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

Kathleen M. Andersen,1 Orit Schieir,2 Marie-France Valois,2 Susan J. Bartlett,2 Louis Bessette,3 Gilles Boire,4 Boulos Harauqi,5 Glen Hazlewood,5 Carol Hitchon,6 Edward C. Keystone,5 Janet Pope,11 Diane Tin,12 J Carter Throne,12 and Vivian P. Bykerk,13 on behalf of CATCH Investigators

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 Hoffman-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.

1Kathleen M. Andersen, MSc: Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; 2Orit Schieir, PhD: University of Toronto, Toronto, Ontario, Canada; 3Marie-France Valois, MSc: McGill University, Montreal, Quebec, Canada; 4Susan J. Bartlett, PhD: McGill University, Montreal, Quebec, Canada, and Johns Hopkins University, Baltimore, Maryland; 5Louis Bessette, MD, MSc: Centre Hôpitalier Universitaire de Québec-Université Laval, Quebec, Quebec, Canada; 6Gilles Boire, MD, MSc: Université de Sherbrooke, Sherbrooke, Quebec, Canada; 7Boulos Harauqi, MD: Institut de Rhumatologie de Montreal, Montreal, Quebec, Canada; 8Glen Hazlewood, MD, PhD: University of Calgary, Calgary, Alberta, Canada; 9Carol Hitchon, MD, MSc: University of Manitoba, Winnipeg, Manitoba, Canada; 10Edward C. Keystone, MD: Mount Sinai Hospital, Toronto, Ontario, Canada; 11Janet Pope, MD, MPH: St. Joseph's Health Care London and University of Western Ontario, London, Ontario, Canada; 12Diane Tin, BSc Phm, J Carter Thorne, MD: Southlake Regional Health Centre, Newmarket, Ontario, Canada; 13Vivian P. Bykerk, MD: Hospital for Special Surgery and Weill Cornell Medicine, New York City, New York. Members of Canadian Early Arthritis Cohort (CATCH) Investigators are as follows: Pooneh Akhavan, Louis Bessette, Gilles Boire, Vivian Bykerk, Ines Colmegna, Sabrina Fallavollita, Derek Haaland, Boulos Harauqi, Glen Hazlewood, Carol Hitchon, Shahin Jamali, Raman Josh, Ed Keystone, Bindee Kuria, Peter Panopalis, Janet Pope, Carter Thorne, Edith Villeneuve, Michel Zummer.

Ms. Andersen has received doctoral training support from the National Heart, Lung, and Blood Institute Pharcacoepidemiology Training Program (grant T32-HL-139426-03) in the United States. Dr. Bartlett has consulted for Pfizer, Union Chimique Belge (UCB), Lilly, Novartis, Merck, Janssen, and AbbVie. Dr. Bessette has received funding for research from Amgen, Bristol-Myers Squibb (BMS), Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, and Novartis; consulting agreements/advisory board membership with Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, and Novartis; and speaker honoraria agreements from Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, and Novartis. Dr. Boire has served on advisory boards for Amgen, BMS, Celgene, Eli Lilly, and Pfizer; has served as a speaker for Merck, BMS, and...
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 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 trials (RCTs) with Astra Zeneca, Bayer, BMS, Merck, Roche, Seattle Genetics, and UCB. Dr. Thorne has served on advisory boards for AbbVie, Amgen, Celgene, Lilly, Medexus/Medac, Merck, Novartis, Pfizer, and Sanofi; has consulted for AbbVie, Centocor, Janssen, Lilly, Medexus/Medec, and Pfizer; has served as speaker for Medexus/Medec; has served on investigator-initiated studies funded by Amgen and Pfizer; and has had RCTs funded by AbbVie, Celgene, CaREBiomed, Novartis, and Pfizer. Dr. Bykerr has consulted for Amgen, Gilead, Sanofi Genzyme/Regeneron, Scipher, Pfizer Pharmaceuticals, and UCB. No other disclosures relevant to this article were reported.

Address correspondence to Vivian P. Bykerr, MD, Hospital for Special Surgery, Department of Rheumatology, 535 East 70th Street, New York, NY 10021. Email address: bykerkv@hss.edu.

Submitted for publication May 4, 2021; accepted in revised form August 5, 2021.
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

| Variable                                                                 | Nonusers (n = 1,330) | Prevalent Users (n = 303) | Nonuser Vs Prevalent User* | New Users (n = 258) | Nonuser Vs New User* |
|-------------------------------------------------------------------------|----------------------|---------------------------|---------------------------|---------------------|----------------------|
| **Demographics**                                                        |                      |                           |                           |                     |                      |
| 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                                                          | 376 (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 (%)                                           | 170 (13)             | 209 (69)                  | 0.25                      | 149 (58)            | 0.02                 |
| ESR, mean (SD), mm/h                                                    | 26.2 (20.6)          | 271 (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 (89)            | 0.14                 |
| Methotrexate use, n (%)                                                 | 943 (71)             | 256 (84)                  | 0.32                      | 202 (78)            | 0.16                 |
| Among users, dose ≥ 20 mg/wk                                            | 632 (47)             | 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.*

*Nonusers, prevalent users, and new users were compared using absolute standardized mean differences.
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 Table 2).
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 |
| --- | --- | --- | --- | --- | --- | --- |
| | Number of Events, n (%) | Number With Follow-Up | Crude OR* (95% CI) | Adjusted OR (95% CI) | Number of Events, n (%) | Number With Follow-Up | Crude OR* (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.

