Prevalence and treatment patterns of psoriatic arthritis in the UK

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Abstract

Objectives. The objectives of this study were to determine the prevalence of PsA in The Health Improvement Network (THIN), a large population-based medical records database in the UK, to examine factors associated with prevalent PsA among patients with psoriasis and to describe the use of DMARDs in patients with PsA.

Methods. Two cohorts were derived from THIN to examine the prevalence of PsA in a cross-sectional study among all patients aged 18–90 years and among a subcohort of 4900 psoriasis patients aged 45–65 years. Prescription codes were used to describe therapies after the diagnosis of PsA. Associations for prevalent PsA among psoriasis patients were assessed using logistic regression analysis.

Results. Among 4.8 million patients in THIN between the ages of 18 and 90 years, 9045 patients had at least one medical code for PsA, giving an overall prevalence of 0.19% (95% CI 0.19%, 0.19%). Of those patients, 45.9% with PsA have been prescribed DMARDs. Among the 4064 confirmed psoriasis patients, the prevalence of PsA was 8.6% (95% CI 7.7%, 9.5%). PsA was more prevalent among patients with severe psoriasis [odds ratio (OR) 3.34; 95% CI 2.40, 4.65], obesity (OR 1.77; 95% CI 1.30, 2.41) and duration of psoriasis for ≥10 years (OR 7.42; 95% CI 3.86, 14.25) in the fully adjusted model.

Conclusion. The prevalence of PsA in THIN is consistent with previous population-based estimates. Limitations include a definition of PsA based on a diagnostic code rather than Classification Criteria for Psoriatic Arthritis (CASPAR) criteria. Given the large population of PsA patients, THIN is an important resource for the study of PsA.

Key words: spondyloarthritis (including psoriatic arthritis), epidemiology, DMARDs, primary care rheumatology.

Introduction

PsA is a chronic inflammatory arthritis associated with psoriasis that can cause joint damage and ultimately disability [1]. Over the past 10 years, observational cohort studies and disease registries established in North America and Europe have informed our understanding of the clinical manifestations of this disorder [2–5]. However, less is known about PsA from a population-based perspective, including prevalence in the general population, how prevalence varies by degree of psoriasis and the factors associated with PsA among patients with psoriasis.

In the few studies examining the epidemiology of PsA in the general population, prevalence estimates range from 0.1% to 0.25% [6–9]. In population-based studies, the estimated prevalence of PsA among patients with psoriasis is 6–11% [10–13]. However, most of the population-based studies have been limited by relatively small numbers of PsA patients in the respective populations. To date, the largest studies of PsA have included fewer than 2000 patients with PsA and were mainly

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Population-based studies are studies that draw subjects from the greater population to arrive at a sample that is representative of the people within that population. Population-based studies contribute a different perspective to our knowledge of PsA compared with clinic-based studies. Advantages include increased generalizability and minimization of selection bias when compared with clinic-based studies, which tend to over-represent patients with more severe disease. Additionally, population-based studies often utilize existing data and possess the large sample sizes needed to investigate disease outcomes with sufficient power.

The Health Improvement Network (THIN) is an electronic primary care medical record database in the UK. It is broadly representative of the UK population in terms of age, sex and geographic distribution. Data are collected on more than 9 million patients from more than 400 practices who are followed on average for >7 years [14]. THIN has been a tremendous resource for population-based epidemiological studies of psoriasis and may be applied to the study of rheumatic disease as well [15]. Therefore the objectives of this study were (i) to determine the prevalence of PsA in THIN overall and among a subcohort of patients with confirmed psoriasis, (ii) to examine factors that are associated with prevalent PsA among psoriasis patients and (iii) to describe the use of DMARDs among patients with PsA.

