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A Bridge Too Far? Real-World Practice Patterns of Early Glucocorticoid Use in the Canadian Early Arthritis Cohort

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Objective. To describe patterns of glucocorticoid use in a large real-world cohort with early rheumatoid arthritis (RA) and assess the impact on disease activity and treatment.

Methods. Data are from adults with new RA (≤1 year) recruited to the Canadian Early Arthritis Cohort (CATCH) and are stratified on the basis of whether a person was prescribed oral glucocorticoids within 3 months of study entry. Disease activity was compared over 24 months. Mixed-effects logistic regression was used for adjusted odds ratios (aORs) of escalation to biologics separately for 12 and 24 months, with random effects terms to account for prescribing patterns clustering by study site.

Results. Among 1891 persons, 30% received oral steroids. Users were older, were less often employed, and had shorter disease duration and higher disease activity. Disease activity improved over time, with early glucocorticoid users starting at higher levels of disease activity. Participants with early oral glucocorticoids were more likely to be on a biologic at 12 months (aOR = 2.4; 95% confidence interval [CI], 1.5-3.7) and 24 months (aOR = 1.9; 95% CI, 1.3-3.0). Despite Canadian clinical practice guidelines to limit corticosteroid use to short-term or 'bridge' therapy, 30% of patients who used oral glucocorticoids still used them 2 years later.

Conclusion. Early steroids were prescribed sparingly in CATCH and were often indicative of more active baseline disease as well as the need for progression to biologics.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by joint inflammation, pain, stiffness, and disability (1). Trajectories of early RA range from mild nonerosive joint symptoms to active destructive arthritis that impairs function, decreases quality of life, and increases comorbidity (2). Early diagnosis and optimized treatment with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and escalation to biologic DMARDs, when needed, can help rapidly control inflammation to minimize disability and improve quality of life (3,4).

The CATCH study was designed and implemented by the investigators and financially supported through unrestricted research grants from: Amgen and Pfizer Canada - Founding sponsors since January 2007; AbbVie Corporation and Hoffmann-LaRoche since 2011; Medexus Inc. since 2013; Merck Canada since 2017, Sandoz Canada, Biopharmaceuticals since 2019, Gilead Sciences Canada since 2020 and Fresenius Kabi Canada Ltd. since 2021. Previously funded by Janssen Biotech from 2011-2016, UCB Canada and Bristol-Myers Squibb Canada from 2011-2018, Sanofi Genzyme from 2016-2017, and Eli Lilly Canada from 2016-2020.

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SIGNIFICANCE & INNOVATIONS

- Although clinical trial data support the efficacy of glucocorticoids as short-term bridge therapy for a few weeks to facilitate rapid control of inflammatory symptoms, our real-world data do not support this as a feasible strategy; nearly one-third of oral steroid initiators did not taper or discontinue these within 24 months.
- Inconsistent with current practice recommendations, we observed that most patients who were initiated on oral glucocorticoids in this Canadian cohort did not use them as bridge therapy. Their use was associated with a poor response to initial disease-modifying antirheumatic drugs as well as a poor prognosis despite the subsequent escalation of therapy, which likely reflects confounding by indication rather than a causal relationship.

Synthetic glucocorticoids have been used for more than 60 years for rapid symptom control (5) and to prevent joint destruction (6), though side effects, including weight gain, osteoporosis, and metabolic dysregulation, are common (7,8). Glucocorticoids also are known to increase the risk of infection (9,10). Data from randomized controlled trials (RCTs) show a beneficial effect of low-dose (≤10 mg prednisone or ≤7.5 mg prednisolone) glucocorticoids on morning stiffness (11,12), tender joints (13), function (14,15), and radiographic progression (6,13,14,16-20). As a result, glucocorticoids are recommended as short-term bridge therapy, rather than long-term disease management, in treat-to-target paradigms in American and European guidelines (21,22) as one of many tools for achieving remission or low disease activity. However, RCTs have limited applicability to clinical practice, in which patients often have more comorbidities, and RA treatment strategies may differ.

