# Diagnostic Prevalence of Ankylosing Spondylitis Using Computerized Health Care Data, 1996 to 2009: Underrecognition in a US Health Care Setting

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## ABSTRACT

**Introduction:** Few studies have assessed the prevalence and features of axial spondyloarthritis (axSpA) and ankylosing spondylitis in diverse, population-based, community settings.

**Objectives:** We used computerized diagnoses to estimate the prevalence of axSpA and ankylosing spondylitis in Kaiser Permanente Northern California (KPNC).

**Methods:** We identified persons aged 18 years or older with 1 or more International Classification of Diseases, Ninth Revision (ICD-9) diagnosis Code 720.X (ankylosing spondylitis and other inflammatory spondylopathies) in clinical encounter data from 1996 through 2009 to estimate the prevalence of axSpA and ankylosing spondylitis. We reviewed medical records to confirm the diagnosis in a random sample and estimated the positive predictive value of computerized data to identify confirmed cases using various case definitions.

**Results:** In the computerized data, 5568 adults had diagnostic codes indicating axSpA. On the basis of our case-finding approach using a single physician diagnosis code for ICD-9 720.X, the point prevalence of these conditions, standardized to the 2000 US Census, was 2.26 per 1000 persons for axSpA and 1.07 per 1000 for ankylosing spondylitis. Less than half of suspected cases saw a rheumatologist. The most specific algorithm for confirmed ankylosing spondylitis required 2 or more computerized diagnoses assigned by a rheumatologist, with 67% sensitivity (95% confidence interval, 64%-69%) and 81% positive predictive value (95% confidence interval, 79%-83%).

**Conclusions:** Observed prevalence in the KPNC population, compared with national estimates for axSpA and ankylosing spondylitis, suggests there is substantial underrecognition of these conditions in routine clinical practice. However, use of computerized data is able to identify true cases of ankylosing spondylitis, facilitating population-based research.

## INTRODUCTION

Axial spondyloarthritis (axSpA) is characterized by chronic inflammatory back pain starting before the age of 45 years that involves sacroiliac joints. *AxSpA* is a relatively new umbrella term that includes ankylosing spondylitis and nonradiographic axSpA. Nonradiographic axSpA refers to an inflammatory spinal condition with symptoms that may be quite similar to ankylosing spondylitis, but where definitive x-ray changes in sacroiliac joints are not present. Most patients with nonradiographic axSpA will have visible inflammation in the sacroiliac joints or spine if advanced imaging such as magnetic resonance imaging (MRI) is performed, and some but not all of these patients will progress to ankylosing spondylitis.[1] The clinical features of inflammatory back pain include symptoms that are worse at night and with rest, improve with exercise, and entail prolonged morning stiffness. Physical examination findings and investigations in patients with axSpA include limitation in range of motion of the chest wall and axial joints, association with human leukocyte antigen-B27 (HLA-B27), and inflammation and/or sclerosis/erosions in the spine and sacroiliac joints. Patients with axSpA carry a substantial burden of disease not only because of musculoskeletal features but also because of extra-articular manifestations that include enthesitis, inflammatory bowel disease, uveitis, psoriasis, and fractures. Treatment options include nonsteroidal anti-inflammatory drugs, nonbiologic disease-modifying antirheumatic drugs such as sulfasalazine (for treatment of peripheral arthritis), and tumor necrosis factor blockers.

Classification criteria for spondyloarthritis have evolved over time, making it challenging to assess the incidence and prevalence of axSpA in population-based settings.[2,3] Two recent studies have investigated the prevalence of axSpA in the US using different methods. The National Health and Nutritional Examination Survey (NHANES) of 2009-2010 concluded that the prevalence of axSpA, using either the Amor or the European Spondyloarthritis Study Group classification criteria, was between 0.9% and 1.4% of the US population, or 9 to 14 per 1000.[4] The NHANES surveys, which are nationally representative, are done by selecting noninstitutionalized US adults through a complex, multistage probability design. Strand et al[5] reported the axSpA prevalence as 0.7% (7 per 1000) by retrospective analysis of patients' medical records from 101 randomly selected US rheumatology practices. Both methods have their advantages and shortcomings, but the axSpA prevalence estimates in these 2 studies are similar.

