Study Title: How does PsAID implementation affect treatment intensification and patient satisfaction in PsA?

Internal Reference Number / Short title: AsseSSing Impact in pSoriatic Treatment (ASSIST)

Ethics Ref: Insert

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Sponsor:	University of Oxford
Funder:	Amgen
Chief Investigator Signature:	
Statistician Signature:	

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, HRA, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

Trial Title: How does PsAID-12 implementation affect treatment intensification and patient satisfaction in PsA?
Protocol Date and Version No: insert

Protocol signature page

The undersigned has read and understood the trial protocol detailed above and agrees to conduct the trial in compliance with the protocol.

Principal Investigator (Please print name)	**Signature**	**Site name or ID number**	**Date**

Following any amendments to the protocol, this page must be updated with the new protocol version number and date and re-signed by the site PI.

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1. KEY CONTACTS

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Funder(s)	Amgen
Clinical Trials Unit	N/A
Collaborator	Springer Healthcare
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2. LAY SUMMARY

Psoriatic arthritis (PsA) is a form of inflammatory arthritis associated with the skin condition psoriasis. A variety of different treatments are used to try to control arthritis and skin psoriasis and management often involves trial and error to find the right medication for the right person. Very little is known about the decisions made to increase treatment in individual patients. Previous research in rheumatoid arthritis found that clinical measures of disease activity, patient reported outcomes and characteristics of the treating doctor all influenced the decision to change therapy in routine practice.

We particularly want to establish whether routine use of the psoriatic arthritis impact of disease (PsAID-12) questionnaire in the clinic setting can enable a better understanding of the impact of PsA on each individual, improve physician-patient communication and lead to appropriate interventions. The PsAID-12 questionnaire is a relatively new European developed questionnaire measuring patient impact across 12 different domains in PsA.

This study will use routine implementation of the PsAID-12 questionnaire and see if this is related to treatment decisions and patient satisfaction. We will also examine other factors that may influence treatment decisions including patient characteristics, physician characteristics, disease activity and quality of patient-physician interactions.

3. SYNOPSIS

Study Title	How does PsAID implementation affect treatment intensification and patient satisfaction in PsA?		
Internal ref. no. / short title	AsseSSing Impact in pSoriatic Treatment (ASSIST) study		
Study registration			
Sponsor	University of Oxford Joint Research Office 1st floor, Boundary Brook House Churchill Drive Headington Oxford OX3 7GB		
Funder	Amgen		
Study Design	Multiple-site, cross-sectional, observational study		
Study Participants	Adult Patients with psoriatic arthritis recruited from rheumatology clinics		
Sample Size	500		
Planned Study Period	This study is a cross-sectional study with only 1 visit involved per participant. Total study period 24 months		
Planned Recruitment period	1st January 2021 – 31st December 2021		
	Objectives	Outcome Measures	Timepoint(s)
Primary	Assess the influence of PsAID-12 score on likelihood of treatment escalation	PsAID-12 questionnaire Treatment escalation recorded in clinic, with reason for decision	Cross-sectional
Secondary	Evaluate the impact of reviewing the PsAID-12	Likert scale “Beyond your usual clinical assessment, how did your review of the patient’s	Cross-sectional

	questionnaire on the physician's decision to change treatment	PsAID-12 questionnaire responses impact on your therapy decision for this patient"	
	Assess the effects of other factors that influence the likelihood of treatment escalation	Treatment escalation in clinic Factors include patient gender, disease duration, comorbidities, physician age, disease activity and PROs. Specifically addressing the impact of PsAID-12 individually and above other factors	Cross sectional
	Determine which factors physicians feel influence treatment decisions in routine practice	NRS of the perceived importance of individual factors that may influence individual treatment decisions	Cross sectional
	Evaluate patient satisfaction and perceived patient effectiveness in the consultation and examine how this links to PsAID-12 score and whether treatment is changed	CollaboRATE and PEPPI questionnaires and their relationship to PsAID-12 scores and treatment change	Cross sectional
	Explore the physicians' views on the use and value of the PsAID-12 tool	Qualitative reports by physicians with themes identified retrospectively	
Intervention(s)	This is an observational study and no interventions will be performed other than routine clinic assessments.		
Comparator	Not applicable		

