Journal of Clinical Epidemiology 114 (2019) 95−103

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

Collection of antirheumatic medication data from both patients and rheumatologists shows strong agreement in a real-world clinical cohort: the Ontario Best Practices Research Initiative—a rheumatoid arthritis cohort

Mohammad Movahedi[a], Angela Cesta[a], Xiuying Li[a], Claire Bombardier[a,b,c,*], OBRI Investigators

[a]*Toronto General Hospital Research Institute, University Health Network, Toronto, Ontario, Canada*
[b]*Department of Medicine (DOM) and Institute of Health Policy, Management, and Evaluation (IHPME), University of Toronto, Toronto, Ontario, Canada*
[c]*Division of Rheumatology, Mount Sinai Hospital, Toronto, Ontario, Canada*

Accepted 10 June 2019; Published online 18 June 2019

Abstract

Objectives: The objective of the study was to examine the agreement between patient- and rheumatologist-reported antirheumatic medication (ARM) use in the Ontario Best Practices Research Initiative.

Study Design and Setting: We included adult patients who enrolled on or after September 1st 2010 and compared ARM use where rheumatologist visits and interviews occurred within 60 days of each other. Kappa statistic was used to measure agreement. We calculated sensitivity, specificity, and positive and negative predictive value, considering patient-reported data as the gold standard. To examine factors associated with agreement, a hierarchical generalized linear model was used. A subset analysis was also completed to compare start and stop dates of ARM.

Results: Overall agreement for ARM was good with higher sensitivity and lower specificity for conventional synthetic disease-modifying antirheumatic drugs compared with biologic disease-modifying antirheumatic drugs. Increased Health Assessment Questionnaire pain index and 28 disease activity score−erythrocyte sedimentation rate (DAS28-ESR) were significantly associated with lower agreement. Reporting stop dates was higher (19.4%) for patient-reported data compared with rheumatologist-reported data (13.1%).

Conclusion: ARM reports had strong agreement particularly for patients who have low disease activity and pain. ARM discontinuation was reported more frequently by patients, which may indicate that patients may be discontinuing use of their rheumatoid arthritis medications before consulting their rheumatologist.

Keywords: Rheumatoid arthritis (RA); Antirheumatic medication; Kappa statistics; Agreement; Data sources; Disease registry

1. Introduction

Although some registries rely on medication data reported directly from physicians, others will collect this information solely through patient reports. Collection of medication use from both patients and physicians could be considered a strength for disease registries and cohorts including rheumatoid arthritis (RA). Medication use obtained through patient interviews is costly and subject to recall bias [1,2]. On the other hand, collecting medication information from physician's offices, using case report forms, does not guarantee complete and accurate data reporting. Greater accuracy and reliability of medication reporting could be gained by using both data sources. For example, medication data would continue to be available through patient interviews for patients not seeing their rheumatologists on a regular basis or patients who decide to switch to a new rheumatologist (i.e., one that may not be participating in the research study). Medication data would also continue to be available through physician reports, for those patients who choose not to participate in interviews. However, to use these two data sources as

* Corresponding author: Division of Rheumatology, Department of Medicine (DOM) and Institute of Health Policy, University of Toronto, Toronto, Ontario, Canada. Tel.: +1 416 340 4800 (6586); fax; +1 888 757 6506.
E-mail address: claire.bombardier@utoronto.ca (C. Bombardier).

https://doi.org/10.1016/j.jclinepi.2019.06.012
0895-4356/

What is new?

Key findings

- Antirheumatic medication use reported by patients and rheumatologists in the Ontario Best Practices Research Initiative registry showed strong agreement; however, medication stop dates were more often reported by patients compared with rheumatologists.

What this adds to what was known?

- We showed that these two data sources could be used interchangeably and are both accurate and reliable sources of medication data in a real-world setting.

What is the implication and what should change new?

- Having more than one source of primary data can minimize the concern of missing data in real-world settings.
- Patients may be stopping their rheumatoid arthritis medications without consulting their rheumatologists.

alternatives for each other and to justify the added cost of collecting medication data from two sources, it is important to consider the strength of agreement between patient- and physician-reported medication use.

Previous studies have shown moderate to good agreement between drug use reported through interviews and claims data [3−10] for medications used in common diseases. Nielson et al. (2008) showed that agreement between surveys and claims data is stronger for cardiovascular and diabetes medication compared with medications used on an as-needed basis [5]. Allin et al. (2013) showed good agreement between self-reported (Canadian community Health Survey) and claims data (Ontario Drug Benefit Program) for oral diabetes medication and moderate agreement for antihypertensive medication in elderly patients [3]. Taipale et al. (2016) examined agreement between self-reported drug use and data in a drug dispensing−based register in elderly Finnish patients. They found good agreement for regularly used drugs but poor agreement for drugs used "as needed" [10].