Registries and other population-based resources are useful to assess the prevalence, incidence, risk factors, and outcomes of diseases

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such as axSpA and ankylosing spondylitis. We used computerized clinical databases maintained by Kaiser Permanente to estimate the prevalence of clinically recognized axSpA in a stable, well-characterized, and ethnically diverse population. As a secondary aim, we evaluated the ability of computerized data to validate cases of axSpA and ankylosing spondylitis.

## METHODS

The study was conducted under the approval of the Kaiser Foundation Research Institute's institutional review board. Because no participant contact was involved and the study involved only a review of existing electronic health record data and associated information (eg, imaging results), no participant consent was obtained or required.

### Study Population

Kaiser Permanente Northern California (KPNC) is a prepaid, comprehensive, integrated care organization that maintains computerized clinical data of all visits, procedures, and prescriptions provided to more than 3 million members in Northern California.

This study included patients with at least 12 months of enrollment in KPNC between 1996 and 2009. Preliminary axSpA cases of patients aged 18 years and older were identified using age on the date of the first diagnosis recorded during the observation period. Because there is no International Classification of Diseases, Ninth Revision (ICD-9) code uniquely appropriate for axSpA, the expectation was that US rheumatologists would use Code 720.X to record such cases. We identified patients with at least 1 assignment of ICD-9 Code 720.X from a physician in the computerized outpatient or inpatient database as preliminary cases. This group of diagnoses included ankylosing spondylitis (Code 720.0), spinal enthesopathy (720.1), sacroiliitis (720.9), and unspecified spondyloarthropathy (720.9). On the basis of the available project resources, an approximate 3% random sample of all preliminary cases was selected for validation using detailed review of the medical record. The sample was stratified on the basis of the type of clinician who recorded the diagnosis (rheumatologist, other clinician), the number of diagnostic codes (1, ≥ 2), the presence of codes for other inflammatory arthritides (rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, or arthritis with inflammatory bowel disease), and prescriptions for disease-modifying antirheumatic drugs.

### Data Collection

Data collection occurred during 2010. Observation began on the later of the date of each patient's enrollment with KPNC or January 1, 1996, and ended on disenrollment or December 31, 2009. Computerized medical information was obtained during 1996 through 2009 and included rheumatologist-recorded diagnosis codes recorded into outpatient data, hospital discharge diagnoses, and laboratory results for HLA-B27. All relevant computerized medical information was obtained for possible cases. A manual chart review was performed on a sample of preliminary cases that had at least 1 computerized diagnostic code for axSpA or ankylosing spondylitis. The main purpose of the chart review was to confirm the diagnosis recorded in the computerized data. A secondary purpose was to obtain information on disease manifestations and family history.

A trained medical record abstractor reviewed the medical records to confirm the diagnosis. The abstractor accessed data from the electronic medical record that was established in 2004 and 2005; in addition, she sometimes referred to clinic notes recorded in the paper-based records created before the transition to the electronic medical record. The abstractor reviewed outpatient notes, hospital discharge summaries, laboratory results, and radiology reports to confirm or rule out the diagnoses using a structured case report form developed by the study team.

### Study Case Definition

Following case validation, the criteria required to satisfy our study's case definition of axSpA and ankylosing spondylitis was two or more clinical diagnoses recorded by a treating rheumatologist in the medical record and occurring on at least two unique calendar days with no qualifiers such as "rule-out" or "possible." Clinic notes by a primary care clinician, without a rheumatologist consult, and indicating joint inflammation in the spine with or without peripheral involvement and without a more specific diagnosis, were reviewed by a single, now retired rheumatologist. The rheumatologist assessed clinical features, including joint inflammation that lasted at least six weeks; associated laboratory test results; and radiology reports and images and reports for sacroiliitis, erosions of the sacroiliac joints, and other radiographic features consistent with axSpA or ankylosing spondylitis.

