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ORIGINAL REPORT

# Validity of psoriatic arthritis and capture of disease modifying antirheumatic drugs in the health improvement network†

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## ABSTRACT

**Purpose** The aims of this study are to examine the validity of diagnostic codes for psoriatic arthritis in The Health Improvement Network (THIN) and to examine the agreement between General Practitioner (GP) report and prescription records for disease modifying antirheumatic drugs (DMARDs).

**Methods** Questionnaires were sent to the GPs of 100 randomly selected patients with at least one medical record code for psoriatic arthritis. The positive predictive value (PPV) for a GP confirmed diagnosis was calculated, and alternative algorithms were examined to determine which method resulted in the highest PPV.

**Results** The PPV for a single code for psoriatic arthritis was 85% (95%CI: 75.8–91.7%). Adding a prescription for a DMARD increased the PPV to 91% but with a substantial loss in sensitivity. Agreement between GPs and prescription data for use of an oral DMARD was 69%.

**Conclusions** The diagnosis codes for psoriatic arthritis used in THIN are valid. All prescriptions for DMARDs may not be accounted for in THIN. Copyright © 2014 John Wiley & Sons, Ltd.

KEY WORDS—psoriatic arthritis; validation; database; disease modifying antirheumatic drug (DMARD); pharmacoepidemiology; the health improvement network

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## INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis that can cause joint damage and disability.[1] Overall, relatively little is known about long term-outcomes in PsA from a population-based perspective. With a prevalence of 0.1–0.25% in the general population, large population-based databases offer an opportunity to better understand long-term outcomes in this relatively rare disease.[2–4]

The Health Improvement Network (THIN), an electronic primary care medical record database in the UK, is a resource for the study of many medical conditions, a variety of which have already been validated.[5–7] THIN includes longitudinal data for over 9000 patients with at least one diagnostic code for psoriatic arthritis between the ages of 18–89, representing the largest population of patients with PsA available for study to date.[9] Psoriasis, in particular, has been extensively studied in THIN, and the positive predictive value (PPV) of a single code is known to be 90%.[8] The prevalence of PsA in THIN and the prevalence of PsA among patients with psoriasis in THIN are similar to a handful of other population-based estimates.[9] However, validation studies have not yet been performed.

In studying inflammatory arthritis such as PsA, ascertaining use of disease modifying antirheumatic

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†This paper was presented in poster form at the International Conference on Pharmacoepidemiology in Montreal, CA, on 26 August 2013. In addition, the positive predictive value and a short summary of the methods were published in a manuscript in Rheumatology (Oxford) in 2013 (referenced below). However, the survey results have not been published. Only the following sentence from the validation study was published in the Rheumatology paper: "Among the 100 GPs of patients with a Read code for PsA selected for query, 87 surveys were returned within 90 days. Seventy-four patients (85.1%, 95% CI 75.8%, 91.7%) had a confirmed diagnosis of PsA. Among these 74 patients, 62 (83.7%) had been seen by a rheumatologist who corroborated the diagnosis."

drugs (DMARDs) is important because these medications may influence long-term outcomes. We previously reported that only 50% of patients with diagnostic codes for psoriatic arthritis in THIN had prescription codes for DMARDs.[9] While this is similar to previous reports from other population-based datasets, it is important to understand the degree to which the use of such therapies is recorded in THIN.

The objectives of this study were to (i) examine the accuracy of diagnostic codes in the medical record for the true diagnosis of PsA and (ii) to examine the agreement between prescription codes in the medical record and General Practitioner (GP) notation of DMARD use in patients with PsA.

## METHODS

### *Study design*

We performed a cross-sectional study within THIN to determine the validity of the diagnosis codes for PsA.

### *Data source*

THIN is a large medical record database in the United Kingdom (UK).[10] THIN processes data collected by participating GP practices and makes it available for research after removing patient identifiers and performing quality assessments. More than 9 million people in 498 practices with an average of 7 years of follow-up per subject are included in the database. Patients in THIN are representative of the general population in the United Kingdom in terms of age, sex, and medical conditions. Information from specialty care may not be captured unless the data are entered by the GP. However, the gatekeeper system in the UK requires that patients see their GP before seeking specialty care and makes the GP the primary contact for all aspects of the patient's care. GPs record data related to patient care including demographics, medical history, laboratories and other diagnostic tests, and prescriptions.[6]

### *Study population*

Patients had at least one READ code[11] for PsA (M160.00, M160.11, M160000, M160100, M160200, M160z00), were age 18–89 at the time of sampling, and were cared for in participating practices.

### *Outcomes*

The GP's confirmation of the diagnosis was used as the reference standard. Secondary outcomes included confirmation of the diagnosis by a rheumatologist and fulfillment of the CASPAR criteria.

