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

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ABSTRACT. ***Objective.*** Our objective was to describe characteristics of Canadian patients with early arthritis and examine differences between those fulfilling 1987 and 2010 rheumatoid arthritis (RA) classification criteria.

Methods. The Canadian Early Arthritis Cohort (CATCH) is a national, multicenter, observational, prospective cohort of patients with early inflammatory arthritis, receiving usual care, recruited since 2007. Inclusion criteria include age > 16 years; symptom duration 6–52 weeks; swelling of ≥ 2 joints or ≥ 1 metacarpophalangeal/proximal interphalangeal joint; and 1 of rheumatoid factor ≥ 20 IU, positive anticitrullinated protein antibodies (ACPA), morning stiffness ≥ 45 min, response to nonsteroidal antiinflammatory drug, or positive metatarsophalangeal joint squeeze test. Data from patients enrolled to March 15, 2011, were analyzed.

Results. In total, 1450 patients met the eligibility criteria (1187 were followed). At baseline, mean age was 53 ± 15 years, symptom duration was 6.1 ± 3.2 months, Disease Activity Score (DAS28) was 4.9 ± 1.6, Health Assessment Questionnaire-Disability Index was 1.0 ± 0.7. Forty-one percent (n = 450) of patients had moderate (3.2 < DAS28 ≤ 5.1) and 46% (n = 505) had high (DAS28 > 5.1) disease activity; 28% of those with baseline radiographs (n = 250/908) had radiographic evidence of erosions. ACPA status was available for 70% (n = 831) of patients; 55% (n = 453) tested positive. Sixty percent (n = 718) of patients were treated with methotrexate (MTX) initially. Of 612 patients without erosions, 63% and 83% fulfilled 1987 and 2010 RA classification criteria, respectively. Seventy-three percent (n = 166) of those who did not fulfill 1987 criteria were newly identified by the 2010 criteria. These patients had less severe disease and more were MTX-naive compared to those satisfying the 1987 criteria. Forty-seven percent of all patients achieved remission at 1 year.

Conclusion. Patients with early RA present with moderate high disease activity; < 50% achieve remission at 1 year, despite MTX treatment in the majority. The 2010 RA classification criteria identify more patients with RA who would previously have been designated as having undifferentiated disease. However, these patients have lower disease activity at the time of identification. (J Rheumatol First Release Aug 15 2012; doi:10.3899/jrheum.120029)

Key Indexing Terms:

RHEUMATOID ARTHRITIS | CLASSIFICATION | COHORT STUDY
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Rheumatoid arthritis (RA) is a chronic inflammatory and destructive joint disease, affecting about 1% of the general population[1]. Recent evidence suggests that early treatment with nonbiologic and/or biologic disease-modifying antirheumatic drugs (DMARD) can limit joint damage and improve longterm clinical outcomes[2,3,4,5]. Better outcomes are obtained with tighter disease control[6,7,8]. Accordingly, the goal of treatment is to achieve and maintain remission early in the course of disease[6,9,10].

While early treatment provides significant benefit, identifying patients early remains challenging. Data from early arthritis clinics across North America, Europe, and Latin America[11,12,13,14,15,16,17] have helped to characterize patients with symptoms of new-onset inflammatory arthritis or undifferentiated polyarthritis, allowing clinicians to better understand the demographic and disease characteristics of these populations. The 2010 RA classification criteria were developed to improve diagnostic sensitivity in early disease[18], potentially allowing earlier diagnosis of RA. Moreover, in recent years the definition of early RA (ERA) in many cohort studies has progressed to include patients with shorter symptom and disease durations. More specifically, recent ERA cohorts have included patients with symptom duration ≤ 1 year, with some cohorts including patients with as little as 1.5 to 3 months of symptoms[11,19,20,21]. Use of 2010 RA classification criteria, along with this evolving definition of ERA and inclusion criteria[22], may also influence demographic and disease characteristics of ERA populations, suggesting that demographics, treatments, and outcomes may differ in more recently established ERA cohorts compared to older ERA cohorts.

We describe the Canadian Early Arthritis Cohort (CATCH), a nationwide, multicenter, observational, prospective, real-world cohort of adults with early inflammatory arthritis. We present an analysis of baseline demographics and disease characteristics for participants and compare baseline demographic and disease characteristics among participants who meet the 1987 American College of Rheumatology (ACR) classification criteria to those who meet the 2010 ACR/European League Against Rheumatism (EULAR) classification criteria. Treatment characteristics and disease state calculated from Disease Activity Score (DAS28) from baseline to 1 year are also described.

MATERIALS AND METHODS

Study design. Data from CATCH were used to analyze baseline demographics and disease characteristics of the ERA population in Canada. Treatment characteristics and remission rates from baseline to 1 year were also analyzed. CATCH comprises adults with new-onset inflammatory arthritis symptoms. The cohort was formed by principal investigators of early arthritis populations located in Sherbrooke, Quebec; Toronto, Ontario; Montreal, Quebec; and Winnipeg, Manitoba, and was extended to other sites throughout Canada with harmonized inclusion criteria and methods. The cohort was developed to study clinical and other research questions, including short- and longterm outcomes in clinical practice. A scientific advisory committee oversees the study with monthly meetings by teleconferences, and an annual meeting with all investigators. Research ethics approval for each site has been obtained.