4. ABBREVIATIONS

BSA	Body surface area
CASPAR	ClASification of Psoriatic ARthritis
CI	Chief Investigator
CRF	Case Report Form
CTRG	Clinical Trials & Research Governance, University of Oxford

EULAR	European League Against Rheumatism
GCP	Good Clinical Practice
GP	General Practitioner
GRAPPA	Group for Research and Assessment of Psoriasis and Psoriatic Arthritis
HAQ	Health assessment questionnaire
HRA	Health Research Authority
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors
NHS	National Health Service
NRS	Numerical rating scale
OMERACT	Outcome Measures in Rheumatology
PEPPI	Perceived Efficacy in Patient-Physician Interactions
PI	Principal Investigator
PIL	Participant/ Patient Information Leaflet
PsA	Psoriatic arthritis
PsAID-12	PsA impact of disease questionnaire
RA	Rheumatoid arthritis
R&D	NHS Trust R&D Department
REC	Research Ethics Committee
RES	Research Ethics Service
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System ®
SOP	Standard Operating Procedure

5. BACKGROUND AND RATIONALE

Psoriatic Arthritis (PsA) is an inflammatory arthritis estimated to occur in 15-30% of people with psoriasis[1] affecting around 150,000 people in the UK[2]. Audit data from Oxford in 2015 shows that 21.5% of patients in the early arthritis clinic have PsA. Two-thirds of people with PsA suffer progressive joint damage with associated disability[3, 4]. People with PsA have similar functional and quality of life impairment to rheumatoid arthritis[5]. PsA is associated with a reduced life expectancy[6] related to the risk of comorbidities, particularly the metabolic syndrome[7]. Direct costs to healthcare are estimated at £2,400 per patient annually in the UK with indirect costs (time lost from work and activities) per patient of over £8,000[8].

Treatment pathways in psoriatic arthritis are not well defined and have to be tailored to the individual given the heterogeneous nature of the condition. PsA can cause inflammation in joints, tendons, soft

tissues, skin, nails and spine in varying patterns. Different therapies are effective for different domains of disease so personalisation of therapy is paramount.

Very little is known about the decision to intensify treatment in PsA in routine practice. In recent years there has been an increasing focus on the idea of treating to target in PsA but this is not widely implemented. Research in Rheumatoid Arthritis (RA) has suggested that 60% of treatment change in RA is related to patient reported outcomes, compared to 40% related to doctor assessed clinical measures. [9]. We wish to study this influence in PsA.

The PsAID is a relatively new questionnaire developed by EULAR to measure patient impact in PsA. This disease-specific measure was developed with prominent patient involvement to ensure that all key physical, social and psychological domains are included. The PsAID-12 (with twelve questions) is designed for use in clinical practice and includes measures of pain, function, participation, sleep, depression, coping and anxiety. [10] It has provisional endorsement by the Outcome Measures in Rheumatology (OMERACT) group to measure health related quality of life and is now being used increasingly in observational and interventional studies. In observational studies of clinical practice, it has been shown to correlate with measures of disease activity and other measures of disease impact, however there has been much less research on the impact of its use in routine clinical practice.

The hypothesis is that the use in clinics of the PsA impact of disease (PsAID-12) questionnaire, specifically knowledge of the overall score and information from the various impact sub-domains, will influence the decision to apply treatment intensification in routine practice. We believe that the routine use of PsAID-12 questionnaires will enable a better understanding by clinicians of the impact of disease on their patients, will improve physician-patient communication and influence treatment interventions. A secondary aim of this study is to evaluate patient satisfaction with their clinician interaction when the PsAID-12 questionnaire is used and whether it is related to treatment change.

Obviously, treatment decisions for individuals are complex and will be based on many different factors. To investigate this further, we will use regression modelling to identify the key factors, in addition to PsAID-12 scores, that may be associated with treatment changes (particularly escalation), including physician characteristics, patient characteristics, inflammatory disease activity and patient reported outcomes.

