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Canadian Patients With Axial Spondyloarthritis Require Almost a Decade To Be Diagnosed Leading to Severe Functional Limitation. Results From the International Map of Axial Spondyloarthritis (IMAS)

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ABSTRACT

Objective: To evaluate the sociodemographic characteristics and disease-related factors associated with diagnostic delay in Canadian patients with axial spondyloarthritis (axSpA).

Methods: Data from 542 Canadian patients who participated in the International Map of Axial Spondyloarthritis online survey were analysed. Diagnostic delay was calculated as the difference between age at diagnosis and age at onset of the first symptoms reported by participants. Univariate and multivariate analyses were used to evaluate possible factors associated with diagnostic delay.

Results: The mean age (± SD) of the surveyed participants was 44.3 ± 13.9 years and 63.1% were female. The average diagnostic delay was 9.0 ± 10.5 years (median, 5.0 years; interquartile range, 1.0–13.8). In the multivariate regression analysis, the three variables most strongly associated with longer diagnostic delay were use of nonsteroidal anti-inflammatory drugs (NSAIDs) (B = 2.991; 95% CI = 1.075–4.909), medium or high functional limitation (B = 1.541; 95%CI = 0.186–2.896), and number of HCPs seen before diagnosis (B = 1.524, 95%CI = 1.072–1.977).

Conclusion: Diagnostic delay continues to be a barrier to optimal care for Canadian axSpA patients. Significant diagnostic delay, associated with a high number of HCP visits prior to diagnosis, high use of NSAIDs, and marked functional limitation in daily life, illustrate the convoluted axSpA patient journey.

1 | Introduction

Axial spondyloarthritis (axSpA) is an insidious and progressive inflammatory disease that can cause irreversible structural damage to the spine and peripheral joints. An early diagnosis is vital so that the optimal management strategies are initiated and patients achieve better outcomes (Furst et al. 2019; Yi et al. 2020). Despite widespread research on axSpA, there remains a lengthy delay between symptom onset and formal diagnosis (i.e., diagnostic delay); indeed, axSpA has one of the longest diagnostic delays among all rheumatic diseases (Poddubnyy et al. 2019).

Patients with unidentified axSpA must confront the onset of disease on their own, relying mostly on symptomatic relief for pain management that fails to slow overall disease progression (Khan 2002). Uncertainty surrounding diagnosis also leads to anxiety (Jovani et al. 2018). Given that early introduction of biological therapy is associated with modification of structural progression of the disease (Zhang et al. 2016), early diagnosis is vital. It may also improve symptoms, relieve psychological distress, ameliorate peripheral and extra-skeletal features, and improve work incapacity. Therefore, it is essential to shorten diagnostic delay in patients with axSpA and establish clinical criteria for early diagnosis by identifying the factors associated with diagnostic delay.

Numerous studies have identified patient characteristics associated with longer diagnostic delay, including female gender (Redeker et al. 2018), manual labour (Bandinelli et al. 2016), younger age at onset of first symptoms (Bandinelli et al. 2016; Redeker et al. 2018), older age at diagnosis (Behar et al. 2018), and a negative human leucocyte antigen B27 (HLA-B27) result (Dincer et al. 2008). Less commonly, peripheral arthritis or dactylitis, more frequent entheseal pain (Behar et al. 2018), and the presence of psoriasis (Redeker et al. 2018) have also been associated with longer diagnostic delay. A family history of axSpA and the presence of inflammatory back pain is associated with a shorter diagnostic delay (Dincer et al. 2008).

The International Map of Axial Spondyloarthritis (IMAS) is a collaboration led by the Health & Territory Research group of the University of Seville and endorsed by the Axial Spondyloarthritis International Federation (ASIF). The goal is to capture the patients' perspective of the holistic burden of axSpA, both psychological and physical, and to help direct patients to appropriate resources in order to reduce the burden of disease. The IMAS project involves a cross-sectional online survey of non-selected patients with a self-reported, clinician-made diagnosis of axSpA, and has been conducted in 13 countries in Europe (Austria, Belgium, France, Germany, Italy, the Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the United Kingdom), 3 countries in Asia (South Korea, Taiwan, and Turkey), and 5 countries in South America (Argentina, Brazil, Colombia, Costa Rica, and Mexico). The project is currently being expanded to other countries, including the United States.

Based on 2846 axSpA patients who participated in the European survey, mean ± SD diagnostic delay was 7.4 ± 8.4 years, mean disease activity was 5.5 ± 2.0 (as measured using the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]), and 61.5% had poor mental health (as measured using the 12-item General Health Questionnaire [GHQ-12]; Garrido-Cumbrera et al. 2019).

The objective of the present study was to use a Canadian adaptation of the IMAS survey to identify factors associated with diagnostic delay of axSpA in Canada, and to compare diagnostic delay to observations in European countries.