All eligible patients referred to participating early arthritis programs across Canada were offered enrollment in CATCH. Patients were referred to rheumatologists by their primary care physician. Patients recruited to the cohort provided written informed consent. The study protocol includes collection of patient- and investigator-reported data, results from routine laboratory testing, and in a subset of participants, samples for biobanking (see Appendix 1). Participants receive usual care, although investigators were encouraged to aim to treat patients to achieve remission, which is supported in the evidence-based literature as an attainable outcome[23].

Patients. The CATCH cohort has recruited patients since January 2007 and recruitment continues. Sites have been added since study inception, and 17 sites across Canada are now participating. Sites are located in urban, suburban, and rural communities. They include both academic and community medical centers. For our study, we included data from participants who were eligible for enrollment in the cohort up to March 15, 2011 (n = 1450). Patients are eligible for enrollment if they are > 16 years old, have joint symptoms for ≥ 6 weeks and ≤ 12 months, and have ≥ 2 swollen joints OR 1 swollen metacarpophalangeal or proximal interphalangeal joint, with 1 of the following features: rheumatoid factor (RF) ≥ 20 IU, positive test for anticitrullinated protein antibodies (ACPA), morning stiffness ≥ 45 minutes, response to nonsteroidal antiinflammatory drug treatment, or a painful metatarsophalangeal joint squeeze test. Patients are not required to meet 1987 ACR criteria for RA at baseline. Patients were excluded if they had psoriatic arthritis or infectious, crystal-induced, or connective tissue diseases. If these diagnoses were identified after inclusion, the patient was withdrawn from the cohort. All participants provided written informed consent before beginning study-related procedures.

The expected sample size for the CATCH cohort is based on an estimated recruitment of roughly 24 patients per site, per year. No limit has been placed on enrollment and no end date for the study has been specified. Data locks occur every 6 months. The analysis presented here includes data from 1187 patients with confirmed ERA or early inflammatory arthritis thought to be RA (or potentially RA) in the opinion of the investigator.

Outcomes. We describe baseline demographic and disease characteristics for patients enrolled in the CATCH cohort. We also compare characteristics among patients meeting 1987 ACR classification criteria and 2010 ACR/EULAR RA classification criteria[18,24]. DAS28 disease activity states were also compared from baseline to 1 year.

Assessments. Data for analysis were collected at the baseline visit, defined as the date of enrollment into the cohort following referral. This was usually within 1 month of referral. Assessments for each patient occur at baseline, then every 3 months for the first year, and every 6 months thereafter. Assessments include a combination of physician- and patient-reported outcomes (Appendix 1). Physician assessments include a record of current and past medications, physical examination, including 66 tender and 68 swollen joint counts, extraarticular manifestations, number of 1987 ACR classification criteria met for diagnosis of RA, and physician global assessment of disease activity. Fulfillment of the 2010 ACR/EULAR classification criteria was determined using the 2010 scorebased algorithm for patients who had all necessary data for this calculation, and for the subset of these

patients who had baseline erosions. The analysis was performed on patients with no baseline radiographs, as well. Patient self-reported data include demographic variables (e.g., age, sex, ethnicity, marital status, and living situation), socioeconomic variables (highest education, employment status), detailed medical and family history, RA disease activity on the Rheumatoid Arthritis Disease Activity Index (RADAI), patient global assessment of disease activity, and Health Assessment Questionnaire-Disability Index (HAQDI)[25,26,27].

Radiographic assessments of the hands and feet are completed at baseline and 6 months, then annually thereafter, for all patients who provide consent as part of their usual care. Radiographs have not yet been subjected to a standardized scoring method, and results presented here indicating the percentage of patients with erosions reflect the nonvalidated readings of multiple assessors.

Standard laboratory assessments were performed at every protocol visit according to a predefined schedule (Appendix 1). A chest radiograph, tuberculosis skin test, and bone mineral density tests were completed at baseline, as required.

All patient data were collected by trained rheumatologists and/or coordinators and entered into an encrypted and password-protected tablet or computer. Data were anonymized and synchronized to a central server. The central database adheres to the principles outlined in the Canadian Standards Association Privacy Code and other legislation and guidelines. Investigators and staff were trained at annual meetings to ensure validity in test measures across sites. Planned data analyses occur biannually.

Statistical analysis. Descriptive statistics (rates and proportions, frequency distributions, means, medians, SD, interquartile ranges) were used to summarize patients' baseline data. P values for categorical data (Table 4A) and data comparing disease activity states between groups over time were calculated using Fisher's exact test[28]. All p values are descriptive only. All statistical analyses were performed using R software[29].

For this analysis, DAS28 was calculated for all patients with available data; disease activity states were defined as follows: remission = DAS28 < 2.6; low disease activity = DAS28 ≥ 2.6 and ≤ 3.2; moderate disease activity = DAS28 > 3.2 and ≤ 5.1; high disease activity = DAS28 > 5.1[30,31].

