WORK DISABILITY IN PSORIATIC ARTHRITIS

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Volume I of I

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DECLARATION

In accordance with the University regulation 16.5 (i) I confirm that this thesis is the result of work done mainly while the author who is registered as a candidate for the Degree of Doctor of Philosophy of this University. Where others have contributed data or assisted with data analyses they are acknowledged accordingly.
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PUBLICATIONS AND CONFERENCE CONTRIBUTIONS ARISING FROM THE WORK OF THIS THESIS


Tillett W, Cavill C, Korendowych E, McHugh N. EuroQol reported health disability demonstrates reduced quality of life remaining constant over time in established psoriatic arthritis. British Society of Rheumatologists annual meeting Brighton 201 No 245

Psoriatic arthritis is an inflammatory arthritis affecting a fifth of patients with skin psoriasis. Inflammation of the joints and tendons causes pain, stiffness, reduced function and disability. Work disability is increasingly recognised as an important, patient centred, functional measure of disease yet little is known about work disability in psoriatic arthritis. The overall aim of my thesis is to examine patient reported work disability in psoriatic arthritis by undertaking the following:

- A systematic review of the relevant literature
- Classification of a cohort of patients to study
- Validation of a commonly used work outcome measure used in other rheumatic diseases
- Selection of a suitable measure of structural damage to inflamed joints for investigating the associations of work disability in longitudinal observational studies.

The results of the systematic review identified limited data reporting high levels of work disability associated with a wide variety of disease and non-disease related factors. The review also identified the lack of a validated outcome measure for use in psoriatic arthritis. I report the classification of a large single centre longitudinal cohort of patients with psoriatic arthritis and evidence supporting the retrospective application of a psoriatic arthritis classification criterion. Subsequently I report a preliminary validation study of the work productivity and activity impairment questionnaire to measure work disability in psoriatic arthritis and a further study comparing the existing measures of structural damage in psoriatic arthritis. Finally I developed and supervised a multicentre observational study to examine the associations of work disability in psoriatic arthritis. The study identified reduced work effectiveness to be associated with measures of disease activity, whereas unemployment was associated with recent disease onset, greater age and worse physical function. The study will provide a valuable cohort for prospective study.
of work disability and the effect of medical treatment and will form part of my planned post-doctoral studies.
AIMS AND OBJECTIVES

Aims
The aims of this thesis are to systematically and critically review the current body of knowledge of work disability in psoriatic arthritis, validate a tool for measuring work disability in psoriatic arthritis, estimate the burden of work disability using this validated tool and investigate the associations with disease activity, structural damage, demographic and social factors.

Objectives
1. To systematically review the current body of knowledge of work disability in psoriatic arthritis.
2. To classify an existing cohort of patients with psoriatic arthritis according to the classification criteria for psoriatic arthritis (CASPAR) criteria modified for retrospective application.
3. To examine the feasibility, construct and discriminative validity of the work productivity and activity specific health questionnaire in psoriatic arthritis.
4. To examine the association between structural damage and work disability through:
   a. Identification of the optimal radiographic tool for use in longitudinal observational studies in psoriatic arthritis through assessment of the feasibility and sensitivity to change in structural joint damage of the four existing radiographic assessment tools.
   b. To determine to what extent structural damage is associated with work disability measured with the work productivity and activity specific health questionnaire using the method selected under (4a).
5. To determine to what extent clinical disease activity, demographic and social factors are associated with work disability measured with the work productivity and activity specific health questionnaire.
CHAPTER I

INTRODUCTION

The aim of my thesis is to examine patient reported Work Disability (WD) in Psoriatic Arthritis (PsA). This will be achieved through a systematic review of the current body of knowledge, identification and classification of an appropriate cohort of patients to study, preliminary validation of a tool to measure WD, assessment of the optimal measure to use for assessment of criterion validity and a cross sectional study to examine the associations of PsA with WD. Here I will set out the reasons for why measuring disease outcome in PsA is important.

PsA is an inflammatory arthritis occurring in 7-42% of patients with psoriasis.\textsuperscript{1} Inflammation of joints and tendons leads to pain, stiffness, reduced movement and subsequent disability. Originally considered a benign disease it is now recognised that PsA can be serious and progressive with significant physical, psychological, functional and social impairment.\textsuperscript{2-5} There is increasing awareness that WD is an important patient centred, quality of life measure of outcome in rheumatic disease. WD has a detrimental impact on an individual’s financial status and quality of life.\textsuperscript{6} Whilst there is a large body of information on the burden of WD in related rheumatic diseases such as rheumatoid arthritis and ankylosing spondylitis\textsuperscript{7} to date there is little data on WD in PsA.\textsuperscript{8, 9} PsA will now be introduced in more detail to explain why separate investigation of WD in this disease is warranted.

\textit{Psoriatic arthritis}

Psoriasis is an inflammatory skin condition affecting 2-3% of the UK population.\textsuperscript{10} The exact prevalence of PsA is unknown. Current estimates suggest 14% of patients with psoriasis in UK general practice\textsuperscript{11} and 20-35% of patients with psoriasis in dermatology clinics have PsA.\textsuperscript{12} In a recent review the mean age of onset of PsA was between 40.7 and 52.0 years (median 47.7).\textsuperscript{13}
**Clinical features**

Psoriatic arthritis has a heterogeneous but distinct clinical phenotype. A number of features help to distinguish PsA from the most common inflammatory arthritis, rheumatoid arthritis. PsA affects men and women equally whereas rheumatoid arthritis is more common in women.\(^{11, 13-15}\) In rheumatoid arthritis peripheral joints are affected in a strikingly symmetrical pattern across rows of joints on both sides. Conversely PsA has a tendency to affect joints along a ‘ray’ such that the metacarpophalangeal (MCP), proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints may be affected along one digit.\(^ {16}\) Rheumatoid arthritis may affect the synovial atlanto-axial joint (joining the 1\(^{st}\) and 2\(^{nd}\) cervical vertebrae) but PsA tends to cause inflammation at other sites in the spine (spondyloarthritis). In 1973 Moll and Wright described five patterns of PsA; symmetrical polyarthritis (15%), asymmetrical oligoarthritis (70%), predominant distal interphalangeal joint disease (5%), predominantly spondyloarthritits (5%) and arthritis mutilans (5%).\(^ {16}\) There is evidence that even these patterns are not fixed and that they may evolve over the course of disease. A longitudinal study of 87 patients with PsA observed that 18 patients changed between phenotypes over a mean follow up of 65 months.\(^ {3}\)

Enthesitis (inflammation of the tendon insertion to bone) and tenosynovitis (inflammation of the tendon and tendon sheath) are further characteristic clinical manifestations of PsA distinguishing it from rheumatoid arthritis. PsA may cause tendon and joint inflammation, together leading to diffuse swelling of an entire digit, termed dactylitis or sausage digit.\(^ {17, 18}\) Ultrasound studies of lower limb entheses have demonstrated that enthesitis is more common than is clinically evident and more common in those with psoriasis than in healthy individuals.\(^ {19, 20}\) Inflammation of these sites will lead to a distinct pattern of symptoms and associated functional impairment.
PsA appears after, or synchronously with, the onset of psoriasis in the majority of patients.\textsuperscript{14, 21} In a minority (18 – 13\%) the arthritis precedes the onset of psoriasis.\textsuperscript{14, 21} Nail pitting (sharply defined depressions in the nail plate) and onycholysis (separation of the nail from the bed) is indistinguishable from that seen in psoriasis.\textsuperscript{22} However nail lesions are more common in patients with PsA than those with psoriasis alone\textsuperscript{23} and in those with DIP joint disease.\textsuperscript{22}

PsA has a characteristic radiographic appearance. Erosions (areas of discrete interruption of the bone surface) and joint space narrowing are seen in most types of inflammatory arthritis. In PsA there are additional changes, which include the presence of bony proliferation (bone growth), periostitis (inflammation of the bone surface), osteolysis (dissolution of bone) and ankylosis (bone fusion across a joint).\textsuperscript{2, 14, 24, 25} In one observational study of a secondary care cohort in the United States two thirds of patients with PsA had radiographic damage at the first visit to a PsA specialist.\textsuperscript{14} A longitudinal study of 139 patients with established PsA demonstrated the progressive nature of the disease. Fifty-eight\% of patients had radiographic damage at baseline (median 5 years disease duration) progressing to 78\% at follow up (median 12 years disease duration).\textsuperscript{26}

In summary PsA is a disease with a varied phenotype, distinct from other forms of inflammatory arthritis, which will have a unique impact upon an individual’s physical, psychological and social functioning. Separate investigation of the impact of this disease is therefore warranted. A more detailed introduction of WD follows in order to explain why this is an important measure of disease outcome.

\textit{Work disability in rheumatic disease}

There has been increasing interest in measuring work disability in rheumatic disease in recent years. This stems from its importance to the individual in terms of financial and emotional wellbeing as well as the wider socio-economic perspective. With the advent and rapid uptake of
highly effective but expensive drug treatments such as anti-Tumour Necrosis Factor (anti-TNF) inhibitors there is a need to provide an economic case for the cost-effectiveness of treatments through health economics analysis. Traditionally this has been through cost of drugs, cost of hospital care and the quality adjusted life years (QALY) system. There is now a growing body of opinion that work disability in terms of productivity should be considered for inclusion in the National Institute of Clinical Excellence (NICE) cost-effectiveness models. 27

Examination of what is known about WD in related conditions can inform studies in PsA. Rheumatoid arthritis predominantly affects the hands and feet causing the same symptoms of pain, stiffness and reduced joint movement. Studies in rheumatoid arthritis have demonstrated that between 20-40% of patients develop WD (absenteeism, sick leave or ill health retirement) in the first 2-3 years of disease onset and that this may be permanent.28-31 In a long term follow up study of early rheumatoid arthritis WD was seen to rise to 80% after 20 years disease duration.32 Ankylosing spondylitis is another related inflammatory arthritis, this time predominantly affecting the spine with symptoms of pain, stiffness and reduced movement. Understanding WD in ankylosing spondylitis is relevant because PsA may also affect the spine in a similar pattern. In an early systematic review of WD in ankylosing spondylitis WD ranged between 3 to 50% after 18 and 45 years of age respectively.33 A Swedish case control study of 122 patients with ankylosing spondylitis over a seven year period reported increased sickness benefit collection, sickness compensation and sick leave amongst those with ankylosing spondylitis compared with age and sex matched controls.34 A Norwegian cross sectional study of 360 patients with ankylosing spondylitis (mean disease duration 22.6 years) reported 43.6% were collecting WD benefit.35 A large cross sectional study of 699 patients with ankylosing spondylitis from the National Spanish Registry investigated prevalence of WD (disability benefit collection) and factors related to it. The mean age of the ankylosing spondylitis population studied was 48.7 years and mean disease duration was 14.1 years. Twenty six per cent were collecting a
work disability pension and this was associated with older age, male sex, longer disease duration, fatigue and radiographic damage.\textsuperscript{36}

WD in rheumatoid arthritis and ankylosing spondylitis is therefore high and occurs early in the disease course. There has therefore been interest in the effect of treatment on WD, in particular studies comparing different classes of drug treatment. Comparison of biological and Disease Modifying Anti-Rheumatic Drugs (DMARD) in rheumatoid arthritis have demonstrated reduced absenteeism, reduced sick leave, higher employment potential and greater levels of employment potential amongst those treated with biologics.\textsuperscript{37} In a study comparing employment levels amongst patients commenced on DMARD (Methotrexate) versus Biologic (Etanercept) reported a close association between clinical improvement and remission and cessation of work.\textsuperscript{37} Patients showing a greater response (70\% versus 20\%) were 72\% less likely to stop working and 55\% less likely miss work.\textsuperscript{37} Data from 139 patients with ankylosing spondylitis in the south Swedish arthritis treatment group register reported higher baseline sick leave than the general population (25\% versus 8\%) and a decline in sick leave in the first 12 months anti-TNF therapy (25\% to 12\%).\textsuperscript{38}

There is therefore a burden of WD in rheumatic diseases. There is also a need to measure WD, as it is only through accurate measurement that we may assess the burden of disability and effect of treatment interventions. The question therefore is how WD is best measured in patients with PsA? It is not possible to assume that measures of WD valid in ankylosing spondylitis or rheumatoid arthritis will perform in the same way in PsA. The many distinguishing features of PsA, not least the presence of skin, enthesal, axial disease and markedly different articular, radiographic and demographic features of PsA may result in unique effects on physical, psychological and social functioning. The following section is a discussion of the measurement of WD.

\textit{Measurement of work disability}
WD may be measured in a variety of ways and there is currently no consensus on the optimal method. Do we measure unemployment, ill health retirement or job loss? Absolute changes in employment are likely to have the greatest impact on an individual but occur infrequently, over periods of years and are therefore unlikely to be detected in short clinical trials or even registries.\textsuperscript{39} Do we measure absenteeism which may be more frequent and therefore detectible and if so do we assess short periods such as hours or longer periods such as days or weeks? Other possibilities include patient reported employability, work instability or work satisfaction. A concept gaining increasing interest is presenteeism; reduced effectiveness while at work as a measure of productivity loss (either taken alone or in combination with absenteeism). At work, reduced effectiveness or shorter periods of absenteeism (such as hours, days, weeks) are likely to occur over a shorter time frame and are therefore a better measure if the ultimate goal is to assess response to treatment. Absenteeism and presenteeism may precede events such as job loss, long term sick leave or retirement due to ill health, are more likely to be reversible, and as such they are more attractive targets for measurement. Finally absenteeism and presenteeism are considered to be the most relevant WD outcomes when considering health economics research.\textsuperscript{40}

PsA is therefore a unique disease with several clinical features distinct from rheumatoid arthritis and ankylosing spondylitis. These distinguishing features may result in differing biological, psychological and social impacts of disease, therefore separate examination of WD in PsA is warranted. In order to establish what is known about WD in PsA and what questions remain, a systematic literature review has been undertaken.
CHAPTER II

WORK DISABILITY IN PSORIATIC ARTHRITIS;
A SYSTEMATIC REVIEW

The first objective of this thesis is to systematically review the current body of knowledge of work disability in psoriatic arthritis. The review was undertaken at the beginning of my study and has subsequently been published.41 The main body of the current chapter has been taken from that review and therefore may include some material already discussed in the introduction.

ABSTRACT

Background
Work disability is an important functional outcome measure in arthritis. There is a large body of information on WD in rheumatic diseases such as rheumatoid arthritis and ankylosing spondylitis, however until now factors that influence work disability in psoriatic arthritis has not been systematically reviewed. My objective was to perform a systematic and critical review of the current literature on work disability and its measurement in psoriatic arthritis.

Methods
A systematic literature search was conducted using Medline, Embase and Cochrane databases. The search strategy was supplemented by a manual search of cited articles. All original English language publications in the form of meta-analyses, randomised controlled trials (RCTs), observational studies and publications in abstract form were included. A quality assessment was made of the articles published in full form.

Results
Nineteen publications (nine in abstract form) were identified. There is intermediate quality evidence that levels of unemployment (20-50%) and WD (16-39%) are high and associated with longer disease duration,
worse physical function, high joint count, low educational level, female gender, erosive disease and manual work. There is sparse low quality evidence that WD is worse in those with PsA than psoriasis alone.

Conclusions
Disability at work in those with PsA is high however data on its associations is limited by the small number of reports and heterogeneity of data collected. Future work should focus on the validation of work disability data collection tools for use in PsA.

INTRODUCTION
Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in 7-42% of patients with psoriasis. Originally considered a benign disease it is now recognised that PsA can be serious and progressive. Prospective studies have demonstrated progression of clinical joint scores and deteriorating functional status with increased disease duration. Patients with PsA also suffer with psoriasis that may itself cause significant physical, psychological, social and functional impairment.

Disability in the workplace inevitably has a significant impact on an individual’s quality of life, financial status as well as society as a whole. There is increasing awareness that work disability in the form of absenteeism (time away from work) and presenteeism (reduced effectiveness at work) are important patient centred, quality of life outcome measure in arthritis. Outcome Measures in Rheumatology (OMERACT) have included participation in the core set of outcome measures in PsA. Whilst there is a large body of information on the burden of WD and the validity of measurement tools in related rheumatic diseases such as rheumatoid arthritis and ankylosing spondylitis to date there is little data on WD in PsA. Assessment and validation of outcome measures of work disability in PsA warrants separate examination given the features that make PsA a unique disease such associated psoriasis, heterogeneity of disease phenotype and comorbidities such as depression, metabolic and cardiovascular disease.
There are a number of observational cohort and controlled PsA studies that have measured aspects of work disability though the current body of evidence on WD in PsA has not yet been synthesised. This review describes a systematic and critical review of the current literature on the burden of work disability and its measurement in PsA.

**METHODS**

**Search strategy**

A search was performed on the 2nd December 2010 in Medline (1950 to present), Embase (1988-present) and Cochrane databases using the following MeSH indexing and Keyword terms respectively; ‘arthritis, psoriatic’, ‘psoriatic arthritis’, ‘work’, ‘employment’, ‘absenteeism’ and ‘presenteeism’. The search strategy was supplemented by a manual reference search of cited articles. All original English language publications in the form of meta-analyses, randomised controlled trials (RCT’s) and observational studies were included. Following review of the abstracts all original articles which contained data on WD in PsA were included for final review. Review articles, those not specific to PsA or not related to work disability were excluded. A literature evaluation form was used to standardise data collection. Publications in abstract form are included however they have not been subject to the same peer review process as fully published articles. In order to accommodate this and avoid placing undue weight to this data the abstracts have not been subject to the quality assessment and are described separately both in the results section and tables.

**Quality assessment**

Due to the differing methodologies employed meta-analysis was not possible. Given the limited amount of published information on WD in PsA we deemed it unfeasible to exclude articles with methodological weakness without significantly limiting the information available. Therefore we have performed a quality assessment based on the presence of seven quality criteria; use of diagnostic criteria for PsA, analysis made
only on those of working age, response rate >80% or loss to follow up <30%, WD defined as due to PsA, use of external WD assessment, avoidance of recall bias and avoidance of confounding. Confounding was considered to be avoided if data was collected and analysed on >3 contextual factors that may influence WD including but not limited to; type of work, assistance at work, education, earnings, depression, comorbidities. This results in an aggregate score out of seven. Study quality was stratified in to three levels; Low <3, Intermediate 3-4, Good ≥5. The criteria used in this study are based on previously published critical reviews of prognostic markers of WD in rheumatic disease.43,44

RESULTS

Search results
The search identified 260 titles of which 94 were duplicates. Of 166 unique results 145 were excluded at abstract review as not specific to PsA, not related to work disability and review articles. Twenty one original articles were included for full text analysis and two further articles were excluded using the same criteria.45,46 Thus nineteen studies were included for final review. Ten studies published in full form and nine in conference abstract form, no Cochrane reviews or meta-analyses were identified (Figure 1).
The ten articles published in full form included 8,585 patients with PsA (Table 1). Study quality and work disability associations are summarised in table 2. There was considerable variability in the work outcome measures used. Furthermore authors occasionally labelled the same work outcome differently. The term work disability may be the label given to ‘disability benefit collection’ 9 or alternatively ‘not working due to ill health’ 39 or even a self-explanatory term not clarified in the
methodology. In this review we have made the exact measure used in each study explicit (Table 1).

Seven studies reported rates of unemployment ranging 20 -50%. Only two cohort studies specifically reported on unemployed caused by PsA rather than all causes, these studies reported unemployment levels of 22% and 23%. Seven studies measured absenteeism (working individuals not currently at work). Two studies measured presenteeism. Two studies used external objective measures of WD (disability benefit/ ill health benefit collection).

The study quality assessment is summarised in table 3. Of the ten fully published articles only one study reached good quality status, two studies were of intermediate quality and seven of low quality. Work disability was the primary outcome measure in only four studies.  

Age
One cohort study investigated the relationship between age and WD and found no association.