This study will use routine implementation of the PsAID-12 questionnaire, using the freely available GRAPPA App, to support an increased understanding by clinicians of the physical, social and psychological impact of psoriatic arthritis (PsA) on their patients' lives, and see if this is related to treatment decisions and patient satisfaction. The study will also seek to learn about the Clinician's views on the value of PsAID-12 as a tool for in their practice both in terms of whether they considered its use impacted on their treatment decision for individual patients and also to collect their overall feedback on the tool.

6. OBJECTIVES AND OUTCOME MEASURES

Objectives	**Outcome Measures**	**Timepoint(s) of evaluation of this**

		outcome measure (if applicable)
Primary objective		
Assess the influence of PsAID-12 score on likelihood of treatment escalation	PsAID-12 questionnaire Treatment escalation recorded in clinic, with reason for decision	Cross-sectional
Secondary objectives		
Evaluate the impact of reviewing the PsAID-12 questionnaire on the physician's decision to change treatment	Likert scale "Beyond your usual clinical assessment, how did your review of the patient's PsAID-12 questionnaire responses impact on your therapy decision for this patient"	Cross-sectional
Assess the effects of other factors that influence the likelihood of treatment escalation	Treatment escalation in clinic Factors include patient gender, disease duration, comorbidities, physician age, disease activity and PROs. Specifically addressing the impact of PsAID-12 individually and above other factors	Cross sectional
Determine which factors physicians feel influence treatment decisions in routine practice	NRS of the perceived importance of individual factors that may influence individual treatment decisions	Cross sectional
Evaluate patient satisfaction and perceived patient efficacy in the consultation and examine how this links to PsAID-12 score and change in treatment	CollaboRATE and PEPPI questionnaires and their relationship to PsAID-12 scores and treatment change	Cross sectional
Explore the physicians' views on the use and value of the PsAID-12 tool	Qualitative reports by physicians with themes identified retrospectively	

7. STUDY DESIGN

This is an observational, cross-sectional study addressing the factors influencing treatment decisions in patients with PsA. Participants will be treated as usual in their routine clinical practice, but decisions on treatment will be recorded – whether treatment is escalated, unchanged or reduced, and why.

The study will be conducted in 25 rheumatology centres in Europe (UK, France, Germany, Spain and Italy) with five centres in each country. Each participant will only attend for one single study visit which is likely to last around 30 minutes in total. This will be alongside their routine clinic visit. The PsAID-12

questionnaire will be implemented on a tablet computer but the remaining outcomes will be collected on paper CRFs and transferred to a database for analysis.

8. PARTICIPANT IDENTIFICATION

8.1. Participating investigators

Each site could have one or more physicians responsible for recruiting and treating patients. The number of participating physicians in each site will be recorded along with their age and sex. Basic features of the sites will also be collected, namely:

- Country
- Patient population size (approximate)
- Type of centre (e.g. principal research centre, district hospital etc)

8.2. Study Participants

Adult participants with a diagnosis of PsA fulfilling the following criteria.

8.2.1. Inclusion Criteria

- Participant is willing and able to give informed consent for participation in the study and complete questionnaires in the local language.
- Aged 18 years or above.
- Diagnosed with PsA according to the ClASification of Psoriatic ARthritis (CASPAR) criteria and diagnosis confirmed by a rheumatologist (Taylor 2006).

8.2.2. Exclusion Criteria

The participant may not enter the study if ANY of the following apply:

- Patients who don't speak or read the local language
- Patients who are not comfortable filling in an app-based questionnaire or paper CRF.
- Patients with a new diagnosis of PsA at the current clinic visit

9. PROTOCOL PROCEDURES

This will be a multi-site, cross-sectional study. It is an observational study in which there will be no intervention to the standard care pathway for patients. The study visit will be aligned with a routine clinic appointment. As more detailed assessments will be performed within the study, these appointments will be slightly longer than standard care.

9.1. Recruitment

Participants will be identified by their treating rheumatologist in the local centre aiming to minimise selection bias by recruiting a random selection of all eligible patients attending the clinic taking into consideration research team availability. They will be invited to join the study at their routine clinic visit.

9.2. Screening and Eligibility Assessment

Once a potential participant, identified by these means, meets with the study team and expresses their interest in the study, they will be provided with a Patient Information Leaflet (PIL) and an opportunity to discuss their eligibility and the details of the study. All potential participants will receive the PIL and will have an opportunity to discuss the study with an investigator as part of the informed consent process during the study visit.