Based on our knowledge to date, the comparability of two or more antirheumatic medication data sources within a registry or a real-world observational cohort has not been studied in Canada. Few studies in other countries have looked at agreement between two different data sources for antirheumatic medication use [11−13]. Noize et al. (2009) found a substantial agreement between interview and reimbursement medication data for drugs used for cardiovascular diseases, diabetes, and neuropsychiatric and rheumatic diseases [13]. Richardson et al. (2013) found poor to moderate agreement between interview-ascertained medication use and pharmacy records among a population aged 50 years or older, for 19 drug classes including antirheumatic medications [11]. Walitt et al. (2008) evaluated the validity of self-reported RA medication data compared with chart review in the Women's Health Initiative [12]. However, they did not assess agreement between the two different data sources. Using U.S. RA registry, one recent study examined patient-reported adherence to methotrexate, which was recorded by rheumatologist at the most recent registry visit [14].

The aim of this study was to examine the strength of agreement (as the primary outcome) between patient- and rheumatologist-reported antirheumatic medication (ARM) use in the Ontario Best Practices Research Initiative (OBRI). We identified individual level factors associated with higher agreement between these two data sources. We also calculated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (as secondary outcomes) overall and by (1) type of ARM (conventional synthetic disease-modifying antirheumatic drugs [csDMARDs] and biologic DMARDs [bDMARDs]); (2) ARM administration route; and (3) ARM start and stop dates.

2. Materials and methods

2.1. Data source and patients

The OBRI is a multicenter registry across Ontario, Canada, collecting data from both rheumatologists and patients with RA followed under routine care. Canada has a publicly funded health care system that covers all services provided by hospitals and physicians. Under the publicly funded health care system, in Ontario, prescription drugs are covered for seniors (≥65 years of age). Canadians must be referred to a rheumatologist through primary health care services (e.g., their family doctor). Once referred, the rheumatologist takes over their RA care. The OBRI incorporates rheumatologist assessments and a unique method of collecting data directly from the patients, using telephone interviewers. Patients in the OBRI are interviewed every 6 months. To minimize recall bias, patients are asked to have all their medication bottles in front of them at the time of the interview. Rheumatologist assessments are conducted as per routine care. All patients have a rheumatologist-confirmed diagnosis of RA with disease onset after 16 years of age and are 18 years of age or older at enrollment into the registry. Between January 2008 and January 2019, 3669 eligible patients across 65 sites gave their consent to participate in rheumatologist evaluations, and 3525 agreed to patient interviews. Institutional research ethics approval was obtained before recruitment.

For this study, we restricted our population to patients who were enrolled in OBRI on or after Sep 1st 2010.

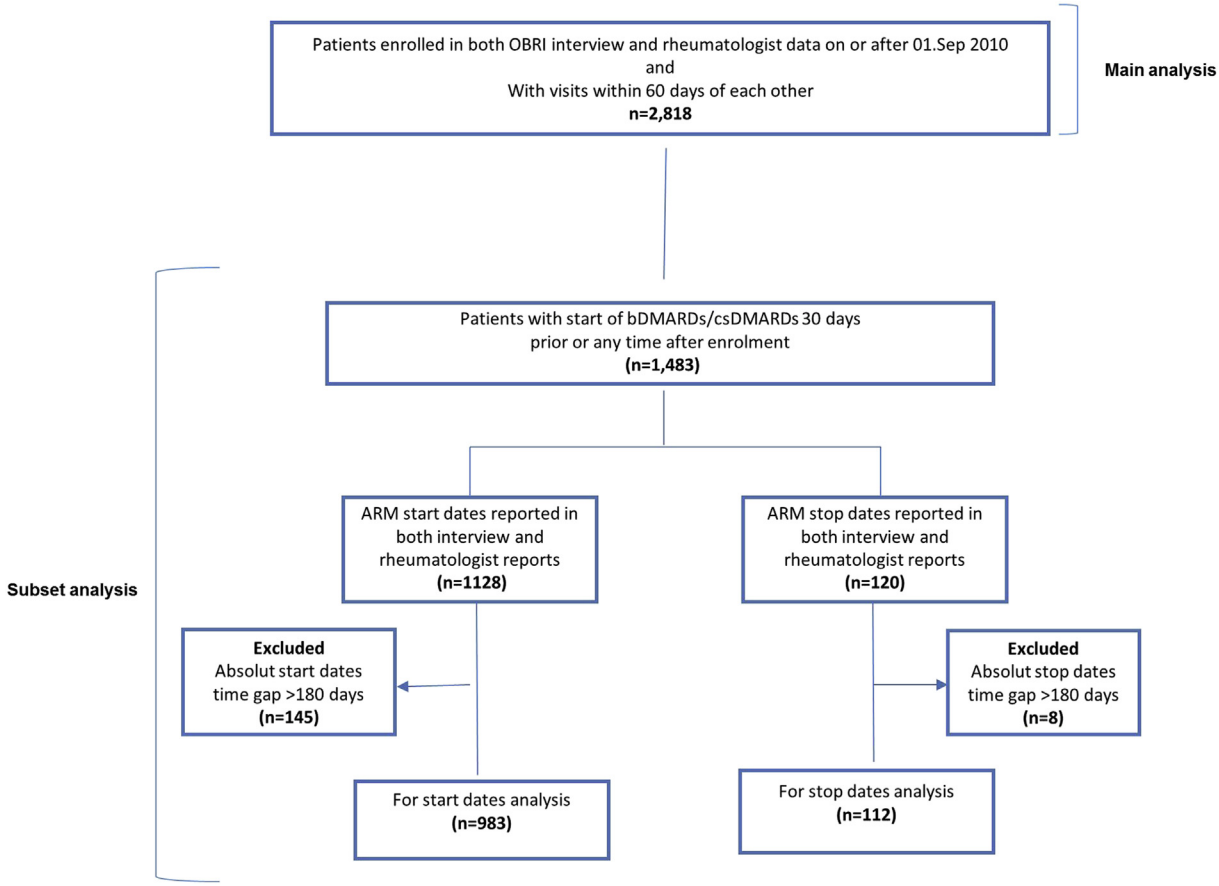

Fig. 1. Cohort selection flowchart. ARM, antirheumatic medication; OBRI, Ontario Best Practices Research Initiative; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; bDMARDs, biologic disease-modifying antirheumatic drugs.