2 | Method

2.1 | Study Population

Canadian participants were recruited between August 2018 and February 2019 by Ipsos SA (formerly GfK), a market research agency, through their existing patient panel of respondents. The Canadian Spondylitis Association recruited additional axSpA patients, who were added to the existing database. Participants were ≥ 18 years of age with a self-reported diagnosis of axSpA (including ankylosing spondylitis and non-radiographic axSpA) and had an axSpA-related visit to a healthcare provider (HCP) in the 12 months prior to completing the survey.

2.2 | Survey

The Canadian adaptation of the original Spanish Atlas of Axial Spondyloarthritis 2017 questionnaire (Garrido-Cumbrera 2017) was performed by an advisory board of axSpA patients and a national steering committee composed of the Canadian Spondylitis Association, local rheumatologists, and axSpA patients. This involved adapting the terminology to the Canadian social, geographical, and legislative context; modifying questions on diagnosis, healthcare, and treatment; validating existing questions and including additional questions proposed by representatives of the patient organisation (Canadian Spondylitis Association) to ensure the survey gathered information on real concerns of Canadian axSpA patients. The final Canadian survey included 109 items related to 13 different areas: sociodemographic characteristics, disability and performance, employment status, daily activities, lifestyle habits, diagnostic journey, healthcare utilization, treatment, comorbidities, mental health, axSpA-specific outcomes, income level, and patient disease-related attitudes and treatment goals (Table S1). Participants completed the survey in either English or French via an online platform. The minimum action required for a response to be considered incomplete was to click on the link to the survey.

2.3 | Diagnostic Delay Assessment

Diagnostic delay was calculated based on self-reported data from the following two items of the Canadian survey: *'Age of onset of first symptoms (pain, inflammation, stiffness) associated with Spondylitis/Spondyloarthritis'* and *'Age at which you were diagnosed with Spondylitis/Spondyloarthritis'*. The diagnosis of HCP speciality was captured in a separate question.

2.4 | Additional Instruments

Disease activity (BASDAI), spinal stiffness, functional limitation (Functional Limitation Index), and psychological distress (GHQ-12) were considered in this analysis, as described in detail by Garrido-Cumbrera et al. (2019).

2.5 | Statistical Analysis

Continuous data are expressed as mean ± SD or *n* (%). Mann–Whitney U tests were used to evaluate the homogeneity of diagnostic delay between Canada and European countries. In the bivariate analysis, Kruskal–Wallis tests were used to evaluate homogeneity in the distribution of diagnostic delay (< 1, 1–5, 6–9 and ≥ 10 years) and quantitative variables. Chi-square tests were used to evaluate the differences between diagnostic delay and categorical variables. Dunn post hoc tests were used to compare subcategories of the dependent variable, diagnostic delay (i.e., < 1, 1–5, 6–9 and ≥ 10 years). A Bonferroni correction was used to correct multiple comparisons.

A univariate linear regression was used to evaluate the linear relationship between diagnostic delay and independent variables. Variables that were significant at the $p < 0.05$ level in the bivariate analysis were included in the univariate regression analysis. Significant predictors ($p < 0.05$) in the univariate analysis were included in the multivariate regression analysis. Multivariate linear regression analysis was used to identify variables independently associated with a longer diagnostic delay.

All comparisons were two-sided and considered statistically significant when $p < 0.05$. Statistical analysis was performed using SPSS version 26.0.

3 | Results

3.1 | Characteristics of Canadian Participants

A total of 542 Canadian patients with self-reported axSpA with a mean + SD age of 44.3 + 13.9 years completed the survey. Most (63.1%) were female. The majority of the participants had college/university education (81.0%), and approximately half were employed (52.6%). This contrasts with the Canadian employment rate (82.7%) for university educated citizens between the ages of 25 and 64 years (Organisation for Economic Cooperation and Development [OECD], 2021). Two out of five participants were members of a patient organisation (41.9%). Most respondents lived in urban centres (93.3%) and within 25 km of a rheumatologist (53.7%). Before diagnosis, patients visited an average of 2.9 specialists and underwent an average of 6.4 tests. Approximately three-quarters of participants had high disease activity (72.1% had BASDAI ≥ 4), 53.1% had psychological distress (GHQ-12 ≥ 3). Most patients had received nonsteroidal anti-inflammatory drug (NSAID) treatment at some point in the past (82.8%), while a smaller proportion had received biologics (58.7%) or DMARDs (36.3%). Since the mean age at the onset of symptoms was 26.4 years and the mean age at diagnosis was 35.0 years, the mean diagnostic delay in Canada was determined to be 9.0 years (Table 1). The median (IQR) diagnostic delay was 5.0 (1.0, 13.8) years (Table 2).

TABLE 1 | Sociodemographic, diagnostic, and clinical characteristics of the analysed population.