Given the retrospective, population-based nature of the study, this case definition was intended to represent a reasonable reference standard to confirm a community-based diagnosis; it was not intended to confirm cases according to formal classification criteria, which would have been infeasible in this setting. The data presented reflected the status of the disease at the time it was assessed and the information available in medical records as part of routine clinical care. The data were not considered to reflect the cumulative prevalence of various manifestations of ankylosing spondylitis based on a systematic, standardized evaluation. During the course of the study and its timeframe in relation to classification criteria for axSpA and the data available to the project (1996-2009), it became apparent that there was not sufficient data available to definitively evaluate the validity of axSpA cases. Therefore, case confirmation was subsequently restricted to ankylosing spondylitis only.

### Disease Manifestations of Ankylosing Spondylitis in Confirmed Cases

Disease manifestations were characterized descriptively and included HLA-B27 positivity; comorbid conditions, including those in the spondyloarthritis family; complications or manifestations of axSpA or ankylosing spondylitis (interstitial lung disease/fibrosis, aortic insufficiency, enthesitis, Achilles tendinitis [heel pain], uveitis/iritis, iridocyclitis, kyphosis, costochondritis); radiographic evidence of syndesmophytes, spondylitis, squaring of vertebral bodies, sacroiliitis, and erosions of the sacroiliac joint; and abnormal results of the Schober test. Because of the community-based and retrospective nature of the study, not all possible clinical and radiologic examinations were performed on all patients; thus, absence of these features did not necessarily imply that the ankylosing spondylitis-associated features of interest were not present, only that they were not assessed or recorded.

### Statistical Analysis

The positive predictive value (PPV) was determined for each of several a priori case-finding algorithms for ankylosing spondylitis. For each a priori algorithm, sensitivity was defined as the number of confirmed cases of ankylosing spondylitis captured by the a priori algorithm divided by the number of confirmed cases with at least 2 ICD-9 Codes 720.X assigned by any physician or 1 such code from a rheumatologist. The PPV was defined as the number of cases captured by the algorithm that was confirmed with the disease during medical record review divided by the number of confirmed plus unconfirmed cases that were captured by the algorithm. We did not compute specificity or negative predictive value because they generally do not fall below 99% for relatively uncommon diseases.

Variables that were examined for inclusion in case-finding algorithms included 1) inpatient and outpatient visits with relevant codes for axSpA or ankylosing spondylitis (720.X), 2) number of visits to a rheumatologist, 3) use of biologic or nonbiologic disease-modifying antirheumatic drugs, and 4) presence of diagnoses for other inflammatory arthritides such as rheumatoid arthritis or psoriatic arthritis. We evaluated multiple possible case-finding algorithms, with the most inclusive (ie, sensitive) algorithm (≥ 1 physician diagnosis of axSpA) used as the basis for comparison with all other algorithms.

All analyses were conducted using SAS version 9.13 software (SAS Institute, Cary, NC). We used the SAS SURVEYMEANS procedure to estimate the PPV and its 95% confidence interval (CI). The procedure took into account that the sampling design was stratified; thus, the overall PPV was weighted.

### Estimation of Point Prevalence

The age- and sex-specific prevalence of axSpA and ankylosing spondylitis was calculated using as the denominator the number of men and women in each age group who were members of KPNC on December 31, 2009. The point prevalence was expressed as the number of adult cases with the disease divided by the number of adults in the Health Plan. The age- and sex-standardized proportion was estimated using the direct method of standardization, with the 2000 US Census population providing weights.[6] The 95% CIs were computed assuming a Poisson distribution.[7]

## RESULTS

### Application of Case-Finding Algorithm

There were 5568 KPNC members with at least 1 inpatient or outpatient diagnosis code of 720.X for ankylosing spondylitis or another inflammatory spondylopathies; of these, 48% were for ankylosing spondylitis specifically (720.0). However, 2965 (53% overall) of these had only a single code assigned by a primary care clinician. We validated the medical record for a random sample of 44 of these 2965 patients, of which only 1 person (PPV, 2%) was confirmed. Because of the low PPV of this definition and resource constraints of the study, we therefore excluded these patients from further consideration.