Methods

Study design and data source

A cross-sectional study was undertaken using THIN. The UK is an ideal health system for capturing medical records data, as the general practitioner (GP) is the primary contact for all aspects of the patient’s care [16]. Participating GPs record data as part of routine patient care (e.g. demographics, medical diagnoses, laboratory data and prescriptions) in the electronic medical record, including recommendations made by specialists in secondary and tertiary care. The data are anonymized and collected by THIN, assessed for quality and made available for research use [17]. The validity of using THIN data for studying a variety of medical outcomes has been widely demonstrated [18, 19].

Study time period

Data were collected between 1994 and 2010. Entry into the cohort was defined as the latest of diagnosis of PsA, 6 months after initial registration with the practice or implementation of Vision software in the patient’s practice. Data were collected until the patient left the practice, the practice was no longer participating in THIN or the end of the study in September 2010.

Study population

Study subjects were aged 18–90 years and enrolled in a practice participating in THIN. Prevalence was first evaluated in the entire THIN population by age and sex, restricting age to 18–90 years. Then, the prevalence of PsA among patients with psoriasis was assessed in a subcohort of THIN patients with a code for psoriasis in whom additional information had been previously obtained from GPs using a questionnaire querying about the validity of the psoriasis diagnosis as well as the duration and severity of psoriasis. As previously described, questionnaires were sent to the GPs of 4900 randomly selected patients with at least one code for psoriasis aged between 45 and 65 years at the time of sampling [15]. This age restriction was selected because this cohort is being followed prospectively for other outcome studies. GPs were asked to confirm the diagnosis of psoriasis and to assess disease severity by categorizing body surface area (BSA; ≤2%, 3–10% and >10%). Psoriasis BSA was expressed as a percentage of the patient’s BSA covered by psoriasis where 1% is equivalent to the size of the patient’s palm. This subcohort was also used to establish the validity of psoriasis medical codes in THIN (positive predictive value 90%) [15].

Definitions of psoriasis and PsA

PsA and psoriasis were defined by the presence of at least one Read code consistent with these diseases (supplementary Tables S1 and S2, available as supplementary data at Rheumatology Online). Patients with juvenile PsA (Read code N045200) diagnosed before the age of 18 years were excluded, as this disease can be phenotypically different from adult-onset PsA [20]. Read codes are a comprehensive hierarchical alphanumeric clinical language developed in the UK to record diagnoses, symptoms and tests, similar to International Classification of Diseases codes [21]. Recorded diagnoses can be made by GPs or specialists.

Validation of PsA diagnosis

GPs of 100 randomly selected patients with at least one Read code consistent with PsA were mailed a survey to ascertain the validity of the diagnosis of PsA. We calculated the positive predictive value for a correct diagnosis of PsA given the presence of one of six Read codes with 95% CI. GPs were additionally asked to report whether or not the diagnosis had been confirmed by a rheumatologist.

Definition of therapies

Patients being treated with medications of interest (e.g. DMARDs, therapies consistent with psoriasis treatments) were identified using a specific Multilex code list if the prescription occurred during the time period of the study (defined above). We assessed the prevalence of having ever been prescribed each therapy as recorded by the GP.

Other covariates

Socio-economic status was assessed by Townsend deprivation scores using quintiles (1–5), with higher quintiles representing more deprivation [22]. These scores are an
area-based measure of deprivation assigned by the patient’s postal code based on census data [23].

Statistical analysis

All statistical analysis was performed using STATA 11.0 (StataCorp, College Station, TX, USA).

The prevalence of PsA in the general population was calculated by dividing the number of patients with PsA (age 18–90 years) by the total number of patients in THIN with data acceptable for research use (age 18–90 years). The prevalence of PsA among psoriasis patients was calculated by dividing the number of patients with PsA by the total number of patients in the psoriasis cohort. Therapy data were summarized descriptively. The final sample size was determined by including all patients fulfilling inclusion criteria in the analysis.