Disease duration
Three studies have reported on the association between WD and disease duration. A cross-sectional Norwegian database study identified longer disease duration independently predicated WD as defined by disability benefit collection. In a German study of patients with rheumatic disease a reduced standardised employment ratio (SER) was demonstrated with increased disease duration irrespective of gender or geographical location (SER falling from 0.94 at 5 yrs to 0.70 at 10yrs in Men). However no such association was seen in the (British society of rheumatologists biologics registry) study of WD. There are no studies investigating WD in early PsA.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample size</th>
<th>Follow up</th>
<th>Country</th>
<th>Age (Mean yrs)</th>
<th>Disease duration (mean yrs)</th>
<th>Work Measure</th>
<th>Work disability</th>
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</thead>
<tbody>
<tr>
<td>Christophers <em>et al</em></td>
<td>CS</td>
<td>53</td>
<td>N/A</td>
<td>Multinational</td>
<td>49</td>
<td>N/A</td>
<td>Employment disadvantages questionnaire (EDQ)</td>
<td>59% PsA pts unemployed, 32% PsA work disabled, 11% Psoriasis work disabled</td>
</tr>
<tr>
<td>Gottlieb <em>et al</em></td>
<td>CS</td>
<td>1122</td>
<td>N/A</td>
<td>USA</td>
<td>48</td>
<td>7.2</td>
<td>Disability and employment</td>
<td>0.4% temporarily disabled, 4% disabled, 8% unemployed</td>
</tr>
<tr>
<td>Kaarela <em>et al</em></td>
<td>PC</td>
<td>13</td>
<td>7.6yrs</td>
<td>Finland</td>
<td>N/A</td>
<td>N/A</td>
<td>Disability pension collection: Ill health retirement Absenteeism</td>
<td>69% of PsA pts were at work compared with: 36% RA, 85-90% AS.</td>
</tr>
<tr>
<td>Kavanaugh <em>et al</em></td>
<td>RCT</td>
<td>200</td>
<td>14wks</td>
<td>USA</td>
<td>47</td>
<td>5.9</td>
<td>Sick days, Productivity VAS, Employability, Employment</td>
<td>16-19% Work disabled and 27-33% Unemployed; Productivity improved by: 67% in treatment arm vs 9% in placebo.</td>
</tr>
<tr>
<td>Mau <em>et al</em></td>
<td>CS</td>
<td>6041</td>
<td>N/A</td>
<td>Germany</td>
<td>45</td>
<td>N/A</td>
<td>Standardised Employment Ratio (SER)</td>
<td>PsA had reduced employment (SER 0.92), PsA (0.94) vs RA, SLE, WG and SSc (0.76-0.81).</td>
</tr>
<tr>
<td>Radtke <em>et al</em></td>
<td>CS</td>
<td>338</td>
<td>N/A</td>
<td>Germany</td>
<td>53</td>
<td>N/A</td>
<td>Employment, absenteeism</td>
<td>50% PsA patients working vs 60% those with PsO, 25% of working PsA patients had taken time off work vs 12% those with Psoriasis</td>
</tr>
<tr>
<td>Roberts <em>et al</em></td>
<td>PC</td>
<td>168</td>
<td>1-10yrs</td>
<td>UK</td>
<td>N/A</td>
<td>N/A</td>
<td>Employment, absenteeism</td>
<td>&gt;1yr of work time was lost, 62% of those with ‘deforming arthritis’ vs 3% with DIPJ and RA alike</td>
</tr>
<tr>
<td>Verstappen <em>et al</em></td>
<td>PC</td>
<td>254</td>
<td>3yrs</td>
<td>UK</td>
<td>45</td>
<td>14</td>
<td>Patient reported disability</td>
<td>39% Work disabled</td>
</tr>
<tr>
<td>Wallenius <em>et al</em></td>
<td>CS</td>
<td>271</td>
<td>N/A</td>
<td>Norway</td>
<td>36</td>
<td>6</td>
<td>Disability benefit collection</td>
<td>33% women &amp; 17% men work disabled</td>
</tr>
<tr>
<td>Zhu <em>et al</em></td>
<td>RC</td>
<td>125</td>
<td>1yr</td>
<td>Hong Kong</td>
<td>48</td>
<td>6.9</td>
<td>Employment</td>
<td>59% of those with peripheral disease were employed vs 39% of those with axial disease.</td>
</tr>
</tbody>
</table>

*RCT (R), Prospective Cohort (PC), Retrospective Cohort (RC), Cross sectional Cohort (CS), Case series/ report (C), Not available (N/A), Rheumatoid arthritis (RA), Ankylosing Spondylitis (AS), Systemic Sclerosis (SSc), Wegener’s Granulomatosis (WG), Systemic Lupus Erythematosus (SLE).*
### Table 2: Work associations reported and study quality assessment

<table>
<thead>
<tr>
<th>Study</th>
<th>Phenotype</th>
<th>High Joint count</th>
<th>Poor physical function (HAQ)</th>
<th>Low Education level</th>
<th>Female gender</th>
<th>Erosive disease</th>
<th>Disease Duration</th>
<th>Manual Work</th>
<th>Work association identified</th>
<th>Quality measure</th>
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<td>Were the sample representative of working age (WD) analysis limited to &lt;18 and &lt;65yrs.</td>
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<td>Were recall bias avoided?</td>
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<td>Were Confounding avoided?</td>
<td>Quality score</td>
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<th>Study</th>
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<td>Were Confounding avoided?</td>
<td>Quality score</td>
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</tbody>
</table>

1. If the information was not available or collected but not analysed a negative answer has been assumed
2. Confounding is considered to be avoided if >3 contextual factors that may influence WD have been corrected for including; Work type, Assistance at work, Education, Earnings, Co morbidities, Depression,

* Although data on confounders was not collected we assume randomisation has been effective mitigating confounding

$^\$ Although this was a UK biologics registry trial diagnostic criteria are not required to qualify for anti-TNF therapy.
Table 3: Study design, demographics and quality principal findings of the 9 papers published in abstract form

<table>
<thead>
<tr>
<th>Source</th>
<th>Study design</th>
<th>Number Pts</th>
<th>WD data</th>
<th>Follow up</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brodszky et al</td>
<td>CS Cost of illness in PsA</td>
<td>183</td>
<td>Sick Reduced Disability benefit</td>
<td>N/A</td>
<td>49% Work disabled</td>
</tr>
<tr>
<td>Gladman et al</td>
<td>RCT ACCALAIM Sub analyses</td>
<td>127</td>
<td>WLQ</td>
<td>12 weeks</td>
<td>23% Unemployed WLQ was reliable and correlated well with patient global activity</td>
</tr>
<tr>
<td>Sampalis et al</td>
<td>RCT ACCALAIM Sub analyses</td>
<td>127</td>
<td>WLQ</td>
<td>12 weeks</td>
<td>Improvement of WLQ after 12 wks of Adalimumab therapy</td>
</tr>
<tr>
<td>Gladman et al</td>
<td>PC Study of Etanercept in PsA</td>
<td>110</td>
<td>HLQ</td>
<td>2yrs</td>
<td>Improvement in productivity, employability and reduced absenteeism at wk 24,</td>
</tr>
<tr>
<td>Gladman et al</td>
<td>RCT ACCALAIM Sub analyses</td>
<td>127</td>
<td>WLQ</td>
<td>12 weeks</td>
<td>Improvement of WLQ after 12 wks of Adalimumab therapy</td>
</tr>
<tr>
<td>Kavanaugh et al</td>
<td>RCT GOREVEAL Study</td>
<td>450</td>
<td>Employability Productivity Absenteeism</td>
<td>1yr</td>
<td>Improvement in productivity, employability and reduced absenteeism at wk 24,</td>
</tr>
<tr>
<td>Kumar et al</td>
<td>CS Willingness to Pay study</td>
<td>72</td>
<td>Employment</td>
<td>N/A</td>
<td>WTP was highest for intimacy, physical comfort, social comfort, emotional health and ability to sleep (median $1000 each).</td>
</tr>
<tr>
<td>Strober et al</td>
<td>RCT CHAMPION and REVEAL Sub analyses</td>
<td>847 Psoriasis pts</td>
<td>WPAI</td>
<td>N/A</td>
<td>WTP was lowest for work or volunteering (median $300). The presence of any co morbidity in those with PsO (including PsA) had impaired quality of life and worse work productivity.</td>
</tr>
<tr>
<td>Tang et al</td>
<td>CS Study from the 2008 National Health and Wellness survey</td>
<td>413</td>
<td>WPAI</td>
<td>N/A</td>
<td>63,000 respondents 413 (0.66%) had PsA: Average of work productivity loss of 42.9%</td>
</tr>
</tbody>
</table>

RCT (R), Prospective Cohort (PC), Retrospective Cohort (RC), Cross sectional Cohort (CS), Case series/ report (C), Work Limitations Questionnaire (WLQ), Health and Labour Questionnaire (HLQ), Work Productivity Activity Index (WPAI), Willingness to Pay (WTP)
**Joint count and radiographic damage**

One study reported a positive association between a high DAS 28 joint count and WD.\(^3^9\) One study reported higher levels of WD in those with axial vs peripheral PsA (39% vs 59%)\(^5^2\) and another higher rates in ‘deforming PsA’ 62% vs distal interphalangeal joint and rheumatoid arthritis like patterns 3%.\(^5^3\) One cross sectional study reported an independent association between those with WD and erosive disease.\(^9\)

**Physical function and quality of life**

Two studies investigated the association between WD and physical function (health assessment questionnaire).\(^9,3^9\) Both studies reported a positive association independent of other measured parameters. One further study \(^4^8\) reported a positive association between the EQ5D (European Quality of life 5 Dimensions) health utility questionnaire and WD independent of age and gender. It should be noted that such a correlation would be expected as contained within the EQ5D is a question referring to problems with ‘usual activities including work’.

**Psoriasis**

Two cross sectional studies compared WD in patients with PsA as compared with psoriasis alone\(^4^8,5^1\), both reported increased work problems in those with PsA. A large cross sectional study of 2009 patients with psoriasis included data on 338 PsA patients.\(^5^1\) Fifty per cent of those with PsA were working vs sixty per cent of those with psoriasis.\(^5^1\) Of those working significantly more patients in the PsA group had taken time off work during the preceding year (25% vs 12%). The questionnaire for this study did specify being unfit for work/ periods of absence from work specifically due to psoriasis rather than PsA which may have biased the results. The second study also reported more work problems in the PsA group 32% vs. Psoriasis alone 11%, \(p=0.0005\).\(^4^8\) No studies have investigated the relative contribution of skin disease and joint disease to WD in patients with PsA however one randomised controlled trial assessing the effect of Infliximab in PsA did demonstrate less WD in those who achieved both 20% improvement in the American College of Rheumatology response criteria (ACR 20) and 75% improvement in the Psoriasis Area and Severity Index (PASI 75) rather than one or neither outcome.\(^5^0\)
Treatment effect

One RCT \(^{50}\) and one observational study \(^{39}\) have investigated the effects of anti-TNF treatment on WD. Analysis from the IMPACT RCT study investigating the efficacy and safety of Infliximab in PsA reported on working status, sick days, productivity visual analogue scale (VAS) and patient reported employability (out of work but could work). \(^{50}\) Productivity improved between baseline and 14 weeks by 67% in treatment arm vs 9% in placebo (median VAS improvement 2.6 vs 0.3). The British society of rheumatologists biologics registry measured WD in patients with PsA, rheumatoid arthritis and ankylosing spondylitis over the first three years of biologic therapy. \(^{39}\) Baseline disability of the 229 patients with PsA was 39%. The study did not demonstrate significant change in work status over three years. Nine working patients became work disabled (6.9%) and 6 work disabled patients started working (6.1%).

Environmental factors

There is very limited data on the role of environmental factors such as type of work, support at work, job satisfaction, or labour market fluctuation on WD. The study by Mau et al reported large differences in the standardised employment ratio (SER) across the economic divide of the old and new federal states in Germany. \(^{54}\) British society of rheumatologists biologics registry data demonstrated an increased rate of becoming WD in those with manual vs non-manual jobs. \(^{39}\)

Personal factors

Limited information is available on the association of WD and sex, marital status, education and earnings in PsA patients. Two large cohort studies have reported female sex to be independently associated with WD. \(^{9,39}\) Two cohort studies have reported low educational level to be independently associated with WD \(^{9,54}\) and one with greater cost of illness. \(^{52}\) The IMPACT study noted no difference in WD between sex after 14 weeks treatment. \(^{50}\)

Comparison with other rheumatic diseases

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Two prospective cohort studies\textsuperscript{39, 49} and one cross sectional study\textsuperscript{54} have compared WD in PsA with other rheumatic diseases. One long term follow up study reported 69\% of PsA patients were at work compared with 36\% rheumatoid arthritis, and 85-90\% ankylosing spondylitis.\textsuperscript{49} This study contained only 13 patients with PsA. The British society of rheumatologists biologics registry registry reported high levels of WD in PsA of 39\% compared with 41\% ankylosing spondylitis, 49\% rheumatoid arthritis.\textsuperscript{39} Mau et al used the standardised employment ratio to compare WD in those with PsA, rheumatoid arthritis, ankylosing spondylitis, Wegener's granulomatosis, systemic lupus erythematosus and systemic sclerosis. Those with PsA had reduced employment (SER 0.92) at a level equivalent to AS (0.94) but better than rheumatoid arthritis, Wegener's granulomatosis, systemic lupus erythematosus and systemic sclerosis (0.76-0.81).\textsuperscript{54}

\textit{Fatigue, Depression, comorbidities}

No studies have investigated the potential relationship between WD and fatigue, depression and comorbidities.

\textit{Data published in abstract form}

Nine studies relating to WD in PsA were published in abstract form. The primary findings are summarised in table 3. They confirm high rates of unemployment and disability reported in the fully published studies. Interestingly these high rates are present irrespective of study design; biologic randomised controlled trials\textsuperscript{56, 57, 59, 62, 64}, cohort studies\textsuperscript{55, 58, 61} or population studies.\textsuperscript{63} Two aspects are noteworthy from this abstract data. Firstly the emerging use of standardised WD questionnaires. The abstracts include data collected with the following instruments; the Work Productivity Activity Index (WPAI)\textsuperscript{62, 63, 65}, Work Limitations Questionnaire (WLQ)\textsuperscript{56, 57}, Employment Disadvantages Questionnaire (EQD)\textsuperscript{48} and Health and Labour Questionnaire (HLQ).\textsuperscript{58} Only one of these studies undertook a validation exercise and these data have been published in two abstracts\textsuperscript{56, 57} (table 3). The work limitations questionnaire was found to demonstrate reliability and sensitivity to change. There was a significant linear relationship between the work limitations questionnaire and Patient Global Assessment (PGA). For every 6.5\% improvement in patient global assessment
there was a 10% improvement in work labour questionnaire (P<0.001). The second finding of interest is the possibility that medical treatment can mitigate work disability. The GOlimumab Randomised EValuation of safty and Efficacy in subjects with psoriatic Arthritis using a human anti-TNF monocLonal antibody (GOREVEAL) RCT reported improvement in productivity at week 24 and additional improvements in lost time from work and employability at week 52. The study examining the safety and efficacy study of adalimumab in PsA- A Canadian open label study to evaluate the saftery and effeCtiveness of adaLimumab when Added to Inadequate therapy for the treatMent of psoriatic arthritis (ACCLAIM) RCT demonstrated an improvement in presenteeism independent of age, sex or disease duration at 12 weeks. Finally a study of Etanercept showed reduced absenteeism after two years; baseline: 0.8 days (+/-2.5 days) within the prior 2 weeks falling to 0.2 days (+/-1.5 days) at month 24.

**DISCUSSION**

Employment is highly contextualised with multiple potential contributory factors that may influence an individual’s level of function or indeed readiness to reduce their working hours. Such factors may include age and proximity to retirement, desire to work, support and flexibility of the employer, family and financial circumstances, education, ability to be flexible in role at work, the extent and access to benefits as well as the current local economic climate. It is on this background that we attempt to measure work disability in patients with psoriatic arthritis.

Work disability was the primary outcome measure in only four studies. The study by Wallenius *et al* is a large cross sectional study measuring disability benefit collection. This is an important study that has identified a number of WD associations (table 2). The study weaknesses should be noted including; that disability pension measure was not specific to PsA, clinical diagnosis rather than diagnostic criteria for PsA were used for entry into the database and the age range included was not full working age (18-45) raising the potential for selection bias. The study by Verstappen *et al* investigates WD during the first three years of anti-TNF therapy. WD was high (39%) and did not change over the 3 years of treatment. This negative result may in part be related to the timing of the baseline
data. Recruitment was determined as ‘within 6/12’ of starting therapy therefore although the study was prospective in design there is a potential here of missing the point of maximal disability prior to biologics and introducing recall bias despite the prospective study design. The 1987 study by Kaarela et al is a Finnish cross sectional study of inflammatory arthritis. 69% of PsA patients were at work compared with 36% rheumatoid arthritis, and 85-90% ankylosing spondylitis. This study is limited by the very small numbers (13 patients with PsA) and calendar bias. Finally the elegant study by Mau et al measuring employment status on 6041 PsA patients was compared with rheumatoid arthritis, ankylosing spondylitis, Wegeners granulomatosis, systemic lupus erythematosus and systemic sclerosis using a standardised employment ratio (SER). A standardised employment ratio of one would mean no difference from the regional average. Those with PsA had reduced employment at a level equivalent to but better than rheumatoid arthritis, systemic lupus erythematosus, Wegeners granulomatosis and systemic sclerosis. The study uses an objective measure but is weakened by the lack of objective diagnostic criteria at entry and the limited scope of WD information collected.

It is apparent that the broad spectrum and variable use of terminology is hindering our understanding of WD in PsA. The majority of the studies report on ‘work disability’ though this may be the umbrella term for; benefit collection, percentage unemployed, frequency of absenteeism, self-reported disability, employability or the index values of a composite score. The most frequently reported measures of WD are employment status (in work or not), absenteeism and to a lesser extent productivity/ presenteeism and disability benefit or retirement collection. A common theme of the more recent studies has been the inclusion of a presenteeism measure. Only two of the trials published in full form assessed presenteeism though six of the RCTs published in abstract form included this measure. Presenteeism is an appealing concept as it is arguably the most feasible and responsive patient reported centred WD measure. Conceptual models of work disability have the common thread of considering work disability as a continuum from presenteeism leading through to short term absenteeism, long term absenteeism and finally job loss. Outcomes earlier in this continuum (presenteeism and short term absenteeism) are more likely to occur more
frequently and are more likely to be reversible than long term absenteeism or unemployment. As a result, measures of employment and long term absenteeism are likely to be less responsive than presenteeism.

When interpreting the individual disease and socioeconomic associations with WD some specific study limitations are worthy of discussion. First, it is not possible to draw any conclusions on the association of WD with age as this has only been investigated in one study that was not specifically powered to detect such an association. Studies investigating WD in rheumatoid arthritis have taken differing approaches when assessing the association age with WD, either analysing all included or only those of working age. It may be most appropriate to assess unemployment only amongst those of working age but extend assessment of absenteeism, presenteeism and productivity loss to those of any age who are in work to give a truest reflection of the impact of disease on work. Second, the association with disease duration has been reported by three studies investigating disability benefit collection, unemployment and self-reported disability and though conflicting the findings are suggestive of an association of longer disease duration with worse disability. Disease duration is likely to have differing effects on each form of WD. It may be postulated that absenteeism and presenteeism will be greatest in early disease but after work and personal adaptations/ accommodations are made this impact will recede. In established disease unemployment may be higher (if adaptations have not worked) leaving only those who are able to remain in work, who in turn may have less presenteeism. Furthermore, no study has investigated WD in early disease, a time known to be important in rheumatoid arthritis. The question of the influence of disease duration on WD is best answered through the prospective study of an inception cohort.

The reports relating to joint disease activity and radiographic damage with WD indicate higher joint counts and erosive disease may be associated with higher levels of WD. Caution should be made when interpreting these findings because these studies have employed the 28 joint counts employed in rheumatoid arthritis (rather than the full PsA 66/68 joint count) and the presence or absence of erosive disease, rather than a validated quantitative radiographic scoring method. There is
more consistent evidence for the association of WD with physical function, reported in two studies, both specifically investigating WD as the primary outcome.\textsuperscript{9, 39} however both studies scored low on the quality assessment, specifically neither applied the CASPAR criteria or defined WD as related to PsA.

When we consider the use of questionnaires to measure WD a large number are available\textsuperscript{66} though none are validated for use in PsA. Of the WD measures used in PsA only WLQ has been subject to any form of validation exercise published in abstract form.\textsuperscript{57, 59} This problem is not isolated to PsA. Despite high quality validation exercises for WD data collection in other diseases such as the WPAI in ankylosing spondylitis\textsuperscript{67} there is still work required to identify a fully validated questionnaire. Recent data comparing estimates of presenteeism reported poor correlation between the following four measures; WLQ, HLQ, HPQ and WPAI.\textsuperscript{68} Although there a number of measures available and there was consensus at the OMERACT 9 meeting that work disability is an important measure\textsuperscript{66} no single tool has yet been endorsed.

The quality assessment process has identified a theme of common weaknesses in the WD data included in these studies. The purpose of our quality assessment was to assist the interpretation of the WD data within studies not to assess the overall quality of the study itself. Table 2 emphasises that despite the apparently moderate number of publications there are common themes that weaken the results. Lack of classification criteria for PsA, failure to apply analysis to the working age population and failure to account for potential confounding factors are the most frequent study deficits. It should be highlighted that our quality assessment has some weaknesses. Firstly confounding is not avoided by simply accounting for 3 or more contextual factors though we felt it important that studies collect data and analysed for potential confounders given the large number of bio, psycho social influences on WD. Secondly we have assumed that defining WD as ‘due to PsA’ is positive, though due to the complex interplay between PsA and its associated comorbidities restricting the outcome in this way may underestimate the burden of disability. Finally the divisions of quality level though necessary for reporting are arbitrary. The use of quality scores has been
debated however the technique allows analysis of a topic where sparse information is available.

**ADDENDUM: Updated literature search 30/05/2013**

A repeat literature search was conducted on the 30/05/2013 identifying five further reports since the search made in December 2010. Three have been fully published and two in abstract form.

A report in abstract form by Gladman et al is now available for more detailed evaluation following publication in full form. The Ratings and Evaluation in Psoriatic Arthritis with Embrel (REPArE) trial is a Canadian multicentre single arm observational study examining the long term effectiveness of Etanercept in the ‘real world’ setting of clinical practice. The primary outcome is physical function measured with the health assessment questionnaire but included WD as a secondary outcome measured with the health and labour questionnaire. The health labour questionnaire reports in four modules, absence from work, reduced productivity at paid work, unpaid labour production and impediments to paid and unpaid labour. The current report is of 24 month data. The mean age was 48.4 years, mean disease duration 8.1 years. Fifty six per cent of patients reported >0.5 improvement in health assessment questionnaire after 24 months treatment with Etanercept and 14% were free of disability. There was no significant change in absenteeism or hours unpaid work. There was a significant decline in mean number of hours of unpaid help that patients reported using in order to take care of home activities such as shopping, household work, childcare, odd jobs (8.0 vs 4.8 hours, 95% CI -6.2 to -0.2 p=0.034). Patient reported impediments to work fell significantly between baseline and follow up 1.5 (sd1.7 p<0.001). Number of hours of paid and unpaid help decreased exponentially with improvement in health assessment questionnaire (p<0.001) and Fatigue Severity Scale (p<0.001). The mean tender and swollen joint counts improved as impediments to work fell (p<0.001). The quality score (as applied in the systematic review) for this WD data was three out of seven, limited by the failure to apply a classification criteria, account for confounding factors, describe WD as related to PsA or use external criterion for WD. In summary this randomised controlled trial adds to the body of
knowledge on the positive effect of treatment on work disability and the correlation of work disability with joint count, fatigue and physical function.