Clinical data are managed by McDougall Scientific Ltd. (website: http://www.mcd-sci.on.ca/), a third-party statistical and clinical data management firm. Clinsys Inc. provides electronic data capture and storage services. Both ensure compliance with standard operating procedures designed to ensure consistency in data collection and minimize missing data and adhere to Health Insurance Portability and Accountability Act guidelines for privacy of data. The CATCH database is analyzed by a trained statistician under direction of the scientific advisory committee and other experts.

RESULTS

Patient disposition and geographic distribution. The study began in January 2007 and is continuing. March 15, 2011, was the cutoff date for data collection for the current analysis. As of this date, 1450 patients had provided consent and initially met eligibility criteria for enrollment. Subsequently, 263 (18.1%) of the patients who provided consent had withdrawn from the cohort, resulting in 1187 patients (81.9%) followed and included in analyses described below (Figure 1). The most common reasons for withdrawal in these 263 patients were loss to followup (n = 68; 25.9%), withdrawal of consent (n = 64; 24.3%), non-ERA diagnosis (n = 57; 23.2%), moved away (n = 40; 15.2%), comorbidity (n = 18; 6.8%), death (n = 11; 4.2%), protocol violation at study entry, where review of the data indicated a symptom duration > 12 months (n = 4; 0.3%), and language barriers (n = 1; < 0.5%). The major non-ERA diagnoses included newly recognized psoriatic arthritis (n = 16), spontaneous resolution or viral/reactive arthritis (n = 13), and progression to connective tissue disease (e.g., scleroderma, vasculitis; n = 4). No specific reason was given for 16 of the 57 patients with a non-ERA diagnosis. Disease severity and baseline characteristics for patients who withdrew were similar to the patient population being analyzed. Of the 1187 patients followed, the majority (80.5%) were enrolled at centers in Ontario (n = 628; 53.0%) and Quebec (n = 328; 27.6%), because 11 of the 18 participating centers are located in those provinces (Table 1). These 2 provinces are the most populous, representing 62% of the Canadian population. Sites are located in 8 of 10 provinces[32].

Demographic and clinical characteristics. Mean age of subjects was 53 ± 15 SD years and 83% (n = 990) were white (Table 1). Overall, 73% (n = 863) were female, and 28% (250 of 908 with available radiographs) had erosions in the hands or feet. The mean symptom duration overall was 6.1 ± 3.2 months. When stratified by year of study entry, there was a trend for median symptom duration to decrease over time between 2007 and 2011 [5.81 (interquartile range, IQR 4.73) vs 4.93 (IQR 3.83) months, respectively; p = 0.22; Table 1]. The proportion of patients with erosions increased with increasing symptom duration; however, there was no difference in symptom duration between patients with and those without erosions at baseline (Appendix 3). The mean tender joint count (TJC; 0–68 joints) was 12 ± 10 and TJC (0–28 joints) was 8 ± 7. The mean swollen joint count (SJC; for 0–68 joints) was 10 ± 8 and SJC (0–28 joints) was 8 ± 6. At baseline, mean DAS28 was 4.9 ± 1.6 and mean HAQ-DI score was 1.0 ± 0.7. Erythrocyte sedimentation rates were 27 ± 23 mm/h and C-reactive protein (CRP) levels were 14 ± 18 mg/l at baseline.

Treatment characteristics. Overall, 65% of patients were treatment-naive or had received < 4 weeks of DMARD treatment at study entry. However, 35% had been exposed to steroids and/or DMARD for over a month at the time of study entry. More than half the 1187 patients received methotrexate (MTX) at or just before the baseline visit (n = 718, 60%), with 31% (n = 223) receiving MTX subcutaneously (Table 2). In the overall population (n = 1187), most MTX users were receiving combination therapy with either hydroxychloroquine (HCQ) and/or sulfasalazine (SSZ; 32%, n = 381/1187). Only 28% (n = 337/1187) were receiving MTX monotherapy. At baseline, 15% (n = 176/1187) were receiving DMARD other than MTX. Only 2% (n = 24) of participants were prescribed biologic agents at baseline, most of which were anti-TNF agents [n = 19, 79%; etanercept, 47% (n = 9) and adalimumab, 42% (n = 8)]. Of the patients followed for at least 1 year (n = 705), 66% (n = 467) were prescribed MTX [41% (n = 190) subcutaneously]. MTX was received in combination with HCQ or SSZ by 43% (n = 303/705), while 23% (n = 164/705) received MTX