In studies of usual care, medication use is at the discretion of the provider. Glucocorticoids are commonly prescribed in older patients with more comorbidities—individuals who also tend to receive biologics less often (23). Steroid use is high in other early RA observational cohorts (24,25), particularly in Europe (26), where early high-dose (30-60 mg/day) prednisone with preplanned tapering over 6 to 9 months is often used (27,28). When used for longer durations (>3 months) or at higher doses (>5-10 mg/day), early glucocorticoids prescribed around the time of diagnosis delayed the start of biologics in some United States prescription drug claims analyses (29) but not others (25,30-32). How these studies and data translate to the use of early glucocorticoids in the Canadian setting, given differences in health care systems and drug reimbursement procedures, also remains unknown. To better understand the use of glucocorticoids in early RA in Canada, a large population with longitudinal follow-up and systematic characterization of changes in disease activity and medication use over time is needed (33). The objective of this study was to describe real-world prescribing patterns associated with early steroid use in Canadian patients with early RA. Specifically, in patients newly diagnosed with RA seen in the usual care settings, we evaluated the prevalence and incidence of glucocorticoid use, as well as disease activity trajectories among users and nonusers over time. We quantified the duration of oral steroid use, as well as concomitant medications.

PARTICIPANTS AND METHODS

Data source and study population. Participants included adults aged 18 and older who were enrolled in the Canadian Early Arthritis Cohort (CATCH) between January 1, 2007, and March 24, 2017. CATCH is a multicenter prospective cohort study of Canadians with early inflammatory arthritis followed in 22 rheumatology clinics across Canada. Consistent with American College of Rheumatology 1987 and 2010 criteria, early inflammatory arthritis was defined as 1 year or less of synovitis, two or more swollen joints, or one or more swollen metacarpophalangeal or proximal interphalangeal joint with at least one of the following: rheumatoid factor (RF) or anti–citrullinated protein antibody (anti-CCP) positivity, 45 minutes or more of morning stiffness, patient-reported improvement with nonsteroidal anti-inflammatory drugs, or a positive metatarsophalangeal squeeze test (34). Data were collected at scheduled visits at 3, 6, 12, and 24 months, reflective of usual care, and investigators were encouraged to follow Canadian RA practice guidelines. We excluded CATCH participants with less than 3 months of follow-up and individuals who started a biologic

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within the first 3 months (to avoid prevalent user and immortal time biases) (35,36).

Ethical approval information. The CATCH study was approved by research ethics boards at each center, and participants provided written informed consent.

Data sharing statement. No data are available.

Patient and public involvement. Patients and the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

Steroid exposure definition. Glucocorticoids were defined using the date that prescription was written for any of the following: prednisone, methylprednisolone, or hydrocortisone. Although CATCH study visits happen every 3 months in the first year, patients may see their physicians more frequently than this cadence. Our analysis used exact date, rather than study visit, for the date of glucocorticoid initiation. Patients were stratified based on three mutually exclusive categories of use by their 3 month follow-up visit (none, new user on or after the date of CATCH cohort entry, and prevalent user on the date of CATCH cohort entry). We allowed for steroid initiation within the first 3 months of study entry to account for a potential lag time for the treating rheumatologist to decide steroid initiation was necessary. Any steroid initiated after 3 months in the CATCH study was not considered exposure in this analysis of early steroid use.

Research personnel were trained to ask participants about start and stop dates, dose, and frequency of csDMARDs and biologics, as well as glucocorticoids. The duration of oral steroid exposure was defined from the first date of use until the date a research coordinator or site physician recorded as the date of last dose.

Covariates. We included sociodemographic and disease-related characteristics in our statistical models, which were adjusted using data from the baseline study visit. These included age, sex, and number of comorbid conditions other than RA. RA clinical variables included months of persistent symptom duration prior to study entry, morning stiffness of at least 1 hour, seropositivity [defined as ever testing positive for either RF or anti-citrullinated protein antibodies (ACPA)], and Disease Activity Score-28 (DAS28) disease activity category. The DAS28 was calculated using whichever acute phase reactant result was available, as it is infrequent in this cohort to have both measured, and we applied the corresponding disease activity cut points according to erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Finally, we adjusted for Physician Global Assessment of Disease Activity, as well as methotrexate use. Random effect terms were used to account for the