Among the 2603 patients remaining who had axSpA or ankylosing spondylitis, 1028 (39%) had 2 or more diagnostic codes by a primary care clinician, 250 (10%) had a single diagnostic code by a rheumatologist (with or without additional codes from a primary care or other type of physician), and 1325 (51%) had 2 or more diagnostic codes by a rheumatologist.

We examined sensitivity and PPV of 4 case-finding algorithms (Table 1). The most inclusive allowed 2 or more diagnoses by a primary care clinician or 1 or more diagnoses by a rheumatologist. By definition (because we excluded possible cases that had only 1 diagnosis code by a primary care clinician), this most inclusive algorithm had 100% sensitivity.

In total, we performed 129 chart reviews to confirm possible ankylosing spondylitis (excluding the 44 chart reviews performed for patients with only a single diagnosis recorded by a primary care clinician). Of these, 80 (62%) were true-positives. The 3 other

**Table 1. Sensitivity and positive predictive value of computerized diagnoses for identifying ankylosing spondylitis in 2603 adults at first recorded diagnosis with 1 or more diagnoses[a]**

| Operational definition | Number in population | Number in stratified sample[b] | Number of true-positives in stratified sample[c] | Number of false-positives in stratified sample[c] | Sensitivity,[d] % (95% CI) | Percentage of diagnoses for AS (ICD-9 code 720.0) | PPV of algorithm to find AS, % (95% CI)[e] |
|---|---|---|---|---|---|---|---|
| ≥ 2 diagnoses in primary care or ≥ 1 diagnosis in rheumatology | 2603 | 129 | 80 | 49 | 100[c] | 80 | 62 (60-64) |
| ≥ 2 diagnoses, any department | 2353 | 102 | 67 | 35 | 96 (95-97) | 80 | 66 (64-68) |
| ≥ 1 diagnosis, rheumatology | 1575 | 83 | 61 | 22 | 72 (70-74) | 94 | 73 (71-76) |
| ≥ 2 diagnoses, rheumatology[f] | **1325** | **56** | **48** | **8** | **67 (64-69)** | 96 | **81 (79-83)** |

[a] Patients aged 18 years or older, from inpatient or outpatient data from Kaiser Permanente Autoimmune Disease Registry, Northern California, 1996 to 2009.
[b] Subjects were sampled for chart review on the basis of the number of visits, the department in which the diagnosis was made, use of disease-modifying antirheumatic drugs, and presence of comorbid autoimmune conditions. The latter 2 variables did not improve the sensitivity or specificity of the algorithm.
[c] Classified on the basis of medical record review.
[d] By definition, given that our search strategy required at least 1 physician diagnosis of ICD-9 code 720.X, and recognizing the likelihood of underascertainment.
[e] Calculated by dividing the number of true-positives by the number in the stratified sample. For example, on the first row, 80 (true-positives)/129 (number in the stratified sample) = 62%.
[f] Boldface indicates most specific algorithm (maximized positive predictive value).
AS = ankylosing spondylitis; CI = confidence interval; ICD-9 = International Classification of Diseases, Ninth Revision; PPV = positive predictive value.

algorithms that we tested were subsets of the most inclusive and considered only the number of diagnostic codes and the department in which they were recorded (Table 1). The sensitivity of the 2 algorithms that required 2 or more physician diagnoses, or 1 or more diagnoses from a rheumatologist, ranged from 72% to 96%, with PPVs ranging from 66% to 73%. The algorithm that maximized PPV required 2 or more diagnoses by a rheumatologist and had a sensitivity of 67% (95% CI, 64%-69%) and PPV of 81% (95% CI, 79%-83%).

Half of the patients with 2 or more rheumatologist diagnoses used biologic or nonbiologic disease-modifying antirheumatic drugs, with the algorithm performing the same in those with and without such drug use. The presence or absence of concomitant diagnoses for other autoimmune diseases did not affect the performance of the algorithm.