Before this date, the interviewers were not collecting start and stop dates for reported ARM. We compared ARM use reports only where rheumatologist visits and interviews occurred within 60 days of each other believing that by restricting the time window between the two data sources, discrepancies would more likely reflect actual changes in the patients' ARM use rather than disagreement in ARM reporting. In a subset analysis comparing start and stop dates reported in the two data sources, we additionally excluded patients who started their ARM more than 30 days before enrollment (Fig. 1).

2.2. Statistical analysis

Characteristics of the cohort at enrollment were described using the mean and standard deviation (SD) for continuous variables or the count and proportion for categorical variables.

In the primary analysis, the prevalence of ARM use overall and for csDMARDs and bDMARDs in the two data sources was compared. To calculate sensitivity and specificity, PPV, and NPV, we arbitrarily selected patient-reported data as the gold standard, acknowledging that unlike diagnostic studies, neither of these two sources is considered the gold standard. The same approach was used for comparing the administration routes for bDMARDs and csDMARDs between the two data sources.

To examine factors associated with agreement of ARM use, hierarchical generalized linear models (HGLMs) (multilevel models) taking into account two levels (patient level and rheumatologist level as patients are nested within rheumatologists) was used [15–17]. The factors considered were patient's age, sex, disease-related factors, and socioeconomic characteristics. Disease-related factors included disease duration, disease activity score–erythrocyte sedimentation rate (DAS28-ESR), physician global score, health assessment questionnaire (HAQ) disability Index, HAQ pain index, and number of comorbidities. Socioeconomic status was measured by marital status, health insurance type (Ontario Health Insurance plan (OHIP)/private health insurance coverage), annual household income, and educational attainment. Sex and academic rheumatologist (rheumatology practices within a university affiliated teaching hospital)/community rheumatologist were also considered as additional-level predictors for agreement. Using HGLM, we calculated intraclass correlation coefficient (ICC) to indicate how much of the total variation in the probability of agreement is accounted for by the rheumatologist.

2.3. Subset analysis

The prevalence, sensitivity, specificity, PPV, NPV, and agreement for ARM start and stop dates for both data sources were calculated in a subset analysis (number of patients = 1483). The absolute time gap (days) for ARM start dates (number of patients = 983) and stop dates (number of patients = 112) available in both patient- and rheumatologist-reported data were also calculated (Fig. 1).

The agreement between patient and rheumatologist reports for all analyses mentioned previously were calculated using Cohen's kappa statistics with 95% confidence interval (95% CI), using patient-reported ARM as the gold standard. Kappa values were interpreted as follows: poor (<0.20), fair (0.20-0.40), moderate (0.41-0.60), good (0.61-0.80), and very good (0.81-1.00) [18].

3. Results

Table 1 shows the characteristics of patients at enrollment. 2,818 patients (78.6% female) were included with a mean (SD) age at OBRI enrollment of 58.0 (13.0) years. Mean (SD) for disease parameters were DAS28: 4.2 (1.6); physician global: 4.0 (2.5); HAQ disability Index: 1.1 (0.8); and HAQ pain index: 1.4 (0.9). Median (interquartile range [IQR]) for disease duration was 4.0 (1.0-12.0) years.

3.1. Agreement in ARM use

The prevalence of ARM use (csDMARDs/bDMARDs) was 98.6% and 99.0% based on patient and rheumatologist reports, respectively. For csDMARDs use, the prevalence was 79.6% based on patient reports and 80.6% based on rheumatologist reports. The prevalence of bDMARDs use was 19.0% and 18.4% in patient and rheumatologist reports (Table 2).

Overall agreement for ARM use between patient- and rheumatologist-reported data was rated as good (kappa: 0.78; 95% CI: 0.72-0.83). Agreement for csDMARDs (kappa: 0.76) and bDMARDs (kappa: 0.89) separately was also rated as good and very good, respectively (Table 2). The sensitivity was higher (99.8%) for csDMARDs compared with bDMARDs (95.6%), whereas specificity in csDMARDs was lower than bDMARDs (64.6% vs. 93.9%). There was a small difference in PPV and NPV between csDMARDs and bDMARDs.

3.2. Characteristics related to patient- and rheumatologist-reported ARM use

There was an overall statistically significant amount of variability in the log odds of agreement between rheumatologists in our analysis sample (HGLM estimate = 1.28; $P = 0.001$). Calculated ICC of 0.28 indicating 28% of total variation in the probability of agreement is accounted for by treating rheumatologist.