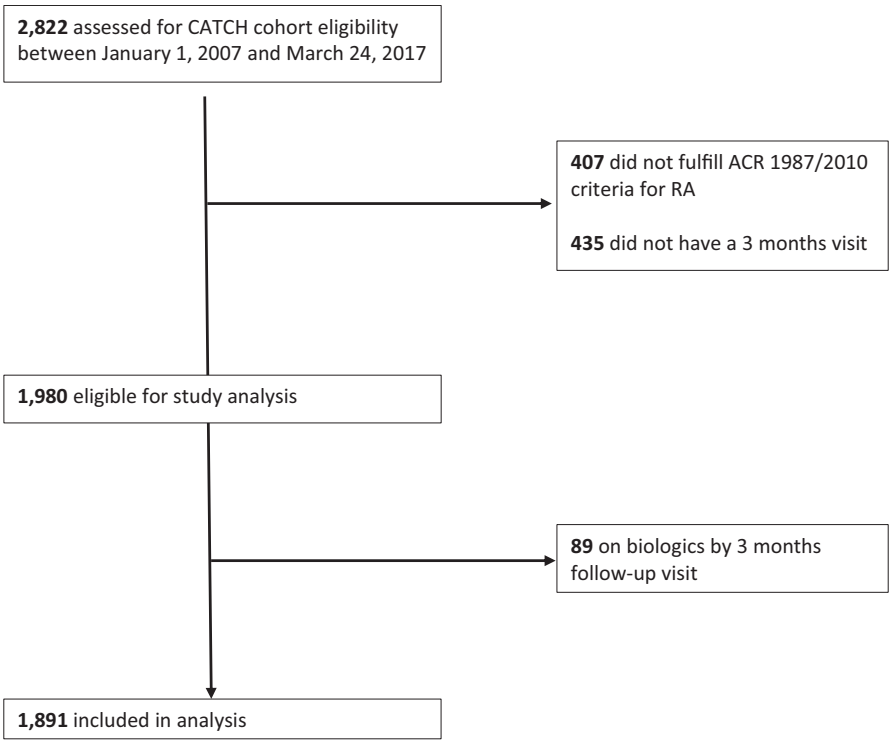

Figure 1. Flow chart of study sample selection (patient counts). ACR, American College of Rheumatology; CATCH, Canadian Early Arthritis Cohort; RA, rheumatoid arthritis.

clustering of treatment patterns within sites. Missing data were infrequent (<10%), and no systematic patterns of missingness were found upon examination; thus, we present a complete case analysis.

Outcomes and statistical analysis. Baseline characteristics were summarized with standard descriptive statistics, with standardized mean differences of more than 10% used to define significant differences between groups in a sample size–independent manner. Changes in disease activity measures (37) were described between steroid groups. We used Kaplan-Meier curves to visually represent the proportion of steroid users who were continuously prescribed steroids over time. Generalized mixed models with a binary distribution were used to calculate adjusted odds ratios (aORs) with 95% confidence intervals (95% CIs) for progression to a biologic drug separately for 12 and 24 months of follow-up, with random effect terms to account for clustering on study site. Models were adjusted for the prespecified covariates described above.

All analyses were performed using SAS version 9.4 statistical software (SAS Institute).

RESULTS

Patient characteristics at steroid initiation. After excluding 89 persons (4%) on biologics by 3 months, a total of 1891 persons were included in this analysis, recruited between January 1, 2007, and March 24, 2017 (Figure 1). Overall, 30% of CATCH participants were prescribed a glucocorticoid within 3 months of follow-up (Table 1). Among them, 303 people began steroids before CATCH study entry; most started within 2 or 3 months before enrollment (mean = 77 days; SD = 105). For the 258 persons who began steroids at or after the date of CATCH study entry, initiation was most often shortly after baseline (mean = 11 days; SD = 22) and was used in people with higher disease activity. There were 109 persons (6% of the analytic cohort, 20% of the glucocorticoid-exposed group) who had both a parenteral and oral steroid within 3 months (Supplemental Table 2).

Table 1. Characteristics of early glucocorticoid users (n = 561, with subdivided groups of prevalent and incidence users) and nonusers