There will be no exceptions made regarding eligibility and all participants must be eligible as defined by all the approved inclusion and exclusion criteria within the protocol.

9.3. Informed Consent

The participant must personally sign and date the latest approved version of the Informed Consent form, in their local language, before any study-specific procedures are performed.

Written and verbal versions of the Participant Information Leaflet will be presented to the participants detailing no less than: the exact nature of the study; what it will involve for the participant; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the Informed Consent. The person who obtained the consent must be suitably qualified and experienced and have been authorised to do so by the Chief/Principal Investigator. A copy of the signed Informed Consent will be given to the participant. The original signed form will be retained at the study site.

9.4. Randomisation

This is a non-randomised study. All participants will be entered into a participant log with dates recorded for informed consent. Any patient not eligible or willing to participate will be recorded in the screening log.

In order to minimise selection bias, sites will invite a random subset of the patients on their list for that month, according to a random list generated by the Statistician. Patients will be recruited until the required number for each month have consented to participate. Further details will be provided in a separate randomisation plan, taking account of how the clinic system at each centre operates.

9.5. Blinding and code-breaking

This is not applicable as this is a non-blinded study.

9.6. Description of study intervention(s), comparators and study procedures (clinical)

There is no intervention, comparator or clinical study procedure involved in this study.

9.7. Assessments

Assessments will be conducted in the following order.

Medical history (~10 min):

We will obtain gender, PsA subtype and disease duration. We will record current and past medication for PsA and psoriasis. We will also record details of treatment changes planned, following the consultation with the treating physician. We will record comorbidities using the Groll comorbidity index.

Clinical Assessments (30min – 15 min assessment, 15 min questionnaires)

- CASPAR Criteria [11]
    - Evidence of current psoriasis
    - Personal history of psoriasis
    - Family history of psoriasis
    - Psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis
    - Evidence of current or documented history of dactylitis
    - Rheumatoid factor (if known)
    - Evidence of new bone formation on radiographs (if known).
- Full clinical disease assessment:
    - Tender and Swollen Joint Count: a full 68 tender and 66 swollen joint count will be performed. Replaced joints will not be counted
    - Dactylitis Assessment using count of tender dactylitic digits
    - Enthesitis Assessment using Leeds enthesitis index [12]
    - Psoriasis body surface area (BSA) in categories [13]
    - Physician's numerical rating scale (NRS) of overall disease activity
- Patient reported outcomes:
    - Global disease activity NRS (0 to 10cm, where 0=excellent, 10=worst possible, over the last week) [14]
    - Participant pain NRS (0 to 10cm, where 0=no pain, 10=worst possible pain, over the last week)
    - Health assessment questionnaire (HAQ) [15]
    - PsA impact of disease (PsAID-12) [10]
        - Total score calculated by using a weighted sum of the scores for the 12 questions in the scale and dividing by 20 (possible range 0 to 10)
    - EQ-5D-5L[16]
    - Widespread Pain Index and symptom severity scale for fibromyalgia[17]

These individual measures can be used to calculate PsA composite scores including the minimal disease activity (MDA) criteria and the disease activity in PsA (DAPSA) score.

Treatment to be prescribed

Full details of the treatment to be prescribed by the clinical team will be recorded comprising:

- Is the treatment regimen to be changed (see section 11.2)
- Details of type of change (see section 11.2)
- Physician's opinion of the reasons driving the treatment decision

    - Assessment of tender/swollen joints/entheses
    - Assessment of skin and nail psoriasis
    - Marker of systemic inflammation (e.g. CRP)
    - Routine patient reported outcomes (e.g. patient global or pain scores)
- Physician's opinion of how the PsAID-12 questionnaire responses influenced the treatment decision today.

Patients' assessment of the consultation

- CollaboRATE questionnaire [18]
    - Top score (score 1 if the patient records the maximum score of 9 for each of the 3 questions in the scale, 0 if not, or missing if any of the 3 questions are not answered)
    - Mean score (Mean of the 3 scores in the scale)
- Perceived efficacy in patient-physician interactions (PEPPI) [19]
    - Total score calculated by summing the scores for the 10 questions in the scale (possible range 10 to 50)

Physicians' overall assessment of PsAID-12 (At the end of the study only)

- Qualitative data seeking the views of the participating physicians on the PsAID-12 tool and its role in management of PsA.