Kavanaugh et al report a placebo controlled randomised controlled trial of the anti-TNF agent Golimumab. This report is a post-hoc analysis from the RCT examining the effect of Golimumab on HRQoL and productivity measured with a visual analogue score 0-10 at weeks 16, 24, 52 and 104. An improvement in productivity was identified at week 24 (2.24± 2.89 p=0.0001). The improvement appeared to be maintained out to week 104 however this did not reach significance (2.89±2.99, p=>0.05). The change in productivity was moderately correlated with the clinical outcome of Disease Activity Score- 28 joint count (DAS28). This study was a post hoc analysis therefore was not powered to detect change in productivity and achieved a quality score of two, perhaps explaining the loss of statistical significance at weeks 52 and 104. The use of a visual analogue score to measure productivity loss is not validated in PsA but has been used in other trials and use of the visual analogue score is well validated in other outcomes such as pain and global activity as reviewed by Mease. A final consideration when interpreting the findings of the study is the highly selected nature of randomised controlled trial participants, reducing the generalizability of the findings. Nonetheless this study adds to the body of evidence that disease activity is associated with productivity loss and may be ameliorated with treatment.

Kristensen at al report a retrospective case control analysis from 191 patients treated with anti-TNF between 2003 and 2009 from the South Swedish Arthritis Treatment Group Register. Work disability information from the Swedish Social Insurance Agency was collected at 30-day intervals from 12 months before the start of treatment until 3 years after and compared to 764 age and sex matched controls. At the start of treatment 67% of the participants were work disabled. WD amongst participants remaining on treatment during the study fell from 12.5 to 10.0 days per month. Logistic regression identified prior work disability, anti-TNF treatment failure, higher age, female sex and longer disease duration as being independently associated with WD. This study achieved a high quality score of six and adds to the evidence for independent associations of WD, as listed, and the
effect of treatment however the findings need to be interpreted with caution. First, confounding by indication should be considered as those commencing anti-TNF will be intrinsically different from others with PsA, likely more severe disease and thus may inflate the associations with clinical activity. Second, the analysis was per-protocol rather than intention to treat and thus will have over-estimated the ‘real world’ efficacy of treatment, participants are followed over the initial phase of treatment and some of the improvement seen may have been regression to the mean. Third, the regression analysis did not include many potentially important factors such as education, work type and comorbidities. Finally Sweden has a particularly supportive social security system for those with ill health and thus this study may reflect higher rates of WD than in other countries. The WD data from this study is of high quality and provides further evidence of the burden of WD in PsA.

Noppakun et al reported data from an Etanercept randomised controlled trial in abstract form. This study compared etanercept 50mg bi-weekly with 50mg once weekly. The aim of the current report was to compare quality of life (EQ5D) and work disability (WPAI) in subjects with PsA vs psoriasis alone. 240 subjects were included for analysis, 84 had PsA. At baseline those with PsA had worse quality of life than psoriasis alone (EQ5D 0.55 vs 0.70 p<0.001) and work impairment (35.8% vs 24.8% p =0.022). At week 24 quality of life and work impairment improved in both groups (0.79 vs 0.85) and work impairment (14% in both groups). The numbers in the study are small and the proportion of participants employed is not reported but taken together will adversely affect the study power. Carter et al reported on data from the US WPAI ‘re-contact study’ in abstract form. Participants were recruited from an internet panel. Inclusion criteria were; age over 18, employed currently or in the last two years and having self-identified as having physician diagnosed atrial fibrillation, neck or lower back pain, PsA, psoriasis or stroke. 498 participants had psoriasis and 347 PsA. Those with PsA patients had higher WPAI scores in all domains than atrial fibrillation or stroke. Psoriasis patients reported more presenteeism than atrial fibrillation or stroke. PsA and psoriasis costs for absenteeism over the preceding seven days were $5748 and $2350 and overall work impairment costs $17413 vs $11790. No statistical comparison was reported between PsA and psoriasis alone. Due to the
potential of confounders and bias in this study it is not possible to draw many specific conclusions. The report does add to the body of evidence that PsA confers greater disability than those with psoriasis alone.

These five studies reported during the latter part of my thesis have added support to the earlier reports that patients with PsA have significant levels of WD, especially patients with more active disease. There is new evidence from highly selective RCT’s that anti-TNF treatment improves WD in the short term.

**CONCLUSION**

This systematic critical review has synthesised the current body of evidence for WD in PsA. We find intermediate quality evidence that WD in PsA is high and is associated with longer disease duration, high health assessment questionnaire, high joint count, low educational level, female sex, erosive disease and manual work. There is sparse low quality evidence that WD may be worse in those with PsA than psoriasis alone. There is no data on WD in early PsA, the relative contribution of psoriasis in those with PsA or the role of other co morbidities such as fatigue, depression or the metabolic syndrome. The evidence that disability at work is mitigated by treatment is limited to a small number of short duration biologics RCTs. There are no WD data collection tools that fulfil the OMERACT criteria for validity for use in PsA.
CHAPTER III

METHODS

Study designs
My thesis employs retrospective (Chapter 5 and 7) and cross sectional (Chapter 6 and 8) study designs in order to achieve its objectives. The individual study designs are discussed in the methods sections of each chapter. Methods and outcome measures used throughout the thesis are discussed in this chapter.

Population
Patients with PsA recruited for study in this thesis fulfil the CASPAR classification criteria. Patients diagnoses prior to the development of the criteria in 2006 fulfil a CASPAR criteria modified for retrospective classification of an existing cohort developed as part of the body of work of this thesis (Chapter 5 and 7). All patients were recruited from the UK. Differing methods of recruitment were used in each study and are discussed separately in each chapter.

Intervention
The body of work in this thesis is observational.

Outcome measures

Work Productivity and Activity Impairment – Specific Health Problem
(WPAI) Questionnaire

The work outcome measure used throughout this thesis is the WPAI (Appendix 1). The WPAI is a patient-reported quantitative assessment of the amount of absenteeism, presenteeism, productivity loss and general activity impairment attributable to a specific health problem. The WPAI is a six item questionnaire asking patients to report the degree to which they experience difficulty at work due to a specific health problem, in this case PsA. The six questions are;

i) Are you currently employed? yes/no.
ii) During the past seven days, how many hours did you miss from work because of problems associated with your psoriatic arthritis? Include hours you missed on sick days, times you went in late, left early, etc., because of your psoriatic arthritis. Do not include time you missed to participate in this study.

iii) During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?

iv) During the past seven days, how many hours did you actually work?

v) During the past seven days, how much did your psoriatic arthritis affect your productivity while you were working? Responses are made on 0 to 10 Visual Analogue Scale (VAS);

vi) During the past seven days, how much did your psoriatic arthritis affect your ability to do your regular daily activities, other than work at a job? As for question five responses are made on a visual analogue scale.

Four main outcomes can be generated from the WPAI and expressed in percentages by multiplying the following scores by 100: 1) Percent work time missed due to PsA, ‘Absenteeism’ = Q2/(Q2 + Q4) for those who were currently employed; 2) Percent impairment while working due to PsA, ‘Presenteeism’ = Q5/10 for those who were currently employed and actually worked in the past seven days; 3) Percent overall work impairment due to PsA, ‘Productivity loss’ Q2/(Q2 + Q4) + [(1 - Q2/(Q2 + Q4)) × (Q5/10)] for those who were currently employed; 4) Percent activity impairment due to PsA Q6/10 for all respondents. For those who missed work and did not actually work in the past seven days, the percent overall work impairment due to PsA will be equal to the percent work time missed due to PsA.

The WPAI has been chosen as the primary work measure in this thesis for a number of reasons. First, the tool measures both absenteeism and presenteeism which are viewed as the most appropriate in health economics research. Second, the WPAI has been validated in the two closest clinical conditions rheumatoid
third, the WPAI reports over one week which minimises the chance of recall bias. A shorter recall period may allow an instrument to be more sensitive to change. Furthermore this is consistent with all the other outcome measures used in this thesis which are also based upon symptoms over the preceding week, thus enabling comparison between measures over the same period of time. Fourth, the WPAI was designed to be feasible and applied by post, comprising of only six questions. Fifth, the WPAI is disease specific such that work disability is attributed specifically to PsA. The advantages and disadvantages of attribution have been discussed in the introduction. Finally, the WPAI was identified at OMERACT 9 to be one of five promising candidates that should be evaluated further.

The WPAI does have some limitations. It only applies to those in employment and may therefore exclude some economically active individuals such as carers, homemakers and volunteers. The questionnaire comprises only six questions which does improve feasibility but means it does not include information on potential contextual factors such as work type, work adaptations and employer influences. This data has been captured in an additional study questionnaire (work questionnaire see below).

**Work Questionnaire**

In order to address some of the weaknesses of the WPAI and collect data on potential confounding and contextual factors of WD, a novel work questionnaire has also been included in the data collection for chapter eight, objective five (appendix 2). This form includes information on work type, reasons for not working, adaptations made at work, perceived helpfulness of the employer (Likert scale), and any non-medication related work therapy such as physiotherapy or occupational therapy.

**The Health Assessment Questionnaire- HAQ**

The health assessment questionnaire is a measure of physical function used in rheumatoid arthritis and is an increasingly accepted and validated measure in PsA. The health assessment questionnaire is a patient-reported assessment of ability to perform tasks
related to daily living. Twenty questions are asked in eight domains; dressing and grooming, rising, eating, walking, hygiene, reach, grip and activities (Appendix 3). Patients rate their ability to perform tasks in these areas from “no difficulty” to “unable to do”, over the prior week. The overall score is reported as a score between 0 and 3. Patients can be classified as; mildly disabled (0-1), moderately disabled (>1-2) or severely disabled (>2-3). Observational studies of patients with PsA have demonstrated functional disability to be significantly higher than that of the healthy population and comparable to rheumatoid arthritis. The longitudinal course of physical function in PsA as an outcome has been studied previously focusing on the transition between predefined health assessment questionnaire states. Older age, female sex, longer disease duration, and higher number of inflamed joints all predict transition between disability states as measured by the health assessment questionnaire. Female sex is associated with an increased likelihood of progression of disability and increasing age associated with a decreased likelihood of improvement. Smoking and delay to diagnosis are associated with higher health assessment questionnaire in established disease. The Minimally Important Difference (MID) of health assessment questionnaire is estimated to be between 0.13 and 0.35. The health assessment questionnaire has been collected for this thesis to investigate the relationships of physical function with WD.

**The EuroQol 5-domain EQ5D**

The European quality of life 5-domain (EQ5D) is patient reported outcome (PRO) measuring of health related quality of life (HRQol) (Appendix 4). The questionnaire consists of five descriptive questions and a visual analogue scale (EQ5Dvas) from 100 (best imaginable health) to 0 (worst imaginable health). A single summary index is generated using a valuation index specific to the UK. The performance of the EuroQol (EQ5D) has been assessed in patients with psoriasis and has been used in observational studies of PsA. It distinguishes well across levels of PsA severity and demonstrates utility gain in patients started on anti-TNF therapy within the first few weeks, sustained over time. The EQ5D has been collected for this thesis to investigate the relationships of general HRQol with WD.

**The Dermatology Quality of Life Index (DLQI)**
The Dermatology quality of life index (DLQI) is a measure of disability experienced by patients with dermatological conditions.\textsuperscript{94} The DLQI is a 10 item patient reported questionnaire which asks patients to attribute the effects of their skin condition on domains of quality of life including, work, leisure activities, personal relationships and embarrassment over the previous week (Appendix 5). Responses are scored 0- ‘not at all’, 1- ‘a little’, 2- ‘a lot’, 3- ‘very much’ resulting in a score from 0-30. It has been validated in psoriasis with evidence for its discrimination and responsiveness as reviewed by Mease in 2011.\textsuperscript{72} The DLQI has been collected for this thesis to investigate the relationships skin specific HRQoL with WD.

**The Functional Assessment of Chronic Illness Therapy- Fatigue (FACIT-fatigue)**

The functional assessment of chronic illness therapy- fatigue (FACIT-fatigue) is a 13 item quantitative measure of fatigue over the prior week (appendix 6).\textsuperscript{95} Responses are on a five point Likert scale of 0- ‘not at all’, 1- ‘a little’, 2- ‘somewhat’, 3- ‘quite a bit’, 4- ‘very much’, the resulting score thus ranges from 0-52. Originally developed for use in anaemia the FACIT-fatigue has evidence for its feasibility, reliability, responsiveness and construct validity in PsA.\textsuperscript{8, 96} FACIT-fatigue has been collected for this thesis to investigate the relationship of fatigue with WD.

**Global Scores**

Patient global scores compliment other scores by encompassing impacts of disease such as systemic feelings of ill health and the burden and side effects of treatments. A recent study undertaken by the GRAPPA network set out to assess the validity and additional utility of domain specific visual analogue scores for Global, Skin and Joint disease activity in PsA (appendix 7).\textsuperscript{97} 319 patients from 18 centres in 10 countries participated. Global visual analogue scores, 66/68 joint counts, skin scores (Psoriasis Area and Severity Index- PASI) and depression scores (Hospital Anxiety and Depression Score- HADS) were assessed at baseline and one week later. Respondents are asked to rate their skin, joints or ‘in all the ways your PsA affects you’ by marking a line on a visual analogue scale. Scores are rated on a horizontal line of 100mm where 0 represents ‘no symptoms’ and
100 represents ‘very poor, severe symptoms’. The global visual analogue score was found to be reliable and correlate closely with joint and skin scores. The skin and joint visual analogue scores offered additional utility when domain severity diverged. Visual analogue scales have been collected for this thesis to investigate the relationships of WD with measures of disease activity.

**Background form**
Demographic data has been included on a background form (appendix 8). Demographic and socioeconomic factors are known to influence WD in related diseases such as rheumatoid arthritis and ankylosing spondylitis. The form for collecting demographic information was developed specifically for this study and includes data on sex, education, smoking and alcohol use, ethnicity, disease and symptom duration and co-morbidities.

**Radiology**
Radiographs of the hands and feet have been scored with the Psoriatic Arthritis Ratingen System (PARS) validated for use in PsA. This is the only scoring system specifically developed for use in PsA rather than adapted from use in rheumatoid arthritis. It includes a measure of bone proliferation which is the only radiographic feature specific to PsA in the CASPAR criteria addition to the ‘truth’ domain of the OMERACT filter. The OMERACT filter is an internationally agreed set of criteria against which an outcome measure can be assessed. A measure is endorsed by OMERACT once all criteria are met. The filter comprises ‘truth’, does it measure what it intends to measure without bias (comprised of face, content, construct and criterion validity), discrimination (comprised of reliability and responsiveness) and feasibility (within the constraints of time, money and practicality).

**Disease Activity in Psoriatic Arthritis (DAPSA)**
The Disease Activity in Psoriatic Arthritis (DAPSA) is a clinical composite disease activity measure. The DAPSA was derived from the Disease Activity in Reactive Arthritis (DAREA) which was a score derived from; a 28 tender and swollen joint count, C-reactive protein (CRP), patient global and pain visual analogue scores summed together. The DAREA was adapted through
substitution of the 28 joint count used in the Disease Activity Score 28 (DAS 28) with the 66/68 tender and swollen joint count to form the DAPSA. This extended joint count accommodates the varied joint involvement of peripheral PsA and is advocated by OMERACT and GRAPPA. The joints included in the 66/68 joint count are; distal interphalangeal (DIP’s), proximal interpalangeal (PIP’s), metacarpaophalangeal (MCP’s), wrists, elbows, glenohumeral, acromioclavicular, sternoclavicular, temporomandibular, hips, knees, ankles, midtarsals, metatarsophalangeal, and the PIP’s of the toes. There is evidence for its feasibility, acceptability, responsiveness and construct validity in PsA. There are other composite measures with evidence for their validity for use in PsA including the Composite Psoriatic Disease Activity Index (CPDAI) and the Psoriatic Arthritis Joint Activity Index (PASJAI) reviewed by Mease. The DAPSA was chosen for this study because it was felt to offer the best balance between feasibility and evidence for its validity in PsA. Feasibility is a critical consideration when undertaking longitudinal observational studies following large numbers of patients at repeated follow up intervals. The DAPSA typically takes less than 5 minutes to obtain. Skin assessment did not reach a significant level in the principle component analysis therefore the DAPSA does not include a skin score which further improves its feasibility. It may be argued that the DAPSA does not fulfil the OMERACT filter for truth because it does not include measures of skin, enthesal or spinal involvement and therefore does not encompass all aspects of PsA. For the purposes of my thesis the domain of skin will be measured a separate patient reported skin visual analogue score and the spinal and enthesal domains under the umbrella of patient global visual analogue score (see Global Scores). This decision to use the DAPSA is supported by a recent comparison of the CPDAI, DAPSA and other composite measures in which the DAPSA performed comparably in discriminating between high and low disease activity. The DAPSA has been collected for this thesis to investigate the relationships of WD with disease activity.

**Reporting**

The systematic review has been conducted and reported in accordance with the Preferred Reporting Items for Systematic reviews and MetaAnalyses- PRISMA recommendations. The observational manuscripts have been conducted and
reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.\textsuperscript{105} The STROBE statement is a checklist of 22 items that was developed in order to strengthen the reporting of observational studies.

\textit{Database and research unit}

The research unit is based at the RNHRD. All study data is held on a database in this unit on a password protected computer in a secure room. The database is supervised by a data protection officer and Caldecott guardian. All the questionnaires and forms used in the studies included in this thesis are paper based. The software used to scan is ‘Teleform’, a Hewlett Packard product developed by Cardiff Software 1991. Forms are created in readable formats and when completed they are then scanned into a password protected Microsoft access database 2003. A pdf form is made simultaneously and stored separately to maintain a duplicate of the original data. The specificity of the scanning is set to 99\%, thereby flagging any queries for manual confirmation. The study master files containing all the regulatory approvals and communications are held securely at the research unit.

\textit{Data entry/ storage}

Data entry is audited monthly against the pdf originals for missing data. Missing data points are then confirmed manually with each site. If an expected questionnaire or data collection form is not received up to two reminders are sent to each participant. If no reply is received the data is recorded as missing. Confirmation of the accuracy of the data scanning process was made by auditing the data from 100 EQ5D questionnaires against the original pdf for misreading. The audit was undertaken on the 10/05/2013 by the author. No data errors were identified.

\textit{Administrative infrastructure}

A database and administrative team were put together from the existing RNHRD research group, Charlotte Cavill as database manager/ data security officer, Mandy Knight and Austin Smith as database administrators and Nina Griffith as
research nurse. Study data is sent to the database team for uploading to the access database using the scanning ‘Teleform’ process.

Analysis
Analyses for chapters our and five were undertaken in SPSS versions 17-20 by the author. Analyses for chapters six and seven were undertaken by Dr G Shaddick (Reader in Mathematics, University of Bath) in statistics package R and this is accredited accordingly. Specific statistical tests used are discussed in the methods section of each chapter.

Funding
This research has been funded through an unrestricted grant from Abbott laboratories ltd. The study undertaken in chapter eight is also supported by the National Institute for Health Research through the Comprehensive Clinical Trials Network.

Ethical approval (LOPAS I and II)
Full ethical approval was given for research conducted in this thesis including the collection and storage of the clinical and radiological data (Table 1).

Table 1: Regulatory Approvals

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<th>Regulatory body</th>
<th>Authorisation number</th>
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<td>Objectives 2, 3, 4a</td>
<td>NREC- Bath</td>
<td>BA74/00-01</td>
</tr>
<tr>
<td></td>
<td>Sponsor- RNHRD</td>
<td>RBB141</td>
</tr>
<tr>
<td>Objectives 4b, 5</td>
<td>NREC- South Wales Panel D</td>
<td>11/WA/0081</td>
</tr>
<tr>
<td></td>
<td>Sponsor- RNHRD</td>
<td>RBB346</td>
</tr>
<tr>
<td></td>
<td>NIHR</td>
<td>10553</td>
</tr>
<tr>
<td></td>
<td>CRN</td>
<td>67424/W</td>
</tr>
</tbody>
</table>

National Research Ethics Committee (NREC)
Royal National Hospital for Rheumatic Diseases (RNHRD)
National Institute for Health Research (NIHR)
Clinical Research Network (CRN) ID
Having addressed the methods used in this thesis we will now move on to the individual studies that answer each of the objectives. The first step is to classify an existing cohort of patients with PsA according to the CASPAR criteria, modified for retrospective application (objective 2). Once this has been achieved a cross sectional study can be undertaken on this group of patients to examine the feasibility, construct and discriminative validity of the WPAI in PsA (objective 3).
CHAPTER IV

CLASSIFICATION OF AN EXISTING COHORT OF PATIENTS WITH PSORIATIC ARTHRITIS USING A THE CASPAR CRITERIA

In order to validate a measure of work disability a well classified cohort of patients with PsA was required to study. Until recently there has been no international consensus on a classification criterion for PsA. In 2006 a classification criteria was agreed upon however this was designed for prospective use. Since 1989 patients with a clinical diagnosis of PsA at the Royal National Hospital for Rheumatic diseases have been followed in a large longitudinal observational study. This current chapter describes a modification of the CASPAR criterion to enable the retrospective classification of this existing cohort. This report has been published and the following is taken from that publication resulting in a small amount of repetition.

INTRODUCTION

Psoriatic arthritis (PsA) is a distinct chronic inflammatory arthritis associated with psoriasis. There are a variety of clinical phenotypes resulting in historic variability in case definition, potentially confounding research. The original classification criteria were developed by Moll and Wright however despite the proposal of a number of other criteria none have been universally accepted. In response to this the CASPAR study group developed a classification criteria specifically for use in clinical research. Their large prospective, multinational study found the CASPAR criteria to be simple to use and demonstrated a sensitivity and specificity of 0.914 and 0.987 respectively. Subsequent studies confirmed these findings.