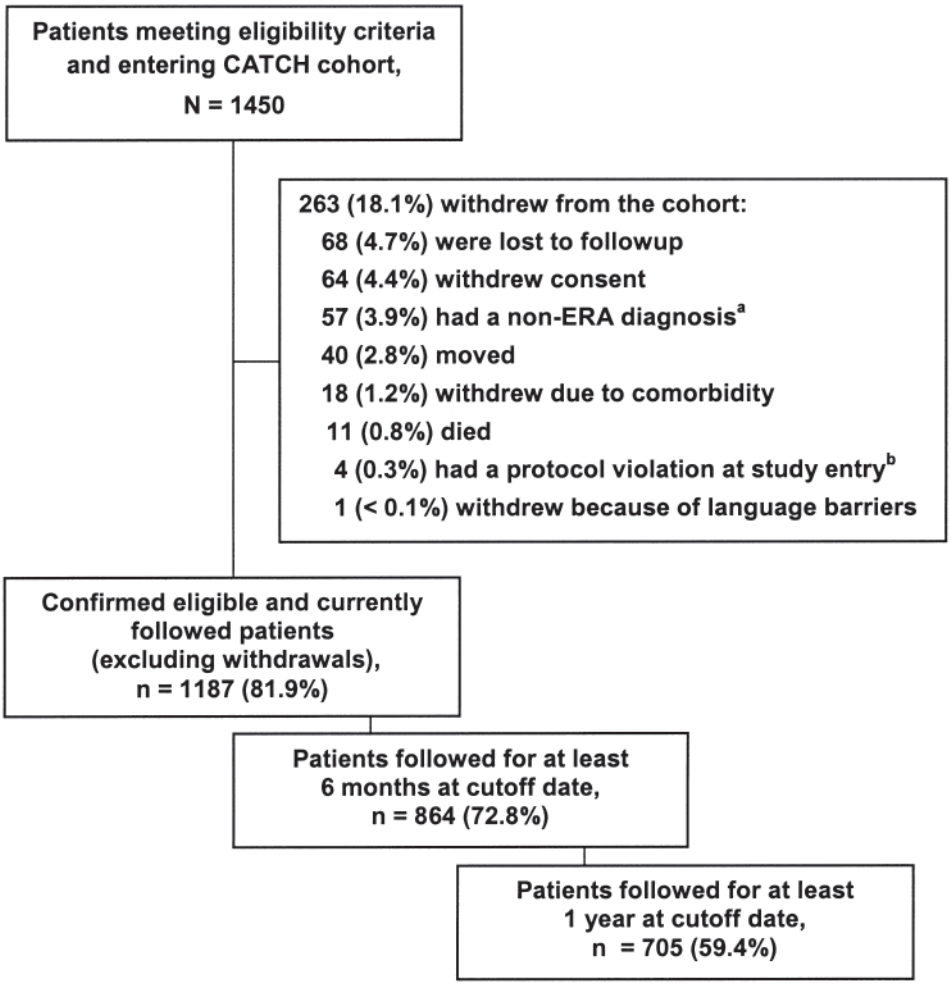

Figure 1. Patient disposition for the Canadian Early Arthritis Cohort (CATCH).

monotherapy and 12% (n = 84) received biologic therapy. Again, the majority of biologic use was with anti-TNF therapies [92%, n = 77; etanercept, 51% (n = 39), and adalimumab, 43% (n = 33)].

Disease activity over time. Overall, 1106 of 1187 patients (93%) had DAS28 scores available at baseline, of whom 46% (n = 505/1106) had high (DAS28 > 5.1), 41% (n = 450/1106) had moderate (3.2 < DAS28 ≤ 5.1), and 6% (n = 66/1106) had low disease activity (2.6 ≤ DAS28 ≤ 3.2), and 8% (n = 85/1106) fulfilled DAS28 remission criteria (DAS28 < 2.6; Table 3A). Of those with available DAS28 scores who were followed for at least 1 year (n = 569/705), 8% (n = 44/569) had high, 31% (n = 178/569) had moderate, and 14% (n = 77/569) had low disease activity scores, while 47% (n = 270/569) were in DAS28 remission (see Appendix 2 for patients followed for only 1 year). Table 3B shows the number of patients receiving corticosteroids (oral or intramuscular) based on the disease activity state at presentation. Overall, < 28% (315/1106) were exposed to corticosteroids before their baseline visit and the majority of those patients presented with moderate or high disease activity (Table 3B).

Patients fulfilling 1987 and 2010 RA classification criteria. Of the 908 patients with radiographs at baseline (Table 1), 855 had the necessary data available to establish a diagnosis of RA using both the 1987 ACR and 2010 ACR/EULAR classification criteria. Of those 855 patients, 243 (28%) had evidence of hand or foot erosions at baseline and 612 (72%) did not. In the 243 patients with baseline erosions, 82% (n = 199) met the 1987 criteria and 80% (n = 195) would meet the 2010 criteria if the score-based algorithm was applied (Table 4A), even though all patients with erosions typical for RA should be classified as RA without applying the score-based algorithm. Participants presenting with erosions at baseline had a higher average baseline DAS28 (5.14 ± 1.63 SD) compared to those without erosions at baseline (4.75 ± 1.57; p < 0.001), a difference of 0.39 (95% CI 0.16–0.61), and more of those with baseline erosions were

Table 1. Demographic and clinical characteristics of patients enrolled in the CATCH cohort by province; as of March 15, 2011 (n = 1187). Data are no. patients (%) unless otherwise specified.