9.8. Subsequent Visits

Not applicable as this is a single visit study

9.9. Sample Handling

No samples will be taken as part of this study.

9.10. Early Discontinuation/Withdrawal of Participants

During the course of the study a participant may choose to withdraw early from the study at any time. According to the design of the study, participants may have the following two options for withdrawal;

1) Participants can withdraw from the study but permit data obtained up until the point of withdrawal to be retained for use in the study analysis. No further data would be collected after withdrawal.

2) Participants can withdraw completely from the study and withdraw the data collected up until the point of withdrawal. The data already collected would not be used in the final study analysis.

In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including, but not limited to:

- Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
- Significant non-compliance with study requirements
- Clinical decision

Participants will not be replaced. The type of withdrawal and reason for withdrawal, where given, will be recorded in the CRF.

9.11. Definition of End of Study

The end of study is the completion of the study visit of the last subject.

10. SAFETY REPORTING

10.1. Definition of Serious Adverse Events

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect.

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

A serious adverse reaction is an SAE which is felt to be related to an intervention or treatment.

10.2. Reporting Procedures for Serious Adverse Events

As this is a non-interventional, observational study, there is no requirement to report adverse events or serious adverse events to any regulatory authority. This study is funded by Amgen and therefore additional reporting is required for adverse events felt to be related to Amgen drugs or devices. This is a requirement of the funding contract.

Reports of safety issues relating to Amgen drugs or devices should be submitted to Amgen safety/quality within the timeframes outlined in the table below. Adverse events/safety issues will only include those reported or occurring during the study visit to the clinical team as this is a single visit cross-sectional study.

Safety Data	Timeframe for submission to Amgen	Send to:
Adverse events considered related to an Amgen drug	Per contractual agreement, send ONLY to Regulatory Agency per local regulatory requirements (spontaneous reporting)	N/A
Serious Adverse Device Effect[a] (SADE)	Within 1 business day of Sponsor awareness	Amgen Safety

Adverse Device Effect (ADE)	Not to exceed 15 calendar days of Sponsor awareness	Amgen Safety
Product Complaint[b]	Immediately, not to exceed 1 business day of Sponsor awareness	Amgen Quality

[a] Adverse device effect is: any adverse event related to the use of a medical device. Adverse device effects include adverse events resulting from insufficient or inadequate instructions for use, adverse events resulting from any malfunction of the device, or adverse events resulting from use error or from intentional misuse of the device.

[b] Product Complaint is: Any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a drug, combination product, or device after it is released for distribution to market or clinic by either: (1) Amgen or (2) distributors or partners for whom Amgen manufactures the material. This includes all components distributed with the drug, such as packaging, drug containers, delivery system, labelling, and inserts. Examples include:

- Device that is damaged or broken
- Bent or blunt needles
- Missing or illegible labelling
- Inability of customer to administer the product
- Product with an unexpected colour, appearance, or particles
- User error (i.e. an act or omission of an act that results in a different combination product or medical device response than intended by the manufacturer or expected by the user, where the user attempted to use the combination product or medical device in good faith and experienced difficulty or deficiency administering the product).

Reports of misuse of a combination product or medical device (i.e. the intentional and improper use of a combination product or medical device not in accordance with the authorized product information) are not considered Product Complaints.

Aggregate safety reports[a] will be sent to Amgen as per the details below

Safety Data	**Timeframe for submission to Amgen**	**Send to**
Annual Safety Report	Annually	NASCR Manager
Other aggregate analyses	At the time of Sponsor submission to any body governing research conduct (e.g. RA, IRB etc)	NASCR Manager
Final (end of study report including): • Unblinding data for blinded studies • Reports of unauthorised use of a marketed product	At the time of Sponsor submission to any body governing research conduct (e.g. RA, IRB etc) but no later than 1 calendar year of study completion	NASCR Manager

[a] Specific requirements are to be outlined in the Research Agreement.