Variables	Mean ± SD or *n* (%)
Sociodemographic	
Age, years	44.3 ± 13.9
Sex, female	342 (63.1)
Education level	
No school completed	1 (0.2)
Primary school	5 (0.9)
High school	97 (17.9)
University/College	439 (81.0)
Residence area, $n = 536$	
Urban	500 (93.3)
Rural	36 (6.7)
Distance from rheumatologist	
Under 25 km	291 (53.7)
25–50 km	127 (23.4)
50–100 km	55 (10.1)
100–150 km	26 (4.8)
Over 150 km	43 (7.9)
Patient organisation membership	227 (41.9)
Body mass index (kg/m^2), $n = 539$	27.8 ± 10.3

(Continues)

TABLE 1 | (Continued)

Variables	Mean ± SD or *n* (%)
Work life	
Job status, employed	285 (52.6)
Occupation, $n = 285$	
Manual worker	66 (23.2)
Non-manual worker	219 (76.8)
Work-related issues	439 (81.0)
Lifestyle habits	
Current smoker	110 (20.3)
Diagnostic journey	
Age at onset of first symptoms, years	26.4 ± 12.0
Age at diagnosis, years	35.0 ± 12.7
Number of HCPs seen prior to diagnosis[a]	2.9 ± 1.6
Number of tests undertaken prior to diagnosis[b]	6.4 ± 10.5
Number of MRI scans prior to diagnosis, $n = 363$	1.7 ± 1.5
Diagnostic delay, years[c]	9.0 ± 10.5
Disease duration since symptom onset, years	17.8 ± 13.7
HLA-B27 positivity, $n = 322$	225 (69.9)
Diagnosed by rheumatologist	
Yes	370 (68.3)
No[d]	172 (31.7)
Treatment	
NSAID	449 (82.8)
DMARD	197 (36.3)
Biologic	318 (58.7)
Psychological health	
GHQ-12 (0–12)[e]	4.0 ± 3.8
Proportion with GHQ-12 ≥ 3[e]	288 (53.1)
Comorbidities and extra-articular manifestations	
History of inflammatory bowel disease	90 (16.6)
History of acute anterior uveitis	161 (29.7)
Disease outcomes	
BASDAI (0–10)[f]	5.3 ± 2.1
Proportion with BASDAI ≥ 4	391 (72.1)
Functional limitation index (0–54)[g]	17.8 ± 11.5
Spinal stiffness index (3–12)	7.4 ± 2.2

Note: $N = 542$ unless otherwise specified.

Abbreviations: BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CT, computed tomography; DMARD, disease-modifying antirheumatic drug; GHQ-12, 12-item General Health Questionnaire; HCPs, healthcare professionals; HLA-B27, human leucocyte antigen B27; IMAS, International Map of Axial Spondyloarthritis; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug.

[a]HCPs included GP; Rheumatologist; Orthopaedic specialist; Physiotherapist; Physical and Rehabilitation Medicine (PRM) specialist, osteopath, chiropractor, and traditional Chinese medicine practitioner.

[b]Tests included HLA-B27, CT, MRI, and ultrasound scans, X-rays, and radionuclide scintigraphy.

[c]The diagnostic delay variable (calculated as the difference between age at diagnosis and age at first symptoms) was ≥ 0 years in 524 participants.

[d]No diagnosed by rheumatologist included GP; Orthopaedic specialist; Physiotherapist; Internal Medicine Specialist; and, Do not know.

[e]GHQ-12, which evaluates mental health, was transformed into a dichotomous score (0-0-1-1) to eliminate bias resulting from the tendency of respondents to choose answers 1 and 4 or 2 and 3 on the 4-point Likert scale. Scores ≥ 3 indicated psychological distress (Organisation for Economic Co-operation and Development (OECD), 2021).

[f]BASDAI is a validated self-administered questionnaire assessing disease activity between 0 (no activity) and 10 (maximum activity). (Barber et al. 2017).

[g]The Functional Limitation Index, explicitly developed for IMAS, assessed the degree of functional limitation in 18 daily life activities. Scores ranged between 0 and 54, indicating low (0–17), medium (18–36), and high limitation (37–54). (Sanchez-Piedra et al. 2018).

3.2 | Comparison With Diagnostic Delay in Europe

Diagnostic delay in Canada was compared with IMAS data collected on axSpA patients in Europe. This analysis revealed that patients in Canada experience significantly longer diagnostic delays than patients in France ($p = 0.004$), Spain ($p = 0.017$), and across the aggregate sample of 13 European countries ($p < 0.001$). In contrast, the diagnostic delay experienced by Canadian axSpA patients was significantly shorter than that observed in Norway ($p < 0.001$; Table 2).