Table 1. Baseline characteristics of patients

Variables	*N* = 2,818
Age, yr	
Mean (SD)	58.0 (13.0)
Median (IQR)	59.0 (50.1-67.2)
Age category, yr, *n* (%)	
≤ 35	156 (5.5)
36-65	1,774 (63.0)
66-75	643 (22.8)
>75	245 (8.7)
Sex, female, *n* (%)	2215 (78.6)
Marital status, married, *n* (%)	1,899 (67.4)
Education, *n* (%)	
High school or less	1177 (41.8)
Postgraduate	1636 (58.0)
Missing	5 (0.2)
Household income class, *n* (%)	
≤ 50,000 CD	933 (33.1)
>50,000 CD	1,358 (48.2)
Missing	527 (18.7)
Health insurance type, *n* (%)	
OHIP	435 (15.4)
OHIP +(ODB or private)	2383 (84.6)
Disease duration, yr	
Mean (SD)	8.1 (9.9)
Median (IQR)	4.0 (1.0-12.0)
Early-onset disease, *n* (%)	986 (35.0)
DAS28-ESR (*n* = 2417)	
Mean (SD)	4.2 (1.6)
Median (IQR)	4.2 (3.1-5.3)
PhGA (range: 0-10), (*N* = 2264)	
Mean (SD)	4.0 (2.5)
Median (IQR)	4.0 (2.0-6.0)
HAQ-DI (range: 0-3), (*N* = 2815)	
Mean (SD)	1.1 (0.8)
Median (IQR)	1.0 (0.4-1.8)
HAQ pain index (range: 0-3), (*n* = 2814)	
Mean (SD)	1.4 (0.9)
Median (IQR)	1.4 (0.6-2.1)
Number of comorbidities, mean (SD)	
Mean (SD)	3.6 (2.6)
Median (IQR)	3.0 (2.0-5.0)
Patients seeing female rheumatologists, *n* (%)	964 (44.8)
Patients seeing academic rheumatologists, *n* (%)	
Community based	954 (44.2)
Academic or mixed based	1,175 (54.6)
Missing	25 (1.2)

Abbreviations: DAS-ESR, disease activity score—erythrocyte sedimentation rate; HAQ-DI, health assessment questionnaire disability index; IQR, interquartile range; OHIP, Ontario Health Insurance Plan; ODB, Ontario drug benefit; PhGA, physician global assessment.

Table 2. Agreement between patient- and rheumatologist-reported ARM use

Patients (n = 2,818)	Prevalence (patient reports) (95% CI) %	Prevalence (rheumatologist reports) (95% CI) %	Sensitivity (95% CI) %	Specificity (95% CI) %	PPV (95% CI) %	NPV (95% CI) %	Kappa[a] (95% CI)
ARM use by name							
bDMARDs	19.0 (18.3-19.7)	18.4 (17.7-19.1)	95.9 (94.9-96.7)	93.9 (92.7-95.0)	95.3 (94.4-96.2)	94.7 (93.6-95.8)	0.89 (0.88-0.91)
csDMARDs	79.6 (78.8-80.2)	80.6 (79.8-81.3)	99.8 (99.7-99.9)	64.6 (59.5-69.6)	98.6 (98.4-98.9)	94.1 (91.1-97.1)	0.76 (0.72-0.80)
Both	98.6 (98.3-98.8)	99.0 (98.8-99.2)	99.9 (99.9-100)	65.5 (58.3-72.7)	99.5 (99.4-99.7)	96.5 (93.1-99.8)	0.78 (0.72-0.83)
ARM use by administration route							
bDMARDs							
SC/injection	62.1 (60.2-64.0)	68.0 (66.0-69.9)	95.3 (93.7-96.7)	95.1 (93.2-96.6)	96.0 (94.6-97.3)	94.4 (92.7-96.1)	0.90 (0.88-0.93)
Infusion	30.3 (28.5-32.3)	26.4 (24.5-28.2)	76.3 (76.3-80.3)	97.0 (95.6-98.1)	92.7 (89.9-95.5)	89.1 (87.1-91.1)	0.77 (0.73-0.81)
csDMARDs							
Oral	79.6 (78.8-80.4)	75.7 (75.0-76.4)	91.7 (91.1-92.4)	68.4 (66.2-70.7)	92.4 (91.7-93.0)	66.6 (64.3-68.9)	0.60 (0.57-0.62)
SC/injection	23.6 (22.9-24.4)	24.2 (23.5-24.9)	68.0 (65.8-70.3)	91.9 (91.2-92.5)	66.6 (64.3-68.9)	92.3 (91.7-92.9)	0.59 (0.57-0.62)

Abbreviations: ARM, antirheumatic medication; ARM, Antirheumatic medication; bDMARDs, biologic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value; SC, subcutaneous.

[a] Kappa statistic key: poor: <0.20; fair: 0.20-0.40; moderate: 0.41-0.60; good: 0.61-0.80; very good: 0.81-1.00.

Table 3 shows factors associated with overall agreement for ARM use. The adjusted HGLM showed that increased HAQ pain index (0.48; 95% CI: 0.33-0.70; P = 0.0002) and increased DAS28-ESR (OR: 0.73; 95% CI: 0.58-0.91; P = 0.01) were significantly associated with lower agreement.