Among the 49 false-positives whose charts were reviewed to confirm ankylosing spondylitis, 10 had other autoimmune diseases, including 5 with rheumatoid arthritis, 2 with inflammatory bowel disease, 1 with both rheumatoid arthritis and inflammatory bowel disease, and 2 with psoriatic arthritis. However, only 4 of these 10 patients had 2 or more rheumatologist diagnoses. Although these individuals might have met diagnostic criteria for axSpA, the diagnostic workup and associated clinical data available were inadequate to systematically assess all reviewed cases for axSpA.

### Prevalence of Axial Spondyloarthritis and Ankylosing Spondylitis

Using the most sensitive definition for axSpA (any 720.X diagnosis code, n = 5568 cases) among patients enrolled in Kaiser Permanente on December 31, 2009, the point prevalence of axSpA, standardized to the 2000 US Census, was 2.26 (95% CI, 2.20-2.32) per 1000. Using a somewhat more specific definition, 2 or more diagnoses in primary care or 1 or more diagnosis in rheumatology (n = 2603), 80% of which were for ankylosing spondylitis, the corresponding estimate was lower by approximately half (1.07 per 1000, 95% CI, 1.03-1.11).

### Characteristics of Ankylosing Spondylitis Cases

Characteristics of the 80 persons confirmed with ankylosing spondylitis were described on the basis of information found in medical records. Most of these specifically mentioned a diagnosis of ankylosing spondylitis. Sixty-one percent of patients were under age 50 years, and 83% were male; 45% were white, 14% Hispanic, and 14% Asian (Table 2). Only 44% had an HLA-B27 test, and only 34% were positive (among those tested). Joint involvement by signs and symptoms was not specifically recorded for 30% of patients. In the remainder, symptoms included the lumbar spine in 55% of patients; x-ray, MRI, or computed tomography evidence for cervical spine involvement in 13%, and sacroiliac and/or hip joint involvement in 26%. About one-fourth of patients had uveitis or iritis.

## DISCUSSION

We estimated the prevalence of axSpA using computerized health care data during 1996-2009. A total of 5568 adults had any diagnostic code indicating axSpA in the computerized data. This led to a point prevalence of axSpA, standardized to the 2000 US census, of 2.26 per 1000. We also reviewed the charts of a random sample of 173 of the 5568 patients. The best (most specific) performing algorithm for ankylosing spondylitis required 2 or more computerized diagnoses by a rheumatologist and had a PPV of 81% (95% CI, 79%-83%) compared with our study case definition.

The incidence and prevalence of ankylosing spondylitis have been described in a number of studies. One report was from the Rochester Epidemiology Project[8] in Minnesota, which identified 158 cases with radiographic sacroiliitis recorded on radiology reports from 1935 to 1989. The overall age- and sex-adjusted incidence rate was 7.3 per 100,000 person-years (95% CI, 6.1-8.4), although prevalence was not reported. Kaipiainen-Seppanen and coworkers[9-11] reported the annual incidence and prevalence of ankylosing spondylitis requiring antirheumatic medication among 87,000 inhabitants of Kuopio, Finland. In 2000, the annual incidence was 6.9 per 100,000 adults (95% CI, 6.0-7.8), very similar to the incidence rate in Rochester, MN, and the prevalence was 1.5 per 1000 (95% CI, 0.8-2.7), very similar to the prevalence we estimated for the KPNC population. In Norway, from 1960 through 1993, the annual incidence of ankylosing spondylitis was 8.71 per 100,000 (95% CI, 6.38-11.04), whereas the estimated point prevalence was 2.6 per 1000 on January 1, 1990.[12] Other reports of the occurrence of ankylosing spondylitis have been reviewed.[13] The prevalence of ankylosing spondylitis was much lower, 0.30 per 1000 (95% CI, 0.26-0.33) in Greece from 1983 through 2002,[14] whereas in Japan it was 0.095 per 1000, based on 990 cases.[15] The prevalence of ankylosing spondylitis has been reported to be relatively high in populations indigenous to circumpolar regions.[15-18]

Key differences between our report and these earlier reports include the size and diversity of the study populations, with the Rochester, Norway, and Sweden populations being largely white with a more restricted genetic background, and the Northern California population reported here being more racially and ethnically diverse. The KPNC population is more diverse than the US population and is 50% white, 6% African American, 22% Hispanic, and 21% Asian.[19,20] Differing calendar periods, disease duration (which affects prevalence estimates), methods for case ascertainment, and fulfillment of diagnostic vs classification criteria are other potential differences that make these reports somewhat difficult to directly compare with one another.