	Nonusers (n = 1,330)	Prevalent Users (n = 303)	Nonuser Vs Prevalent User[a]	New Users (n = 258)	Nonuser Vs New User[a]
Age, mean (SD), yr	54 (15)	57 (16)	0.19	57 (15)	0.20
Female sex, n (%)	998 (75)	196 (65)	0.22	177 (69)	0.13
Employed, n (%)	771 (58)	137 (45)	0.26	117 (45)	0.26
Education at or less than the high school level, n (%)	550 (41)	136 (45)	0.08	122 (47)	0.12
Overweight or obese, n (%)	620 (47)	123 (41)	0.12	86 (33)	0.29
Weight missing	396 (30)	118 (39)	0.19	132 (51)	0.44
Ever smoker, n (%)	740 (56)	182 (60)	0.08	144 (56)	0.00
Number of comorbidities other than RA, n (%)					
0	318 (24)	64 (21)	0.07	53 (21)	0.07
1	326 (25)	75 (25)	0.00	57 (22)	0.07
2	240 (18)	48 (16)	0.05	58 (22)	0.10
≥3	438 (33)	115 (38)	0.10	88 (34)	0.02
Symptom duration, mean (SD), mo	6.0 (3.0)	5.6 (3.0)	0.13	4.6 (2.6)	0.50
Morning stiffness ≥1 h, n (%)	760 (57)	209 (69)	0.25	149 (58)	0.02
ESR, mean (SD), mm/h	26.2 (20.6)	27.1 (24.5)	0.04	35.9 (27.3)	0.40
CRP, mean (SD), mg/L	13.4 (17.6)	16.3 (19.1)	0.16	21.9 (22.7)	0.42
TJC28, mean (SD)	8 (6)	8 (7)	0.00	11 (7)	0.46
SJC28, mean (SD)	7 (6)	7 (6)	0.00	10 (7)	0.46
Seropositive, n (%)	898 (68)	198 (65)	0.06	143 (55)	0.27
Missing	213 (16)	45 (15)	0.03	33 (13)	0.09
DAS28 (from ESR or CRP if ESR is missing), mean (SD)	4.9 (1.4)	4.8 (1.4)	0.07	5.6 (1.4)	0.50
CDAI, mean (SD)	26.2 (13.4)	25.1 (13.8)	0.08	32.8 (15.0)	0.46
Physician Global Assessment, 0-10, mean (SD)	4.8 (2.5)	4.8 (2.5)	0.00	5.6 (2.4)	0.33
Patient Global Assessment (range, 0-10), mean (SD)	5.8 (2.9)	5.3 (3.1)	0.17	6.4 (2.9)	0.21
HAQ-DI (range, 0-3), mean (SD)	1.0 (0.7)	1.0 (0.7)	0.00	1.2 (0.7)	0.29
Pain (range, 0-10), mean (SD)	5.5 (2.8)	5.1 (2.9)	0.14	6.3 (2.6)	0.30
Fatigue (range, 0-10), mean (SD)	5.0 (3.0)	5.0 (3.1)	0.00	6.0 (2.9)	0.34
Use of any DMARD, n (%)	1187 (89)	292 (96)	0.27	241 (93)	0.14
Methotrexate use, n (%)	943 (71)	256 (84)	0.32	202 (78)	0.16
Among users, dose ≥20 mg/wk	632 (67)	185 (72)	0.11	105 (52)	0.31
Oral steroids average daily dose, mean (SD), mg	N/A	13.1 (11.8)	N/A	12.4 (8.7)	N/A
Oral steroids maximum daily dose, mean (SD), mg	N/A	16.0 (13.7)	N/A	15.1 (10.8)	N/A

Abbreviations: CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28, disease activity score-28; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; HAQ-DI, health assessment questionnaire disability index; N/A, not applicable; RA, rheumatoid arthritis; Vs, versus.

[a] Nonusers, prevalent users, and new users were compared using absolute standardized mean differences.