Univariable and multivariable logistic regression were performed to assess whether psoriasis severity was a predictor for prevalent PsA. The model was adjusted for age, sex, BMI, duration of psoriasis and smoking status closest to the time of sampling. Age at GP assessment of psoriasis was modelled as a continuous variable while BMI, duration of psoriasis, smoking and BSA were modelled as categorical variables. Only patients with complete data were included in the model: 11.5% of the 4064 patients with confirmed psoriasis had missing data (BSA or BMI). Sensitivity analyses included modelling age as a categorical rather than a continuous variable, modelling age as an effect modifier and including only patients followed by their GP at least once yearly on average. Results were expressed as odds ratios (ORs) with 95% CIs. All $P$-values were two-sided. All data in this study were anonymous to the investigators. This study was approved by the University of Pennsylvania Institutional Review Board and Cegedim’s Scientific Review Committee.

Results

Among 4 785 619 patients in THIN between the ages of 18 and 90 years with data acceptable for research purposes, 9045 patients had at least one medical Read code for PsA, yielding an overall prevalence of 0.19% (95% CI 0.185%, 0.193%) (Fig. 1). Prevalence peaked in the fifth decade at 0.36% (Table 1). Of the 9045 patients with PsA, 4588 (50.7%) were male. Median age at the first medical code for PsA was 44.8 years [interquartile range (IQR) 34.7–55.8]. The majority of patients (67.7%) received their first PsA code between ages 30 and 60 years (Fig. 2). Within each age category, the male to female ratio was approximately 1:1.

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.

Of the patients with PsA, 6631 (73.3%; 95% CI 72.4%, 74.2%) also had a recorded diagnosis of psoriasis. In the majority (6631; 72.4%), the diagnosis of psoriasis preceded the diagnosis of PsA. In 10.8% the medical code for PsA was entered before the psoriasis diagnosis, and in 16.8% the diagnosis of psoriasis was entered within 3 months of the diagnosis of PsA.

In Table 2 we present the prevalence of DMARD use after PsA diagnosis among patients with PsA. A total of 4155 (45.9%) patients with PsA have been prescribed DMARDs. Among the 9045 patients with PsA, 4836 (53.5%) had no prescriptions for DMARDs, 2819 (31.2%) had been prescribed one DMARD, 1049 (11.6%) two different DMARDs and 341 (3.8%) three or more DMARDs. Thirty patients (0.3%) were recorded as receiving etanercept, adalimumab or infliximab. Nearly two-thirds of patients had been prescribed NSAIDs, while 1952 (22%) had received oral corticosteroids. A total of 6492 (73%) PsA patients had received medications consistent with psoriasis treatment. Finally, pain medications including opiates and tramadol were prescribed in 2142 (23.7%) and 2142 (19.7%) of patients, respectively.

Next, we examined the prevalence of PsA among a subcohort of patients with psoriasis. The subcohort was created by randomly selecting 4900 patients with at least one code for psoriasis. Questionnaires were sent to GPs and 4634 were returned, a 95% response rate. The psoriasis diagnosis was confirmed by the physician in 4064 patients (90%; 95% CI 89%, 91%) as described previously in detail [15]. Among the 4064 confirmed psoriasis...
patients, there were 365 individuals with a diagnosis of PsA, giving a prevalence of 8.6% (95% CI 7.7%, 9.5%). Baseline characteristics were not significantly different between those with and without PsA: age [median 56 years (IQR 51–62) for both groups], sex (55% vs 51% male) and socio-economic status by Townsend deprivation score. However, patients with PsA had a significantly longer duration of psoriasis (10–19 years) than patients without PsA (5–9 years).

Psoriasis severity in terms of BSA was obtained for 3895 confirmed psoriasis patients (BSA data were missing in 4.2%): 52.5% had mild psoriasis (<2% BSA), 35.4% had moderate psoriasis (3–10% BSA) and 12.2% had severe psoriasis (>10% BSA). Patients with more extensive skin psoriasis had a significantly higher prevalence of PsA. The prevalence of PsA among each of the severity categories increased in a dose-dependent manner.