* Crude model accounts for clustering on study site.

**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.
GLUCOCORTICOIDS IN CATCH COHORT

Taken together, these findings are consistent with selective glucocorticoid prescription are unable to discontinue 2 years later. Early glucocorticoids were associated with the need to intensify therapy that represents the standard of care. However, we found that a large proportion needed these medications much longer than bridge use. Thus, patterns we observed may inform future propensity score analyses, in which factors 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.

Study conception and design. Andersen, Haraoui, Bykerk

Acquisition of data. Bartlett, Basset, Boire, Haraoui, Hazlewood, Hitchon, Keystone, Pope, Thorne, Bykerk

Analysis and interpretation of data. Andersen, Schieir, Valois

REFERENCES

1. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016;388:2023–38.
2. Barnabe C, Sun Y, Boire G, Hitchon CA, Haraoui B, Thorne JC, et al. Heterogeneous disease trajectories explain variable radiographic, function and quality of life outcomes in the Canadian Early Arthritis Cohort (CATCH). PLoS One 2015;10:e0135327.
3. Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Bournpas D, Burmester G, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631–7.
4. Smolen JS, Breedveld FC, Burmester GR, Bykerk V, Dougados M, Emery P, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. Ann Rheum Dis 2016;75:3–15.
5. Hench P. Effects of cortisone in the rheumatic diseases. Lancet 1950;2:483–4.
6. Kirwan JR. The effect of glucocorticoids on joint destruction in rheumatoid arthritis. The Arthritis and Rheumatism Council Low-Dose Glucocorticoid Study Group. N Engl J Med 1995;333:142–6.
7. Benedek TG. History of the development of corticosteroid therapy. Clin Exp Rheumatol 2011;29 Suppl 88:5–12.
8. Morrison E, Capell HA. Corticosteroids in the management of early and established rheumatoid disease. Rheumatology (Oxford) 2006;45:1058–61.
9. Listing J, Gerhold K, Zink A. The risk of infections associated with rheumatoid arthritis, with its comorbidity and treatment. Rheumatology (Oxford) 2013;52:53–61.
10. Dixon WG, Suss S, Hudson M. The association between systemic glucocorticoid therapy and the risk of infection in patients with rheumatoid arthritis: systematic review and meta-analyses. Arthritis Res Ther 2011;13:R139.
11. Deandrade JR, McCormick JN, Hill AG. Small doses of prednisolone in the management of rheumatoid arthritis. Ann Rheum Dis 1964;23:158–62.
12. Buttgereit F, Doering G, Schaeffler A, Witte S, Sierakowski S, Gronmica-Ilhe E, et al. Efficacy of modified-release versus standard prednisone to reduce duration of morning stiffness of the joints in rheumatoid arthritis (CAPRA-1): a double-blind, randomised controlled trial. Lancet 2008;371:205–14.
13. van Everdingen AA, Jacobs JW, Siewertsz van Reesema DR, Bijlsma JW. Low-dose prednisone therapy for patients with early active rheumatoid arthritis: clinical efficacy, disease-modifying properties, and side effects: a randomized, double-blind, placebo-controlled clinical trial. Ann Intern Med 2002;136:1–12.
14. Harris ED, Jr., Emkey RD, Nichols JE, Newberg A. Low dose prednisone therapy in rheumatoid arthritis: a double blind study. J Rheumatol 1983;10:713–21.
15. de Jong PH, Hazes JM, Barendregt PJ, Huisman M, van Zeiden D, van der Lubbe PA, et al. Induction therapy with a combination of DMARDs is better than methotrexate monotherapy: first results of the TREACH trial. Ann Rheum Dis 2013;72:72–8.
16. Boers M, Verhoeven AC, Markusse HM, van de Laar MA, Westhovens R, van Denderen JC, et al. Randomised comparison of combined step-down prednisolone, methotrexate and sulphasalazine with sulphasalazine alone in early rheumatoid arthritis. Lancet 1997;350:309–18.
17. Svensson B, Boonen A, Albertsson K, van der Heijde D, Keller C, Hafstrom I. Low-dose prednisolone in addition to the initial disease-modifying antirheumatic drug in patients with early active rheumatoid arthritis reduces joint destruction and increases the remission rate: a two-year randomized trial. Arthritis Rheum 2005;52:3360–70.