The 2009-2010 NHANES study is the largest effort to date to assess the prevalence of axSpA in the US.[4] They calculated the prevalence of axSpA to be 14 per 1000 in US adults. This figure is 6 times higher than the prevalence we estimated from the KPNC population. There are several possible explanations for this discrepancy. First, there are major differences in the study designs. Whereas NHANES was designed to actively search for axSpA in a prospective manner in the general US population, the KPNC study was a retrospective analysis of computer records from a community-based patient population. To assess the prevalence of axSpA, NHANES investigators used a specifically designed case ascertainment tool that systematically searched for spondyloarthritis features found during spondyloarthritis-focused physical examinations, as well as systematically assessed for HLA-B27, applying the criteria of Amor and the European Spondyloarthritis Study Group.[1,3] In contrast, clinicians in KPNC were not actively searching for spondyloarthritis, and the study design is a retrospective capture of the computerized data for diagnoses made not just by specialists but also by primary

care physicians, and made without applying these classification criteria. Strand et al[5] estimated the prevalence of axSpA in the US to be 7 per 1000, and 3 per 1000 for ankylosing spondylitis, half that reported by NHANES, despite being conducted in US rheumatologists' practices. Our study showed that many patients suspected of spondyloarthritis were not referred by primary care clinicians to rheumatologists, supported by our data showing that 48% of all 720.X cases were ankylosing spondylitis (720.0) but 94% of 720.X cases seen by rheumatologists were ankylosing spondylitis.

The second major reason for the low prevalence of axSpA in our study may suggest underascertainment of these cases in clinical practice. Indeed, the necessary data to support classifying patients according to our study case definition (much less apply the formal classification criteria for axSpA or ankylosing spondylitis) were frequently absent in the KPNC records. We also call attention to the distinction between population prevalence, the proportion of patients with a diagnosed disease of interest throughout the entire population, vs diagnostic prevalence (which we assessed in this study) Diagnostic prevalence is the proportion of people who have a diagnosis of the disease based on diagnostic codes, physician diagnoses, or other features determined when they seek medical attention. For most conditions, some patients will have the disease of interest, yet it is undiagnosed; diagnostic prevalence would not include these patients and therefore would be expected to underestimate the true disease prevalence. The study by Strand et al[5] noted that the US rheumatologists did not diagnose one-fourth of cases of axSpA even though they fulfilled the Assessment of SpondyloArthritis International Society classification criteria and were subsequently discovered by retrospective chart assessment. It is likely that the underascertainment of these cases in general practice by nonspecialists is even higher, indicating a need for increased awareness.[21-23]

**Table 2. Demographic and disease manifestations among 80 confirmed cases of ankylosing spondylitis from Kaiser Permanente Northern California, 1996 to 2009**

| Characteristic | n (%) |
|---|---|
| **Sex, male** | 66 (83) |
| **Age, years** | |
| 18-29 | 9 (11) |
| 30-39 | 18 (23) |
| 40-49 | 22 (27) |
| 50-59 | 15 (19) |
| 60-69 | 11 (14) |
| 70-89 | 5 (6) |
| **Race/ethnicity** | |
| White | 36 (45) |
| Hispanic | 11 (14) |
| Asian | 11 (14) |
| African American | 2 (2) |
| Other/multiracial/unknown | 20 (25) |
| **Disease duration, years** | |
| 0-4 | 12 (15) |
| 5-9 | 13 (16) |
| 10-19 | 14 (18) |
| ≥ 20 | 34 (42) |
| Not recorded | 7(9) |
| **Laboratory and imaging tests** | |
| HLA-B27 test performed | 35 (44) |
| HLA-B27 positive (% of those tested) | 12 (34) |
| X-rays of SI joints and/or spine | 61 (76) |
| CT of SI joints and/or spine | 6 (8) |
| MRI of SI joints and/or spine | 16 (20) |
| **Associated immune-mediated disease diagnoses (present at any time)** | |
| None or unmentioned | 60 (75) |
| Psoriasis or psoriatic arthritis | 2 (2) |
| JIA/JRA | 1 (1) |
| Inflammatory bowel disease | 2 (2) |
| Reactive arthritis | 4 (5) |
| Undifferentiated spondyloarthropathy | 2 (2) |
| Other | 7 (9) |