To assess whether psoriasis severity was a risk factor for PsA, a multivariable logistic regression model was used and included psoriasis extent (mild, moderate, severe), BMI category, duration of psoriasis category, smoking, age and sex (Table 3). Age and sex were not confounders in the model. Predictors of prevalent PsA among psoriasis patients after adjusting for all factors in the model included severe (OR 3.34; 95% CI 2.40, 4.65) and moderate psoriasis (OR 1.49; 95% CI 1.10, 1.99) compared with mild disease, BMI >30 (OR 1.77; 95% CI 1.30, 2.41) and duration of psoriasis for >10 years (OR 7.42; 95% CI 3.86, 14.25). Smoking was not significant in the model, with ex-smokers having an OR of 0.86 (95% CI 0.65, 1.15) and current smokers having an OR of 0.77 (95% CI 0.56, 1.04). Sensitivity analyses, including modelling age as a categorical rather than continuous variable, modelling age as an effect modifier and restricting to only patients followed by their GP at least once yearly on average did not significantly change the results.

**Discussion**

The prevalence of PsA among the THIN population was 0.19% (95% CI 0.185%, 0.193%) and among patients with confirmed psoriasis was 8.6% (95% CI 7.7%, 9.5%). The age and sex distributions of PsA in THIN are consistent with previous studies [6, 9, 24, 25]. The large sample size in this study allowed us to calculate prevalence by age and sex with precision. This peak in prevalence in the fifth decade was also noted by Love et al. [6] in a study of PsA prevalence in Iceland. These results are likely to be generalizable to the UK, as THIN is broadly representative of the UK population [19].

The diagnosis of PsA in this study is based on a medical records diagnosis code recorded by the GP. The positive predictive value for psoriasis is known to be 90% and this study found that the positive predictive value for a PsA diagnostic code is 85% [15]. PsA is difficult to diagnose, even for rheumatologists [26]. While it is possible that we...
Table 2: Medications prescribed among patients with PsA

<table>
<thead>
<tr>
<th>Medication</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMARDs</td>
<td></td>
</tr>
<tr>
<td>Any DMARD</td>
<td>4155 (45.9)</td>
</tr>
<tr>
<td>MTX</td>
<td>3003 (33.2)</td>
</tr>
<tr>
<td>SSZ</td>
<td>1891 (20.9)</td>
</tr>
<tr>
<td>LEF</td>
<td>480 (5.5)</td>
</tr>
<tr>
<td>HCO</td>
<td>250 (2.8)</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>192 (2.1)</td>
</tr>
<tr>
<td>AZA</td>
<td>152 (1.7)</td>
</tr>
<tr>
<td>Biologics</td>
<td>30 (0.3)</td>
</tr>
<tr>
<td>MMF</td>
<td>12 (0.1)</td>
</tr>
<tr>
<td>Anti-inflammatories</td>
<td></td>
</tr>
<tr>
<td>Oral steroids</td>
<td>1952 (21.6)</td>
</tr>
<tr>
<td>Parenteral steroids</td>
<td>850 (9.4)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>6629 (73.3)</td>
</tr>
<tr>
<td>Aspirin</td>
<td>1649 (18.2)</td>
</tr>
<tr>
<td>Pain medication</td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>1786 (19.7)</td>
</tr>
<tr>
<td>Opiates</td>
<td>2142 (23.7)</td>
</tr>
<tr>
<td>Therapies consistent with psoriasis</td>
<td></td>
</tr>
<tr>
<td>Topical therapies for psoriasis</td>
<td>6465 (71.5)</td>
</tr>
<tr>
<td>Any psoriasis therapy</td>
<td>6492 (71.8)</td>
</tr>
</tbody>
</table>