	Patients (%)
Province	
Alberta	50 (4.2)
British Columbia	38 (3.2)
Manitoba	38 (3.2)
New Brunswick	0 (0.0)
Newfoundland and Labrador	33 (2.8)
Northwest Territories[a]	0 (0.0)
Nova Scotia	44 (3.7)
Nunavut[a]	0 (0.0)
Ontario	628 (53.0)
Prince Edward Island[a]	0 (0.0)
Quebec	328 (27.6)
Saskatchewan	28 (2.4)
Yukon[a]	0 (0.0)
All provinces	1187 (100)
Characteristic, all subjects at baseline (n = 1187, unless otherwise noted)	
Mean age, yrs (± SD)	53 ± 15
No. white (%)	990 (83)
No. female (%)	863 (73)
Mean symptom duration, mo ± SD[b]	6.1 ± 3.2
Median symptom duration, mo, by year of study entry (IQR)	
2007, n = 143	5.81 (4.73)
2008, n = 276	5.78 (5.59)
2009, n = 350	5.21 (4.03)
2010, n = 370	5.24 (3.86)
2011, n = 48[c]	4.93 (3.83)
No. with RF test at baseline[d] (%)	1063 (90)
No. RF-positive (%)	651 (61)
No. with ACPA test at baseline[e] (%)	831 (70)
No. ACPA-positive (%)	453 (55)
No. with radiographs at baseline[f] (%)	908 (76)
No. with erosions at baseline (hands, feet) (%)	250 (28)
TJC (0–68)	12 ± 10
TJC (0–28)	8 ± 7
SJC (0–68)	10 ± 8
SJC (0–28)	8 ± 6
DAS28, n = 1106	4.9 ± 1.6
ESR, mm/h[g]	27 ± 23
CRP, mg/l[h]	14 ± 18
Patient global assessment VAS, mm	57 ± 30
Physician global assessment VAS, mm	47 ± 25
Fatigue VAS, mm	5.2 ± 3.0
Pain VAS, mm	5.5 ± 2.8
HAQ-DI (0–3)	1.0 ± 0.7
No. with baseline DMARD (%)	841 (71)
No. with steroids (oral, intramuscular, or intraarticular) at baseline (%)	316 (27)
No. on MTX at baseline (%)	677 (57)

[a] Patients from Nunavut, Northwest Territories, Prince Edward Island, and Yukon were referred to centers in Manitoba and Ontario. [b] Defined as time from symptom onset. [c] p = 0.22, compared to 2007 mean symptom duration. [d] 10% of cohort missing data. [e] 30% of cohort missing data. [f] 24% of cohort missing data. [g] Normal reference range < 20 mm/h. [h] Normal reference range < 8 mg/l. ACPA: anticitrullinated protein antibodies; CRP: C-reactive protein; DAS: Disease Activity Score; DMARD: disease-modifying antirheumatic drugs; ESR: erythrocyte sedimentation rate; HAQ-DI: Health Assessment Questionnaire-Disability Index; IQR: interquartile range; MTX: methotrexate; TJC: tender joint count; SJC: swollen joint count; VAS: visual analog scale; RF: rheumatoid factor.

started on MTX than those without erosions (p = 0.02).

The 612 patients without erosions at baseline represent the eligible population to whom the score-based algorithm from the 2010 criteria should be applied. In these patients, 63% (n = 384) met 1987 ACR classification criteria and 83% (n = 510) met the 2010 criteria (Table 4A). When the criteria were applied to those patients without baseline radiographs, 167/220 (76%) met the 1987 criteria and 185/220 (84%) met the 2010 criteria. Overall, 62 of the 612 patients did not meet either set of classification criteria and represent true undifferentiated arthritis (Table 4A). Among the 612 patients without erosions at baseline, 385 had at least 1 year of followup. At 1 year, 10/326 (3%) of those fulfilling 2010 criteria and 7/59 (12%) of those not fulfilling 2010 criteria were not treated with DMARD or biologics. Examining baseline characteristics for the 612 patients without erosions, similar proportions of those that satisfied the 1987 ACR criteria (80%) and of those newly identified by 2010 ACR/EULAR criteria (81%) had a DAS28 ≥ 3.2 (Table 4B). However, fewer patients identified only by the 2010 criteria (32%) had a DAS28 > 5.1 than patients identified by the 1987 criteria (52%). Overall, 31% of those meeting 1987 criteria and 51% of those newly identified by 2010 criteria were MTX-naive at study entry.

DISCUSSION

We describe demographics and disease characteristics of patients enrolled in the CATCH cohort and compare characteristics of patients meeting the 1987 and 2010 RA classification criteria. To our knowledge, CATCH is the largest multicenter nationwide ERA cohort in North America that started in the post-biologic era and specifically focused on ERA. Indeed, other nationwide multicenter cohorts, such as the CORRONA database in the United States, have been informative in describing populations with established RA; however, CATCH provides perspectives on the subpopulations of patients with ERA[33]. Baseline data show that the mean disease duration for patients enrolled in the cohort was about 6 months and median symptom duration decreased slightly between 2007 and 2011. Most patients had moderate or high disease activity at enrollment. Most were treated with MTX, with baseline combination DMARD therapy used more frequently than monotherapy. The 2010 ACR/EULAR RA classification criteria identified several new patients as having RA compared to the 1987 criteria. These patients tended to have less severe disease at baseline and more of these patients were MTX-naive at enrollment. This finding highlights the potential influence of implementing the 2010 ACR/EULAR RA classification criteria on ERA patient characteristics and suggests that characteristics of ERA populations may change as use of the 2010 RA classification criteria becomes more widespread. Participants presenting with erosions at baseline had a higher average baseline DAS28 and more were started on MTX com-

Table 2. Treatment received by patients at 3 different timepoints, i.e., at the time of the indicated visit. Data are no. (%).