3.3 | Analysis of Diagnostic Delay in Canada

Patients with the greatest diagnostic delay (≥ 10 years) were significantly older (48.5 ± 11.1 years) than patients with a shorter diagnostic delay of 1–5 years or 6–9 years ($p < 0.001$; Table 3). Mean (SD) age was 46.0 ± 16.4 years for patients with < 1-year diagnostic delay, 41.1 ± 14.8 for 1–5 years delay, and 42.2 ± 11.2 years for 6–9 years delay. Half of the patients with a diagnostic delay ≥ 10 years (54.3%) belonged to a patient organisation. In contrast, only 24.7% of patients with a diagnostic delay < 1 year belonged to a patient organisation ($p < 0.001$). Furthermore, patients with a longer diagnostic delay had attended more visits to specialists and had undergone more tests before diagnosis ($p < 0.001$). Significantly more patients with ≥ 10 years diagnostic delay than patients with 1–5 years of diagnostic delay had received an axSpA diagnosis by a rheumatologist (77.7% vs. 63.3%; $p = 0.012$).

Compared to patients with a diagnostic delay of 1–5 years or 6–9 years, significantly more patients with a longer diagnostic delay had higher functional limitation ($p = 0.047$). The proportion of patients with pelvic inflammation was greater in patients with 6–9 years (50%) and ≥ 10 years (50%) versus < 1-year diagnostic delay (27.2%; $p = 0.004$). Patients with the longest diagnostic delay had more mental comorbidities than patients in the other diagnostic delay categories ($p < 0.001$). Patients with a diagnostic delay of 1–5 years had fewer physical comorbidities (1.7 ± 2.1) than those with ≥ 10 years of diagnostic delay (2.1 ± 2.2; $p = 0.041$). Patients who experienced ≥ 10 years diagnostic delay were significantly younger at the onset of symptoms than patients who experienced < 10 years of diagnostic delay. The vast majority (87.5%) of patients with ≥ 10 years of diagnostic delay had work-related issues, while a significantly lower proportion (70.4%) of patients with < 1 year of diagnostic delay experienced such issues ($p = 0.004$). A greater

TABLE 2 | Comparison of diagnostic delay in Canada and Europe.

Country	Sample size[a]	Diagnostic delay		
		Mean ± SD	Median (IQR)	*p*
Canada	524	9.0 ± 10.5	5.0 (1.0, 13.8)	NA
France	626	6.9 ± 8.2	4.0 (1.0, 10.0)	0.004[b]
Norway	504	10.6 ± 9.9	8.0 (2.0, 17.0)	< 0.001[b]
Spain	550	8.5 ± 7.7	6.0 (3.0, 12.0)	0.017[b]
Pan-European aggregated sample (13 countries)[c]	2652	7.4 ± 8.4	4.0 (1.0, 11.0)	0.040[b]

Abbreviations: IQR, interquartile range; NA, not applicable.
[a]Sample size included patients who responded to both questions used to derive diagnostic delay (i.e., 'Age of onset of first symptoms (pain, inflammation, stiffness) associated with Spondylitis/Spondyloarthritis' and 'Age at which you were diagnosed with Spondylitis/Spondyloarthritis').
[b]Mann–Whitney test versus Canada.
[c]The Pan-European aggregated sample included patients from Austria, Belgium, France, Germany, Italy, the Netherlands, Norway, Russia, Slovenia, Sweden, Switzerland, the United Kingdom, and Spain (Garrido-Cumbrera et al. 2019).

TABLE 3 | Bivariate and post hoc analyses of variables in relation to diagnostic delay.

Variable	Diagnostic delay[a]				
	< 1 year (*n* = 81)	1–5 years (*n* = 199)	6–9 years (*n* = 60)	≥ 10 years (*n* = 184)	*p*
Sociodemographic					
Age, years	46.0 ± 16.4	41.1 ± 14.8[b]	42.2 ± 11.2[b]	48.5 ± 11.1[c,d]	< 0.001[e]
Sex, female	47 (58.0)	119 (59.8)	38 (63.3)	130 (70.7)	0.098[f]
Distance from rheumatologist (< 25 km)	45 (55.6)	112 (56.3)	37 (61.7)	92 (50.0)	0.579[f]
Patient organisation membership	20 (24.7)[b]	74 (37.2)[b]	26 (43.3)	100 (54.3)[c,g]	< 0.001[f]
Work life					
Occupation, manual worker	10 (27.0)	25 (21.2)	9 (30.0)	20 (22.2)	0.707[f]
Left or lost job due to AS/axSpA[h]	4 (80.0)	10 (76.9)	1 (20.0)	10 (76.9)	0.100[f]
Difficulty finding work due to AS/axSpA	45 (55.6)	115 (57.8)	38 (63.3)	124 (67.4)	0.430[f]

(Continues)

TABLE 3 | (Continued)