| Characteristic | n (%) |
|---|---|
| **Joint involvement by signs/symptoms** | |
| Lumbar spine | 44 (55) |
| SI joint/hip | 21 (26) |
| Cervical spine/neck | 10 (13) |
| Shoulder | 2 (3) |
| Thoracic spine | 4 (5) |
| Knee | 3 (4) |
| Ankle | 3 (4) |
| Not recorded | 24 (30) |
| **Complications** | |
| Uveitis or iritis | 19 (24) |
| Kyphosis | 4 (5) |
| Achilles tendinitis | 2 (3) |
| Enthesitis | 1 (1) |
| None | 55 (69) |
| **Positive Schober test** | 31 (39) |
| **Family history of autoimmune disease[a]** | |
| Mother/father/sibling | 19 (24) |
| Grandparent/distant relative | 8 (10) |
| **Medication use[b]** | |
| Oral glucocorticoids | 27 (34) |
| Etanercept | 14 (18) |
| Adalimumab | 5 (6) |
| Infliximab | 4 (5) |

[a] Family history of any of the following diseases: Addison disease, adult Still disease, alopecia areata, ankylosing spondylitis or axial spondyloarthritis, asthma, autoimmune hepatitis, Behçet syndrome, CREST syndrome, Crohn disease, dermatomyositis/polymyositis, diabetes (type 1), Graves disease, Guillain-Barré syndrome, idiopathic thrombocytopenic purpura, inflammatory bowel disease, JIA/JRA, Meniere disease, mixed connective tissue disease, myasthenia gravis, pemphigus vulgaris, pernicious anemia, primary biliary cirrhosis, Sjögren syndrome, psoriasis, psoriatic arthritis, Raynaud disease, Reiter syndrome (reactive arthritis), rheumatoid arthritis, sarcoidosis, spondyloarthropathy excluding ankylosing spondylitis, systemic lupus erythematosus, systemic sclerosis (scleroderma), Hashimoto thyroiditis, ulcerative colitis, uveitis/iritis, and vasculitis.

[b] Used anytime between 1996 and 2009.

CT = computed tomography scan; HLA = human leukocyte antigen; JIA/JRA = juvenile idiopathic arthritis or juvenile rheumatoid arthritis; MRI = magnetic resonance imaging; SI = sacroiliac.

A third reason for the low prevalence of axSpA in our study may be that some patients with chronic low back pain are cared for by chiropractors, not physicians. Such patients will not be found in Health Plan data but will be captured in population-based studies like NHANES.

For all these reasons, and because early identification and treatment of axSpA might prevent patients from progressing to ankylosing spondylitis, it is important to identify these conditions earlier. Early identification might be facilitated by an educational campaign directed at clinicians, or a screening program targeted at patients who have back pain with inflammatory features that began at an early age of onset (eg, age < 40 years).[24]

We required patients to have at least one year of enrollment in KPNC to be included in the study. Differing amounts of data available in future studies could affect the estimated prevalence of ankylosing spondylitis and its manifestations, and should be considered when comparing across populations.