### *Sampling*

Surveys were sent to the GPs of 100 randomly selected patients with a medical code for PsA cared for in practices that agreed to participate in surveys (250 practices, approximately half of practices contributing to THIN). Surveys were mailed in January 2012 by Cegedim's Additional Information Services so that individual patient information was anonymous to the investigators.

### *Variables*

Variables collected from the medical record included age at sampling, sex, date of diagnosis, rheumatology and dermatology consultation codes, history of osteoarthritis (OA) or rheumatoid arthritis (RA), diagnosis codes for psoriasis, and prescriptions for oral DMARDs (methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, azathioprine, cyclosporine), biologic DMARDs (etanercept, infliximab, adalimumab), and oral corticosteroids. Data from the medical record were collected between 1994 and 2010.

### *Instrument*

GPs were asked to complete a survey (Supplemental Document) to ascertain accuracy of PsA diagnosis, disease characteristics, and history of DMARD use. The survey was designed by dermatologists, rheumatologists, and epidemiologists with assistance from a GP consultant in the UK.

### *Analysis*

Descriptive statistics were used to compare characteristics among responders and non-responders and among those with confirmed PsA and without PsA. The PPV and 95% confidence interval were calculated for each algorithm with the GP confirmed diagnosis as the reference standard. Strategies for defining PsA included (i) 1 code for PsA, (ii) 2 codes for PsA, (iii) 1 code for PsA and 1 code for psoriasis, (iv) 1 code for PsA and 1 DMARD prescription, (v) a code for PsA in the absence of RA or OA, and (vi) a code for PsA and a code for a rheumatology consultation. Additionally, among patients with a GP response, we calculated the sensitivity and specificity for algorithms ii through vi. In this analysis, the presence or



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absence of the additional requirement (e.g. a second code for PsA) was considered the "test," and the GP's confirmation of the diagnosis was considered the "reference standard." Finally, we examined percent agreement between GP and medical record notation of DMARDs use. Percent agreement was calculated as the number of times the medical record and the GP agreed on the use of DMARDs over the total number of observations.

## RESULTS

Of the 100 surveys sent, 87 were returned within 90 days. Practitioners who did not respond belonged to different practices than those who did respond, and patients for whom the survey was not returned had a median year of diagnosis 10 years earlier than those patients whose forms were returned—1987 versus 1997, respectively. Otherwise, there were no significant differences between the characteristics of patients for whom the survey was returned and those for whom the survey was not completed.

The GP confirmed the diagnosis in 74 of 87 patients with at least one diagnosis code for PsA (PPV 85.1%, 95%CI: 75.8–91.7%). Of those with confirmed PsA, 62 (83.7%) had been seen by a rheumatologist who corroborated the diagnosis and 43 met Classification for Psoriatic Arthritis (CASPAR) criteria.[12] The remaining 31 records did not have enough information to examine CASPAR criteria.

The characteristics of the patients for whom surveys were returned are found in Table 1. Compared to patients with a non-confirmed diagnosis, those with confirmed PsA were more likely to be male, referred to a rheumatologist, and prescribed a DMARD although only the latter was statistically significant ($p = 0.049$). The other characteristics were similar between the two groups.

Clinical features of patients with confirmed PsA are shown in Table 2. The median time since diagnosis was approximately 5 years. GPs reported a history of joint swelling in the majority (72%). Among the 74 patients with confirmed PsA, the GP reported "unknown" for all of the PsA features in 6 patients, and one patient was noted to have "none" of the features. The body surface area (BSA) of psoriasis was minimal in 39 patient (53%), moderate in 17 (23%), and severe in 14 (19%). The GP did not know the extent of psoriasis in 4 patients (5%). While all but 4 GPs provided a psoriasis BSA, only 74% of patients with confirmed PsA had a code for psoriasis. Many of the other clinical features were not recorded or were noted as unknown by the GP.

Next, alternative algorithms for defining PsA were examined (Table 3). Of the algorithms tested, none had a substantially higher PPV than a single code for PsA except when a DMARD prescription was required (PPV 91%, 76.3–98.1). However, this