Variable	Diagnostic delay[a] < 1 year (*n* = 81)	1–5 years (*n* = 199)	6–9 years (*n* = 60)	≥ 10 years (*n* = 184)	*p*
Work-related issues due to AS/axSpA	57 (70.4)[b]	162 (81.4)	44 (73.3)	161 (87.5)[g]	0.004[f]
Diagnostic journey					
Age at onset of first symptoms, years	32.0 ± 15.3[b]	28.9 ± 11.2[b]	26.4 ± 9.2[b]	21.0 ± 9.0[c,d,g]	< 0.001[e]
Number of HCPs seen prior to diagnosis	2.0 ± 1.1[b,c,d]	2.7 ± 1.4[b,g]	3.1 ± 1.7[b,g]	3.7 ± 1.6[c,d,g]	< 0.001[e]
Number of tests undertaken prior to diagnosis	5.2 ± 15.8[b,c,d]	6.3 ± 10.3[g]	7.2 ± 11.6[g]	6.9 ± 7.3[g]	< 0.001[e]
Number of MRI scans prior to diagnosis	1.5 ± 0.8	1.8 ± 2.1	1.5 ± 0.9	1.8 ± 1.3	0.359[e]
Diagnosed by rheumatologist	52 (64.2)	126 (63.3)[b]	44 (73.3)	143 (77.7)[c]	0.012[f]
HLA-B27 positivity	22 (71.0)	80 (67.2)	27 (65.9)	91 (74.0)	0.573[f]
Treatment					
NSAID	59 (72.8)[b]	162 (81.4)	51 (85.0)	167 (90.8)[g]	0.002[f]
DMARD	32 (39.5)	70 (35.2)	23 (38.3)	66 (35.9)	0.900[f]
Biologic	39 (48.1)[d]	114 (57.3)[d]	42 (70.0)[c,g]	116 (63.0)	0.038[f]
Psychological health					
GHQ-12 (0–12)	3.5 ± 3.6	3.9 ± 3.9	3.7 ± 3.9	4.3 ± 3.9	0.378[e]
Anxiety	23 (28.4)[b,d]	62 (31.2)	26 (43.3)[g]	78 (42.4)[g]	0.040[f]
Depression	26 (32.1)	64 (32.2)	22 (36.7)	80 (43.5)	0.121[f]
Comorbidities and extra-articular manifestations					
Number of mental comorbidities	0.8 ± 1.1[b]	0.9 ± 1.0	1.0 ± 1.0	1.3 ± 1.1[g]	0.001[e]
Number of physical comorbidities	2.3 ± 2.7	1.7 ± 2.1[b]	2.3 ± 3.4	2.1 ± 2.2[c]	0.041[e]
Disease outcomes					
BASDAI (0–10)	5.4 ± 2.2	5.2 ± 2.2	4.9 ± 2.0	5.5 ± 2.0	0.254[e]
Spinal stiffness, severe	25 (30.9)	49 (24.6)	17 (28.3)	61 (33.2)	0.315[f]
Functional limitation, medium–high	40 (49.3)	90 (45.3)[b]	25 (41.6)[b]	111 (60.3)[c,d]	0.047[f]
Body area with inflammation, pelvis	22 (27.2)[b,d]	81 (40.7)	30 (50.0)[g]	92 (50.0)[g]	0.004[f]

Note: Results are expressed as mean ± SD or *n* (%).
Abbreviations: AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DMARD, disease-modifying antirheumatic drug; GHQ-12, 12-item General Health Questionnaire; HCPs, healthcare professionals; HLA-B27, human leucocyte antigen B27; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug.
[a]Sample size included patients who responded to both questions used to derive diagnostic delay (i.e., *'Age of onset of first symptoms (pain, inflammation, stiffness) associated with Spondylitis/Spondyloarthritis'* and *'Age at which you were diagnosed with Spondylitis/Spondyloarthritis'*).
[b]$p < 0.05$ compared to ≥ 10 years diagnostic delay. A Bonferroni correction was used to correct multiple comparisons.
[c]$p < 0.05$ compared to 1–5 years.
[d]$p < 0.05$ compared to 6–9 years.
[e]Kruskal–Wallis homogeneity test.
[f]Chi-square test. Significant differences between subcategories (Dunn post hoc test) are shown as follows.
[g]$p < 0.05$ compared to < 1 year.
[h]Question available only to respondents who reported being unemployed.

proportion of patients with longer diagnostic delay had used biological therapy ($p = 0.038$) or NSAIDs ($p = 0.002$; Table 3).

Univariate linear regression revealed that a longer diagnostic delay was associated with older age ($B = 0.212$), patient organisation membership ($B = 3.234$), age at onset of first symptoms ($B = -0.341$), a greater number of HCPs seen before diagnosis ($B = 2.424$), diagnosis by rheumatologist ($B = 1.716$), medium or high functional limitation ($B = 3.678$), pelvic inflammation ($B = 2.887$), greater mental comorbidities ($B = 1.554$), greater physical comorbidities ($B = 0.388$), presence of anxiety ($B = 2.089$) and treatment with NSAIDs ($B = 3.126$; Table 4).

Variables independently associated with longer diagnostic delay were determined using a multiple linear regression model. These included treatment with NSAIDs ($B = 2.992$), medium or high functional limitation ($B = 1.541$), greater number of HCPs seen before diagnosis ($B = 1.524$), greater number of mental comorbidities ($B = 0.930$), diagnosis by rheumatologist ($B = 0.793$), younger age at onset of first symptoms ($B = -0.532$) and older age ($B = 0.408$; Table 4).