Therapy	At Baseline, n = 1187	At 6 Months, n = 864	At 1 Year, n = 705
MTX (All)	718 (60)	597 (69)	467 (66)
Subcutaneous	223 (31)	243 (41)	190 (41)
MTX with HCQ and/or SSZ	381 (32)	392 (45)	303 (43)
MTX monotherapy	337 (28)	205 (24)	164 (23)
DMARD other than MTX	176 (15)	93 (11)	84 (12)
No DMARD	293 (25)	174 (20)	154 (22)
Biologic (all)[a]	24 (2)	72 (8)	84 (12)
Anti-TNF (all)	19 (79)	68 (94)	77 (92)
Adalimumab	8 (42)	25 (37)	33 (43)
Etanercept	9 (47)	35 (51)	39 (51)
Infliximab	2 (11)	5 (7)	3 (4)
Golimumab	0 (0)	3 (4)	2 (3)
Abatacept	1 (4)	4 (6)	7 (8)
Tocilizumab	4 (17)	0 (0)	0 (0)
Rituximab	0 (0)	1 (1)	0 (0)
Corticosteroids[b]	316 (27)	160 (19)	101 (14)

[a] Some patients are receiving more than 1 biologic between visits because their biologics were switched. These patients are identified independently for each biologic that they receive. [b] Includes depomedrol/methylprednisolone (parenteral); kenalog/triamcinolone (parenteral); prednisolone (oral); prednisone (oral). DMARD: disease-modifying antirheumatic drugs; HCQ: hydroxychloroquine; MTX: methotrexate; SSZ: sulfasalazine; TNF: tumor necrosis factor.

Table 3A. No. (%) patients by diagnosis, i.e., DAS28 disease state over time.

	Baseline[a], n = 1187	3 Months, n = 969	6 Months, n = 864	1 Year[b], n = 705
No. patients with DAS28 available[c]	1106 (93)	764 (79)	708 (82)	569 (81)
DAS28 remission (< 2.6)	85 (8)	197 (26)	249 (35)	270 (47)
Low DAS28 (≥ 2.6 and ≤ 3.2)	66 (6)	114 (15)	109 (15)	77 (14)
Moderate DAS28 (> 3.2 and ≤ 5.1)	450 (41)	314 (41)	249 (35)	178 (31)
High DAS28 (> 5.1)	505 (46)	139 (18)	101 (14)	44 (8)

[a] Baseline defined as the first visit. [b] See Appendix Table 2 for DAS28 disease states for patients followed for only 1 year. [c] Percentages for each DAS28 disease state category were calculated using values from this row as the followup denominator. DAS: Disease Activity Score.

Table 3B. Patients by DAS28 disease state, for patients receiving corticosteroids at baseline.

Patients With Baseline[a] DAS 28 (n = 1106)[b]	Corticosteroids, n = 315 (28%)	No Corticosteroids, n = 791 (72%)	p
Proportion of patients[c], n (%)			
DAS28 remission (< 2.6)	27 (2)	58 (5)	—
Low DAS28 (≥ 2.6 and ≤ 3.2)	15 (1)	51 (5)	—
Moderate DAS28 (> 3.2 and ≤ 5.1)	114 (10)	336 (30)	—
High DAS28 (> 5.1)	159 (14)	346 (31)	—
Mean DAS28			
DAS28 remission (< 2.6)	1.81	1.87	0.72
Low DAS28 (≥ 2.6 and ≤ 3.2)	2.89	2.88	0.84
Moderate DAS28 (> 3.2 and ≤ 5.1)	4.25	4.23	0.70
High DAS28 (> 5.1)	6.40	6.19	0.01

[a] Baseline defined as the first visit. [b] Denominator for all percentages is n = 1106 patients. [c] See Appendix 2 for DAS28 disease states for patients followed for only 1 year. DAS: Disease Activity Score.

Table 4A. Analysis of patients to whom the new 2010 ACR/EULAR diagnostic criteria should be applied: number of patients fulfilling the 1987 and 2010 RA diagnostic critera. Data are numbers of patients.