Table 2. Mean disease activity scores over time, by early steroid use

	Time Since CATCH Cohort Entry				
	6 Months	9 Months	12 Months	18 Months	24 Months
Clinical Disease Activity Index, mean (SD)					
Early glucocorticoid	9.0 (12.8)	6.6 (11.5)	6.3 (9.5)	5.3 (10.6)	4.0 (7.5)
Not prescribed	6.6 (12.9)	5.5 (10.0)	5.0 (9.0)	4.0 (9.0)	4.0 (8.0)
Tender joints (range, 0-28), mean (SD)					
Early glucocorticoid	2 (5)	1 (4)	1 (3)	1 (3)	0 (2)
Not prescribed	1 (4)	1 (3)	1 (3)	0 (2)	0 (2)
Swollen joints (range, 0-28), mean (SD)					
Early glucocorticoid	1 (4)	0 (3)	0 (2)	0 (2)	0 (1)
Not prescribed	1 (3)	0 (2)	0 (2)	0 (2)	0 (1)
Pain (range, 0-10), mean (SD)					
Early glucocorticoid	3.0 (4.7)	3.0 (4.0)	2.0 (3.0)	2.0 (4.0)	2.0 (3.0)
Not prescribed	2.0 (4.0)	2.0 (3.1)	2.0 (3.2)	2.0 (3.9)	1.9 (3.9)
Patient Global Assessment (range, 0-10), mean (SD)					
Early glucocorticoid	3.0 (4.5)	3.0 (4.0)	2.9 (4.0)	2.5 (4.0)	2.0 (4.0)
Not prescribed	2.0 (4.0)	2.0 (3.9)	2.0 (4.1)	2.0 (3.5)	2.0 (3.6)
Physician Global Assessment (range, 0-10), mean (SD)					
Early glucocorticoid	1.5 (3.2)	1.0 (2.9)	0.7 (2.0)	0.5 (2.0)	0.2 (1.8)
Not prescribed	1.0 (3.0)	1.0 (2.0)	0.8 (2.0)	0.3 (2.0)	0.1 (1.0)
HAQ-DI (range, 0-3), mean (SD)					
Early glucocorticoid	0.50 (1.00)	0.50 (1.00)	0.38 (1.00)	0.38 (1.00)	0.25 (1.00)
Not prescribed	0.38 (0.88)	0.25 (0.75)	0.25 (0.75)	0.25 (0.75)	0.25 (0.75)
Erythrocyte sedimentation rate, mean (SD), mm/h					
Early glucocorticoid	13.0 (18.0)	12.0 (15.0)	11.0 (16.0)	12.0 (18.0)	10.0 (17.0)
Not prescribed	12.0 (16.0)	11.0 (17.0)	11.0 (17.0)	10.0 (16.0)	11.0 (17.0)
C-reactive protein, mean (SD), mg/L					
Early glucocorticoid	3.0 (6.0)	3.0 (5.9)	3.0 (5.6)	3.0 (6.0)	3.0 (6.0)
Not prescribed	2.9 (5.1)	2.5 (4.5)	2.7 (5.0)	2.7 (5.0)	3.0 (5.0)

Abbreviations: CATCH, Canadian Early Arthritis Cohort; HAQ-DI, health assessment questionnaire disability index.

The mean oral steroid dose was 12.8 mg (SD = 10.5). As compared with nonusers, participants receiving glucocorticoids were significantly older, less likely to be employed, and had a shorter disease duration (Supplemental Table 1). HAQ-DI scores were similar (1.0 nonusers versus 1.1 users). Combination steroid users had several comorbidities and elevated markers of baseline disease activity (ESR, CRP, and morning stiffness) as well as methotrexate use (Supplemental Table 2).

Patient characteristics and disease activity measures over time by early steroid exposure. Disease control, as measured by a variety of disease activity measures, improved over 24 months (Table 2). Although the early glucocorticoid group started at higher levels of disease activity on each measure, no differences remained by 24 months. The proportion of participants with moderate or high disease activity, as measured by Clinical Disease Activity Index (Figure 2) and also by DAS28 (Supplemental

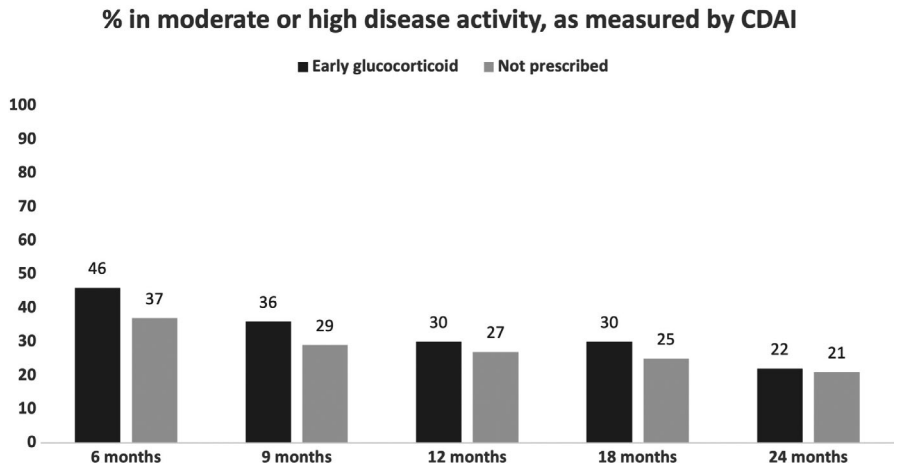

Figure 2. Longitudinal changes in Clinical Disease Activity Index (CDAI), by early steroid exposure groups.