3.3. Subset analysis for reported start and stop dates

3.3.1. ARM administration route agreement

The route of administration was reported as 62% subcutaneous (SC) or injection based on patient reports and 68% based on rheumatologist reports, whereas the prevalence of infusions for bDMARDs was higher (30.3%) in the patient reports compared with rheumatologist reports (26.4%). The agreement in SC administration route for bDMARDs was rated as very good (kappa: 0.90; 95% CI: 0.88-0.93), whereas the agreement was moderate for oral and SC routes of csDMARDs (kappa: 0.60 and 0.59, respectively (Table 2)).

3.3.2. Start and stop date agreement

For this subset analysis, 1,483 patients were included. After reviewing the outliers (i.e., absolute time gap > 180 days), the majority were found to be data entry errors and were therefore excluded from the analysis. The prevalence of reported start dates of ARM was 77.6% and 82.2% based on patient and rheumatologist reports, respectively. The prevalence of reporting stop dates was higher (19.4%) for patient reports compared with rheumatologist reports (13.1%). Sensitivity and PPV were higher, and specificity and NPV were lower for start dates compared with stop dates.

Overall agreement between patient and rheumatologist reports were rated as moderate (kappa: 0.49; 95% CI: 0.45-0.53) and poor (kappa: 0.20; 95% CI: 0.16-0.25) for start and stop dates, respectively (Table 4).

3.3.3. Start and stop date absolute time gap

The absolute time gap between start dates of all ARMs was approximately 1 week (median: 8 days; 1.0-40.0). Fig. 2A shows the distribution of the absolute time gap (days) between patient and rheumatologist reports for start by ARM type. The absolute time gap for csDMARDs was shorter (median: 7 days; IQR: 1-36) compared with bDMARDs (median: 14 days; IQR: 1-63).

With respect to the absolute time gap in stop dates for all ARMs, 50% of records showed a time gap of 15.5 days (IQR: 6-61) between patient and rheumatologist reports. The time gap in reported stop dates was similar for csDMARDs (15.5 days; 6-46) compared with bDMARDs (16.0 days; 7-99.5) (Fig. 2B).

4. Discussion

In this study, we found good agreement between rheumatologist- and patient-reported ARM use. The slightly higher ARM use reported by rheumatologists may reflect

Table 3. Hierarchal generalized linear models for assessing impact of selected characteristics on agreement between patient- and rheumatologist-reported ARM use

	Odds ratio (95% CI), *P*-value	
Patients (n = 2,818)	**Univariable analysis**	**Multivariable analysis**
Age, yr	**0.99 (0.97-0.99), 0.03**	0.98 (0.96-1.00), 0.13
Sex		
Male	Ref	Ref
Female	0.72 (0.51-1.02), 0.07	0.66 (0.35-1.22), 0.18
Marital status		
Single/divorced/widow	Ref	Ref
Married	1.07 (0.82-1.40), 0.61	1.02 (0.61-1.69), 0.95
Education		
High school or less	Ref	-
Postsecondary	0.93 (0.71-1.22), 0.60	0.69 (0.42-1.15), 0.16
Household income class		
≤50,000 CD	Ref	Ref
>50,000 CD	0.96 (0.71-1.29), 0.76	1.03 (0.60-1.78), 0.90
Insurance type, *n* (%)		
OHIP	Ref	Ref
OHIP +(ODB or private insurance)	**0.52 (0.34-0.80), 0.003**	0.47 (0.19-1.17), 0.10
Disease characteristics		
RA disease duration	**0.97 (0.96-0.98), <0.0001**	0.99 (0.97-1.02), 0.70
DAS28-ESR	**0.85 (0.77-0.94), 0.001**	**0.73 (0.58-0.91), 0.01**
PhGA	**0.92 (0.86-0.98), 0.01**	1.13 (0.98-1.29), 0.09
HAQ-DI	**0.74 (0.62-0.88), 0.001**	1.61 (1.03-2.52), 0.06
HAQ-pain index	**0.60 (0.51-0.70), <0.0001**	**0.48 (0.33-0.70), 0.0002**
Comorbidity number	0.96 (0.92-1.01), 0.13	1.04 (0.95-1.15), 0.40
Characteristics of consulted rheumatologists		
Patients seeing female rheumatologist	0.93 (0.48-1.79), 0.82	1.04 (0.43-2.55), 0.92
Patients seeing academic/mixed rheumatologist		
Community based	Ref	Ref
Academic based	0.81 (0.42-1.56), 0.44	0.58 (0.23-1.46), 0.25

Abbreviations: ARM, antirheumatic medication; CI, confidence interval; DAS-ESR, disease activity score–erythrocyte sedimentation rate; HAQ-DI, health assessment questionnaire disability index; OHIP, Ontario health insurance plan; ODB, Ontario drug benefit; PhGA, physician global assessment; RA, rheumatoid arthritis.

Bolded *P* values are < 0.05.

the reporting of RA medications that are prescribed but for various reason, not filled by the patient (i.e., because of fear of side effects, medication cost, or delays in getting prescriptions filled). The prevalence of both bDMARDs and csDMARDs use was comparable between the two data sources.