TABLE 4 | Univariate and multivariate regression analyses of variables in relation to diagnostic delay.

	Univariate regression		Multivariate regression	
Variable	**Beta**	**95% CI**	**Beta**	**95% CI**
Age, years	0.212	0.150, 0.275	0.408	0.350, 0.466
Patient organisation membership	3.234	1.426, 5.042	0.495	−0.883, 1.874
Work-related issues due to AS/axSpA	2.248	−0.041, 4.537	NA	NA
Age at onset of first symptoms, years	−0.341	−0.412, −0.270	−0.532	−0.597, −0.467
Number of HCPs seen prior to diagnosis	2.424	1.901, 2.946	1.524	1.072, 1.977
Number of tests undertaken prior to diagnosis	0.056	−0.029, 0.141	NA	NA
Diagnosed by rheumatologist	1.716	0.745, 2.686	0.793	0.007, 1.578
Treatment, NSAID	3.126	0.692, 5.560	2.992	1.075, 4.909
Treatment, biologic	1.393	−0.441, 3.227	NA	NA
Anxiety	2.089	0.218, 3.960	NA	NA
Number of mental comorbidities	1.554	0.756, 2.353	0.930	0.299, 1.561
Number of physical comorbidities	0.388	0.018, 0.758	−0.217	−0.517, 0.083
Functional limitation, medium–high	3.678	2.216, 5.141	1.541	0.186, 2.896
Body area with inflammation, pelvis	2.887	1.081, 4.694	−0.064	−1.465, 1.337

Abbreviations: AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; CI, confidence interval; HCPs, healthcare professionals; NA, not applicable; NSAID, nonsteroidal anti-inflammatory drug.

4 | Discussion

In this sample of Canadian patients with axSpA, the average diagnostic delay was 9.0 years with half of the patients experiencing a diagnostic delay of at least 5 years. Moreover, Canada has a longer diagnostic delay than other European countries studied by IMAS and than the Pan-European average (7.4 years). One of the main reasons for this difference may be due to a shortage of rheumatologists in Canada. A study from 2016 estimated that there are between 0 and 0.8 full-time rheumatologists per 75,000 inhabitants, depending on the province/territory investigated. These figures consistently fall short of the Canadian Rheumatology Association recommendations of one rheumatologist per 75,000 population (Barber et al. 2017). In contrast, Spain and France have 2.0 and 3.4 rheumatologists per 100,000 inhabitants, respectively (Sanchez-Piedra et al. 2018; Conseil national de l'Ordre des médecins 2021). However, self-management of symptoms and general practitioners who do not refer patients to specialists may also contribute to the long delay in diagnosis. This shortage of rheumatologists in Canada could make it difficult for patients with axSpA to access a rheumatologist, which could impact the time to diagnosis. Furthermore, a study carried out in Canada showed that the median waiting time from referral to rheumatologist consultation was 74 days (Widdifield et al. 2016).

In Canada, the factors most associated with a longer diagnostic delay were the use of NSAIDs, medium or high functional limitation, and a higher number of HCPs seen before diagnosis. This contrasts with the findings in Europe, where younger age at symptom onset, female gender, a higher number of HCPs seen before diagnosis, and being diagnosed by a rheumatologist were the factors most associated with a longer diagnostic delay (Garrido-Cumbrera et al. 2022).

Living at a distance of more than 25 km from a rheumatologist was not associated to diagnostic delay. This is contrary to expectations, as a study indexed in the Ontario Best Practices Research Initiative (OBRI) registry found that remote distances (≥ 100 km) to rheumatologists played a role in increasing diagnostic delay for patients with rheumatoid arthritis, even if its predictive power was lower than regional rheumatology supply or income level (Widdifield et al. 2014). The parameters that were found to be associated with diagnostic delay were a greater number of HCP visits and non-MRI tests performed prior to diagnosis. These findings indicate that subtler cases of axSpA required a greater number of specialists and tests to rule out other pathologies (less probably) or that some of these visits or tests were misguided decisions by key personnel in the diagnostic journey (more probable). The latter is reinforced by the fact that the probability of the axSpA diagnosis being made by a rheumatologist is also associated with diagnostic delay and the number of tests undertaken before diagnosis loses its predictive value over the number of HCP visits in the multivariate analysis. Similar findings were reported by research conducted in the United States, which found that only 37% of patients reporting back pain were referred to rheumatologists and received a diagnosis of ankylosing spondylitis. The remainder were referred to other HCPs, thus delaying diagnosis (Deodhar et al. 2016). In the same vein, Canadian patients go through an excessively high number of specialists and tests until they finally reach a rheumatologist who is able to make the correct diagnosis. These data suggest that other HCPs fail to correctly identify an inflammatory process as the cause of low back pain and often attribute their symptoms to a mechanical aetiology. This would lead to incorrect referrals to HCPs other than a rheumatologist, such as physiotherapists (visited by 51.8% of patients prior to diagnosis), orthopaedic specialists (21.1%), or chiropractors (14.1%).