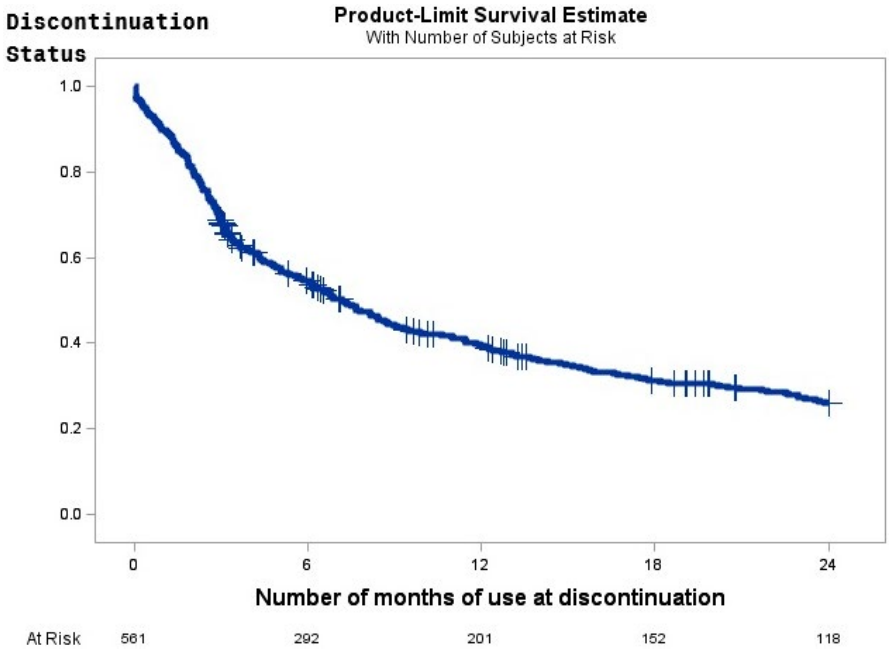

Figure 3. Number of months from oral steroid initiation to discontinuation. Participants who were still using oral steroids at the end of their follow-up, or at 24 months if there was more than 24 months of follow-up, were censored.

Figure 1), at each time point was greater in the early glucocorticoid group than in the group not prescribed glucocorticoids. Results were similar when restricted to persons with at least 24 months of follow-up, suggesting that there was a random loss to follow-up rather than systematic patterns of loss to follow-up (data not shown).

Among the subset of patients who initiated glucocorticoids early in CATCH follow-up, 30% were either unable to discontinue by 2 years or were persistently using oral steroids at the last date of follow-up (Figure 3).

Early steroid use and progression to biologics. Among participants with at least 12 months of follow-up data, 159 (10%) initiated a biologic by 12 months; among those with at least 24 months of follow-up, 199 (15%) initiated a biologic. Unadjusted risk ratios suggest that early glucocorticoid use significantly increased risk of biologic use at 12 months (risk ratio = 2.2; 95% CI, 1.7-3.0) and 24 months (risk ratio = 1.9; 95% CI, 1.4-2.4). Compared with nonusers, participants with early glucocorticoid use were significantly more likely to be prescribed a biologic by 12 months (aOR = 2.4; 95% CI, 1.5-3.7) and 24 months (aOR = 1.9; 95% CI, 1.3-3.0) (Table 3).

DISCUSSION

To our knowledge, this is the first study to show that in Canadian early RA care, steroid use is mostly directed to patients with severe and active disease. As expected, disease activity improved over follow-up for all groups, consistent with the treat-to-target paradigm in Canada. Early use of glucocorticoids was associated with higher disease activity at baseline, creating a greater relative difference by 24 months than non–steroid-exposed persons;

Table 3. ORs with 95% CIs for biologic initiation by 12 months and 24 months of follow-up, by early steroid exposure

	12 Months				24 Months			
	Number of Events, n (%)	Number With Follow-Up	Crude OR[a] (95% CI)	Adjusted OR (95% CI)	Number of Events, n (%)	Number With Follow-Up	Crude OR[a] (95% CI)	Adjusted OR (95% CI)
Early oral glucocorticoids	77 (16)	483	2.2 (1.5-3.1)	2.4 (1.5-3.7)	89 (22)	396	1.9 (1.4-2.7)	1.9 (1.3-3.0)
Not prescribed	82 (7)	1137	1.0 (ref)	1.0 (ref)	110 (12)	911	1.0 (ref)	1.0 (ref)