The timeframe of the study prevented us from confirming cases of axSpA,[25,26] and we recognize the possibility that some cases that could not be confirmed as ankylosing spondylitis nevertheless had some features that might suggest this condition (eg, concomitant psoriatic arthritis, 2 or more rheumatologist diagnoses). However, we were able to confirm potential ankylosing spondylitis cases. Only 1610 (29%) of the 5568 patients with at least one 720.X diagnosis in the present study population were inferred to truly have ankylosing spondylitis, suggesting that a single diagnosis code alone is not appropriate. The best performing algorithm (based on maximizing PPV) required 2 or more computerized diagnoses by a rheumatologist and had a sensitivity of 67% and a PPV of 81%. Other investigators have used computerized health care data to ascertain the prevalence of ankylosing spondylitis,[11,27-33] but only 2 studies of which we are aware have validated a case-finding algorithm for ankylosing spondylitis.[31,34] The Veterans Affairs study reviewed medical records for 10 patients with 1 or more rheumatologist-assigned diagnostic code for ankylosing spondylitis as well as for other patients with rheumatic diagnoses.[31] The study investigators reported a single diagnosis in the Rheumatology Department to have a PPV of 83% (CI, 78%-89%) with a sensitivity of 91% (CI, 87%-95%), although they did not include nonrheumatologists' diagnoses of ankylosing spondylitis in the denominator when computing sensitivity. As in the present study, requiring use of disease-modifying antirheumatic drugs greatly reduced the sensitivity of case finding and was not helpful.[31] A separate study conducted in The Health Improvement Network involving 85 patients found that a single diagnostic code for ankylosing spondylitis had a PPV of 72%, and the best performing algorithm for ankylosing spondylitis had a PPV of 89% and required 2 ankylosing spondylitis codes more than 7 days apart.[34] It is possible that rheumatologists assigned ankylosing spondylitis diagnoses to patients who actually had nonradiographic axSpA, which would have lowered the PPV. This circumstance may lessen with transition to use of the ICD-10 system given that the relevant diagnostic codes are somewhat more dissimilar between ankylosing spondylitis (M45) and other specified inflammatory spondylopathies such as nonradiographic axSpA (M46.8). We also acknowledge that the sensitivity computed was predicated on an initial case-finding strategy that used ICD-9 codes. Alternate approaches (eg, presence of HLA-B27 or physician notes mentioning ankylosing spondylitis in the electronic health record) may be useful in the future to maximize sensitivity.

A positive HLA-B27 test has been strongly linked to ankylosing spondylitis. HLA-B27 has a very high prevalence among the native peoples of the circumpolar arctic and the subarctic regions of Eurasia and North America and in some regions of Melanesia, and it is present throughout Eurasia; however, the genotype is virtually absent among native populations of South America, Australia, and many equatorial and Southern African populations.[12] In the sample of our 80 confirmed ankylosing spondylitis cases, only 45% were white, and only 44% were tested for HLA-B27. It is possible that only patients for whom the diagnosis of ankylosing spondylitis was uncertain were tested for the presence of HLA-B27. Restated, patients for whom physicians had greater certainty of ankylosing spondylitis on the basis of clinical and radiographic findings may be less likely to be tested for HLA-B27. Because these patients presumably would have a higher prevalence of HLA-B27, this might account for the lower-than-expected prevalence of HLA-B27 in our sample, and the fact that most (two-thirds) were not tested.

Methods used for case finding in any study will depend on the research question, the setting, and the costs of overascertainment and underascertainment with respect to validity and precision. A case-finding strategy that is insensitive but has a high PPV, such as recruitment through rheumatology clinics, likely will yield fewer and more severe cases. The algorithms we examined provided the typical trade-off between specificity (and PPV) and sensitivity. A case-finding algorithm with high sensitivity is useful for studies requiring complete ascertainment but requires additional resources to confirm cases through a second-stage review of medical records. Case-finding algorithms with higher specificity and PPVs are useful when two-stage case ascertainment is impractical. We found that two or more computerized diagnoses for ankylosing spondylitis from a rheumatologist provided the best combination of sensitivity and PPV.

## CONCLUSION

Identification of an algorithm using computerized data enables efficient identification of ankylosing spondylitis and should be useful for advancing understanding of medical service utilization, long-term outcomes, and medication safety. Studying the natural history of the disease and the potential for early intervention to prevent progression from axSpA to ankylosing spondylitis is likely to be fruitful in future investigations. ❖

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