Whilst the CASPAR criteria can be used with confidence in prospective trials, to my knowledge its performance when used retrospectively has not yet been assessed. Much of the observational research in PsA relies on cohorts established prior to the development of the CASPAR criteria. It is essential that such cohorts
can be appropriately classified. I have set out to investigate the feasibility and performance of the CASPAR criteria when used to retrospectively classify an existing study cohort.

PATIENTS AND METHODS

The CASPAR criteria were applied to records from 480 patients from the RNHRD PsA cohort and 100 consecutive controls with inflammatory arthritis from a general rheumatology clinic. The CASPAR criteria consist of confirmed inflammatory articular disease (joint, spine or enthesal) with at least three points from the following features:

1. Current psoriasis (2 points)
2. A personal or family history of psoriasis (1 point)  
   (Unless current psoriasis is present, first or second degree relative)
3. Dactylitis (1 point)  
   (Current or prior history recorded by a Rheumatologist)
4. Juxtaarticular new bone formation, hands or feet, (1 point)  
   (Ill-defined ossification near joint margins- excluding osteophyte formation- on plain hand and feet radiographs)
5. Rheumatoid factor negativity (1 point)
6. Psoriatic nail dystrophy (1 point)  
   (Onycholysis, pitting, and hyperkeratosis observed on current physical examination)

I adapted this score for retrospective use from medical records in such a way that; ‘inflammation’ and ‘current psoriasis’ were scored if they had ever been confirmed by a Rheumatologist in the PsA clinic. This study was conceived, led and reported by myself. To optimise feasibility once three points had been scored (indicating PsA according to the CASPAR criteria) the records were not further scrutinised. Two raters reviewed all records (Myself and co-author Dr Luisa Costa). Inter-rater reliability was assessed based on duplicate scoring of twenty records. The diagnostic gold standard was expert clinical diagnosis by a clinician with longstanding expertise in PsA. In cases of doubt where the clinical diagnosis was of PsA and did not fulfil CASPAR criteria the records and radiology were reviewed in full for consensus (Myself, Dr Luisa Costa and Professor N McHugh). Two sensitivity and specificity analyses were performed.
The first excluded those with a clinical diagnosis of PsA but who did not have sufficient data available to confirm the classification with the CASPAR criteria. The second analysis was performed on all records including those with missing data.

RESULTS
Nine case records were missing or destroyed leaving 471 cases from the PsA cohort. On review, 456 cases had PsA. The diagnosis had changed over time in fifteen cases and they were entered into the control group. Of the 115 controls 96 had rheumatoid arthritis, five OA, three reactive arthritis (ReA), three seronegative arthritis, three undifferentiated arthralgia, two ankylosing spondylitis, one spondyloarthritis and two systemic sclerosis (demographics table 1). Four percent of the control group had current or personal history of psoriasis consistent with current prevalence estimates of between 0.6%-4%. 28 (4.6%) of the records were reviewed for consensus assessment.

Table 1
CASPAR study participant demographics and disease phenotype

<table>
<thead>
<tr>
<th></th>
<th>PsA (n=480)</th>
<th>Control group (n=115)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age year (n=456)</td>
<td>57.4 (13.2)</td>
<td>65 (+/-14.1)</td>
</tr>
<tr>
<td>Age onset of Arthritis years (n=456)</td>
<td>39.5 (13.8)</td>
<td>56.8 (+/-14.4)</td>
</tr>
<tr>
<td>Age at onset of Psoriasis years (n=456)</td>
<td>30.3 (15.4)</td>
<td>N/A</td>
</tr>
<tr>
<td>Sex- Female %</td>
<td>53.1%</td>
<td>73%</td>
</tr>
<tr>
<td>Rheumatoid Factor +ve % (n= 416)</td>
<td>2.9%</td>
<td>64%</td>
</tr>
<tr>
<td>Anti-Cyclic Citrullinated Peptide +ve % (n=363)</td>
<td>1.3%</td>
<td>43%</td>
</tr>
<tr>
<td>Phenotype (n=316)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal interphalangeal joint (DIPJ)</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>DIPJ and Polyarthritis</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>Monoarthritis</td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td>Mutilans</td>
<td>1.9%</td>
<td></td>
</tr>
<tr>
<td>Oligoarthritis</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Oligoarthritis and Spondyloarthritis</td>
<td>3.9%</td>
<td></td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>59.4%</td>
<td></td>
</tr>
<tr>
<td>Polyarthritis and Spondyloarthritis</td>
<td>8.5%</td>
<td></td>
</tr>
<tr>
<td>Spondyloarthritis</td>
<td>1.9%</td>
<td></td>
</tr>
</tbody>
</table>

Of the 456 patients with a physician diagnosis of PsA eight did not fulfil CASPAR criteria. For only one of these information regarding all the CASPAR
criteria was available. For a further seven patients either no radiographs or no RhF test results were available to enable a complete assessment. Sensitivity and specificity were 99.7% and 99.1% respectively. Sensitivity remained high even after inclusion of the seven case records with missing data (Sensitivity 98.2%, Specificity 99.1%).

The objectivity of the CASPAR assessment resulted in excellent inter-rater reliability. Of the twenty records reviewed there was full agreement in eighteen cases. Both raters also identified the same two records as cases of doubt for consensus review. Both raters found the CASPAR to be easy and quick to use. 52% of the PsA cases fulfilled criteria based on current psoriasis, a negative rheumatoid factor, as well as inflammation; each readily accessible from the case records.

**DISCUSSION**

The CASPAR criteria could be applied prospectively to established research cohorts but waiting for all the patients to attend clinic would take years. The ability to use a classification tool retrospectively is therefore important. We have found the CASPAR criteria to be easy and practical to use for three reasons. First, the majority of cases reached the required 3 points quickly from inflammation, current psoriasis and a negative rheumatoid factor. Second, the objectivity of the criteria made inter rater reliability high with minimal training. Third, removing the requirement to scrutinise the records after sufficient points had been reached further improved the feasibility. Finally, missing data points are a reality of observational research however the sensitivity and specificity were found to be similar to previous reports even when data points were missing.

This study is potentially weakened by three factors. First, there is the lack of a gold standard which has been a concern in prior reports. The approach involving experienced physicians diagnosis is a recognised method which has been applied in prior studies. Second, through modification of the CASPAR criteria to allow ‘current psoriasis’ and inflammation to be scored at any time rather than at the same clinical assessment we have potentially increased the sensitivity. The initial sensitivity of the criteria was 91% reported by Taylor.
however subsequent reports have all estimated the sensitivity to be between 97 and 100%\textsuperscript{108-110} limiting the degree to which we can overestimate it. Furthermore specificity is of greater importance when classifying a research cohort. Finally, we have not compared the performance of the CASPAR criteria to other criteria. These comparisons have already been made elsewhere in the literature\textsuperscript{76, 110, 114} and the purpose of this study was to assess whether the feasibility and performance characteristics were maintained when the CASPAR criteria were used retrospectively.

In conclusion, this study demonstrates that the feasibility, specificity and sensitivity of the CASPAR criteria are maintained when adapted for retrospective use to classify an established research cohort from medical records even in those with missing data. This modification of the CASPAR criteria for retrospective use addresses objective 2 of this thesis. I will now describe a cross sectional study undertaken to address objective 3 of this thesis, to explore the validity of the WPAI in PsA.
CHAPTER V

WORK DISABILITY IN ESTABLISHED PSA- A PRELIMINARY VALIDATION OF THE WORK PRODUCTIVITY AND ACTIVITY INDEX

This current chapter relates to objective three of my thesis, to examine the feasibility, construct and discriminative validity of the Work Productivity and Activity Index- Specific Health Problem (WPAI) questionnaire in PsA. This study has been reported resulting in a small amount of repetition.115

BACKGROUND
Psoriatic arthritis is a distinct inflammatory arthritis associated with psoriasis. PsA is a heterogeneous disease; patients have skin and joint disease but may also have manifestations such as enthesitis, axial disease, uveitis, the metabolic syndrome and other less well defined factors related to long term inflammation such as fatigue. All these elements combine to have a significantly detrimental effect on physical function and quality of life.82 Work is of central importance to patients and it is now well recognised that Work Disability (WD) is an important, patient centred quality of life outcome that needs further investigation.116 WD is an umbrella term encompassing a spectrum of disability ranging from presenteeism (reduced effectiveness at work) through to absenteeism and unemployment. There is no universally accepted measure of WD although a number have been proposed and it is a subject of current interest within the Worker Productivity Special Interest Group (WP-SIG) of Outcome Measures in Rheumatology (OMERACT).117

Unemployment and WD in PsA is high, with estimates for each ranging between 16-39% and 20-50% respectively.41 Preliminary evidence suggests that longer disease duration, worse physical function, high joint count, low educational level, female sex, erosive disease and manual work are all associated with increased WD in PsA41 However accurate interpretation of predictive factors is hampered by the variety of outcomes used and lack of a validated measure.
The Work productivity activity index specific health problem questionnaire (WPAI) is a patient reported questionnaire used to assess the impact of disease on work productivity. The questionnaire has been validated in a number of chronic conditions including ankylosing spondylitis and rheumatoid arthritis and has been used in psoriasis. I set out to assess the feasibility, construct and discriminative validity of the WPAI in patients with PsA.

**METHODS**

This cross sectional validation study was undertaken as part of the Long term Outcomes in Psoriatic Study I (LOPAS I). Since 1989 patients with PsA at the Royal National Hospital for Rheumatic Diseases, Bath, UK have been included in the longitudinal observational study with prospective collection of clinical outcome measures during their routine clinical follow up and biannual postal patient reported outcome measures. This present validations study was conceived, led and reported by myself. Adults with PsA of any disease duration are eligible for inclusion in the study. All participants fulfilled the ClASsification for Psoriatic Arthritis- CASPAR criteria. All 380 patients participating in the postal study were sent the following questionnaires; health assessment questionnaire, Patient Global Visual analogue scale (PtG), EuroQol (EQ5D), Dermatology Life Quality Index (DLQI), the Functional Assessment of Chronic Illness Therapy Fatigue score (FACTIT-F) and the WPAI.

The WPAI questionnaire asks patients to report the degree to which they experience difficulty at work due to a specific health problem, in this case PsA. There are six questions in total; 1 = currently employed- yes/no; 2 = hours missed due to PsA; 3 = hours missed for other reasons; 4 = hours actually worked; 5 = degree to which PsA is affected productivity while working using a 0 to 10 Visual Analogue Scale (VAS); 6 = degree to which PsA is affects productivity in regular unpaid activities (using a VAS). The recall period for questions 2 to 6 is seven days. Four main outcomes can be generated from the WPAI and expressed in percentages by multiplying the following scores by 100: 1) Percent work time missed due to PsA, ‘Absenteeism’ = Q2/(Q2 + Q4) for those who were currently employed; 2) Percent impairment while working due to PsA, ‘Presenteeism’ =
Q5/10 for those who were currently employed and actually worked in the past seven days; 3) Percent overall work impairment due to PsA, ‘Productivity loss’ \( \frac{Q2}{Q2 + Q4} + \left(1 - \frac{Q2}{Q2 + Q4}\right) \times \left(\frac{Q5}{10}\right) \) for those who were currently employed; 4) Percent activity impairment due to PsA Q6/10 for all respondents. For those who missed work and did not actually work in the past seven days, the percent overall work impairment due to PsA will be equal to the percent work time missed due to PsA.

Statistical analysis was undertaken in SPSS v17. Descriptive statistics were used to provide demographic information. Due to the non-Gaussian distribution of the data nonparametric tests were used. Spearman’s correlation coefficient was used to estimate the correlation of the WPAI with other outcome measures validated for use in PsA\(^2\) as an estimate of construct validity. Mann-Whitney U was used to assess whether the WPAI was able to discriminate between better or worse PsA defined by the median of each outcome in order to estimate discriminative validity. Using the OMERACT model feasibility was determined by ease of application, given the constraints of time, money and interpretability.

This study was approved through the Bristol research ethics committee and participants signed informed consent in accordance with the Declaration of Helsinki.
RESULTS

Two hundred and seventy patients responded (71.0%). Ninety-five percent fulfilled CASPAR criteria for PsA, 50% were male, mean age was 57 (standard deviation- SD 13.0), mean PsA duration was 17years (SD 10.6) and the mean Psoriasis duration was 25years (SD 14.9).

Outcome measures are reported in Table 1. 190 patients were of UK working age (18-65years) and 131 were still working. Of those still working absenteeism, presenteeism and work productivity loss secondary to PsA over the last week were 4.7%, 21.1% and 24.0% respectively. Of the fifty nine patients of working age not working fourteen were not working because of their PsA, twelve were not working for other reasons and thirty three were retired.

Table 1

Comparison of disease outcome measures by working status

<table>
<thead>
<tr>
<th>Outcome</th>
<th>All (n=270)</th>
<th>Working age (n=190)</th>
<th>Working age working (n=131)</th>
<th>Working age not working (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAQ Global Median (IQR)</td>
<td>2.0 (1.0)</td>
<td>2.0 (1.0)</td>
<td>2.0 (1.0)</td>
<td>2.0 (2.0)</td>
</tr>
<tr>
<td>HAQ DI Median (IQR)</td>
<td>0.62 (1.2)</td>
<td>0.62 (1.13)</td>
<td>0.62 (1.00)</td>
<td>1.00 (1.62)</td>
</tr>
<tr>
<td>Pain VAS Median (IQR)</td>
<td>2.6 (3.8)</td>
<td>2.60 (4.8)</td>
<td>2.2 (3.1)</td>
<td>4.4 (4.70)</td>
</tr>
<tr>
<td>EQ-5Dvas Median (IQR)</td>
<td>70.0 (35.0)</td>
<td>70.0 (25.0)</td>
<td>75 (35.0)</td>
<td>60 (44.0)</td>
</tr>
<tr>
<td>EQ5Dindex Median (IQR)</td>
<td>0.69 (0.21)</td>
<td>0.69 (0.21)</td>
<td>0.73 (0.18)</td>
<td>0.60 (0.32)</td>
</tr>
<tr>
<td>DLQI Median (IQR)</td>
<td>2.0 (3.0)</td>
<td>2.0 (3.0)</td>
<td>2.0 (3.0)</td>
<td>2.0 (6.75)</td>
</tr>
<tr>
<td>FACIT-fatigue Median (IQR)</td>
<td>38.0 (19.5)</td>
<td>18.2 (16.0)</td>
<td>20.6 (14.0)</td>
<td>17.3 (19.0)</td>
</tr>
</tbody>
</table>

Health assessment questionnaire (HAQ), disease index (DI), visual analogue score (VAS), Euroqol 5 domain (EQ5D), dermatology quality of life index (DLQI), functional assessment of chronic illness therapy fatigue (FACIT-fatigue), Inter quartile range (IQR).

We found the WPAI to be low cost (paper and postage costs only) and quick to apply (six questions). We also found the WPAI easy to analyse and interpret. The results are expressed as a percentage over the preceding week, rather than alternative tools that report hours absent from work which is a harder measure to analyse and compare.
Correlations with other outcome measures and discrimination between better and worse PsA states are reported in Table 2. Statistically significant Spearman rank correlation coefficients are reported are stratified as strong (>0.60), moderate (0.40 to 0.59) and weak (0.20 to 0.39).\textsuperscript{118} Absenteeism demonstrated weak correlation with health assessment questionnaire, EQ5D index and FACIT-fatigue. Presenteeism showed strong correlation with the patient global visual activity scale/ health assessment questionnaire, EQ5D index and FACIT-fatigue, moderate correlation with pain and weak correlation with the DLQI. Work productivity loss showed strong correlation with patient global visual activity scale/ health assessment questionnaire, EQ5D index and FACIT-fatigue and moderate correlation with pain.

Table 2

WPAI correlation with other measures (construct validity) and discrimination between better and worse PsA states (discriminative validity).

<table>
<thead>
<tr>
<th>WPAI Correlations with other measures</th>
<th>Patient global</th>
<th>Pain VAS</th>
<th>HAQ DI</th>
<th>EQ5D Index</th>
<th>DLQI</th>
<th>FACIT-fatigue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spearman R correlations; Construct validity</td>
<td>0.16</td>
<td>0.13</td>
<td>0.39*</td>
<td>-0.28*</td>
<td>-0.1</td>
<td>0.27*</td>
</tr>
<tr>
<td>Absenteeism</td>
<td>0.54*</td>
<td>0.43*</td>
<td>0.60*</td>
<td>-0.63*</td>
<td>0.25*</td>
<td>0.64*</td>
</tr>
<tr>
<td>Presenteeism</td>
<td>0.56*</td>
<td>0.41*</td>
<td>0.65*</td>
<td>-0.65*</td>
<td>0.15</td>
<td>0.64*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WPAI discrimination between better and worse health status, (median of each measure)</th>
<th>Mann Whitney U- Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discriminative validity</td>
<td>Absenteeism</td>
</tr>
<tr>
<td>Presenteeism</td>
<td>-5.38*</td>
</tr>
<tr>
<td>Productivity loss</td>
<td>-4.72*</td>
</tr>
</tbody>
</table>

* p<0.05

Work productivity and activity index (WPAI), Health assessment questionnaire (HAQ), disease index (DI), visual analogue score (VAS), Euroqol 5 domain (EQ5D), dermatology quality of life index (DLQI), functional assessment of chronic illness therapy fatigue (FACIT-fatigue)

Spearman correlations-estimate of construct validity by correlating with other measures of disease activity
Mann Whitney U- Z score- estimate of responsiveness through differentiation between high and low disease activity states defined by other measures of disease activity.
The Mann-Whitney U test demonstrated the WPAI measurement of presenteeism and productivity loss was able to differentiate between better and worse PsA states as measured by patient global activity, health assessment questionnaire, EQ5D and FACIT fatigue (Table 2). For example when patients were grouped into those with better physical function (health assessment questionnaire score below the median) and those with worse physical function (health assessment questionnaire score above the median) those with better physical function reported less presenteeism (8.9% SD 13.9 versus 30.9% SD 22.2). The measure of absenteeism differentiated between better and worse PsA states only in the domains of physical function (health assessment questionnaire), and quality of life (EQ5D).

**DISCUSSION**

To my knowledge this is the first attempt to validate a work outcome measure in PsA. Whilst a variety of WD measures are available I chose to investigate the WPAI for three reasons. First, it includes measures of both absenteeism and presenteeism, the two core WD measures as determined at OMERACT 10. Second, the recall period is one week, as are most of the other outcomes in this study. To assess the construct validity of the WPAI we have conducted correlation coefficients with other outcome measures therefore it is crucial the measures assess the same period of time. A short recall time minimises the risk of recall bias and has a greater potential for detecting change in a condition subject to relapse and remission, two desirable features if the intention is to apply the tool to study change in WD over time and the effect of treatment. Third, there is good evidence for the validity of the WPAI in the two most closely related conditions rheumatoid arthritis and ankylosing spondylitis and it has also been used in psoriasis.

I have found the WPAI easy and quick to apply, low cost and readily interpretable, thus fulfilling the OMERACT criteria for feasibility. The WPAI estimates of presenteeism and productivity loss correlated with health assessment questionnaire, EQ5D and FACIT fatigue. The correlation with DLQI was either absent or poor but this may relate to the skin disease characteristics of our cohort.
The majority had mild skin involvement and a small minority had marked skin disease. Absenteeism showed weaker correlations as is the case in similar studies in rheumatoid arthritis and ankylosing spondylitis. In the present study this finding may be related to the smaller numbers reporting a period of absenteeism. A current leading model of disability at work suggests individuals pass through escalating disability states from presenteeism, absenteeism, temporary unemployment to permanent unemployment or retirement. Under this model we would expect periods of presenteeism would be more common and lead on to absenteeism if disease deteriorates or adaptation is not possible.

I report moderate work disability in PsA patients of working age. Direct comparison of disability levels with other diseases such as rheumatoid arthritis and ankylosing spondylitis cannot be made without inclusion of locally matched disease controls. PsA patients in this study all had established disease and are from a well classified single secondary care centre in the UK.

The findings of this study should be interpreted taking into account some methodological considerations. The Spearman is a measure of association only and does not infer causality. This is a cross sectional study and the recall period of the outcome measures used is only one week introducing the possibility that longer term disability or fluctuations in disease activity may not have been captured (discussed further in the discussion section of this thesis). The WPAI asks patients to attribute their WD to psoriatic arthritis rather than their general health which may be difficult for patients to do. However if the goal is to study the effect of disease specific treatment on WD a disease specific tool is desirable. Furthermore in a study of WD in rheumatoid arthritis results were participants were similar for WD in general and WD secondary to rheumatoid arthritis. The cohort in our study had established disease with a mean age of (57years) and a relatively long mean PsA duration (17years), though the majority were still of working age (70%). It is therefore possible our estimates of WD are high as the cohort is more likely to have advanced damage as a result of longstanding disease. With the relative lack of participants with early disease we may also have an underestimated the effect of more recent inflammatory joint disease on WD. Finally the study population are from a single centre in the UK.
and the impact of country specific social security systems on disability pensions and sick leave is well recognised\textsuperscript{119}.