Younger age at symptom onset is another factor associated with longer diagnostic delay. Mechanical pain—caused by stress on the bones, discs, or nerves of the spine—is more common in the consultation demands of young patients, while rheumatic processes tend to be associated with older age (Khan 2002). Only in the past decade have international guidelines recommended that general practitioners refer patients with chronic low back pain to a rheumatologist (Koes et al. 2010). Therefore, young age at symptom onset may lead HCPs to conclude that the origin of back pain is mechanical rather than inflammatory. Following this logic, patients who present at a young age may be overlooked and not diagnosed until much later in life. Age at completion of the Canadian IMAS survey was also related to diagnostic delay, as older patients reported greater diagnostic delay. However, based on a post hoc analysis of the Canadian data, significant differences in mean age were found between patients in the longest diagnostic delay group (≥ 10 years) and those in the groups with either 1–5 years or 6–9 years of diagnostic delay. These results align with another study demonstrating a correlation between age and diagnostic delay (Fallahi et al. 2016). The shorter time to axSpA diagnosis in more recent years could be explained by greater awareness of the disease (Navarro-Compán, Ermann, and Poddubnyy 2022).

Additionally, the use of NSAIDs increased steadily with greater years of diagnostic delay. NSAIDs are unlikely to have a direct impact on diagnostic delay. However, for young patients and those with less obvious developed forms of the disease, the use of NSAIDs could provide temporary relief or reduce symptoms sufficiently to mask the disease and thus contribute to delaying diagnosis.

Results from this study provide some insights into the consequences of a delayed diagnosis in axSpA patients. The data reveal that a delayed diagnosis ≥ 10 years is associated with increased functional limitation. As previous studies have shown, a delay in diagnosis could lead to a delay in the initiation of early and optimal treatment, potentially triggering greater functional limitation and disability (Fernandez-Carballido et al. 2017). If diagnostic delay is sufficiently long, it could even lead to the appearance of irreversible structural damage (Danve et al. 2019) prior to a confirmed diagnosis of axSpA.

In the Canadian IMAS sample, 53.1% of respondents scored above the GHQ-12 threshold for psychological distress (≥ 3). This is substantially higher than the psychological distress rate of 13.2% observed using the same criteria in the Canadian general population (Mann et al. 2011). Using K10, a scale that assesses psychological distress through domains similar to GHQ-12, the rate of psychological distress in the Canadian general population varies between 9% and 20% depending on sociodemographic characteristics (Mann et al. 2011). According to the World Health Organisation, the prevalence of anxiety and depressive disorders in Canada are 4.9% and 4.7%, respectively (World Health Organization [WHO] 2021). The present IMAS data highlight the psychological toll that axSpA places on Canadian patients compared to the general population. As diagnostic delay increases, a greater proportion of patients express anxiety. The relationship between anxiety and diagnostic delay disappears in the multivariate analysis, as the number of mental health comorbidities explains a greater variability. This implies that the association between psychological health and diagnostic delay is not limited to the stress produced by mere diagnostic uncertainty, but rather that diagnostic delay is associated with overall psychological impairment. Until diagnosed and properly managed, axSpA can be associated with worsening in the physical health of patients through symptoms of chronic pain and stiffness. The latter may lead to a worsening of the patient's mental health. Further research is needed to establish whether diagnostic delay is sufficient to impair psychological health, or whether it impacts psychological health through worsening disease outcomes and loss of function. Conversely, patients with poorer psychological health could be less inclined to seek medical care, and mental disorders could delay and complicate the axSpA diagnosis. Regardless, it is important to ensure that psychological services reach axSpA patients, particularly those who have undergone a long journey to diagnosis.

Patient organisations are a valuable source of information and support for patients (Nikophorou et al. 2017), which is why we included patient organisation membership in our analyses. In Canada, longer diagnostic delay increases the likelihood of becoming a member of a patient organisation. It is likely that people with greater diagnostic delay are more motivated to join patient organisations. This could also be explained by the fact that members of patient organisations tend to be older than their non-member counterparts (data not shown). We acknowledge that patients invariably join patient organisations after receiving a diagnosis. Using patient organisation membership as an independent variable in our analysis means that we are unable to determine the consequences of being part of a patient organisation, its impact on the patient journey and the axSpA disease course. However, this could form the basis of a subsequent analysis on the importance of patient organisations.

A key strength of this study is the use of validated scales for the evaluation of disease activity and mental health. In addition, being able to compare our results with the findings from European countries is another strength. According to the most recent Canadian Census data (2016), the survey respondents were representative of the general Canadian population in terms of age (mean age in Canada is 41 years; Statistics Canada 2021).