The agreement in reporting of SC/injection route was better compared with infusions for bDMARDs (0.90 vs. 0.77). Perhaps, some patients are not able to accurately report on the route of bDMARDs because they cannot distinguish between the two route options provided (i.e., SC/injection vs infusion).

Table 4. Agreement between patient and rheumatologist reports for ARM start and stop dates

Patients (n = 1483)	**Prevalence (patient reports) (95% CI) %**	**Prevalence (rheumatologist reports) (95% CI) %**	**Sensitivity (95% CI) %**	**Specificity (95% CI) %**	**PPV (95% CI) %**	**NPV (95% CI) %**	**Kappa[a] (95% CI)**
Start dates	77.6 (76.0-79.2)	82.2 (80.7-83.7)	92.4 (91.1-93.5)	53.1 (48.9-57.2)	87.2 (85.8-88.6)	66.8 (62.3-71.1)	0.49 (0.45-0.53)
Stop dates	19.4 (17.9-21.0)	13.1 (11.8-14.5)	27.6 (23.5-31.3)	90.4 (89.1-91.6)	40.7 (35.4-46.2)	83.8 (82.3-85.3)	0.20 (0.16-0.25)

Abbreviations: ARM, antirheumatic medication; CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

[a] Kappa statistic key: poor: <0.20; fair: 0.20-0.40; moderate: 0.41-0.60; good: 0.61-0.80; very good: 0.81-1.00.

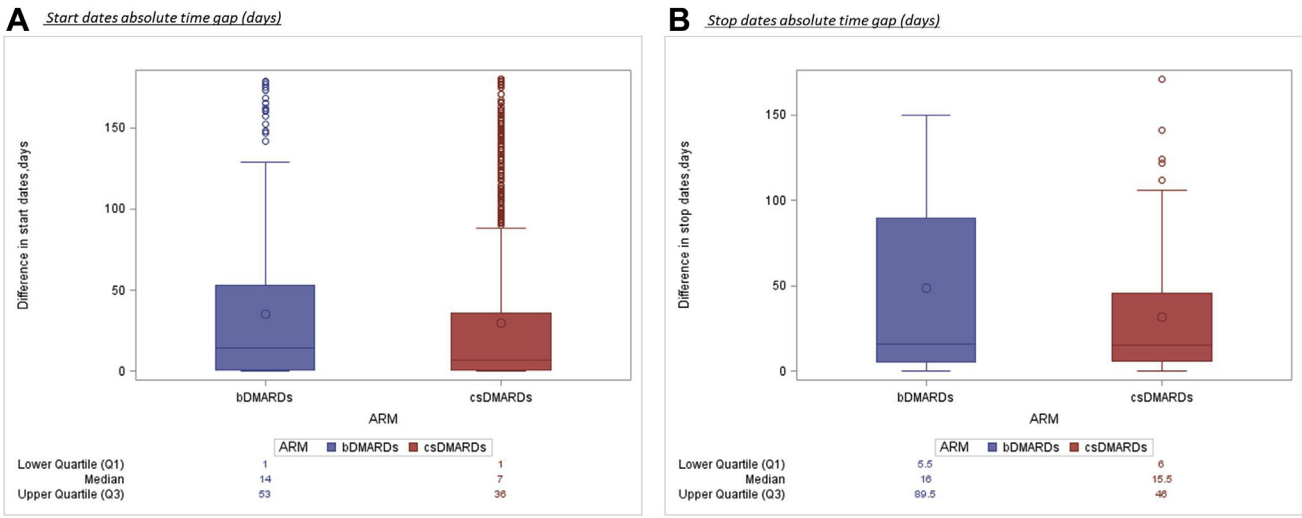

Fig. 2. Box and whisker plots for absolute time gap in start (A) and stop dates (B) as reported by patients and rheumatologists. ARM, antirheumatic medication; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; bDMARDs, biologic disease-modifying antirheumatic drugs.

We found moderate and poor agreement between the two data sources, for reporting ARM start and stop dates, respectively. Patients are more likely to report stop dates compared with rheumatologists. One possible reason for this important finding could be that patients may occasionally stop taking their medications before advising or consulting with their rheumatologist. Further exploration of this outcome is warranted. For example, a more detailed examination of the patient-reported reason for these medication stops would allow us to better understand why this is happening and possibly allow us to improve patient care. For example, the patient may have stopped taking the medication because they experienced side effects, because they are feeling better and believe they no longer need them, or because they simply ran out of their medications.

Overall, the median gap time for reporting start dates between the two data sources was smaller for csDMARDs (8 days) compared with bDMARDs (14 days). One possible reason is that patients can refer to their medication bottles for the start date of oral medications, but may not be provided with a record of their biologic infusion dates (i.e., these medications are mostly administered through infusion clinics).

In multivariate HGLMs, the agreement between patients and rheumatologists was better for patients with lower disease and lower pain scores. Lack of adherence to prescribed medications may partly explain why we found less agreement between patient- and rheumatologist-reported ARM use in patients with higher disease scores. Patients who feel they are not being optimally treated may be less likely to take their medications as prescribed by their rheumatologist or the higher scores in disease activity may be a consequence of their lack of adherence to their prescribed medications. Ahluwalia et al. found that patients in the OBRI with higher physician global scores were less likely to be adherent to their RA medications [19].