Abbreviations: CI, confidence interval; OR, odds ratio; ref, reference; DAS28-ESR, disease activity score - erythrocyte sedimentation rate; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.
[a] Crude model accounts for clustering on study site.
[b] Adjusted for age, sex, number of comorbidities other than rheumatoid arthritis, symptom duration, morning stiffness lasting more than 1 hour, seropositivity, as well as DAS28-ESR (or CRP if ESR was missing), Physician Global Assessment, and methotrexate use. Random effects terms for study site were used, with robust standard errors adjusted for clustering on study site. In the adjusted models, 386 persons with 12 months of follow-up and 304 persons with 24 months of follow-up were excluded because of missing data.

absolute measures of disease activity were similar. Importantly, early glucocorticoids were associated with the need to intensify drug use over time. Nearly one in three people who have an early glucocorticoid prescription are unable to discontinue 2 years later. Taken together, these findings are consistent with selective steroid use in an advanced disease activity population, sometimes referred to as "confounding by indication" or "channeling bias."

One possible explanation for the findings is that the early use of glucocorticoids in more active disease and severe symptoms may reflect a clinician's concerns about exposing their patients with less active baseline disease to additional side effects if there is not a strong indication for steroid use. Our results are similar to recent findings from administrative claims in the United States, which showed that glucocorticoids did not reduce biologic use, but add an in-depth analysis of clinical data that provides further insight into how glucocorticoids are used and in whom. Among early glucocorticoid users, the odds of progression to a biologic at 12 and 24 months were nearly double those of people not prescribed early glucocorticoids.

Overall, 30% of the cohort initiated oral glucocorticoids close to their study enrollment date, and 20% of these patients received both oral and parenteral steroids over the first 3 months. The rationale for using both was not queried, but using combination glucocorticoids as a strategy to gain faster disease control, and then being able to stop oral steroids sooner, may have been one motivator. Drug use findings are important, as future drug safety and effectiveness analyses require a rich understanding of which patients are exposed to a given therapy, and our findings may inform future propensity score analyses, in which factors identified in this work can be used to predict the probability of drug exposure, in this cohort as well as others.

Strengths of the study include the use of a large, well-characterized cohort of patients with early RA with comprehensive longitudinal disease activity measures. Data are from real-world patients treated in rheumatology clinics across Canada. Rheumatologists participating in the study meet annually to review treat-to-target strategies and major RA treatment recommendations, with the goal of achieving sustained remission as quickly as possible. Patients were followed at regular intervals, and treatment was escalated if patients had not yet achieved remission (or low disease activity, if it was not possible to achieve remission). In Canada, almost all patients with RA can access biologic therapy if they have failed a guideline-based therapy with one or more csDMARDs. Steroid use is not mandated in the Canadian health care system, and guidelines suggest use for short periods of time as bridge therapy. However, we found that a large proportion needed these medications much longer than bridge use. Thus, patterns we observed of steroid use represent those typical of real-world practice in the context of having access to health care and relatively similar access to therapy that represents the standard of care.

This study has limitations. Initially, the CATCH study did not have a widespread collection of oral steroid dose, nor did it distinguish the parenteral injections as intramuscular or intra-articular. Although these data were ultimately added later using protocol amendments, they were not available for the earlier participants of this cohort. We also could not account for cases in which treatments were recommended but declined by patients or cases in which patients did not adhere to prescribed therapies. Furthermore, reasons for use, either by the physician or patient, were not captured. Other unmeasured factors also may have impacted decisions about whether to initiate, continue, or stop using glucocorticoids, as well as other long-term disease activity measures.

In conclusion, these results from a Canadian clinical setting suggest that initiation of low-dose glucocorticoids early in the course of new RA occurs mostly in severe disease and predicts the need for biologics in the upcoming 2 years. Our results did not find significant differences in disease control 24 months later when comparing glucocorticoid users and nonusers, which is likely a reflection of their use among a subset of persons with more severe disease rather than a true lack of effectiveness. Early use of steroids was frequently prolonged, perhaps as a longer-term option rather than a true bridge therapy as patients wait for access to advanced therapies and for treatment escalation to take effect. Thus, in the Canadian clinical practice sites participating in this observational study, glucocorticoids were not used as short-term bridge therapy envisioned in practice recommendations.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Ms Valois and Dr Schieir had full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the analysis.

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