We acknowledge that this survey has some limitations. Since the aim of the IMAS survey was to capture the real-world perspective of Canadian patients with axSpA, it relied on self-reported data. We did not attempt to confirm patient diagnosis against physician reports or clinical registries. Furthermore, the use of non-selected patients led to sample bias in terms of education level and gender (63.1% of respondents were female, which is above the proportion [50.9%] reported for the Canadian population; Nikophorou et al. 2017). However, this bias is common in online surveys, a method that is documented to be less favourable with men and more accessible to people with a higher level of education (Smith 2021). Another limitation is the use of previously non-validated scales or indices to evaluate certain factors, such as functional limitations in daily life and spinal stiffness. Finally, it is not possible to conclude a cause-and-effect relationship in a cross-sectional study. To establish causality, it would be necessary to carry out a longitudinal study. The rate of survey completion was not considered

a limitation of the study, as the minimum action required was to click on the link of the survey and was comparable to that of surveys of a similar length conducted by Ipsos SA (personal communication). Furthermore, respondents recruited through the Canadian Spondylitis Association received no incentive for survey completion.

5 | Conclusion

Despite recent advances, diagnostic delay continues to be a barrier to optimal care for Canadian axSpA patients. Considerable diagnostic delay, together with a high number of HCP visits prior to diagnosis, high NSAID use, and high degree of functional limitation illustrate the convoluted axSpA patient journey. The present findings highlight the need for patient-centric management and monitoring improvements to shorten the journey towards diagnosis and facilitate treatment access.

Author Contributions

The authors confirm contribution to the paper as follows: Study conception and design: Proton Rahman, Marco Garrido-Cumbrera, Jose Correa-Fernández, Patrick Leclerc, Robert D. Inman; Data collection: Proton Rahman, Marco Garrido-Cumbrera, Sherry Rohekar, Michael G. Mallinson, Elie Karam, Algis V. Jovaisas, Nigil Haroon, Jeff Beach, Artur J. de Brum-Fernandes, Martin Cohen, Jonathan Chan, Jose Correa-Fernández, Patrick Leclerc, Robert D. Inman; Analysis and interpretation of results: Proton Rahman, Marco Garrido-Cumbrera, Sherry Rohekar, Michael G. Mallinson, Elie Karam, Algis V. Jovaisas, Nigil Haroon, Jeff Beach, Artur J. de Brum-Fernandes, Martin Cohen, Jonathan Chan, Jose Correa-Fernández, Patrick Leclerc, Robert D. Inman; Draft manuscript preparation: Proton Rahman, Marco Garrido-Cumbrera, Sherry Rohekar, Michael G. Mallinson, Elie Karam, Algis V. Jovaisas, Nigil Haroon, Jeff Beach, Artur J. de Brum-Fernandes, Martin Cohen, Jonathan Chan, Jose Correa-Fernández, Patrick Leclerc, Robert D. Inman. All authors reviewed the results and approved the final version of the manuscript.

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Ethics Statement

The Canadian adaptation of the International Map of Axial Spondyloarthritis (IMAS) patient questionnaire and its French translation were approved by Advarra IRB (Columbia, Maryland). The requirement for obtaining informed consent was waived since Advarra IRB determined that the Canadian privacy requirements for a waiver of consent had been met.

Conflicts of Interest

Proton Rahman received consulting fees from Abbott, AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Novartis and Pfizer, and has also received research grants from Janssen and Novartis. Marco Garrido-Cumbrera had a research collaboration with Novartis Pharma AG. Sherry Rohekar received honoraria and/or participated in advisory boards for AbbVie, Amgen, BMS, Celgene, Eli Lilly, Fresenius Kabi, Gilead, Janssen, Merck, Novartis, Pfizer, Roche, Sandoz and UCB. Michael G. Mallinson received honoraria and/or participated in advisory boards for AbbVie, Janssen, Novartis and Pfizer. Elie Karam has no conflicts of interest. Algis V. Jovaisas received honoraria and participated in advisory boards for Amgen, Eli Lilly, Novartis, Pfizer, Sandoz and Sanofi. Nigil Haroon has no conflicts of interest. Jeff Beach has no conflicts of interest. Artur J. de Brum-Fernandes has no conflicts of interest. Martin Cohen received honoraria/consulting fees and/or participated in advisory board/speakers bureau events for AbbVie, Amgen, Celgene, Celltrion, Fresenius Kabi, Gilead, Janssen, Lilly, Novartis, Organon, Pfizer, Roche, Sandoz, Sanofi, and UCB. Jonathan Chan received honoraria and/or participated in advisory boards for AbbVie, Amgen, BMS, Celgene, Eli Lilly, Fresenius Kabi, Gilead, Janssen, Merck, Novartis, Organon, Pfizer, Roche, Sandoz, Viatris and UCB. Patrick Leclerc is an employee of Novartis Canada. José Correa-Fernádez has no conflicts of interest. Robert D. Inman received consulting fees from AbbVie, Janssen, Lilly, Novartis, Sandoz and UCB.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.