**CONCLUSION**

The findings of this study address objective three of this thesis, providing evidence for the feasibility, construct and discriminative validity of the WPAI in PsA. Further prospective study should further validate the WPAI through assessment of its sensitivity to change with clinical parameters such as joint count, inflammatory markers and radiographic damage as well as estimate the minimally clinically important difference of the WPAI in PsA. Objective 4a, identification of the optimal tool for the radiographic assessment of PsA in longitudinal observational studies will now be assessed. The WPAI and the selected radiographic measure can then be applied in the cross sectional study in chapter seven, to assess the extent to which structural damage (objective 4b), clinical disease activity, demographic and social factors are associated with WD measured with the WPAI (objective 5).
CHAPTER VI

THE FEASIBILITY, RELIABILITY AND SENSITIVITY TO CHANGE OF FOUR RADIOGRAPHIC SCORING METHODS IN PATIENTS WITH PSA

Investigating the association of work disability with disease severity is an important aspect of understanding the relationship between disease and disability. The definitive measure of disease severity is evidence of structural damage determined by radiographic damage. There are a number of radiographic measures used in psoriatic arthritis but no agreement regarding which is the optimal measure to use in observational studies and there are no comparison studies upon which to base an informed decision. This current study addresses objective four (a) of my thesis to assess the feasibility, reliability and sensitivity to change of four radiographic scoring methods in longitudinal observation studies of psoriatic arthritis (PsA). This study has been reported resulting in a small amount of repetition.121

INTRODUCTION

The measurement of radiographic joint damage is essential in characterising disease severity, progression and prognosis. Radiographic damage has been demonstrated in psoriatic arthritis (PsA) in both early and established disease.26, 122 It is a core outcome measure in both randomised control trials (RCTs) for novel therapies as well as longitudinal observational studies and is included in the core set of outcomes recommended for use in PsA clinical trials by the Outcome Measures in Rheumatoid Arthritis (OMERACT) consortium.42

Several scoring methods have been proposed for use in PsA including the Modified Sharp score (MSS)123, 124, the Sharp-van der Heijde modified method (VDH)124, 125, Modified Steinbroker (STB)126 and psoriatic arthritis Ratingen score (PARS)98. With the exception of the Ratingen method these scoring methods were designed and validated for use in rheumatoid arthritis and subsequently modified for use in PsA.
The choice of radiographic outcome measure to use in PsA RCTs and longitudinal observational studies was discussed at the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) annual meeting 2012 in Stockholm. There was consensus that the Sharp-van der Heijde modified was the optimal tool to use in RCTs (where sensitivity to change is often the most important attribute of the outcome measure) but the most appropriate tool for use in LOS is yet to be determined. Agreement on the use of a single measure in LOS would improve comparison of study results between cohorts, pooling data and potentially aid meta-analyses. I set out to assess the feasibility, reliability and sensitivity to change of four radiographic scoring methods in PsA in order to inform discussion on the optimal method for longitudinal observational studies.

**METHODS**

This study was conceived, led and reported in the journal of Arthritis Care Research by myself. Postero-anterior radiographs of the hands and feet from fifty consecutive patients commenced on anti-Tumour Necrosis Factor (anti-TNF) therapy for PsA at the Royal National Hospital for Rheumatic Diseases were included. Radiographs taken at the point of anti-TNF commencement and two years prior were scored with each of the Steinbroker, modified Sharp, Sharp-van der Heijde modified method and psoriatic arthritis Ratingen methods. This selection of participants and radiographs was designed to capture patients likely to have sustained active disease and thus progression of radiographic damage upon which the sensitivity to change of each method could be compared. All radiographs included a ‘phantom phalanx’ as a reference for normal bone density. All selected patient’s fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria after retrospective assessment of case records.

**Radiographic scoring methods**

The radiographic techniques are described briefly below and summarised in Table 1. The Steinbroker is a global technique that scores the joints of the hands and feet for soft tissue swelling or periarticular osteopenia, erosion, joint space narrowing, total destruction (lysis or ankylosis) on a single scale. The Steinbroker was originally developed for use in rheumatoid arthritis and was modified for use in PsA through inclusion of the distal interphalangeal joints (DIPJs). The
modified Sharp and Sharp-van der Heijde modified methods are composite methods that score erosion and joint space narrowing separately and then are summed together in a total score. The Sharp-van der Heijde method was originally developed for use in rheumatoid arthritis then modified for use in PsA. The modified Sharp method was again adapted from the original method used in rheumatoid arthritis. The method I have used in this study is the same as that described by Ravindran et al. with the addition that I have included the feet as originally described by van der Heijde. Finally the psoriatic arthritis Ratingen method is the only method to be developed specifically for use in PsA. The psoriatic arthritis Ratingen method is a composite method that scores erosion and bony proliferation characteristic for PsA which are then summed in a total score.

Radiographic methods
Standard antero-posterior radiographs of the hands and forefeet were taken on to Kodak DirectView phosphor storage plates. Directly after the images were captured the phosphor plates were scanned and digitised using the Kodak DirectView CR 950 system. Images were then viewed and scored on the Centricity Web viewer (V3.0.10) on a standard Hewlett Packard monitor (1440-900 pixel spacing) with the images preserved at the original 1:1 ratio, all other viewing tools were allowed.

Reading strategy
Two readers, WT (myself) and DJ (co-author Dr Deepak Jadon) trained in the four scoring methods. Using two readers reduces the impact of potential reading errors or bias that can arise from a from a single reader or scoring by consensus where a senior assessor may influence the reading of the junior member. The training in scoring methods involved pre-study training in the precise definitions of radiographic findings of PsA as described by Taylor et al., literature review of each method, contact with the original authors for clarification where required, then practice with supervision and discussion with an experienced musculoskeletal radiologist (Co-author Dr Graham Robinson) over a two month period. To determine reliability, ten sets of hand and feet radiographs were scored by both WT and DJ with all four techniques in random order to assess inter-rater
reliability, and then scored one month later to estimate intra-rater reliability. The remaining 40 radiographs were then scored (20 by WT and 20 by DJ) with the prior score and radiographs available to optimise sensitivity to change. An assumption of progression only was made for all scores, thus no improvement was recorded.

Statistical analysis
Statistical analysis was performed by Dr G Shaddick, department of mathematics, University of Bath, UK. Demographic data was analysed using descriptive statistics. Feasibility was estimated using the average time taken to score each method. Measurement error was estimated by re-scoring ten films by the same rater (intra-rater reliability) and by the other rater (inter-rater reliability). Differences are reported as recommended using both intra-class correlation coefficients (ICC) and visually by plotting the difference in change of scores against the mean change by both raters (Bland-Altman plots).

Sensitivity to change is reported using multiple methods to allow comparison with prior reports. A two-way analysis of variance was performed with an interaction between patient and time leaving a residual from which the Standard Error of the Mean (SEM) could be estimated. The Standardised Response Mean (SRM) is a unit-less expression of change calculated as the ratio of the mean difference between baseline and follow up score divided by the standard deviation of this difference. An SRM of >0.8 is considered to have a high potential of detecting change. I also report the Smallest Detectable Change (SDC) defined as the smallest difference that can be detected over and above measurement error. A similar method of reporting this is the Smallest Detectable Difference (SDD). The SDD is a less appropriate method to use in this study because I have assessed radiographs with the prior film and score available meaning the assessments cannot be considered to be truly independent. In this instance the SDD will overestimate the measurement error, however, I have reported the SDD to allow for comparison with prior reports. I also report the SDC and SDD as a percentage of the total scores to allow comparison between methods.
The study was approved by the Bath Research Ethics Committee and has been conducted in accordance with the Declaration of Helsinki. All participants signed informed consent.

RESULTS
All patients fulfilled CASPAR criteria for psoriatic arthritis. The mean age of patients at the baseline assessment was 50 years (sd 12.1; median 53 years, range 49). The mean disease duration at baseline was 10 years (sd 8.4; median 8 years, range 29). The mean interval between radiographs was 25 months (sd 9.6; median 26 months, range 36). The mean (sd) baseline score for the Steinbrocker, psoriatic arthritis Ratingen, modified Sharp and Sharp-van der Heijde methods were 15.4 (21.63), 13.2 (25.23), 26.3 (39.05) and 26.8 (38.25).

The intra-rater reliability was high for all methods (Table 2). The baseline inter-rater reliability was high for the Sharp-van der Heijde, modified Sharp and psoriatic arthritis Ratingen scores at 0.95 (95% confidence interval (CI) 0.83-0.99), 0.94 (95% CI 0.78-0.96) and 0.89 (95% CI 0.64-0.97), respectively. The baseline inter-rater reliability for the Steinbroker was low at 0.42 (95% CI -0.21-0.81). Review of the 10 films revealed the source to be poor agreement on the presence of periarticular osteopenia in three of the ten cases. All 50 baseline radiographs were therefore scored using the Steinbroker by both readers to better reflect the frequency of osteopenia in PsA and hence more accurately estimate the performance of the Steinbroker. The baseline inter-rater reliability for all 50 radiographs was 0.88 (95% CI 0.77-0.94).

The sensitivity to change of the methods is reported in Table 3. Using the SDC expressed as a percentage of the total score allows comparison between scores. The Sharp-van der Heijde score has the greatest ability to detect change followed by the modified Sharpe score, psoriatic arthritis Ratingen and Steinbroker at 1.2%, 1.4%, 2.1% and 2.9% respectively. The sensitivity to change of the methods using the SRM demonstrated the Sharp-van der Heijde followed by the modified Sharp score to have the greatest ability to detect change at a level approaching 0.80. The Steinbroker and psoriatic arthritis Ratingen showed less sensitivity to change with levels of 0.46 and 0.44 respectively.
<table>
<thead>
<tr>
<th>Scoring methods</th>
<th>Scales</th>
<th>Total erosion score</th>
<th>Total JSN score</th>
<th>Total score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STB</strong></td>
<td>42 Joints of the hands and feet: Scale 0-4</td>
<td>N/A</td>
<td>N/A</td>
<td>168</td>
</tr>
<tr>
<td></td>
<td>0 is normal.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 is juxta-articular osteopenia or soft tissue swelling.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 indicates the presence of any erosion.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 the presence of erosion and joint space narrowing.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 total joint destruction (lysis or ankylosis).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MSS</strong></td>
<td>54 joints (42 hands, 12 feet) for erosion: scale 0-5</td>
<td>270</td>
<td>216</td>
<td>486</td>
</tr>
<tr>
<td></td>
<td>0 = no erosion.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = one discrete erosion or involvement of &lt; 21% of the joint are by erosion.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = two discrete erosions or involvement of 21-40% of the joint.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = three discrete erosions or involvement of 41-60% of the joint.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = four discrete erosions or involvement of 61-80% of the joint.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 = extensive destruction involving more than 80% of the joint.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VDH</strong></td>
<td>52 joints (42 hands, 10 feet) for erosion: scale 0-5 (hands) 0-10 (feet)</td>
<td>320</td>
<td>208</td>
<td>528</td>
</tr>
<tr>
<td></td>
<td>0 = no erosions.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = discrete erosion.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = large erosion not passing the midline.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = large erosion passing the mid-line.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = combination of below</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 = combination of below</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PARS</strong></td>
<td>52 joints (42 hands, 10 feet) for JSN: scale 0-4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0 = normal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = asymmetrical minimal narrowing with loss of up to a maximum of 25%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = definite narrowing with loss of up to 50% of the normal space</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = definite narrowing with loss of 50–99% of the normal space or subluxation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = absence of a joint space, presumptive evidence of ankylosis, or complete subluxation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PARS</strong></td>
<td>40 joints (30 hands, 10 feet) for proliferation: scale 0-4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0 = normal.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 = bony proliferation measured from the original bone surface of 1-2mm, or clearly identifiable bone growth not exceeding 25% of the original diameter of the bone.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 = bony proliferation of 2-3mm or bone growth between 25 to 50%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 = bony proliferation &gt;3mm or bone growth &gt;50%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 = bony ankylosis.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Steinbroker method (STB), Sharp van der Heijde method (VDH), Modified Sharp method (MSS), Ratingen method (PARS), Joint space narrowing (JSN) *Proliferation
Table 2

Inter/ Intra-rater reliability of each scoring method

<table>
<thead>
<tr>
<th>Method</th>
<th>Range</th>
<th>Inter rater reliability (95% CI)</th>
<th>Intra rater reliability (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Baseline</td>
<td>Follow up</td>
</tr>
<tr>
<td>STB</td>
<td>0-168</td>
<td>0.42 (-0.21-0.81)</td>
<td>0.40 (-0.23-0.81)</td>
</tr>
<tr>
<td>STB (n=50)</td>
<td></td>
<td>0.88 (0.77-0.94)</td>
<td></td>
</tr>
<tr>
<td>MSS</td>
<td>0-486</td>
<td>0.94 (0.78-0.96)</td>
<td>0.96 (0.86-0.99)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0-270</td>
<td>0.77 (0.35-0.94)</td>
<td>0.64 (0.10-0.90)</td>
</tr>
<tr>
<td>JSN</td>
<td>0-216</td>
<td>0.96 (0.86-0.99)</td>
<td>0.94 (0.81-0.99)</td>
</tr>
<tr>
<td>VDH</td>
<td>0-528</td>
<td>0.95 (0.83-0.99)</td>
<td>0.99 (0.96-1.00)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0-320</td>
<td>0.91 (0.70-0.98)</td>
<td>0.92 (0.72-0.98)</td>
</tr>
<tr>
<td>JSN</td>
<td>0-208</td>
<td>0.96 (0.87-0.99)</td>
<td>0.92 (0.73-0.98)</td>
</tr>
<tr>
<td>PARS</td>
<td>0-360</td>
<td>0.89 (0.64-0.97)</td>
<td>0.90 (0.65-0.97)</td>
</tr>
<tr>
<td>Destruction</td>
<td>0-200</td>
<td>0.69 (0.18-0.91)</td>
<td>0.69 (0.18-0.91)</td>
</tr>
<tr>
<td>Proliferation</td>
<td>0-160</td>
<td>0.90 (0.67-0.97)</td>
<td>0.85 (0.52-0.96)</td>
</tr>
</tbody>
</table>

Modified Steinbroker method (STB), Sharp-van der Heijde modified method (VDH), Modified Sharp method (MSS), psoriatic arthritis Ratingen score (PARS), Joint space narrowing (JSN)
Figure 1.
Bland-Altman plots to illustrate reliability of radiographic assessment between the two assessors. Difference in radiograph score between each rater plotted against mean score for each radiograph from both raters.

![STB](image1.png)

![MSS](image2.png)

![PARS](image3.png)

![VDH](image4.png)

Modified Steinbroker method (STB), Sharp-van der Heijde modified method (VDH), Modified Sharp method (MSS), psoriatic arthritis Ratingen score (PARS). STB original 10 plots in grey, full 50 baseline plots in black.

The feasibility of each method was estimated based on the mean time taken to score each film. The Steinbroker took the least time to score followed by the psoriatic arthritis Ratingen, Sharp-van der Heijde and modified Sharp at 6.2 minutes, 10.5 minutes, 14.4 minutes and 14.6 minutes respectively.


**DISCUSSION**

Radiographic assessment of joint damage in PsA is an important outcome measure in longitudinal observational studies, however the optimal method for use in this setting has not been determined and to our knowledge there are no reports comparing the existing methods. I report a comparison of four radiographic scoring methods used in PsA to inform discussion on the optimal method for use in the longitudinal observational setting.

In terms of feasibility each of these methods are readily available and interpretable as a simple summative score. The time required to apply each method differs considerably in our study from 6.2 minutes to 14.6 minutes. An essential attribute of a scoring method for use in longitudinal observational studies is that it can be readily learned and applied feasibly. The ‘feasibility barrier’ has resulted in very limited radiographic data collection from observational cohorts. As may be expected, the Steinbroker global score is the most feasible and the time required to apply the composite scores is proportional to the number of areas scored (psoriatic arthritis Ratingen<Sharp-van der Heijde<modified Sharp). Whilst there is no threshold of time beyond which a score becomes unfeasible, the Sharp-van der Heijde and modified Sharp scores are more challenging in terms of time required for application in longitudinal observational studies.

In this current study I have found good agreement between assessors and good test-re-test reliability. The exception was osteopenia in the Steinbroker. The inter/intra-rater reliability estimates for this study (baseline inter 0.88 and intra for both readers 0.99/ 1.0) are comparable with the original reports (inter 0.86 and intra for both readers 0.81/ 0.80)\(^\text{126}\). I have found the inter-rater reliability was poor (0.42) amongst the initial ten patients due to disagreement in three cases of possible osteopenia but rose to more acceptable levels (0.88) when applied to all 50 patients because less osteopenia was seen. The prevalence of periarticular osteopenia in PsA has not been reported but is thought to be less than rheumatoid arthritis\(^\text{131}\). Our group has previously reported a strong correlation between the modified Sharp score and periarticular osteopenia, present in 25 of the 73 PsA patient hand and feet radiographs included in the study\(^\text{26}\). Radiographic
osteoopenia is dependent on radiographic technique, varying according to choice of projection, exposure and capture media, thus may vary significantly between time-points and radiographers. Determining the presence of osteopenia is also subjective and therefore prone to variation. For these reasons osteopenia was removed from a number of radiographic scoring techniques in rheumatoid arthritis. It may be argued therefore that any potential benefits of retaining osteopenia in a measure for use longitudinal observational studies of PsA are outweighed by these disadvantages.

Regarding sensitivity to change we found the smallest detectable change to be greater than the mean change over two years in all techniques which is an important finding. The smallest detectable difference/ smallest detectable change and minimal detectable difference are study specific (a function of mean change and measurement error) but are infrequently reported in trials. There are no previous reports directly comparing the sensitivity to change of the Steinbroker, modified Sharp or Sharp-van der Heijde in PsA. The original psoriatic arthritis Ratingen method reported a minimal detectable change (calculated from the square root of the standard deviation of the inter-rater variance) for the total score, proliferation score and destruction score of 16.5, 8.4 and 11.5, respectively, which are comparable with our smallest detectable difference of 12.7, 5.8 and 7.3, respectively. Guillemin et al. examined the reproducibility and sensitivity to change of five methods including the Sharp-van der Heijde in rheumatoid arthritis. The mean change in the Sharp-van der Heijde score exceeded the smallest detectable difference for the total, erosion and JSN scores in their study (9.7, 5.8 and 7.2, respectively) yet the smallest detectable difference remains comparable with our study (10.8, 7.3 and 7.3, respectively). Sharp et al examined the variability of precision of the modified Sharp method among readers from the datasets of six studies in rheumatoid arthritis. Considerable variability between readers and the mean smallest detectable difference was greater than the mean progression, as we have found in our present study. I found that the smallest detectable difference/ change (normalised as a percentage of the total score to allow comparison) estimates were ranked as might be expected (Steinbroker>psoriatic arthritis Ratingen>modified Sharp>Sharp-van der Heijde). The smallest detectable difference/ change is largest for the global Steinbroker
score which assesses radiographic change as either present or absent rather than graded, thereby allowing less flexibility to detect change. The Sharp-van der Heijde score is consistently the most sensitive to change than the score from which it was derived (the modified Sharp score). Finally the psoriatic arthritis Ratingen score is more sensitive than the Steinbroker as it is a composite rather than global score allowing grading of erosion and proliferation but not as sensitive as the modified Sharp and Sharp-van der Heijde scores partly because it includes the wrist as a single joint rather than multiple small joints.

Other parameters within the scoring methods are worth noting. The soft tissue swelling element of the Steinbroker is an additional source of variability, particularly at the MTPJs there is a less clear view of the soft tissues. The scoring of JSN is not specific to PsA and can occur in concurrent osteoarthritis and thus over-estimate progression of PsA. The psoriatic arthritis Ratingen includes a measure of proliferation which was the only radiographic change sufficiently specific to PsA to justify inclusion in the CASPAR criteria for PsA\textsuperscript{76}. Finally, the composite scores preserve data separately on erosion, joint space narrowing or in the case of the psoriatic arthritis Ratingen proliferation, whereas such information is limited in a global score.

The findings of this study should be interpreted in light of certain methodological limitations. I have not blinded the chronological order of radiographs and have had the prior score available for comparison when scoring. This introduces the possibility of expectation bias, potentially overestimating change. However, blinding to films may result in failure to detect progression. This was demonstrated in a study of rheumatoid arthritis which showed that blinding assessors to the chronology of films can introduce a measurement error that results in a loss of signal and hence underestimation of progression.\textsuperscript{128} A second study from the same group showed that expert raters agreed most when the sequence of films was known.\textsuperscript{136} Furthermore, two of the methods, the psoriatic arthritis Ratingen and Sharp-van der Heijde scores were both developed in unblinded studies with known chronological order and so we have applied these tools as they were developed. The purpose of this present study is to identify which radiographic scoring method has the appropriate properties to be used in
longitudinal observational studies where radiographs are obtained and scored in routine clinical practice thereby un-blinded and in known chronological order. It is not feasible to consider storing radiographs for future scoring in a blinded study as this would be too time consuming. Even the quickest score to perform, the Steinbroker, is used routinely in only one centre (Toronto psoriatic arthritis research unit). Radiographs are scored un-blinded in known chronological order at the end of a routine clinic using a consensus approach (unpublished communication, Dr D Gladaman). This allows a gradual accumulation of data over many years that would be unfeasible to perform retrospectively. The un-blinded approach taken in this study is therefore in keeping with the methodology used in the development of two of the scores and importantly is the way the tool is intended to be used in practice but this method does introduce the risk of expectation bias.

We have selected patients with established disease in the two years prior to anti-TNF therapy and therefore likely to have progressive disease in order to study and compare the sensitivity to change of each method. The exact chronology of radiographic change in psoriatic arthritis is not yet established and therefore it is possible the scores may perform differently in early disease. A final potential limitation is that we have scored the radiographs with the assumption of no improvement as stipulated in the Sharp-van der Heijde scoring instructions. We applied the same rule to all methods to avoid biasing the results. Unblinded reporting may have had the effect of overestimating the standardised response mean of the Steinbroker which includes soft tissue swelling which may well improve over the study period.

I have found that the modified Sharp and Sharp-van der Heijde methods are the most reliable and sensitive to change in this present study, but took longer to perform. The Steinbroker is the most feasible but lacks the sensitivity of the modified Sharp and Sharp-van der Heijde methods. The smallest detectable change of the psoriatic arthritis Ratingen is close to that of the modified Sharp and Sharp-van der Heijde methods but is quicker to perform and may be more specific to PsA through inclusion of proliferation. The findings of this study can be used
to inform discussion on potential modifications and further study of these existing radiographic scoring methods for use in PsA longitudinal observational studies.