Characteristic	Do Not Meet 2010 Criteria	Meet 2010 Criteria	Total (%)
Patients with radiographs and no erosions at baseline (n = 612)[a]			
Do not meet 1987 criteria	62	166	228 (37)
Meet 1987 criteria	40	344	384 (63)
Total (%)	102 (17)	510 (83)	612 (100)
Treatment characteristics of patients with radiographs and no erosions at 1 year followup (n = 385)[b]			
Do not receive DMARD or biologics within 1 year	7	10	17 (4)
Receive DMARD/biologics within 1 year	52	316*	368 (96)
Patients with no radiographs at baseline (n = 220)			
Do not meet 1987 criteria	17	36	53 (24)
Meet 1987 criterai	18	149	167 (76)
Total (%)	35 (16)	185 (84)	220 (100)
Patients with radiographs and erosions at baseline (n = 243)[a]			
Do not meet 1987 criteria	12	32	44 (18)
Meet 1987 criteria	36	163	199 (82)
Total (%)	48 (20)	195 (80)	243 (100)

[a] Totals are out of the 855 patients with baseline radiographs and data available to calculate both the 1987 ACR and new 2010 ACR/EULAR criteria. In total, 53 (5.8%) patients out of 908 with radiographs available at baseline did not have sufficient data to apply both sets of criteria. [b] Number of patients (out of 612 without erosions) who have 1-year of followup who were validated against the need for MTX or DMARD. * p = 0.0078, Fisher's exact test. DMARD: disease-modifying antirheumatic drug; MTX: methotrexate. ACR: American College of Rheumatology; EULAR: European League Against Rheumatism.

Table 4B. Analysis of patients to whom the new 2010 ACR/EULAR diagnostic criteria should be applied. Baseline characteristics for those with radiographs and no erosions meeting 1987 vs 2010 ACR/EULAR criteria, n = 612 (patients without baseline erosions of the 855 patients with data available to calculate both 1987 ACR and 2010 ACR/EULAR criteria). Data are numbers of patients (%).

Characteristic	Meet 1987 Criteria, n = 384 (63%)	Meet 2010 Criteria, n = 510 (83%)	Newly Identified by 2010 Criteria, n = 116 (19%)
DAS28 ≥ 3.2	307 (80)	444 (87)	94 (81)
DAS28 > 5.1	200 (52)	240 (47)	37 (32)
≥ 6 tender and swollen joints	238 (62)	296 (58)	49 (42)
MTX-naive at study entry	119 (31)	189 (37)	59 (51)
Symptoms > 12 weeks	330 (86)	134 (85)	95 (82)
Elevated CRP or ESR	265 (69)	347 (68)	73 (63)

DAS: Disease Activity Score; MTX: methotrexate; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ACR: American College of Rheumatology; EULAR: European League Against Rheumatism.

pared to those without baseline erosions. Providers were aware of baseline radiographic status and this likely influenced this prescribing pattern.

Data from our study provide a basis for understanding how characteristics of patients with undifferentiated inflammatory arthritis may change because of evolving diagnostic criteria and treatment standards. Many ERA cohorts that developed in the pre-biologics era set inclusion criteria that reflected the previous standards of care and therefore may report patient characteristics that differ from ERA cohorts established in the post-biologic era. The Leiden Early Arthritis Cohort, for example, is a single-center, prospective, inception cohort established in 1993 that includes patients with suspected arthritis with < 2 years of symptom duration[17]. The Amsterdam Early Arthritis cohort was also established in the pre-biologics era (1995) and recruits patients with < 3 years' disease duration[15,16]. With current standards of care shifting toward earlier diagnosis and treatment, recruitment for more recently established ERA cohorts, including CATCH, NOR-VEAC (Norwegian Very Early Arthritis Cohort)[11], and REACH (Rotterdam Early Arthritis Cohort)[14], has moved toward inclusion of patients with shorter disease or symptom durations, potentially allowing for earlier treatment. The CATCH cohort has more use of combination DMARD and more remission at 1 year despite less steroid use, which supports the concept that ear-

lier treatment yields better outcomes[34,35] or may also reflect geographic differences in practice patterns. The decrease in baseline symptom duration between 2007 and 2011 in our study also suggests that patients are being seen earlier in the course of their disease, which may reflect increased awareness of the need for earlier diagnosis and treatment. These data may also reflect that initiation of ERA clinics allows more rapid assessment of patients, as suggested[36]. It should also be noted that many ERA cohorts use the terms "symptom duration" and "disease duration" interchangeably, which can lead to ambiguity in interpreting different datasets. The term "disease duration" is often intended to mean the duration since diagnosis of disease rather than the time from symptom onset. Studies evaluating diagnosis have shown that there can be a significant lag between symptom onset and diagnosis and perhaps inclusion criteria should be clarified to differentiate between symptom and disease duration.

Like other cohort studies, the CATCH study provides an opportunity to validate clinical diagnostic and assessment tools and helps to raise awareness of practice patterns for ERA patients in region-specific clinical settings. We did not primarily seek to formally validate the 2010 ACR/EULAR criteria; however, several other early arthritis cohorts have performed these analyses[37] and this will be an interesting focus for future studies on the CATCH cohort. Nationwide recruitment from multiple centers allows for large numbers of patients to be analyzed and increases the generalizability of study results compared to recruitment with single-center studies, where recruitment and sample size may be limited. Centralized documentation of procedures and patient management, as well as regular investigator meetings, also improves standardization of protocols and offers convenience and easy access to data for all investigators.