11. STATISTICS AND ANALYSIS

11.1. Statistical Analysis Plan (SAP)

The plans for the statistical analysis of the study are outlined below. There will be a separate SAP document in use for the trial with a more detailed description of the planned analysis.

11.2. Outcome variables

The primary outcome variable is whether an escalation in current treatment for PsA is required. An escalation in treatment consists of one or more of the following:

- Increase in dose of current medication
- Increase in frequency of dose administration
- Change in route of administration (i.e. from oral to sc MTX if dose not reduced)
- Initiation of a new medication in addition to existing therapy (including steroid >5mg prednisolone, conventional, targeted synthetic, or biologic DMARD)
- Initiation of a new medication as a switch from existing therapy (including steroid >5mg prednisolone, conventional, targeted synthetic, or biologic DMARD)

Reduction of therapy will also be collected, defined as any of the following:

- Decrease in dose of current medication
- Decrease in frequency of dose administration
- Change in route of administration, where not covered as described under “Escalation” above
- Stopping a medication

If the patient is retained on the same treatment regimen as they were on before the clinic visit, this will be considered as “No change”

Details of treatment prior to (at the start of) the appointment and subsequent to the appointment (including any treatment changes) will be collected.

Secondary outcomes comprise the following:

Patient data:

- PsA impact of disease (PsAID-12) scores
- Patients’ satisfaction with consultation as measured by the COLLABORATE scores
- Perceived efficacy on patient-physician interaction score (PEPPI)
- Other assessments performed (see 9.7) will be used for the analysis of factors affecting treatment decisions but do not represent outcomes per se

Physician data:

- Physician’s opinion of the reasons driving the treatment decision
    - Assessment of tender/swollen joints/entheses
    - Assessment of skin and nail psoriasis
    - Marker of systemic inflammation (e.g. CRP)
    - Routine patient reported outcomes (e.g. patient global or pain scores)
- Physician’s opinion of how the PsAID-12 questionnaire responses influenced the treatment decision today.

11.3. Description of the Statistical Methods

A stratified estimate of the percentage of patients requiring an escalation in PsA treatment will be derived, with clinic as the stratum. For the primary outcome, logistic regression will be used to investigate the effect of the total PsAID-12 score on the probability of modifying treatment, after adjusting for clinic. This analysis will not take account of other possible predictive factors: see later paragraph in this section. The odds ratio will be estimated for unit increases in PsAID-12 score with associated 95% confidence interval.

Logistic regression will be used to investigate the relationship between various factors and the decision to change treatment. Potential factors to be investigated include:

- Patient characteristics (gender, disease duration, comorbidities, including presence of fibromyalgia)
- Physician characteristics (age)
- Disease activity characteristics (Patient global, physician global, joint counts, BSA, enthesitis, dactylitis)
- Disease impact characteristics (PsAID-12, Patient pain, HAQ, SF-36)

Various logistic regression models will be fitted to the data to identify the factors having most influence on the decision to escalate treatment. Once a suitable model has been identified, the term for PsAID-12 will be added to see its effect on that model. This will be done by assessing the goodness of fit of the models with and without PsAID-12, and also by estimating the odds ratio associated with a unit increase in PsAID-12 score, after fitting other predictive terms.

The collaboRATE scores will be used to assess the degree of patients' satisfaction with their consultation and the relationship between these scores and the decision to change treatment, and other key outcomes, will be investigated in summary tables and/or graphs.

The PEPPI scores will be used to assess the patients' own perceived level of confidence in interacting with the physician during the consultation. The relationship between these scores and the decision to change treatment, and other key outcomes, will be investigated in summary tables and/or graphs.

The characteristics of the patient population with regard to demographics, severity and duration of PsA and HRQoL, and characteristics of the participating centres (age/sex of physicians, country and type of centre), will be summarised in tables.

Other variables will be summarised in tables of descriptive statistics.

The study team will do a detailed review of all the physicians' reports of the use of PsAID-12 in order to identify emerging themes. These will be summarised and reported on qualitatively. For example, themes may include the value of insight provided by the PsAID-12 and the balance between the extent of pain and patients' ability to cope.