For the purposes of my thesis I have chosen the psoriatic arthritis Ratingen score as the measure of radiographic damage for two reasons. It is the only score that includes PsA specific radiographic change though the inclusion of bone proliferation. Furthermore the psoriatic arthritis Ratingen offers an appropriate balance of feasibility (over the modified Sharp and Sharp-van der Heijde methods) and sensitivity to change (over the Steinbroker) for the study undertaken in chapter eight.

The body of work of this thesis thus far has related to a review of the literature (chapter I) and then the development or assessment of classification criteria (chapter II) and outcome measures (chapters III and IV). The final results chapter of this thesis applies these measures and criteria to a cross sectional study of WD in PsA to address explore the associations of WD with structural damage (objective 4b), disease activity, clinical patient reported outcome measures, demographic and socioeconomic factors (objective five).
CHAPTER VII

DISEASE AND SOCIOECONOMIC ASSOCIATIONS OF WORK DISABILITY IN PSORIATIC ARTHRITIS

This current chapter explores the associations of work disability with structural damage (objective 4b), disease activity, clinical PRO’s, demographic and socioeconomic factors (objective five). In order to achieve these objectives and to allow future longitudinal study of WD as part of planned postdoctoral studies a multicentre observational cohort study design has been employed in a study named Long Term Outcomes in Psoriatic Arthritis II (LOPAS II). This chapter, and hence the objectives 4b and 5 will be addressed through analysis of the cross sectional baseline data from LOPAS II. I conceived the LOPAS II study protocol, led the funding, ethical approval, running and reporting of the study. The body of work in this chapter have been published resulting in some minor duplication (In Press).

INTRODUCTION

The existing body of knowledge relating to WD in PsA has been reviewed in chapter II. In summary there is intermediate quality evidence that levels of unemployment (20-50%) and WD (16-39%) are high and associated with longer disease duration, worse physical function, high joint count, low educational level, female sex, erosive disease and manual work. There is sparse low quality evidence that WD is worse in those with PsA than psoriasis alone. Interpretation of this data is hampered by the small number of reports and heterogeneity of data collected. In particular data on the associations of WD are limited by the prior lack of a validated measure. I set out to determine to what extent structural damage, clinical disease activity, demographic and social factors are associated with unemployment, absenteeism, presenteeism and productivity loss measured with the work productivity and activity index.

METHODS

LOPAS II is a multicentre observational cohort study of four hundred patients with PsA conceived to explore the associations of WD with disease activity and
study the effect of drug treatment. Hospitals at twenty three sites across England participated in this study (figure 1), recruited through support from the National Institute of Health Research (NIHR). Patients fulfilling CASPAR criteria for PsA commencing a new DMARD or anti-TNF treatment were recruited to this two year follow up study. Follow up was based on routine clinical care such that follow up was twelve weekly if the treating clinician considered the psoriatic arthritis to be poorly controlled and six monthly if well controlled. LOPAS II is an observational study with no treatment protocol, individual treatment decisions were made by the treating clinician. The following outcome data was collected at the routine clinic visits: physician assessment (DAPSA composite score) and patient reported outcomes (physical function- health assessment questionnaire, health related quality of life- EQ5D, fatigue- FACIT, skin specific quality of life-DLQI, global and domain specific disease activity visual analogue scores, comorbidities, demographic details, education, location, employer awareness/helpfulness Likert scale) and international standard classification of occupations- ISCO work type. Radiographs of the hands and feet were taken at the baseline visit and scored with the psoriatic arthritis Ratingen score. Work disability was assessed with the WPAI which reports work disability as percentage of; absenteeism (work time missed), presenteeism (impairment at work/ reduced effectiveness) and work productivity loss (overall work impairment/ absenteeism plus presenteeism). Details regarding the individual outcomes are found in the methods chapter. The patient information sheet and consent form can be found in appendix 9 and 10 respectively.

Statistical analysis
Statistical analysis of demographic data has been undertaken in SPSS v20 by the author (WT). Associations between potential explanatory variables and unemployment status were examined using multivariate logistic regression and with per cent presenteeism and productivity loss amongst those of working age using multivariate linear regression models. The distribution of absenteeism showed small numbers in a number of categories and was converted into a binary variable representing either present (0%) or absent (100%) and analysed using multivariate logistic regression. The regression analyses were undertaken using the statistical package R (2011) by GS. All measured variables were considered
for inclusion, including location. Age demonstrated a non-linear relationship therefore a quadratic term was applied. Two way interactions were considered in all models but no significant effects at this level were observed.

**RESULTS**
The number of recruits contributed from each centre is displayed in figure 1.

![Figure 1](image_url)

**Figure 1** Location of study sites for the LOPAS II study. Sites are labelled by number recruited at each site.

Of the 400 participants three hundred and eighteen were of UK working age (18-65 years), mean age 46.8 years (sd 11.02), mean disease duration 5.8 years (sd 8.00), 49.9% female. Two hundred and twenty six of the study participants (64%)
were in work with a further ten over retirement age, but still working. Ninety two participants of working age (26%) were unemployed. Comparison of demographic, clinical, radiographic and socioeconomic factors of those working (any age) and those not working (18–65 years only) are presented in table 1.

Absenteeism, presenteeism and productivity loss of the 236 participants in work the mean was 14% (sd 29.0), 39% (sd 27.2) and 46% (sd 30.4) respectively (figure 2).

Figure 2 LOPAS II participant patient reported work disability amongst employed participants over the preceding seven days measured with the WPAI estimated

Negative influences upon remaining in employment included greater age, duration of two to five years and worse physical function (Table 2). The effect of age was an odds ratio (OR) of 0.99 (95% CI 0.994 to 0.999, p=0.02) such that for every additional year the risk of unemployment increases by 1%. This change is only
Table 1 LOPAS II comparison of study participants working (any age) and those unemployed (working age)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not Working (working age) N= 92</th>
<th>Working (any age) N=236</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEMOGRAPHIC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age mean(sd)</td>
<td>55 (14.7)</td>
<td>48 (11.01)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sex male (%)</td>
<td>44%</td>
<td>50.1%</td>
<td>0.318</td>
</tr>
<tr>
<td><strong>DISEASE FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis duration years mean (sd)</td>
<td>8 (9.8)</td>
<td>5.8 (7.77)</td>
<td>0.045</td>
</tr>
<tr>
<td>DAPSA mean (sd)</td>
<td>45 (26.1)</td>
<td>45 (29.7)</td>
<td>0.930</td>
</tr>
<tr>
<td>68 Tender joint count mean (sd)</td>
<td>17 (14.8)</td>
<td>15 (11.6)</td>
<td>0.284</td>
</tr>
<tr>
<td>66 Swollen joint count mean (sd)</td>
<td>8 (6.9)</td>
<td>7 (6.8)</td>
<td>0.578</td>
</tr>
<tr>
<td>CRP mean (sd)</td>
<td>14 (18.2)</td>
<td>15 (29.8)</td>
<td>0.676</td>
</tr>
<tr>
<td>Global VAS 0-100 mean (sd)</td>
<td>62 (23.8)</td>
<td>66 (65.8)</td>
<td>0.960</td>
</tr>
<tr>
<td>Pain VAS 0-100 mean (sd)</td>
<td>61 (24.9)</td>
<td>65 (66.1)</td>
<td>0.566</td>
</tr>
<tr>
<td>Joint VAS 0-100 mean (sd)</td>
<td>62 (22.9)</td>
<td>68 (91.5)</td>
<td>0.780</td>
</tr>
<tr>
<td>Skin VAS 0-100 mean (sd)</td>
<td>39 (30.3)</td>
<td>46 (93.1)</td>
<td>0.769</td>
</tr>
<tr>
<td>HAQ 0-3 mean (sd)</td>
<td>1.3 (0.78)</td>
<td>1 (0.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EQ5D VAS 0-100 mean (sd)</td>
<td>0.4 (0.36)</td>
<td>0.5 (0.28)</td>
<td>0.013</td>
</tr>
<tr>
<td>FACIT mean (sd)</td>
<td>22 (10.9)</td>
<td>21 (9.9)</td>
<td>0.247</td>
</tr>
<tr>
<td>DLQI 0-30 mean (sd)</td>
<td>5 (5.9)</td>
<td>4 (5.3)</td>
<td>0.297</td>
</tr>
<tr>
<td>Radiographic score:</td>
<td>19 (31.7)</td>
<td>8 (16.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any co-morbidity * yes</td>
<td>52%</td>
<td>31%</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>SOCIOECONOMIC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WPAI %</td>
<td>n/a</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Absenteeism</td>
<td>14% (28.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presenteeism</td>
<td>39.0% (27.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Productivity loss</td>
<td>40.0% (30.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activity Impairment</td>
<td>49% (26.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISCO work type valid % (n)</td>
<td></td>
<td></td>
<td>0.819</td>
</tr>
<tr>
<td>Managers</td>
<td>11% (8)</td>
<td>12% (27)</td>
<td></td>
</tr>
<tr>
<td>Professionals</td>
<td>20% (14)</td>
<td>18% (40)</td>
<td></td>
</tr>
<tr>
<td>Associate professionals</td>
<td>23% (16)</td>
<td>21% (47)</td>
<td></td>
</tr>
<tr>
<td>Clerical</td>
<td>12% (8)</td>
<td>7% (16)</td>
<td></td>
</tr>
<tr>
<td>Sales</td>
<td>8% (6)</td>
<td>14% (33)</td>
<td></td>
</tr>
<tr>
<td>Skilled agricultural</td>
<td>4% (3)</td>
<td>2% (5)</td>
<td></td>
</tr>
<tr>
<td>Craft</td>
<td>8% (6)</td>
<td>13% (29)</td>
<td></td>
</tr>
<tr>
<td>Plant operators</td>
<td>3% (2)</td>
<td>6% (13)</td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>11% (8)</td>
<td>7% (15)</td>
<td></td>
</tr>
<tr>
<td>Military</td>
<td>0% (0)</td>
<td>0% (0)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>n/a (21)</td>
<td>n/a (10)</td>
<td></td>
</tr>
<tr>
<td>Employer aware</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Very helpful</td>
<td>5% (2)</td>
<td>25% (41)</td>
<td></td>
</tr>
<tr>
<td>Helpful</td>
<td>18% (7)</td>
<td>35% (58)</td>
<td></td>
</tr>
<tr>
<td>No help required</td>
<td>42% (16)</td>
<td>30% (49)</td>
<td></td>
</tr>
<tr>
<td>Unhelpful</td>
<td>21% (8)</td>
<td>7% (11)</td>
<td></td>
</tr>
<tr>
<td>Very unhelpful</td>
<td>13% (5)</td>
<td>3% (5)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>n/a (54)</td>
<td>n/a (71)</td>
<td></td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td>0.081</td>
</tr>
<tr>
<td>No formal education</td>
<td>1% (1)</td>
<td>0% (0)</td>
<td></td>
</tr>
<tr>
<td>Lower secondary</td>
<td>63% (56)</td>
<td>49% (110)</td>
<td></td>
</tr>
<tr>
<td>Upper secondary</td>
<td>12% (11)</td>
<td>26% (58)</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>24% (21)</td>
<td>25% (56)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>n/a (3)</td>
<td>n/a (11)</td>
<td></td>
</tr>
</tbody>
</table>

*Comorbidities yes if any of Diabetes, Hypertension, Hypercholesterolemia, Cerebrovascular disease or Cardiovascular disease, % displayed is the valid per cent.

Difference between working/ not working ANOVA P value.

DAPSA - disease activity in psoriatic arthritis, CRP - C reactive protein, VAS visual analogue scale, HAQ health assessment questionnaire, EQ5D Euroqol 5 domains score, FACIT functional assessment of chronic illness therapy, DLQI dermatology quality of life index, WPAI work productivity and activity questionnaire

ISCO International classification of occupation
likely to achieve clinical significance when considered over decades. Disease duration of 2 to 5 years exerted a strongly negative influence upon remaining in employment OR 0.41 (95% CI 0.180-0.953 p=0.03). The association of worse physical function with unemployment was also strong, such that the risk of unemployment increased by OR 0.56 (0.343 – 0.926, p=0.02) for every increase of 1 in the health assessment questionnaire (HAQ score range 0-3). Finally employer helpfulness exerts a strongly positive influence on remaining in employment. If participants rated an employer as helpful the likelihood of employment was increased by an OR of 15.10 (95% CI 4.658-69.355, p=<0.01). This positive effect was sustained even if the participant perceived that no help is required, OR 3.22 (95% CI 1.264-8.229, p<0.01).

Table 2 Associations with employment/ unemployment (working age)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1- logistic Employed</th>
<th>Odds Ratio (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.01 (0.000 to 1.622)</td>
<td>p=0.07</td>
</tr>
<tr>
<td>Age years</td>
<td>1.31 (1.029 to 1.672)</td>
<td>p=0.03</td>
</tr>
<tr>
<td>Age (quadratic) years</td>
<td>0.99 (0.994 to 0.999)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Disease duration 2-5 years (n=61)</td>
<td>0.41 (0.180 to 0.953)</td>
<td>p=0.03</td>
</tr>
<tr>
<td>Disease duration &gt;5 years (n=80)</td>
<td>1.36 (0.557 to 3.319)</td>
<td>p=0.49</td>
</tr>
<tr>
<td>HAQ 0-3</td>
<td>0.56 (0.343 to 0.926)</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Employer very helpful (n=63)</td>
<td>15.10 (4.658 to 48.753)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Employer helpful (n=43)</td>
<td>17.46 (4.395 to 69.355)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>No help required (n=59)</td>
<td>3.22 (1.264 to 8.229)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Employer unhelpful (n=18)</td>
<td>1.29 (0.325 to 5.155)</td>
<td>p=0.72</td>
</tr>
<tr>
<td>Employer very unhelpful (n=9)</td>
<td>0.39 (0.039 to 3.942)</td>
<td>p=0.42</td>
</tr>
</tbody>
</table>

Intercept: represents the odds ratio when all variables are zero such that age is zero, disease duration 0-1 years, global/ joint VAS zero, HAQ zero, Employer unaware, Significant associations in bold.

Absenteeism as a binary variable (present or absent over the prior week) was associated with worse joint activity visual activity scale (0-100) such that for every increase in of 10 the OR of absenteeism increased by 4% (OR 1.04 (95% CI 1.018-1.055, p=<0.01)).
Greater global, joint specific disease activity and worse physical function exerted a negative influence on presenteeism and productivity loss (Table 3). For every increase in global disease activity visual analogue scale (0-100) of 10 there was an increase of presenteeism of 2% (estimate 0.02, 95% CI 0.001-0.053, p=0.01) and 3% for productivity loss (estimate 0.03, 95% CI 0.003-0.055, p=0.01). Worse physical function was strongly associated with more presenteeism and productivity loss. For every increase in health assessment questionnaire of 1 presenteeism was 47% higher (estimate 0.63, 95% CI 0.005-1.200, p=0.03) and productivity loss 12% higher (estimate 0.12, 95% CI 0.066-0.182, p<0.01).

**Table 3** Associations with presenteeism and productivity loss amongst those working (any age) n=200

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 2- Linear</th>
<th>Model 3- Linear</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Presenteeism (0-1)</td>
<td>Productivity loss (0-1)</td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.02 (-0.114 to 0.074) p=0.67</td>
<td>-0.05 (-0.143 to 0.040) p=0.27</td>
</tr>
<tr>
<td>Disease duration 2-5 years (n=36)</td>
<td>0.02 (-0.066 to 0.112) p=0.61</td>
<td></td>
</tr>
<tr>
<td>Disease duration &gt;5 years (n= 63)</td>
<td>-0.09 (-0.167 to -0.021) p=0.01</td>
<td></td>
</tr>
<tr>
<td>Global activity VAS 0-10</td>
<td>0.02 (0.001 to 0.053) p=0.01</td>
<td>0.03 (0.001 to 0.06) p&lt;0.01</td>
</tr>
<tr>
<td>Joint activity VAS 0-10</td>
<td>0.03 (0.006 to 0.055) p=0.01</td>
<td>0.02 (0.000 to 0.049) p=0.05</td>
</tr>
<tr>
<td>HAQ 0-3</td>
<td>0.63 (0.005 to 1.200) p=0.03</td>
<td>0.12 (0.066 to 0.182) p&lt;0.01</td>
</tr>
</tbody>
</table>

Intercept: represents the estimate when all variables are zero such that age is zero, disease duration 0-1 years, global/joint VAS zero, HAQ zero, Employer unaware, Significant associations in bold

**DISCUSSION**

I report the associations of unemployment, absenteeism, presenteeism and productivity loss amongst a well classified cohort of patients with PsA.

With regards to unemployment we report the novel findings that greater age and recent disease are associated with unemployment. Furthermore patient reported employer awareness and helpfulness exerts a strongly positive influence on remaining in employment, even if patients perceive no help is required.
The British society of rheumatologists biologics register is the only study to date to investigate the influence of age upon employment and did not find an association.\textsuperscript{39} The study by Wallenius \textit{et al} examined disability benefit collection in a cohort of patient with PsA aged between 18-45 years controlled for age in their regression.\textsuperscript{9} In this present study the absolute effect of each year of age upon becoming unemployed is small, an increase of 1\% for every additional year of age. PsA is however a chronic disease and when considered over decades this effect would become a clinically meaningful burden.

Four studies have previously reported that increasing disease duration negatively influences remaining in employment.\textsuperscript{9, 39, 54, 73} The finding in our present study of increased unemployment in those with early disease (2 to 5 years) is an interesting one and in keeping with the finding of high levels of unemployment in the first five years of rheumatoid arthritis reviewed by Nikiphorou \textit{et al}\textsuperscript{137}. Reports in rheumatoid arthritis have been inconsistent as reviewed by de Croon \textit{et al}.\textsuperscript{43} The findings in this present study of increased unemployment in those with disease for 2-5 years do differ from prior reports in PsA and differences in study designs may account for this. First, two studies were restricted to patients on anti-TNF introducing the possibility of confounding by indication.\textsuperscript{39, 73} Second, differing social security systems may influence an individual’s decision to stop work and the other three studies were conducted in countries other than the UK; Germany\textsuperscript{54} Norway\textsuperscript{9} and Sweden\textsuperscript{73}. Finally I have measured relatively short duration absenteeism with the WPAI which has a recall period of one week whereas these prior studies were based on government social security benefit collection records thus measuring more long-term absence from work.

To my knowledge this is the first time patient reported employer helpfulness has been investigated in PsA. The findings of this study suggest that patient reported employer awareness and helpfulness are positively associated with remaining in employment, even if patients perceive no help is required. The strength of the association between employer helpfulness and employment in the regression model may account for variables identified in previous studies such as worse physical function\textsuperscript{9, 39, 70}, joint disease\textsuperscript{39, 70, 71}, fatigue\textsuperscript{70}, erosive disease\textsuperscript{9}, sex\textsuperscript{9, 39, 73} and education\textsuperscript{9, 54} not achieving significant associations and inclusion into the
final models. This finding emphasises the multifactorial influences upon WD and the importance of accounting for as many potentially confounding factors as possible.

Relating to absenteeism, presenteeism and productivity loss amongst those at work we report that only disease activity factors rather than demographic or socioeconomic factors influence performance. Specifically in this present study greater global, joint specific disease activity and worse physical function exerted a negative influence on presenteeism and productivity loss. Furthermore disease activity measures appear to exert a greater influence than severity (radiographic damage), which did not achieve inclusion into the final models. This is an interesting finding suggesting that although there are multiple potential influencing factors targeting disease may be appropriate when considering approaches to reducing absenteeism, presenteeism and productivity loss.

Prior studies have reported reduced patient reported work productivity amongst those taking anti-TNF for PsA\textsuperscript{39, 70, 71} however we report this finding amongst a wider population of patients taking both DMARD and anti-TNF treatment. The magnitudes of the associations of presenteeism with global and joint specific disease activity are modest (2% and 3% per 10% increase respectively). There is no data on the minimally important difference of presenteeism in PsA and this is a subject of further research by our group.

The finding that global and joint specific activity but not the domain of skin disease (skin specific activity visual analogue score or DLQI) reached statistical significance in the final models is consistent with prior reports comparing patients with PsA and those with psoriasis alone. Two studies have reported increased WD amongst patients with PsA versus patients with psoriasis alone.\textsuperscript{48, 51} To my knowledge this is the first study reporting the relative impact of joint and skin disease on WD and indicates that joint disease exerts the greatest influence in this cohort. It should be noted that the level of skin activity compared to joint activity was low (39% skin visual analogue versus 62% joint visual analogue amongst those not working). It is known that domains of disease activity can be divergent in PsA and the selection of patients in this study was from rheumatology clinics in
those having treatment escalation for PsA. By including people with relatively mild skin disease I may have overestimated the relative influence of the joint domain. Nonetheless the finding in this study that disease activity measures, which are potentially reversible, exert a negative influence upon performance at work adds strength to the theory that presenteeism/ productivity loss can be improved with treatment.

This study has a number of strengths and scores six out of seven (high quality) when measured against the quality measure from the systematic review in chapter three. The first strength is that the cohort is well classified; all participants fulfil the CASPAR criteria for PsA. Second work disability is the primary endpoint for LOPAS II and thus has data on multiple potential confounding factors available for inclusion in the analysis and we have measured a variety of types of WD (unemployment, absenteeism, presenteeism and productivity loss). Participants have been recruited regardless of age and this has enabled the dual analysis of unemployment amongst those of working age and measures of reduced effectiveness (WPAI) amongst those in work regardless of age. Third this is the first study to measure WD in PsA with a tool that has preliminary evidence for its validity PsA. Finally the multicentre nature of the study increases the generalizability of the findings.