18. Wassenberg S, Rau R, Steinfeld P, Zeidler H. Very low-dose prednisolone in early rheumatoid arthritis retards radiographic progression over two years: a multicenter, double-blind, placebo-controlled trial. Arthritis Rheum 2005;52:3371–80.
19. Bakker MF, Jacobs JW, Welsing PM, Verstappen SM, Tekstra J, Ton E, et al. Low-dose prednisone inclusion in a methotrexate-based, tight control strategy for early rheumatoid arthritis: a randomized trial. Ann Intern Med 2012;156:329–39.
20. Jacobs JW, van Everdingen AA, Verstappen SM, Bijlsma JW. Followup radiographic data on patients with rheumatoid arthritis who participated in a two-year trial of prednisone therapy or placebo. Arthritis Rheum 2006;54:1422–8.
21. Singh JA, Saag KG, Bridges SL, Aki EA, Bannuru RR, Sullivan MC, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol 2016;68:1–26.
22. Smolen JS, Landewe RBM, Bijlsma JWJ, Burmester GR, Dougados M, Kershbaumer A, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis 2020;79:685–99.
23. Arnold MB, Bykerk VP, Boire G, Harauoi BP, Hitchon C, Thorne C, et al. Are there differences between young- and older-onset early inflammatory arthritis and do these impact outcomes? An analysis from the CATCH cohort. Rheumatology (Oxford) 2014;53:1075–86.
24. De Witt EM, Lin L, Glick HA, Anstrom KJ, Schulman KA, Reed SD. Pattern and predictors of the initiation of biologic agents for the treatment of rheumatoid arthritis in the United States: an analysis using a large observational data bank. Clin Ther 2009;31:1871–80.
25. George MD, Sauer BC, Ting CC, Cannon GW, England BR, Kerr GS, et al. Biologic and glucocorticoid use after methotrexate initiation in patients with rheumatoid arthritis. J Rheumatol 2019;46:343–50.
26. Roubille C, Rincheval N, Dougados M, Ripo RM, Daures JP, Combe B. Seven-year tolerability profile of glucocorticoids use in early rheumatoid arthritis: data from the ESPOIR cohort. Ann Rheum Dis 2017;76:1797–802.
27. Landewe RB, Boers M, Verhoeven AC, Westhovens R, van de Laar MA, Markusse HM, et al. COBRA combination therapy in patients with early rheumatoid arthritis: long-term structural benefits of a brief intervention. Arthritis Rheum 2002;46:347–56.
28. Duru N, van der Goes MC, Jacobs JW, Andrews T, Boers M, Buttgereit F, et al. EULAR evidence-based and consensus-based recommendations on the management of medium to high-dose glucocorticoid therapy in rheumatic diseases. Ann Rheum Dis 2013;72:1905–13.
29. Spivey CA, Griffith J, Kaplan C, Postlethwaite A, Ganguli A, Wang J. A retrospective analysis of corticosteroid utilization before initiation of biologic DMARDs Among patients with rheumatoid arthritis in the United States. Rheumatol Ther 2018;5:255–70.
30. Kim G, Bramer JC, Rascati K, Richards K. Factors associated with the initiation of biologic disease-modifying antirheumatic drugs in Texas Medicaid patients with rheumatoid arthritis. J Manag Care Spec Pharm 2015;21:401–7.
31. Desai RJ, Rao JK, Hansen PA, Fang G, Maciejewski ML, Farley JE. Predictors of treatment initiation with tumor necrosis factor-alpha inhibitors in patients with rheumatoid arthritis. J Manag Care Spec Pharm 2014;20:1110–20.
32. Jin Y, Desai RJ, Liu J, Choi NK, Kim SC. Factors associated with initial or subsequent choice of biologic disease-modifying antirheumatic drugs for treatment of rheumatoid arthritis. Arthritis Res Ther 2017;19:159.
33. Bykerk VP. Low-dose glucocorticoid use does not reduce biologic use in early ra, nor do biologics reduce the need for glucocorticoids. J Rheumatol 2019;46:331–2.
34. Bykerk VP, Jamal S, Boire G, Hitchon CA, Harauoi B, Pope JE, et al. The Canadian Early Arthritis Cohort (CATCH): patients with new-onset synovitis meeting the 2010 ACR/EULAR classification criteria but not the 1987 ACR classification criteria present with less severe disease activity. J Rheumatol 2012;39:2071–80.
35. Ray WA. Evaluating medication effects outside of clinical trials: new-user designs. Am J Epidemiol 2003;158:915–20.
36. Sussia S. Immortal time bias in pharmaco-epidemiology. Am J Epidemiol 2008;167:492–9.
37. Aletaha D, Neill VP, Stamm T, Uffmann M, Pfugelbeil S, Machold K, et al. Acute phase reactants add little to composite disease activity indices for rheumatoid arthritis: validation of a clinical activity score. Arthritis Res Ther 2005;7:R796–806.