Rheumatologist ARM reporting had a very high sensitivity and was found to be accurate and valid when compared with patient reports. These findings suggest that the two sources of data are interchangeable. Therefore, by collecting these data from two different sources, we are able to minimize missing medication data. This is an important consideration for long-term follow-up studies where participant attrition is often a major concern. In the OBRI, a number of patients who are no longer being seen by the rheumatologist who enrolled them into the cohort (i.e., an OBRI investigator) continue to participate in the OBRI through interview-reported data, whereas some patients who are too busy to participate in interviews continue to participate in OBRI rheumatologist-reported data. We have specifically considered ARM reporting in patients with RA in a real-world setting, which does not appear to have been addressed by any previous studies in Canada. Previous studies have mostly considered other drug classes, different data sources, and different settings; however, in spite of this limitation, our results are consistent with most of these studies [3,5,7,9,10,13,20].

Among studies which investigated the agreement between two data sources for ARM use, Kehoe et al. (1994) [21] compared self-reported medical history and medication use with information form the participant's physicians in a case-control study. They found some differences between patient and physician reports for arthritis (15%) and aspirin medication (21%) but little differences for other diseases or medication (e.g., antihypertensive).

Similar to our study results, Noize et al. (2009) also found good agreement between interview-reported and reimbursement medication data for drugs used for musculoskeletal diseases [13]. Richardson et al. (2013) assessed the agreement between interview-ascertained medication use and pharmacy records for 19 drug classes including ARMs [11]. They found moderate or poor agreement for antiinflammatory

and antirheumatic products (kappa = 0.54). However, they considered all types of ARM including folic acid, steroids, and nonsteroid agents, which may be the reason for the lower agreement (i.e., patient recall is not good for nonspecific antirheumatic agents and medications taken "as needed").

In a recent RA study by Curtis et al. (2016), where patient self-reported medication was considered the gold standard, it was shown that of 228 patients whose rheumatologist reported current methotrexate use at the time of the most recent registry visit, 45 (19.7%) had discontinued or missed $\geq$ 1 dose in the last month [14]. This is consistent with our finding of a lower ARM discontinuation or stop date prevalence reported by rheumatologists compared with patients.

4.1. Limitations

Although we found good to very good agreement in RA medication reporting between the two data sources in the OBRI cohort, these findings are relevant to settings with similar procedures and may not be generalizable to all registries or observational studies. Regardless, these findings are important because they describe a novel method for collecting reliable and accurate medication data in the real-world setting and support the accuracy of using either source of RA medication data.

5. Conclusion

The results of this study suggest that there is strong agreement between patient- and rheumatologist-reported ARM use. The agreement is even better for patients who have lower disease activity and pain. Our results also suggest that some patients are discontinuing their RA medications before consulting their rheumatologist and recommend this finding be further investigated. Based on the results of this study, we believe it is acceptable to use either of these two data sources and to use them interchangeably, to minimize missing data when conducting research in a real-world setting. With the increasing role of real-world data in health care decisions and the current trend toward using high-quality real-world evidence for regulatory decisions, this study provides an example of how registry data can be collected accurately and reliably and how missing data can be minimized.

CRediT authorship contribution statement

Mohammad Movahedi: Conceptualization, Data curation, Formal analysis, Methodology, Validation, Writing - original draft, Writing - review & editing. **Angela Cesta:** Conceptualization, Data curation, Funding acquisition, Project administration, Resources, Writing - original draft, Writing - review & editing. **Xiuying Li:** Data curation, Methodology, Software, Writing - review & editing. **Claire Bombardier:** Conceptualization, Investigation, Validation, Funding acquisition, Resources, Supervision, Writing - review & editing.

Acknowledgments

The authors would like to thank all investigators participating in the OBRI: Drs. Ahluwalia, V., Ahmad, Z., Akhavan, P., Albert, L., Alderdice, C., Aubrey, M., Aydin, S., Bajaj, S., Bell, M., Bensen, B., Bhavsar, S., Bobba, R., Bombardier, C., Bookman, A., Cabral, A., Carette, S., Carmona, R., Chow, A., Chow, S., Choy, G., Ciaschini, P., Cividino, A., Cohen, D., Dixit, S., Haaland, D., Hanna, B., Haroon, N., Hochman, J., Jaroszynska, A., Johnson, S., Joshi, R., Kagal, A., Karasik, A., Karsh, J., Keystone, E., Khalidi, N., Kuriya, B., Larche, M., Lau, A., LeRiche, N., Leung, Fe., Leung, Fr., Mahendira, D., Matsos, M., McDonald-Blumer, McKeown, E., Midzic, I., Milman, N., H., Mittoo, S., Mody, A., Montgomery, A., Mulgund, M., Ng, E., Papneja, T., Pavlova, P., Perlin, L., Pope, J, Purvis, J., Rohekar, G., Rohekar, S., Ruban, T., Samadi, N., Sandhu, S., Shaikh, S., Shickh, A., Shupak, R., Smith, D., Soucy, E., Stein, J., Thompson, A., Thorne, C., and Wilkinson, S.