The findings of this study need to be interpreted in light of certain methodological limitations. The multicentre study design allows a better reflection of socioeconomic status of the UK population and recruitment over an achievable timeframe. However there are a number of design limitations this introduces. First, the twenty-three recruiting centres were located across England though did not include London, potentially limiting the generalisability of the results. I have employed a spatial model to assess for geographic variation in WPAI however and no differences were detected. Second, the study design needed to be minimally burdensome to patients and clinicians to be taken on at multiple National Health Service (NHS) sites across the UK. This means that the data collection forms needed to be short enough to be feasible in this setting. As a result some data that may have been useful has not been collected to optimise feasibility such as a clinicians assessment of the psoriasis with a psoriasis area and
severity score (PASI). The PASI score was deemed too time consuming to conduct in clinical practice and the collection of the visual analogue score for skin and DLQI have both been collected and are known to correlate well with the PASI score.\textsuperscript{72, 97} Third, involving multiple sites increases the number of assessors thereby increasing measurement error for the clinically assessed tender and swollen joint count. I have made every effort to minimise inter rater variance across sites by providing one-to-one joint count training at the lead site (Royal National Hospital for Rheumatic Diseases- RNHRD), providing standardised joint count training material (DVD, poster and booklet) and encouraging the same assessor to perform all assessments at each site.\textsuperscript{138} Fourth, the inclusion criteria and sample size calculation were based on the prospective study to determine the difference between change in presenteeism between DMARD and anti-TNF treatment therefore the study that, after discussion at the transfer viva and with NJM and CdeV will now be undertaken as postdoctoral studies. Fifth, the study participants were recruited to the LOPAS II study at the time a new drug was commenced and therefore represent a group with active disease. Through selection of a cohort with active disease the influence of disease activity on WD may be over emphasised. Sixth, with respect to the assessment of employer helpfulness it should be noted that the Likert scale used in this study has not been validated. Further work to validate this measure is planned as part of post-doctoral studies. Finally there are some potential confounding factors that have not been included in this study such as depression, financial status and desire to work. Nonetheless the findings of this present study are certainly applicable to patients with active PsA and add to the evidence that active disease adversely affects WD.

In conclusion greater age, recent disease onset (2 to 5 years disease duration) and worse physical function exert a negative influence on remaining in employment. Patient reported employer awareness and helpfulness exerts a strongly positive influence on remaining in employment, even if patients perceive no help is required. In contrast in those who remain at work reduced effectiveness (presenteeism and productivity loss) are associated with the disease activity measures of greater global, joint specific visual analogue scales and worse physical function. Further prospective study is underway to investigate whether
ameliorating disease activity improves absenteeism, presenteeism and productivity loss.
CHAPTER VIII
DISCUSSION

The aims of my thesis were to systematically and critically review the current body of knowledge of work disability in psoriatic arthritis, examine the validity of the WPAI, estimate the burden of work disability using this tool and investigate the associations with disease activity, structural damage, demographic and social factors. My thesis reports a new body of knowledge addressing these objectives. The weaknesses of the individual studies have been discussed in the individual chapters and are not specifically revisited here. In this chapter I will discuss the findings of my thesis, by order of each objective, highlighting the key findings and their wider meaning before finally considering potential directions for further research.

OBJECTIVE ONE

Objective one of my thesis was to systematically review the current body of knowledge of work disability in PsA. I report the first systematic review of work disability in psoriatic arthritis, with the following key findings:

- There is intermediate quality evidence that work disability in PsA is high and is associated with longer disease duration, high health assessment questionnaire, high joint count, low educational level, female sex, erosive disease and manual work.
- There is sparse low quality evidence that work disability may be worse in those with PsA than psoriasis alone.
- There is no data on work disability in early PsA, the relative contribution of psoriasis in those with PsA or the role of other co morbidities such as fatigue, depression or the metabolic syndrome.
- Finally the evidence that disability at work is mitigated by treatment is limited to a small number of short duration biologics RCTs.

There has been increasing focus on work as an outcome in rheumatic disease during the conduct of this thesis. The journal ‘Rheumatology’ dedicated a themed edition to ‘work in rheumatic disease’ in 2012 (Issue 51) highlighting this
interest. More recently a study reported in abstract form by Gossec et al has drawn attention to the importance of work from the individual patient’s perspective. This study, presented at the EULAR conference in 2013 reported the preliminary development of a new ‘impact of disease’ score— the Psoriatic Arthritis Impact of Disease score (PsAID). This project incorporated the patient perspective from its inception with the intention of better capturing the true impact of disease. The first step in the PSAID study was to identify and select domains of disease to be included in the score. Focus group sessions were used to identify domains. One hundred and thirty nine participants were then asked to rank the identified domains according to the impact on their lives (physically, mentally and socially). A novel and interesting finding here was that work was found to be a high priority, ranking fourth highest behind pain, skin disease and fatigue. The importance attributed to work disability by patients with PsA will be recognised by incorporation of work in the PsAID.

The findings of the systematic review conducted in chapter two highlight the extent of the gaps in our current understanding of WD in PsA and identifies areas for further study including; the lack of a validated outcome measure, the lack of information in early disease and the incomplete understanding of the influencing factors. The review may also be used as a source of evidence to quantify the impact of disease in PsA. Quantifying the burden of disease is an important consideration when justifying the need for costly research and the systematic review will be a useful source of evidence.

The findings of the systematic review have informed the conducted of the research in my thesis beyond identifying the current body of knowledge. The review identified the lack of consensus on a measure of WD. Therefore I selected a work outcome that would allow separate analysis of individual work outcomes from presenteeism, absenteeism, productivity loss through to unemployment. This has enabled examination of influencing factors of each type of work disability. During the conduct of the systematic review it became clear that many studies had restricted the age of participants, making interpretation of the findings complex, as entire demographic bands were not included (such as those over retirement age who are still in work). Viewing this as a limitation to prior studies
I have not restricted the age of participants in the study examining associations with work disability (chapter seven). Having no age restriction allows individual analyses amongst those of working age when examining absolute levels of employment and analysis of those in work, irrespective of age, when assessing absenteeism and presenteeism.

Summarising the body of knowledge relating to work disability in psoriatic arthritis was hampered by a number of factors. First, there have been multiple outcome measures used in the research to date. These include, but are not limited to: unemployment, government records of disability benefit collection, absenteeism from work over varying lengths of time and patient productivity loss calculated in different ways (chapter 2, Tables 1 and 3). Multiple outcomes may be expected in any emerging field, until consensus is achieved, and this is certainly the case in work disability. In addition to a lack of consensus it has become clear that there is poor agreement between the existing candidate measures. This poor agreement leads to further uncertainty when comparing results between studies. Second, the differing populations and study designs amongst the small number of studies make meaningful comparison of the results difficult. Of particular note the studies to date are from a range of different countries, each with differing social security systems and therefore different incentives for leaving or remaining in the work place.

In summary the study of work disability in psoriatic arthritis is an emerging field with evidence from a small number of diverse studies that there is a high burden of disability, no consensus on a measurement tool and a wide variety of disease and non-disease related influencing factors. Evidence from the review has informed the conduct of the studies undertaken in my thesis and may be used in a wider setting to inform future research as well as contributing to the body of evidence relating to the burden and impact of PsA.

**OBJECTIVE TWO**

In order to examine the validity of the WPAI it was necessary to classify an existing cohort of patients to study. Objective two was therefore to classify an existing cohort of patients with PsA, according to the CASPAR criteria. The
cohort of patients’ at the Royal National Hospital for Rheumatic Diseases was started in 1989, however consensus on the use of the CASPAR classification criteria was only reached relatively recently in 2006. Prospective re-classification of this cohort was deemed unfeasible so it was necessary to assess the performance of the CASPAR criteria when applied retrospectively from medical case notes. I report the novel finding that:

- The feasibility, specificity and sensitivity of the CASPAR criteria are maintained when adapted for retrospective use to classify an established research cohort from medical records even in those with missing data.\(^{77}\)

This study has allowed the appropriate classification of an existing cohort of patients to study in order to address objective three. The wider application of this study is limited, as there are relatively few pre-existing cohorts in the wider research community that need to be retrospectively classified. Nonetheless it is important that any such cohorts are appropriately classified, as evidenced by the identification of fifteen patients amongst the RNHRD cohort whose diagnosis had changed from PsA since their original inclusion. Decision making in rheumatology practice is dynamic as clinical diagnosis can and does change over time, sometimes very gradually over years. As researchers we need to remain vigilant to such changes in long term observational cohorts and have appropriate, feasible and validated classification tools. Therefore the evidence presented in this study may be used to classify existing cohorts with confidence, thereby allowing confident interpretation of study findings.\(^{76}\)

**OBJECTIVE THREE**

Objective three of this thesis was to examine the feasibility, construct and discriminative validity of the WPAI in PsA. I report the following novel findings supporting the validity of the WPAI in psoriatic arthritis:\(^{121}\)

- Evidence supporting the feasibility of the WPAI in psoriatic arthritis though ease of application, low cost and ready interpretation.
- Evidence for the construct validity of the WPAI through correlation with other domains of disease activity including patient reported global disease activity, pain, physical function, health related quality of life and fatigue.
Evidence for the discriminative validity of the WPAI through discrimination between better or worse disease defined by the medians of: patient reported global disease activity, pain physical function, health related quality of life and fatigue.

This study therefore provides evidence supporting the validity of the WPAI in psoriatic arthritis. When considering the remaining aspects of validity according to the OMERACT filter the domain of responsiveness of the WPAI in PsA is yet to be determined. Responsiveness incorporates both sensitivity to change and stability of a measure when there has been no clinical change. Validation studies of the WPAI in rheumatoid arthritis and ankylosing spondylitis have demonstrated the tool has good responsiveness.\textsuperscript{67, 79} A prospective study is required to assess this domain and there are plans to address this as part of post-doctoral studies.

There are many work outcome measures available, as reviewed by Beaton et al, and the rationale for my selecting the WPAI has been discussed in the methods section.\textsuperscript{66} Briefly the WPAI is one of a small number of measures selected for further assessment by the OMERACT work special interest group and there is good evidence for its validity in two closely related conditions, rheumatoid arthritis and ankylosing spondylitis.\textsuperscript{67, 79} Despite these reports and the evidence reported in this thesis supporting the validity of the WPAI, doubt remains over the levels of agreement between the existing measures. A recent study has demonstrated poor agreement in the estimates of productivity loss between four existing methods.\textsuperscript{68} In this study of 250 patients with OA and rheumatoid arthritis the average numbers of lost hours (SD) over the prior two weeks due to presenteeism measured by the HLQ, WLQ, HPQ, and WPAI were 1.6 (3.9), 4.0 (3.9), 13.5 (12.5), and 14.2 (16.7) respectively.\textsuperscript{68} The cause of this poor agreement has yet to be determined. It is possible these differences arise from underling differences in the psychometric properties of the questionnaires. Each questionnaire has been developed independently and the differences in the questions and calculation methods may underpin the variance. However certain methodological considerations may in part account for these findings. The questionnaires have differing recall periods (HPQ and WPAI one week, HLQ and WLQ was two weeks) and arthritis is a variable condition with symptoms of
relapse and remission that may occur over very short periods of time, thus introducing variance to this study. The questionnaires were applied in the same order to all participants, possibly resulting in a high missing rate for the HLQ which was the last questionnaire. The results of any study examining work disability with these instruments should to be interpreted with caution until the underlying causes of these discrepancies are clarified.

The assessment of work disability is in its relative infancy and although I have undertaken a study examining the validity of the WPAI in psoriatic arthritis questions (posed by members of the OMERACT work group) remains relating to the measurement of work disability. These questions include:\textsuperscript{66,119}

- How best to combine information on absenteeism and presenteeism?
- Should general work impairment or activity specific be measured?
- How to incorporate job transition or adaptation in a measure of disability?
- What should the length of recall be; weeks, months or years?
- Should work disability be attributed to disease or should it remain unrestricted?
- Should only paid work be assessed or should unpaid work be included?
- Exactly what aspect of work disability should be measured?

Historically aspects such as absenteeism, presenteeism, productivity loss, impairment, job instability (perceived risk of work cessation) and impaired performance have all been measured. There was increasing consensus at the OMERACT 10 meeting that a measure combining absenteeism and presenteeism should be taken forward for further development and six measures including the WPAI were selected as having potential.\textsuperscript{140} Therefore when considering the findings of this study in the wider context it may be considered that I have added information on the validity of one measure in PsA but ultimately an alternative or entirely new measure of WD may be taken forward by the wider research community, limiting the future use of these findings.

In summary I report new evidence supporting the feasibility, construct validity and discriminative validity of the WPAI in psoriatic arthritis. These findings
support the use of the WPAI in patients with PsA but do not constitute a full validation as the domain of responsiveness is yet to be determined.

**OBJECTIVE FOUR (a)**

Objective four (a) of this thesis was to assess the feasibility, reliability and sensitivity to change in structural joint damage of the four existing radiographic assessment methods in psoriatic arthritis. The use of plain radiographs to assess structural damage is routine in clinical practice and an important measure of structural damage in longitudinal observational studies. Plain radiographs are inexpensive, quick to perform, acceptable and readily interpretable. There was agreement amongst experts at the radiographic assessment workshop at the annual GRAPPA meeting in Stockholm 2012 that the Sharp-van der Heijde modified method was the optimal method for use in short duration randomised controlled trials however there was no agreement on the optimal method for longitudinal observational studies. I report the first comparison of four radiographic scoring methods in psoriatic arthritis with the novel findings that:

- The modified Sharp score and van der Heijde methods are the most reliable and sensitive to change but take longer to perform.
- The Steinbrocker method is the most feasible but lacks the sensitivity of the modified Sharp score and van der Heijde method.
- The smallest detectable change of the Ratingen method is close to that of the modified Sharp score and van der Heijde method but is quicker to perform and may be more specific to PsA through inclusion of bony proliferation.

The selection of any outcome measure, including a radiographic one, is always likely to remain a study specific decision. In particular individual studies will have differing requirements for truth, reliability and feasibility. For example outcome in a genetic association study may rank specificity to disease highest when choosing a method and as such the Ratingen may be the most appropriate as it includes bony proliferation, the only radiographic feature sufficiently specific to PsA to achieve inclusion in the CASPAR criteria. Alternatively a short duration phase III drug trial may prioritise sensitivity to change and thus the van der Heijde
may be most appropriate. The findings of this study have enabled a data driven selection of the Ratingen method on the basis of feasibility, specificity and sensitivity to change.

When considering the findings of this study in the wider context of psoriatic arthritis research this data may inform the selection of radiographic methods in other observational studies of PsA. This is the first study to report the minimal detectable change of the Steinbrocker and Modified Sharp Scores in PsA and this data can be used to inform sample size calculations for future studies. The data can also inform discussion on radiographic outcome in observational studies with a view to more consistency in the use of a single measure. Consistency in the use of the same method introduces the possibility of increasing the collaboration of data between cohorts, comparison between studies and possibly meta-analyses. If no consensus can be achieved the data from this study may allow the development of a novel radiographic score in psoriatic arthritis, potentially derived through mathematic reduction to achieve maximum sensitivity to change from the minimum areas scored. Such a score would then need to be assessed on a larger scale, including on patients with early psoriatic arthritis.

In summary I report new data comparing the feasibility, reliability and sensitivity to change of four radiographic scoring methods in psoriatic arthritis. This evidence has allowed a data driven selection of the most suitable measure for use in my study but the results may be used by the wider PsA research community to make a data driven selection of study specific measures, calculate sample size or potentially develop a novel measure.

**OBJECTIVE FOUR (b) & FIVE**

Objectives four (b) and five of this thesis were to determine the extent to which radiographic damage, clinical disease activity, demographic and social factors are associated with WD measured with the WPAI. In this multicentre, cross sectional observational study I report the novel findings that amongst those with PsA of working age:

- Greater age, recent disease onset (2 to 5 years disease duration) and worse physical function exert a negative influence on remaining in employment.
• Patient reported employer awareness and helpfulness exerts a strongly positive influence on remaining in employment, even if patients perceive no help is required. These findings are in contrast with those of any age who remain at work where presenteeism and productivity loss are associated with the disease activity measures of:

• Greater global activity, joint specific activity and worse physical function.

Gaining further understanding of the breadth of the work disability concept and highly contextual nature of WD were seen as key issues at OMERACT 10. The importance of separately measuring individual WD perspectives was specifically highlighted. This study has been designed to separately analyse the individual perspectives of productivity loss, presenteeism, absenteeism and unemployment. A broad range of contextual factors were included in addressing objective five of this thesis. An interesting finding of this study has been the identification of the association of patient reported employer helpfulness (chapter seven, table two) with remaining in employment. Employer attitude has been discussed as conceptually important by Sandqvist and Henriksson and voted as important to investigate at the OMERACT 10 work SIG, but to my knowledge this is the first report of the positive influence of employer attitude upon remaining in employment. This association was not seen with presenteeism, absenteeism or productivity loss. Investigation of this finding in a prospective study would allow confirmation of any temporal relationship between patient reported employer attitude and unemployment.

It should be noted that there are contextual factors that were not included in this present study including; co-worker attitude (in addition to employer attitude), depression, job satisfaction/ motivation, individual income need and demands and support at home. The latter was the top rated contextual factor at the OMERACT 10 work SIG, receiving 26% of votes. These potentially important confounding factors may also influence the reported findings. The strength of the association of employer helpfulness rarely assessed in work studies, that replaced other more frequently reported associations (such as sex, education, work type and
radiographic damage) in the regression model. This highlights the effect that missing confounding factors may have upon study findings and thus the importance of confirmation in prospective studies.

The association of radiographic damage with presenteeism, absenteeism and productivity loss was not sufficiently strong to warrant inclusion in the final regression models. The associations of disease activity measures with WD ‘pushed’ demographic, social factors as well as out radiographic damage of the model (chapter seven, table three). This finding supports the notion that, despite the many influencing factors, presenteeism could be a responsive measure reflecting disease activity. The association of radiographic damage with unemployment was also insufficiently strong to warrant inclusion in the final regression model replaced with age, disease duration, physical function and employer helpfulness (chapter seven, table two). The findings of this study indicate that unemployment, the work disability ‘endpoint’, may be associated with demographic and social factors (employer helpfulness) rather than structural damage or disease activity.

The influence of time upon work disability also warrants discussion as both work disability and psoriatic arthritis may fluctuate over time. As discussed in the introduction and the systematic review of this thesis there are multiple factors that may influence WD and their relative contribution may change over time. For example a period of economic recession followed by recovery may directly impact upon employment. Additionally the psoriatic arthritis may relapse and remit over days, weeks or months. The WPAI measures disease only over a one week period and may therefore fail to capture change outside this timeframe and potentially interact with the findings of any study using the WPAI, or any other measure with a short recall period. Conversely a recall period of one week may be regarded as a strength of the WPAI. Over a longer period (such as a month in the case of the WLQ) the response would be an average of flares and remissions over that time. The process of averaging will thereby potentially both underestimate the effect of disease activity (by including periods of remission) and miss fluctuations thus resulting in a less responsive measure. The study comparing four WD measures in rheumatoid arthritis and osteoarthritis by Zhang
et al support this theory with the finding that measures of WD over longer recall periods estimate WD lower than those that measure over a shorter time such as the WPAI.\textsuperscript{68} Finally a measure with a short recall period of one week minimises the risk of recall bias and allows direct comparison with other disease outcome measures such as the HAQ, DLQI, VAS, EQ5D, FACIT which all have a recall period of one week. I would therefore suggest that a measure of WD with a shorter recall period is desirable but does introduce the risk of interacting with study findings by missing WD outside the recall period.

In summary I present new data on the associations of patient reported work disability in psoriatic arthritis from a well classified cohort of patient’s recruited from across the UK. Presenteeism and productivity loss amongst those in work are associated with the disease activity measures. This is in contrast to unemployment which is associated with age, disease duration, physical function and employer helpfulness.
Future work

The lack of evidence relating to work disability in early PsA identified in the systematic review and has not been addressed in this thesis. Studies in rheumatoid arthritis suggest that work disability occurs early in disease and may be irreversible as reviewed by de Croon et al.\textsuperscript{43} There is therefore a case for assessing factors that influence work disability in early PsA with a view to developing a strategy for preventing or minimising the impact in early disease. This could be addressed with a mixed methods inception cohort study, qualitative interviews exploring influencing factors followed by quantitative assessment with medical and patient reported assessment over the first five years of disease.

Another area of limited evidence identified in the systematic review is the effect of medical treatment upon work disability. There is evidence suggesting biological therapy with anti-TNF treatment can improve work disability but this evidence comes from short duration drug RCT’s and thus relates to a highly select group of patients with limited follow up.\textsuperscript{41} A prospective study of the ‘real world’ effect of disease modifying and anti-TNF treatment on WD is underway as part of planned post-doctoral studies (LOPAS II, appendix 9).

The lack of consensus on the existing measures of work disability and the possible development of a new measure are the subject of on-going research.\textsuperscript{117} Once a consensus has been achieved this will enable more confident interpretation of the findings of individual research projects and comparison of cohorts.

Once these three areas of measurement, influencing factors in early disease and the effect of treatment have been addresses the next step may be to consider an interventional case control study comparing multidisciplinary intervention. Such a study would compare a novel intervention aimed specifically at the improvement and prevention of work disability compared with standard best practice care.
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APPENDIX

APPENDIX 1

Work Productivity and Activity Index

Psoriatic Arthritis
Work Productivity and Activity Impairment Questionnaire
Specific Health Problem V1.0 (WPAI:SHP)

First Name  
Surname  

The following questions ask about the effect of your psoriatic arthritis on your ability to work and perform regular activities. Please fill in the blanks or tick a number, as indicated.

1) Are you currently employed (working for pay)?
   No   Yes
   If NO, check “NO” and skip to question 6.

The next questions are about the past seven days, not including today.

