0.47	
Annual Income class during follow-up, n (%)			
- < \$ 50,000	Ref	-	-
- ≥ \$50,000	1.10 (0.87-1.38), 0.43		
Smoking history during follow-up, n (%)			
- Never smoked	Ref	-	-
- Former smoker	0.99 (0.80-1.23), 0.95	-	
- Current smoker	0.96 (0.71-1.29), 0.80		
<u>Health insurance information</u>			
Health insurance, n (%)			
- No private	Ref	-	-
- Private	1.08 (0.83-1.40), 0.58		
% prescription covered by health insurance, during follow-up	1.01 (1.00-1.02), 0.25	-	-
<u>Disease parameters</u>			
Disease duration at baseline	0.99 (0.99-1.01), 0.70	-	-
Early RA			
- No	Ref	-	-
- Yes	1.04 (0.84-1.29), 0.70		
Ever presence of erosion, n (%)			
- No	Ref	-	-
- Yes	0.96 (0.82-1.12), 0.57		
RF positive, n (%)			
- No	Ref	Ref	Ref
- Yes	0.79 (0.64-0.99), 0.04	0.74 (0.56-0.97), 0.03	0.73 (0.56-0.96), 0.02
DAS28 during follow-up	1.10 (1.02-1.18), 0.02	0.98 (0.87-1.11), 0.74	-
Physician global score during follow-up	1.10 (1.05-1.15), <0.0001	1.12 (1.04-1.20), 0.003	1.10 (1.04-1.15), 0.001
HAQ disability index during follow-up	1.09 (0.97-1.24), 0.15	0.89 (0.74-1.08), 0.25	-
Comorbidity number during follow-up	0.96 (0.90-1.01), 0.11	0.94 (0.87-1.01), 0.11	0.92 (0.85-0.99), 0.02
<u>Medication information</u>			
Prior csDMARDs use at baseline			
- No	Ref	-	-
- Yes	1.18 (0.89-1.57), 0.25		
Prior bDMARDs use at baseline			
- No	Ref	-	-
- Yes	1.04 (0.83-1.29), 0.76		

Number of prior csDMARDs at baseline	1.08 (1.01-1.15), 0.03	1.03 (0.94-1.13), 0.57	-
Number of prior bDMARDs at baseline	1.04 (0.93-1.15), 0.50	1.04 (0.93-1.15), 0.50	-
csDMARDs use during follow-up			
- No	Ref	-	-
- Yes	1.12 (0.90-1.29), 0.69		
bDMARDs use during follow-up			
- No	Ref	-	-
- Yes	1.04 (0.85-1.29), 0.69		
Steroid use during follow-up			
- No	Ref	Ref	-
- Yes	1.26 (1.00-1.60), 0.05	1.04 (0.72-1.51), 0.83	
NSAIDs use during follow-up			
- No	Ref	Ref	Ref
- Yes	1.90 (1.54-2.34), <0.0001	1.78 (1.28-2.48), 0.001	1.75 (1.29-2.38), 0.003
Number of ARM during follow-up	1.30 (1.19-1.43), <0.0001	1.22 (1.03-1.44), 0.02	1.23 (1.07-1.40), 0.003
<u>Physician information</u>			
Female gender, n (%)	1.21 (0.99-1.47), 0.06	1.18 (0.90-1.53), 0.23	-
Academic position, n (%)			
- Community-based	Ref	Ref	-
- Academic or mixed based	1.24 (1.02-1.51), 0.03	1.07 (0.82-1.39), 0.62	
Location of clinical site, n (%)			
- Urban	Ref	-	-
- Rural	1.13 (0.88-1.45), 0.33		
Distance from patient residence, n (%)			
- ≤ 25 Km	Ref	-	-
- > 25 km	1.13 (0.93-1.38), 0.22		