OBRI was funded by peer-reviewed grants from CIHR, Canada, Ontario Ministry of Health and Long-Term Care, Canada, Canadian Arthritis Network, Canada, and unrestricted grants from AbbVie, Amgen, Celgene, Hospira, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sanofi, & UCB. Dr. Bombardier holds a Canada Research Chair in Knowledge Transfer for Musculoskeletal Care and a Pfizer Research Chair in Rheumatology.

Authors' contribution: M.M. and C.B. contributed to study conception and design. X.L., M.M., and A.C. contributed to acquisition of data. M.M. and C.B. contributed to analysis and interpretation of data. M.M. and A.C. contributed to drafting of the manuscript. M.M., A.C., C.B., and X.L. contributed to critical revision.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2019.06.012.

References

[1] Klungel OH, de Boer A, Paes AH, Herings RM, Seidell JC, Bakker A. Influence of question structure on the recall of self-reported drug use. J Clin Epidemiol 2000;53:273−7.
[2] Paganini-Hill A, Ross RK. Reliability of recall of drug usage and other health-related information. Am J Epidemiol 1982;116:114−22.
[3] Allin S, Bayoumi AM, Law MR, Laporte A. Comparability of self-reported medication use and pharmacy claims data. Health Rep 2013;24(1):3−9.
[4] Haapea M, Miettunen J, Lindeman S, Joukamaa M, Koponen H. Agreement between self-reported and pharmacy data on medication

use in the Northern Finland 1966 Birth Cohort. Int J Methods Psychiatr Res 2010;19(2):88−96.
[5] Nielsen MW, Sondergaard B, Kjoller M, Hansen EH. Agreement between self-reported data on medicine use and prescription records vary according to method of analysis and therapeutic group. J Clin Epidemiol 2008;61:919−24.
[6] Pit SW, Byles JE, Cockburn J. Accuracy of telephone self-report of drug use in older people and agreement with pharmaceutical claims data. Drugs Aging 2008;25(1):71−80.
[7] Rikala M, Hartikainen S, Sulkava R, Korhonen MJ. Validity of the Finnish prescription register for measuring psychotropic drug exposures among elderly finns: a population-based intervention study. Drugs Aging 2010;27(4):337−49.
[8] Sarangarm P, Young B, Rayburn W, Jaiswal P, Dodd M, Phelan S, et al. Agreement between self-report and prescription data in medical records for pregnant women. Birth Defects Res A Clin Mol Teratol 2012;94(3):153−61.
[9] Sjahid SI, van der Linden PD, Stricker BH. Agreement between the pharmacy medication history and patient interview for cardiovascular drugs: the Rotterdam elderly study. Br J Clin Pharmacol 1998;45(6):591−5.
[10] Taipale H, Tanskanen A, Koponen M, Tolppanen AM, Tiihonen J, Hartikainen S. Agreement between PRE2DUP register data modeling method and comprehensive drug use interview among older persons. Clin Epidemiol 2016;8:363−71.
[11] Richardson K, Kenny RA, Peklar J, Bennett K. Agreement between patient interview data on prescription medication use and pharmacy records in those aged older than 50 years varied by therapeutic group and reporting of indicated health conditions. J Clin Epidemiol 2013;66:1308−16.
[12] Walitt BT, Constantinescu F, Katz JD, Weinstein A, Wang H, Hernandez RK, et al. Validation of self-report of rheumatoid arthritis and systemic lupus erythematosus: the Women's Health Initiative. J Rheumatol 2008;35:811−8.
[13] Noize P, Bazin F, Dufouil C, Lechevallier-Michel N, Ancelin ML, Dartigues JF, et al. Comparison of health insurance claims and patient interviews in assessing drug use: data from the Three-City (3C) Study. Pharmacoepidemiol Drug Saf 2009;18(4):310−9.
[14] Curtis JR, Bharat A, Chen L, Greenberg JD, Harrold L, Kremer JM, et al. Agreement between rheumatologist and patient-reported adherence to Methotrexate in a US rheumatoid arthritis registry. J Rheumatol 2016;43:1027−9.
[15] Enders CK, Tofighi D. Centering predictor variables in cross-sectional multilevel models: a new look at an old issue. Psychol Methods 2007;12(2):121−38.
[16] Ene M, Leighton E, Blue G, Bell B. Multilevel models for categorical data using SAS PROC GLIMMIX: The Basics. Columbia, SC: SAS tehnical report 3430, University of South Carolina, SAS Institute In; 2015.
[17] Moerbeek M. The consequence of Ignoring a level of nesting in multilevel analysis. Multivariate Behav Res 2004;39(1):129−49.
[18] Landis JR, Koch GG. An application of hierarchical kappa-type statistics in the assessment of majority agreement among multiple observers. Biometrics 1977;33:363−74.
[19] Ahluwalia V, Rampakakis E, Movahedi M, Cesta A, Li X, Sampalis JS, et al. Predictors of patient decision to discontinue anti-rheumatic medication in patients with rheumatoid arthritis: results from the Ontario best practices research initiative. Clin Rheumatol 2017;36(11):2421−30.
[20] Lau HS, de Boer A, Beuning KS, Porsius A. Validation of pharmacy records in drug exposure assessment. J Clin Epidemiol 1997;50:619−25.
[21] Kehoe R, Wu SY, Leske MC, Chylack LT Jr. Comparing self-reported and physician-reported medical history. Am J Epidemiol 1994;139:813−8.