2) During the past seven days, how many hours did you miss from work because of problems associated with your psoriatic arthritis? Include hours you missed on sick days, times you went in late, left early, etc., because of your psoriatic arthritis. Do not include time you missed to participate in this study.
   Hours

3) During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?
   Hours

4) During the past seven days, how many hours did you actually work?
   Hours  (If "0", skip to question 8.)
5) During the past seven days, how much did your psoriatic arthritis affect your productivity while you were working?

Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If psoriatic arthritis affected your work only a little, choose a low number. Choose a high number if psoriatic arthritis affected your work a great deal.

Consider only how much psoriatic arthritis affected productivity while you were working:

<table>
<thead>
<tr>
<th>Psoriatic arthritis had no effect on my work</th>
<th>Psoriatic arthritis completely prevented me from working</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

TICK A NUMBER

6) During the past seven days, how much did your psoriatic arthritis affect your ability to do your regular daily activities, other than work at a job?

By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If psoriatic arthritis affected your activities only a little, choose a low number. Choose a high number if psoriatic arthritis affected your activities a great deal.

Consider only how much psoriatic arthritis affected your ability to do your regular daily activities, other than work at a job:

<table>
<thead>
<tr>
<th>Psoriatic arthritis completely prevented me from doing my daily activities</th>
<th>Psoriatic arthritis had no effect on my daily activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

TICK A NUMBER
APPENDIX 2

Work Questionnaire

Psoriatic Arthritis - Work Questionnaire

Please answer the following questions about your working life.

1) If you are working how would you best describe your work?
   - [ ] Employed full time
   - [ ] Employed part time
   - [ ] Self Employed
   - [ ] Volunteering
   - [ ] Home maker
   - [ ] Full time education
   - [ ] Not working

2) If you are not working which of the following best describes your situation?
   - [ ] Retired
   - [ ] Off work because of psoriatic arthritis
   - [ ] Off work for another reason
   - [ ] Unemployed and seeking work
   - [ ] None of the above

3) If you are working have you needed to make any work changes because of your psoriatic arthritis?
   - [ ] Yes
   - [ ] No
   - [ ] Not applicable

If yes what changes have you needed to make. Please mark any that apply to you;
   - [ ] Additional equipment
   - [ ] Physical modification of workstation
   - [ ] Reduced hours
   - [ ] Change in role at work (within your current work)
   - [ ] Change to completely new work
   - [ ] Other

4) What is (or was) your job title?

LCPAS2 Additional work questionnaire Version 1.3, Feb 2011
5) Does (or did) your employer know you have psoriatic arthritis;
   Please mark one only;
   □ Yes □ No □ Not applicable □ Don't Know

   If your employer is / was aware of your arthritis how helpful are / were they with your arthritis related needs at work such as offering flexible hours, modifications to your work station or change of role at work?
   □ Very helpful □ Helpful □ No help required □ Unhelpful □ Very unhelpful

6) If you are working or hoping to return to work have you had any therapies aimed at improving your disability at work such as occupational therapy or physiotherapy problems?
   □ Yes □ No □ Not applicable □ Don't Know

7) Is your psoriatic arthritis currently satisfactory when you take into account your general functioning and your current pain?
   Please mark one only;
   □ Yes □ No □ Not relevant

8) How would you describe the change in your psoriatic arthritis since your last clinical appointment?
   Please mark one only;
   □ Much better □ Somewhat better □ Same/ No change □ Somewhat worse □ Much worse

9) Overall how severe is your psoriatic arthritis currently?
   □ Unnoticeable □ Very Mild □ Mild □ Moderate □ Severe □ Unbearable

10) If you have any additional comments that you would like to make then please do so here:

   ________________________________________________________________
   ________________________________________________________________
   ________________________________________________________________
   ________________________________________________________________
   ________________________________________________________________

LOPAS2 Additional work questionnaire Version 1.2, Feb 2011
APPENDIX 3

Health Assessment Questionnaire

Psoriatic Arthritis Health Assessment Questionnaire

Forename

Surname

Date of Birth

Section 1 – Health Assessment questionnaire

We are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments at the end of this form.

Please tick the one response which best describes your usual abilities over the past week.

1) Dressing and Grooming
   Are you able to:
   - Dress yourself including shoelaces and doing buttons?
   - Shampoo your hair?

2) Rising
   Are you able to:
   - Stand up from an armless straight chair?
   - Get in and out of bed?

3) Eating
   Are you able to:
   - Cut your meat?
   - Lift a full cup or glass to your mouth?
   - Open a new carton of milk (or soap powder)?

4) Walking
   Are you able to:
   - Walk outdoors on flat ground?
   - Climb up 5 steps?

Please tick any AIDS or DEVICES that you usually use for any of these activities:

- Walking stick
- Devices used for dressing (button hook, zipper pull, long handled shoe horn etc)
- Walking frame
- Built-up or special utensils
- Crutches
- Special or built-up chair
- Wheelchair
- Other (specify)

Please tick any categories for which you usually need ASSISTANCE FROM ANOTHER PERSON

- Dressing and Grooming
- Rising
- Eating
- Walking
1039285154

Please tick the one response which best describes your usual abilities over the past week.

1) **Hygiene**
   Are you able to:
   - Wash and dry your entire body?  
   - Take a bath?  
   - Get on and off the toilet?  

2) **Reach**
   Are you able to:
   - Reach and get down a 5lb object (e.g. bag of potatoes) from just above your head?  
   - Bend down to pick clothing from the floor?  

3) **Grip**
   Are you able to:
   - Open car doors?  
   - Open jars which have previously opened?  
   - Turn taps on and off?  

4) **Activities**
   Are you able to:
   - Run errands and shop?  
   - Get in and out of a car?  
   - Do chores such as vacuuming, housework or light gardening?  

Please tick any AIDS or DEVICES that you usually use for any of these activities:

- Raised toilet seat
- Bath Rail
- Bath seat
- Long-handled appliances for reach
- Jar opener (for jars previously opened)
- Other (specify)  

Please tick any categories for which you usually need HELP FROM ANOTHER PERSON:

- Hygiene
- Reach
- Gripping and opening things
- Activities

**Section 2 - Pain**

**How strong has the pain in your joints been in the past week?**

Please mark on the line to indicate the severity of the pain:

No pain  ________________  Pain as bad as it could be

**Section 3 - Patients Global Assessment**

How active is you arthritis today?

*Not active at all*  1  2  3  4  5 *Extremely active*

For office use only:

- Dressing & grooming
- Rising
- Eating
- Walking
- Pain Vas
- Hygiene
- Reach
- Grip
- Activity
APPENDIX 4

EuroQol five domain

Psoriatic Arthritis EQ-5D

First Name: ____________________________
Surname: ____________________________

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility
- [ ] I have no problems in walking about
- [ ] I have some problems in walking about
- [ ] I am confined to bed

Self Care
- [ ] I have no problems with self-care
- [ ] I have some problems washing or dressing myself
- [ ] I am unable to wash or dress myself

Usual Activities (e.g. work, study, housework, family or leisure activities)
- [ ] I have no problems with performing my usual activities
- [ ] I have some problems with performing my usual activities
- [ ] I am unable to perform my usual activities

Pain/Discomfort
- [ ] I have no pain or discomfort
- [ ] I have some pain or discomfort
- [ ] I have extreme pain or discomfort

Anxiety/Depression
- [ ] I am not anxious or depressed
- [ ] I am moderately anxious or depressed
- [ ] I am extremely anxious or depressed
APPENDIX 5

Dermatology Quality of Life Index

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1) Over the last week, how **itchy, sore, painful or stinging** has your skin been?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all

2) Over the last week, how **embarrassed or self-conscious** have you been because of your skin?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all

3) Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home or garden**?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all
   - [ ] Not relevant

4) Over the last week, how much has your skin influenced the **clothes** you wear?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all
   - [ ] Not relevant

5) Over the last week, how much has your skin affected any **social** or **leisure** activities?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all
   - [ ] Not relevant

6) Over the last week, how much has your skin made it difficult for you to do any **sport**?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all
   - [ ] Not relevant

7) Over the last week, has your skin prevented you from **working** or **studying**?
   - [ ] Yes
   - [ ] No
   - [ ] Not relevant

   If "No", over the last week how much has your skin been a problem at **work** or **studying**?
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all

8) Over the last week, how much has your **skin** created problems with your **partner** or any of your **close friends or relatives**?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all
   - [ ] Not relevant

9) Over the last week, how much has your **skin** caused any **sexual difficulties**?
   - [ ] Very much
   - [ ] A lot
   - [ ] A little
   - [ ] Not at all
   - [ ] Not relevant

10) Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home **messy**, or by taking up **time**?
    - [ ] Very much
    - [ ] A lot
    - [ ] A little
    - [ ] Not at all
    - [ ] Not relevant
APPENDIX 6

FACIT Fatigue score

**Psoriatic Arthritis**

**FACIT Fatigue Scale (Version 4)**

<table>
<thead>
<tr>
<th>Statement</th>
<th>Not at all</th>
<th>A little bit</th>
<th>Somewhat</th>
<th>Quite a bit</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>I feel fatigued.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I feel weak all over.</td>
<td></td>
<td></td>
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<tr>
<td>I feel listless (&quot;washed out&quot;).</td>
<td></td>
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<tr>
<td>I feel tired.</td>
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<tr>
<td>I have trouble starting things because I am tired.</td>
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<tr>
<td>I have trouble finishing things because I am tired.</td>
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<tr>
<td>I have energy.</td>
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<tr>
<td>I am able to do my usual activities.</td>
<td></td>
<td></td>
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<tr>
<td>I need to sleep during the day.</td>
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<tr>
<td>I am too tired to eat.</td>
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<tr>
<td>I need help doing my usual activities.</td>
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<tr>
<td>I am frustrated by being too tired to do the things I want to do.</td>
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</tr>
<tr>
<td>I have a limit to my social activity because I am tired.</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Below is a list of statements that other people with your illness have said is important. Please tick one box per line to indicate your response as it applies to the past 7 days.
APPENDIX 7

Visual Analogue Scores

Psoriatic Arthritis
Patients assessment scores

First Name
Surname

The aim of this questionnaire is to measure how much each aspect of your condition has affected you OVER THE LAST WEEK.

Please indicate on each scale how good or bad your condition has been by drawing a vertical mark STRAIGHT DOWN ACROSS EACH LINE.

Global score
In all the ways in which your PSORIATIC ARTHRITIS, as a whole affects you, how would you rate the way you have felt over the last week.

Excellent [ ] Poor [ ]

Pain
How strong has the PAIN in your JOINTS been in the past week?
No pain [ ] Pain as bad as it could be [ ]

Joint assessment
In all the ways in which your ARTHRITIS affects you, how would you rate the way you have felt over the last week.
(Please mark on the line and tick the box to indicate the severity of your arthritis)

Excellent [ ] Poor [ ]

Skin assessment
In all the ways in which your PSORIASIS affects you, how would you rate the way you have felt over the last week.

Excellent [ ] Poor [ ]

LOPAS2 patient assessment form May 2011 Version 1.0
APPENDIX 8

Background Form

0917630691
Study No.: PSA \\
Date:  \\

Background Form
Long Term Outcome in Psoriatic Arthritis II

Please use addressograph label or complete by hand

First Name: \\
Surname: \\
Date of Birth: ___ / ___ / ___

GP Name: \\
GP address: \\

Section 1: Background data

1) What is your marital status? 
- Married
- Single
- Divorced
- Separated
- Widowed
- Living with partner

2) What is your ethnic group?

White: 
- British
- Irish
- Other

Black or Black British: 
- White & Black Caribbean
- White & Black African
- White & Asian
- Other

Asian or Asian British: 
- Indian
- Pakistani
- Bangladeshi
- Other

Chinese or other: 
- Chinese
- Other

If other: please give details: 

3) At which stage did you finish your education?

- No formal education
- Primary school (generally finishes at 10-12 yrs)
- Lower secondary school (GCSE / O level or equivalent, generally finishes 16 yrs)
- Upper secondary school (A level or equivalent, generally finishes 18 yrs)
- University (generally finishes 21-23 yrs)

4) Have you ever drunk alcohol?

- I currently drink alcohol
- I used to drink alcohol
- I have never had alcohol

- Average number of units per week

5) Have you ever smoked?

- I currently smoke
- I used to smoke
- I have never smoked

Please provide details.

- No. per day
- Years smoked
- Years since smoked

LPAS2 Background from Version 1.2, January 2011
Section 2: Arthritis
1) When did the symptoms of arthritis start? _____ Year symptoms began
2) When was your arthritis diagnosed? _____ Year diagnosed
3) Which joint was first affected by arthritis? 

Section 3: Psoriasis
1) When did the symptoms of psoriasis start? _____ Year symptoms began
2) When was your psoriasis diagnosed? _____ Year diagnosed
3) Have you ever seen a dermatologist? Yes ☐ No ☐
4) Are you currently seeing a dermatologist? Yes ☐ No ☐
5) Have you ever had psoriasis of the nails? Yes ☐ No ☐ Don’t know ☐
   (e.g. nails thickened, pinna, yellow...)

Section 4: Past Medical History
1) Have you ever suffered from: [please tick all that apply and provide details]
   ☐ Heart problems
   ☐ Stroke
   ☐ Diabetes
   ☐ High Blood Pressure
   ☐ High Cholesterol

If you have any other medical conditions please provide details below

[Signature]
Section 5: Medications
Have you been prescribed any of the following drugs. If yes please provide details about when you started and finished them and why you stopped taking the medication.

☐ Methotrexate

☐ Sulphasalazine

☐ Leflunomide

☐ Hydroxychloroquine

☐ Anti - TNF Drugs

☐ Ciclosporine

☐ IM Gold

☐ Prednisone

☐ Other

Reason for stopping

Start Date (mm/yy) / End Date (mm/yy)

If other please give details
Section 6: Family History
If any of your family have had any of the following conditions then please tick all that apply and provide details

- [ ] Heart problems
- [ ] Stroke
- [ ] Diabetes
- [ ] High Blood Pressure
- [ ] High Cholesterol
APPENDIX 9

Patient Information Sheet

Royal National Hospital for Rheumatic Diseases
NHS Foundation Trust
Upper Borough Walls
Bath, BA1 1RL
Telephone 01225 485941
Facsimile 01225 421202

STUDY INFORMATION SHEET I
VERSION 1.4 JULY 2011

LONG TERM OUTCOME IN PSORIATIC ARTHRITIS II

Names of Researchers: Dr William Tillett, Dr Neil McHugh, Dr Stuart Kyle, Dr Richard Haigh, Sr Nicola Waldron, Sr Nina Griffith, Mrs Charlotte Carmichael

Invitation
We would like you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. The study is being organised by Dr William Tillett from the Royal National Hospital for Rheumatic Diseases (RNHRD) in Bath but you may have been approached by your local hospital who are also participating in the study.

Part I

Why are we doing this research?
We are interested in finding different and better ways to measure psoriatic arthritis. It is only through measuring arthritis that we can assess if our treatments are working and which ones are best. Traditionally we have assessed how bad arthritis is by counting affected joints and performing blood tests. We now realise there are other, perhaps better ways such as measuring aspects of quality of life, functioning and disability at work. Our study will investigate disability at work and how to measure it.

Why have I been invited?
You have been asked to participate because you have arthritis associated with psoriasis and are having your treatment changed.

Do I have to take part?
No, being part of the study is absolutely voluntary and if you prefer not to take part, your decision will be accepted without question. You will not have to give a reason and your future care would certainly not be affected in any way.

What will happen if you take part?
We would like to observe your arthritis over the next two years. We will not change or delay any of your normal treatment or ask you to take any experimental medications. We will monitor your arthritis in a number of ways; firstly by sending you questionnaires in the post to fill in and post back to us, secondly by collecting the...
information from your normal appointments such as the examination of your joints and your blood tests results and finally by taking x-rays of your hands and feet at the beginning and end of the study.

We would like to send you a set of questionnaires now then again in two weeks, four weeks, three months then every six months for two years. This will be a total of 8 sets of questionnaires during the two years of the study. It will take approximately 30 minutes to complete the questionnaires on each of the 8 occasions. You can then return them by post in a pre-paid envelope.

If you decide to take part in the study we will check to see if you have had recent x-rays of your hands and feet and an up-to-date blood test. If you have not had these x-rays within the last 3 months or a blood test in the last week we will ask you to come to your local hospital at your convenience over the next few days for these tests. Apart from this one occasion at the start of the study you will not be asked to attend any clinic appointments or hospital visits in addition to your routine care.

What are the risks of taking part?
This is an observational study meaning we will simply be observing your arthritis during your routine care, if you chose to participate we will not change or withhold any of your normal treatment.

The only risk involved with this study relates to the x-rays we would like to take. Performing x-rays every two years is routine at the RNHRD to confirm treatment is working but not all hospitals do this. You may have had x-rays within the last two years in which case the first x-ray would perform would be additional to your routine care. There are no immediate side effects from x-rays and the dose of radiation is very low. We are all exposed to radiation from the air we breathe, the food we eat and even from space and this is called ‘background radiation’. Background radiation varies across the United Kingdom but the amount from these x-rays is about the same two hours in an aeroplane or a holiday to Cornwall.

What are the possible benefits of taking part?
The overall results of the study will increase our understanding of psoriatic arthritis but will not be of direct benefit to you.

Contact details
If you have any questions about the study either ask the clinic staff to contact your local research team or alternatively Sr Nina Griffith or a member of the Bath Psoriatic Research Unit would be happy to answer your questions by;

Telephone on 01225 448 444 or 07531 802 371
By e-mail: pna@birdbath.org.uk

Thank you for reading so far – if you are still interested, please go to Part II
Part II

What would happen to my information?
It may be necessary to read sections of your medical notes to record all of the information about your arthritis. Your information will be kept in a secure locked room on a password protected database at the Bath Institute for Rheumatic Diseases where the RNHRD’s Bath Psoriatic Research Unit is based. The security of this database is monitored by a data protection officer. Your information will be allocated a study number and kept as strictly confidential. Only the research team at your hospital and the RNHRD will know the study number that applies to you.

We may wish to use the information we collect in future studies or contribute to international research in psoriatic arthritis such as an international database. If this is the case the information we use will be anonymous and there will be no way of identifying you. You may not wish for us to use your information in this way so we have included a separate option on the consent form for this.

Will anyone else know I am doing this?
We will inform your GP you are participating in this research so they have all the information if you have further queries or want to be involved in other research at other hospitals.

What will happen to the samples I give?
The blood test samples taken to assess the activity of your arthritis will be analysed and disposed of as normal in your local hospital laboratory. We will not store or process any samples as part of this study.

Who is organising and funding the study?
Dr Tillett is organising the study which is funded by Abbott pharmaceuticals. Abbott produce Humira which is a drug used to treat psoriatic arthritis. The purpose of this study is not to investigate this drug, the funding from Abbott is unrestricted and they will not be involved with the interpretation or publication of the results. Nobody will benefit financially from this study.

Expenses and payment
We are unable to pay volunteers for taking part but you will be reimbursed any travel expenses incurred attending any additional hospital visits.

What happens when the research stops?
Your normal care will continue at your regular hospital. After the two years are over we will simply stop sending you questionnaires and stop collecting the information from your clinic visits.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people called the Research Ethics Committee to ensure the research is fair. This study has been reviewed and approved by South East Wales Research Ethics Committee (Panel D).

What to do next?
Thank you for taking a few minutes to consider this study.

- I would like to take part in this study.
  - Please ask the clinic staff to contact the research team for you who can assist with the forms and organise any tests you may need before you go home.
    - Alternatively
      - You can go home now and wait for us to telephone you tomorrow as you have discussed with your doctor.

- I would like more information about this study before I decide.
  - You can now either:
    - Ask the clinic staff to contact the research team for you and we can come discuss the study now.
      - Alternatively
        - You can go home now and wait for us to telephone you tomorrow as you have discussed with your doctor.

- I do not want to take part in this study.
  - Please let the clinic nurses know so they can tell your doctor.
  - Thank you for taking the time to consider this study. No further action is required, we will not contact you and your normal care will not be affected in any way.

If you would like to discuss the study please either ask the clinic staff to contact your local research team or alternatively Sr Nina Griffith and the research team at the RNRHD can be contacted in a number of ways at any time in working hours;

1. Mobile telephone: 07531 802 371
2. Alternatively landline telephone on 01225 465941 to discuss the consent form further.
3. E-mail on psa@birdbath.org.uk

If we are not able to answer the telephone please leave a message with your contact details and we will telephone you back.
APPENDIX 10

Patient Consent form

Study No:  
Hosp No:  

Royal National Hospital for Rheumatic Diseases

INFORMED CONSENT FORM I
LONG TERM OUTCOME IN PSORIATIC ARTHRITIS II
Version 1.4 2011

Please fill in your name, date of birth, read the following statements and tick as many boxes as appropriate.

Forename  
Surname  
DOB  

Names of Researchers: Dr William Tillett, Dr Neil McHugh, Dr Stuart Kyle, Dr Richard Haigh, Staff Nurse Nicola Waldron, Miss Charlotte Carmichael

Please initial box(es)

1  I have read the patient information sheet I version 1.4, had an opportunity to ask questions, discuss the study and received satisfactory answers to any questions. I understand that I am free to withdraw from the study at any time, without having to give a reason and without affecting future care.

2  I understand that sections of any of my medical notes may be looked at by responsible individuals in the research team or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.

3  I agree to participate in the above study and for my information to be stored on the Psoriatic arthritis database at the Royal National Hospital for Rheumatic Diseases (RNHRD) and for my GP to be informed about my participation.

4  I give consent for my information to be used anonymously to contribute to international research in psoriatic arthritis as part of an international database.

5  I give consent for my information to be used anonymously for future research by the Bath Psoriatic Arthritis Research Unit at the RNHRD.

6  I give permission for the Bath Psoriatic Arthritis Research Unit to contact me about participating in any future studies.

Name of Patient  
Date  
Signature  

Researcher  
Date  
Signature  

LOPAS II Consent form I version 1.4