Table 1. Patient characteristics

| | PsA | No PsA | Not returned |
|---|---|---|---|
| Number | 74 | 13 | 13 |
| Male *N* (%) | 41 (55%) | 4 (31%) | 4 (31%) |
| Age mean (SD) | 56.7 (14.7) | 58.1 (12.9) | 61.4 (4.3) |
| Osteoarthritis | 17 (23%) | 3 (23%) | 3 (23%) |
| Rheumatoid arthritis | 12 (16%) | 3 (23%) | 1 (8%) |
| Psoriasis | 55 (74%) | 10 (77%) | 11 (85%) |
| Rheumatology consultation | 52 (70%) | 8 (62%) | 8 (62%) |
| PsA codes | | | |
| M160.00 (psoriatic arthropathy) | 71 | 12 | 11 |
| M160.11 (psoriatic arthritis) | 6 | 0 | 0 |
| M160000 (psoriatic spondylitica) | 0 | 0 | 1 |
| M160100 (distal interphalangeal psoriatic arthropathy) | 0 | 0 | 0 |
| M160200 (arthritis mutilans) | 0 | 0 | 0 |
| M160z00 (psoriatic arthropathy NOS) | 1 | 1 | 1 |
| Number of PsA codes | | | |
| 1 | 39 (53%) | 7 (54%) | 7 (54%) |
| 2 | 18 (24%) | 4 (31%) | 1 (8%) |
| 3+ | 17 (23%) | 2 (15%) | 5 (38%) |
| Oral DMARD prescription* | 31 (42%) | 3 (23%) | 7 (54%) |
| Number of DMARD prescriptions in medical record | | | |
| 0 | 43 (58%) | 10 (77%) | 10 (77%) |
| 1 | 23 (31%) | 1 (8%) | 1 (8%) |
| 2+ | 8 (11%) | 2 (15%) | 2 (15%) |

*Refers to an oral DMARD prescription anytime between registration and date of survey.

Table 2. Disease features among patients with confirmed psoriatic arthritis

| | Present | Not present | Unknown |
|---|---|---|---|
| Morning stiffness | 18 (24%) | 17 (23%) | 37 (50%) |
| Inflammatory back pain | 22 (30%) | 26 (35%) | 26 (35%) |
| Joint swelling | 53 (72%) | 12 (16%) | 9 (12%) |
| Dactylitis or sausage digit | 13 (18%) | 34 (46%) | 27 (36%) |
| Nail disease | 13 (18%) | 21 (28%) | 40 (54%) |
| DIP joint involvement | 20 (27%) | 22 (30%) | 32 (43%) |
| Oligoarthritis | 26 (35%) | 28 (38%) | 20 (27%) |
| Polyarthritis | 36 (49%) | 23 (31%) | 15 (20%) |
| Spondylitis | 7 (9%) | 39 (53%) | 28 (38%) |
| X-ray confirmation | 9 (12%) | 33 (45%) | 32 (43%) |
| Family history of psoriasis | 12 (16%) | 13 (18%) | 49 (66%) |

This table includes only patients with a diagnosis of PsA confirmed by the GP.



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lowered the sensitivity (42%) of the algorithm as less than half of subjects had a prescription for a DMARD.

Finally, agreement between prescription records for DMARDs and GP report of DMARD use was examined. Among the 87 patients with a returned survey, 34 (46%) had at least one prescription for an oral DMARD in THIN and all, but 3 patients were confirmed to have used DMARDs by the GP (PPV = 91%, 95% CI 0.76–0.98). The GP noted a history of oral DMARD use in an additional 20 patients without a prescription record for an oral DMARD in THIN. In 6 patients, the GP did not know the patient's treatment history, and these patients did not have prescriptions for DMARDs in THIN. Percent agreement was 66.7% (95%CI: 56–76%). Of the patients with confirmed PsA, none had a prescription record for a biologic DMARD, but 6 GPs reported that the patient was using or had used a biologic DMARD. Of note, four of the six had previous prescriptions for oral DMARDs in THIN.

## DISCUSSION

In this validation study, we have demonstrated that a single READ code for psoriatic arthritis reliably identifies patients with a diagnosis of PsA in THIN with a PPV of 85% using GP confirmation of the diagnosis as the reference standard. Thus, THIN is a valid database for the study of PsA based on this definition. While adding a prescription for a DMARD increased the PPV to 91%, substantially fewer patients met the criteria. Since performing this validation study, we have published a study on mortality among patients with PsA stratified by DMARD prescription receipt.[13] There was no significant difference in mortality between patients with (HR 1.06, 95%CI: 0.95–1.19) versus without (HR 0.94, 95%CI: 0.80–1.10) a DMARD prescription, suggesting that, while a DMARD prescription may slightly increase the PPV, these two populations may be similar.