Among 9045 patients with PsA, the number and percentage of patients who were prescribed each therapy after the diagnosis of PsA and after implementation of Vision medical record software in the practice in order to most accurately capture prescription recording. Medications included in each of the categories are the following: DMARDs included MTX, SSZ, LEF, HCQ, ciclosporin, AZA, MMF or TNF-α inhibitors including adalimumab, infliximab and etanercept. Oral steroids: betamethasone, beclometasone, dexamethasone, deflazacort, cortisone acetate, fluoroactonides, hydrocortisone, methylprednisolone, prednisolone, prednisone, triamcinolone. Parenteral steroids: dexamethasone, hydrocortisone, triamcinolone, nadelone. NSAIDs: tiaprofenic, tenoxicam, sulindac, rofecoxib, piroxicam, naproxen, ketoprofen, indometacin, ibuprofen, flurbiprofen, etodolac, diclofenac, dexibuprofen, celecoxib, parecoxib, lumircacoibx, valdecoxb, benoxaprofen, fenbufen, flurbiprofen, indoprofen, ketorolac, meloxicam, nabumetone, nimesulide, phenylbutazone, tolmetin, mefanamic acid, diflunisal, etoricoxib. Opiates: codeine (excluding cough syrups), buprenorphine, diamorphine, dihydrocodeine, fentanyl, methadone, morphine, oxycodone. Topical therapies: topical steroids: tar, salicylic acid, dithranol, topical tacrolimus, topical pimecrolimus, vitamin D analogues (calcipotriol and calcitriol), topical retinoids (tazarotene). Topical steroids: alclometasone, beclometasone, clobetasone, betamethasone, desoximetasone, diflucortolone, flucinolone, fluocortolone, fluodroxyxoyctide, fluticasone, hydrocortisone, mometasone, triamcinolone, clobetasol, fluocinonide, halcinonide, desonide. Psoriasis therapies: topical steroids, tar, salicylic acid, dithranol, topical tacrolimus, retinoids (etretinate, acitretin), psoralen + UVA light therapy (PUVA) and phototherapy.

The analysis of the impact of psoriasis severity on the prevalence of PsA in a population-based setting advances our understanding of the epidemiology of PsA. The strongest associations with PsA were obesity, psoriasis severity and psoriasis duration. Current smoking, while suggested to be protective of PsA in other studies, was not significantly associated with prevalent PsA in this study. We have since further characterized the association with obesity and have found it to be a significant independent risk factor for the development of PsA among patients with psoriasis [32]. One of the concerns with this association is that we may be capturing increased OA associated with obesity. However, the association between psoriasis severity and the development of PsA has been reported in other studies as well, some of which included patient exams to confirm inflammatory arthritis [11, 13, 33]. However, previous studies have not demonstrated an association between skin and joint disease activity. The association between psoriasis severity and PsA prevalence may help explain the difference in prevalence between clinic-based and population-based studies. It is possible that patients with more severe psoriasis are seen more frequently by their GP and are therefore more likely to receive a diagnosis of PsA; however, a sensitivity analysis restricting patients to those followed at least yearly on average did not significantly change the results. While these data suggest that patients with severe psoriasis are more apt to have PsA, it is important to note that the majority of patients with PsA still have mild psoriasis, as mild psoriasis is much more common in the general population [34, 35]. This is the largest examination of drug utilization among PsA patients from a population-based perspective since Love et al. [6] described the drug utilization patterns of 131 patients with PsA in Iceland in 2007, and Shbeeb et al. [12] reported the treatments of 66 PsA patients in Olmsted County, Minnesota, in 2000. We found higher rates of disease-modifying therapy use (~50%) as compared with the reported 10 of 66 patients on DMARDs in the study from Minnesota, but very similar patterns to those noted in Iceland, Western Norway and previous
dermatology clinic-based studies in the USA [25, 35]. We may be underestimating the prevalence of DMARD use given that specialists may also prescribe DMARDs. TNF-\(\alpha\) inhibitors may be particularly susceptible to incomplete recording because, in the UK, these medications are prescribed only by hospital consultants [36]. It is possible that a GP is not aware that a patient is currently using a TNF-\(\alpha\) inhibitor, that they may not record it in the medical record or that it is only captured in a free-text field. Fewer than 15% of the PsA patients in this study qualified for this class of medications based on the data available, as they are first required to fail two oral DMARDs before proceeding to a TNF-\(\alpha\) inhibitor [36, 37].