There are study limitations worth noting. As with any cohort study, loss to followup may also lead to selection bias, particularly if nonrandom, systematic mechanisms contribute to the loss of observations. Currently, overall attrition for the study is < 20%, of which < 5% was classified as loss to followup for unknown reasons, which may help minimize the effect of this bias and ensure that data represent a random sampling of the Canadian ERA population. ACPA status was not available from 30% of patients because it is not covered as a reimbursable test throughout Canada, and baseline radiographs were not available from 24%, because this cohort is based on a standard of care, and not all patients consented to having radiographs at baseline. A central laboratory was not used for the RF, ACPA, and CRP measurements, which may have led to variability in these measurements across sites, but helps support generalization of the findings in real-life nationwide settings. We were limited in our analysis of patients fulfilling the 2010 or 1987 classification criteria, because of missing data. We had 17 patients who could not be classified as having RA by either criteria set because of missing radiographs. We had an additional 56 patients who could be identified by only 1 of the criteria sets, also because of missing baseline radiographs. Thus 1.4% of our patients could not be classified with confidence using either set of criteria. In our cohort, 24% of patients did not have baseline radiographs, but there were sufficient data to classify them as having RA using at least 1 set of criteria. Thus in real-world cohort studies it may be prudent to apply both sets of criteria.

Although Canada has a universal healthcare plan, it does not have a national pharmacy care plan, so differences in provincial reimbursement criteria for biologics may influence the type of treatments received across provinces and lead to region-specific treatment trends that are not evident when data from all centers are analyzed collectively. Separate analyses based on a longer duration of followup are planned regarding the effects of province-specific reimbursement on certain patient outcomes. It should also be noted that CATCH is a study of usual care in Canada and therefore treatment practices may change with time. The effects of these changes may be difficult to assess as standards of care continue to evolve; however, by defining remission as the desired treatment outcome, the effect of different treatment approaches and newer therapies can be assessed using a common endpoint. The diagnosis of patients was a clinical diagnosis. For most patients, investigation sites were not yet incorporating the new 2010 RA classification criteria, because they were published only 3 months before the cutoff date for this dataset. On average, patient baseline characteristics were similar among centers, although 80.5% of patients were from Ontario and Quebec. All these factors should be taken into consideration when interpreting data and assessing the generalizability to clinical practice.

Overall, our study shows the characteristics of the ERA population in Canada and suggests that the majority of patients referred to early arthritis clinics have moderate to high disease activity and are treated with MTX in combination with other DMARD. The proportion in remission at 1 year is quite high compared to older cohorts, which could reflect patients being recruited earlier and the evolution of trends in treatment[38,39]. The majority of these patients fulfill the 1987 ACR criteria and even more score ≥ 6 on the 2010 ACR/EULAR classification criteria. The 2010 RA classification criteria identify more patients with RA who would previously have been designated as having undifferentiated disease. However, these patients have lower disease activity at the time of identification. Further investigation is needed to fully address the influence of the 2010 criteria on patient care in terms of time to diagnosis, treatment, remission, quality of life, and work productivity.

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Appendix 1. Schedule of patients' assessments.

Visit	MD	RN	Patient Questionnaire	Physician Questionnaire	Long Labs[a]	Short Labs[b]	Chest Radiograph	TB Test	Hands/Feet Radiographs	BMD
Baseline	X	X	X	X	X[c]	X	X	X	X	PRN
3 months[d]	X	X	X	X		X				
6 months	X	X	X	X		X			X	
9 months	X	X	X	X		X				
12 months	X	X	X	X	X				X	
Q 6 months	X	X	X	X		X				
Q 1 year[e]	X	X	X	X	X				X	

[a] Complete blood counts, acute phase reactants, liver function tests, creatinine, cholesterol tests, rheumatoid factor, anticitrullinated protein antibodies, any other tests (usually at baseline only) that diagnose RA. [b] Routine tests used to monitor methotrexate/DMARD therapy. [c] At baseline visits, baseline test (long labs + extra labs). [d] Patients will be seen by MD and RN 4–6 weeks after baseline visit to review medication and side effects, only if they do not have another rheumatologist. [e] For any interim visits, routine care will be provided. Q: at; MD: physician assessment; RN: nurse assessment; TB: tuberculosis; BMD: bone mineral densitometry; PRN: as required; RA: rheumatoid arthritis; DMARD: disease-modifying antirheumatic drug.

Appendix 2. DAS28 disease states for patients followed for 1 year; of 705 followed for 1 year, 554 had DAS28 data available at both baseline and 1 year. Data are no. patients (%).

	Baseline[a] n = 554	1 Year, n = 554
DAS28 remission (< 2.6)	47 (8)	263 (47)
Low DAS28 (≥ 2.6 and ≤ 3.2)	28 (5)	75 (14)
Moderate DAS28 (> 3.2 and ≤ 5.1)	222 (40)	172 (31)
High DAS28 (> 5.1)	257 (46)	44 (8)

p = 10e-16 (paired t-test). [a] Defined as the first visit. DAS: Disease Activity Score.

Appendix 3. Patients with and without erosions at baseline have similar symptom duration. Data are no. (%).

Symptom Duration	Erosion	No Erosion	p
All	246	643	0.9312
< 3 months	44 (18)	115 (18)	0.5581
≥ 3 and ≤ 6 months	89 (36)	249 (39)	0.4610
> 6 months	113 (46)	279 (43)	0.2988

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