The strengths of this study include the 87% response rate within a relatively short period of time, random sampling among all enumerated subjects, and ascertainment of clinical variables. GP report of psoriasis BSA mirrors a previous study examining the validity of codes for psoriasis. The results of this study are generalizable to the use of THIN and likely also to the Clinical Practice Research Datalink (CPRD), formerly known as the General Practice Research Database, as the two databases use the same data collection system and approximately half of the practices in THIN also participate in CPRD.[6]

Limitations include the possibility of selection bias in that practices agreeing to participate in surveys may be different from practices who do not participate. Next, GPs may not be equipped to answer questions about the patient's arthritis, as suggested by the relative lack of information about clinical disease activity in patients with confirmed PsA. And, given the difficulty diagnosing PsA even among rheumatologists, the diagnosis may be incorrect despite GP confirmation. However, the majority of these patients had been seen by a rheumatologist who corroborated the diagnosis. We were unable to collect information from the rheumatologist to support the rheumatologist's diagnosis of PsA including examination findings. Finally, this validation study examines the validity of codes for PsA in representing the presence of actual disease. There are likely patients with a code for psoriasis who also have PsA but do not have a medical record code for PsA.[14] Unfortunately, we are unable to capture these patients. This is a challenge associated with studying PsA from a population-based perspective.

Table 3. Alternative algorithms for defining psoriatic arthritis

| | Total | Confirmed | PPV (%) 95% CI | Sensitivity* | Specificity* |
|---|---|---|---|---|---|
| One PsA code | 87 | 74 | 85.1 (75.8–91.8) | N/A | N/A |
| PsA + DMARD | 34 | 31 | 91.2 (76.3–98.1) | 41.9 | 76.9 |
| PsA + PsO | 65 | 55 | 84.6 (73.5–92.4) | 74.3 | 23.1 |
| Two PsA codes | 41 | 35 | 85.4 (70.8–94.4) | 47.3 | 53.8 |
| PsA and No OA code | 67 | 57 | 85.1 (74.3–92.6) | 77.0 | 23.1 |
| PsA and No RA code | 72 | 62 | 86.1 (75.9–93.1) | 83.8 | 23.1 |
| PsA + Rheum code | 59 | 51 | 86.4 (75.0–94.0) | 68.9 | 38.5 |
| PsA + PsO + DMARD | 27 | 26 | 91.2 (76.3–98.1) | 35.1 | 92.3 |

PsA = psoriatic arthritis, PsO = psoriasis, OA = osteoarthritis, RA = rheumatoid arthritis, Rheum code = code referring to rheumatology consultation, DMARD = Disease Modifying Antirheumatic Drug.

*These columns represent the sensitivity and specificity of the additional code (e.g. DMARD prescription) for a verified diagnosis of PsA by GP report among patients with at least one code for psoriatic arthritis. They do not represent overall sensitivity and specificity of the algorithm (including the PsA code) as false negatives are unavailable (i.e. we did not sample patients without PsA codes).



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In conclusion, THIN is a valid database for the study of the psoriatic arthritis. With more than 9000 cases of psoriatic arthritis, this cohort represents a tremendous resource for future studies examining long-term outcomes in PsA and risk factors for development of psoriatic arthritis.

## CONFLICT OF INTEREST

Dr Gelfand serves as a consultant to Amgen, Abbott, Centocor, Celgene, Novartis, Eli Lilly, and Pfizer and has received honoraria; He has received grants from Amgen, Abbott, Pfizer, Eli Lilly, Novartis, and Genentech. Dr. Hennessy has consulted for Amgen, Bristol-Myers Squibb, Astra-Zeneca, Millenium Pharmaceuticals, and CSL Behring, and received research funding from Bristol-Myers Squibb and Astra-Zeneca. The remaining authors do not have competing interests.

Cegedim Strategic Data (CSD) Medical Research UK is an expert in UK anonymous patient data. The data was collected by Cegedim and the GPs through an anonymized process using Cegedim's Additional Information Services. CSD is a commercial organization that supplies data and trains and supports researchers in the use of primary care patient data. Data are available for use in medical research in the academic setting as well as in industry for a fee which varies depending on the type of data requested. Aside from undergoing ethical review by the Scientific Review Committee at Cegedim, independent academic groups who voluntarily act as an ethical review body, changes to the protocol were not made by the company. We did not receive financial support or other forms of computational or analytical support from Cegedim/THIN.

### KEY POINTS

- The positive predictive value of a diagnostic code for psoriatic arthritis in a UK medical record database, The Health Improvement Network (THIN), was 85% when using the GP confirmation as the reference standard.
- Large medical record databases such as THIN are excellent resources for the study of long-term outcomes in large cohorts of patients with psoriatic arthritis.
- Disease modifying anti-rheumatic drug prescriptions are not fully captured in primary care medical record databases such as THIN.

## ETHICS STATEMENT

This study was approved by the University of Pennsylvania Institutional Review Board and the Cegedim Scientific Review Committee. Methods conform to the STROBE statement.[15]

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