Potential limitations of the study include the use of GP coding to define PsA, incomplete information on NSAID and TNF-\(\alpha\) inhibitor use, lack of information on PsA disease severity and the use of a cross-sectional study design. Completeness of information is a concern in utilizing medical record databases. For example, THIN does not contain information on PsA disease activity. However, in general, most information about the patient should be recorded, and from previous studies we know that \(-90\%\) of information from specialists is captured [39]. Furthermore, in medical record databases, a diagnosis may be recorded once rather than at every visit [40, 41]. Thus we may miss cases of PsA that were recorded in a previous practice but not recorded in the current practice. NSAID use may be under-reported as patients have access to these medications over the counter, although we have included a number of prescription-only NSAIDs in this study. Furthermore, in older individuals, aged \(\geq 60\) years, capture of NSAID use is likely to be complete, as they are entitled to free prescriptions [42]. Finally, as this is a cross-sectional study, we cannot make inferences about the temporal relationship between BSA, psoriasis duration and BMI and the development of PsA. For this reason, a longitudinal cohort study of risk factors for the development of PsA is needed.

This study of more than 9000 PsA patients, the largest cohort to date, suggests that THIN is an excellent resource for the study of PsA. The findings contribute to the literature providing population-based estimates of PsA prevalence among both the general population and among confirmed psoriasis patients, drug utilization patterns in PsA patients and predictors for prevalent PsA among psoriasis patients. Future studies are required to identify clinical predictors for the development of incident PsA among psoriasis patients, to explore the natural history of PsA and to investigate health outcomes related to PsA such as mortality and cardiovascular events.

Table 3: Psoriasis BSA as a predictor of PsA

<table>
<thead>
<tr>
<th>Model variable</th>
<th>Age- and sex-adjusted OR (95% CI)</th>
<th>Fully adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis severity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3% BSA</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>3-10% BSA</td>
<td>2.16 (1.63, 2.85)</td>
<td>1.49 (1.1, 1.99)</td>
</tr>
<tr>
<td>&gt;10% BSA</td>
<td>5.89 (4.35, 7.97)</td>
<td>3.34 (2.40, 4.65)</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>25-30</td>
<td>1.19 (0.90, 1.58)</td>
<td>1.11 (0.82, 1.49)</td>
</tr>
<tr>
<td>&gt;30</td>
<td>1.96 (1.47, 2.61)</td>
<td>1.77 (1.30, 2.41)</td>
</tr>
<tr>
<td>Psoriasis duration, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2-9</td>
<td>3.77 (1.99, 7.15)</td>
<td>3.23 (1.67, 6.43)</td>
</tr>
<tr>
<td>(\geq 10)</td>
<td>10.38 (5.64, 19.11)</td>
<td>7.42 (3.86, 14.25)</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>0.87 (0.67, 1.13)</td>
<td>0.86 (0.65, 1.15)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.76 (0.58, 1.01)</td>
<td>0.77 (0.56, 1.04)</td>
</tr>
<tr>
<td>Age</td>
<td>0.99 (0.97, 1.01)</td>
<td>0.99 (0.97, 1.01)</td>
</tr>
<tr>
<td>Sex</td>
<td>0.83 (0.67, 1.04)</td>
<td>0.83 (0.65, 1.07)</td>
</tr>
</tbody>
</table>

The results of logistic regression modelling with prevalent PsA as the outcome. Age and sex were not significant in the model. The age- and sex-adjusted models for each risk factor independently are shown in the left column and for the fully adjusted model in the right column. The \(P\)-value for trend was significant for psoriasis severity, BMI and psoriasis duration (for all \(P < 0.001\)).

The prevalence of PsA is 19/10,000 people in the UK.

Psoriasis severity, psoriasis duration and obesity are strongly associated with PsA in the UK.

Half of patients with PsA in the UK receive disease-modifying therapies.

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Supplementary data are available at Rheumatology Online.

References


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Supplementary data

Supplementary data are available at Rheumatology Online.