11.4. Sample Size Determination

The initial sample size calculation was based on the need to estimate the percentage of patients for whom treatment is modified, with a stated degree of precision. This was defined as a 95% confidence interval for the percentage with width 10 percentage points (e.g. 25% to 35% for a percentage of 30%). This is based on data from the GRACE study which recruited 503 patients worldwide and found that 32%

underwent a treatment change, the majority escalation for active disease (Helliwell et al, ARD 2013; 72: 986). For a percentage of 30% (i.e. 30% of patients requiring treatment change), a study of 333 patients would have 80% power to estimate a percentage of 30% requiring change with a confidence interval of ±5% (Source: SAS® PROC POWER). A larger percentage of patients needing treatment change or a more precise estimate (narrower confidence interval) would require a larger sample size. For example, if the proportion requiring treatment escalation is 50%, then 390 patients would be required for the study to have at least an 80% chance of obtaining a 95% confidence interval of width 10 percentage points (i.e. 45% to 55%).

In order to investigate the effect of the total PsAID-12 score on the proportion, the sample size can be calculated using the method in Hsieh (1998). For example, if the effect of an increase in 1 s.d. of the PsAID-12 score is to increase the chance of intensifying the treatment from 30% to 40%, approximately 316 patients would be required for power of 95% and two-sided alpha of 5%

For the secondary outcome of assessing the importance of the various factors on an event (in this case the decision to intensify treatment), a rule of thumb is 10 patients experiencing the event per factor. If 15 factors affecting the decision to change treatment are to be investigated then this would require at least 150 patients requiring a treatment change, which for a percentage of 30% would need 500 patients in total. If the percentage requiring a treatment change is less than 30% then reliable estimates of the effect of fewer factors could be derived. Conversely, with a frequency of treatment change closer to 50% of patients, the effects of more factors could be estimated. It is likely that there could be some missing data but this will be checked carefully at source sites. There is no follow up required for this cross-sectional study so we have not accounted for loss to follow up.

11.5. Analysis populations

For clinical outcomes, all participants will be included as enrolled. No other patient populations will be defined.

11.6. Decision points

No interim analysis will be performed.

11.7. Stopping rules

There are no planned stopping rules.

11.8. The Level of Statistical Significance

The level of significance to be used is 0.05 unless otherwise stated.

11.9. Procedure for Accounting for Missing, Unused, and Spurious Data.

Patients with missing data on the primary study outcome (change of therapy) will be excluded from the relevant analysis but will be described in the study report, especially the extent of the missing data and the reasons for it. Missing covariate information will not necessarily lead to automatic exclusion from analysis. The extent of missing data of all kinds will be fully investigated and imputation methods may be used if appropriate. Details will be given in the SAP.

Missing scores on individual items of questionnaires will be handled as detailed in the corresponding scoring manual.

In this study, intention to treat analysis is not relevant given the study design.

11.10. Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any deviation(s) from the original statistical plan will be described and justified in the protocol and/or in the final report.

11.11. Health Economics Analysis

Not applicable.

11.12. Bias

The study is observational and not randomised, so is subject to various types of bias. Selection bias can occur through the type of patients invited to participate at each centre, or in the choice of participating centres.

Study centres are to be selected based on the potential population size, the ability to perform the study, and variety of hospital/clinic settings to provide a cross-section of different clinics. At each centre, a random subset of eligible patients presenting at routine clinics each month during the study time frame will be invited to participate. This is to try and avoid subjective decisions by the physicians as to who they invite to join the trial. A log will be kept of those who do and do not agree to participate to see whether the refusal rate is similar across all participating sites. A high refusal rate could lead to significant bias in that the recruited patients may not reflect the general PsA population. The recruitment rates for each centre will be summarised in the study report. Demographic and other disease characteristics will be used to summarise the study population across sites to see whether they are consistent and to assess the extent to which they reflect the general PsA population.

The primary outcome of the study is treatment change, which is by definition, a subjective choice. The study investigators will be asked to make treatment decisions based on the information available to them, as they would usually do. Since the aim of the study is to assess the influence of PsAID-12 on the decision, care must be taken not to unduly influence participating physicians as to what factors they should consider when making any treatment decisions.

The various PRO instruments will be completed by the patients themselves to avoid any possible influence by research staff at the study sites. In particular, questionnaires assessing the level of satisfaction with the consultation (i.e. PEPPI and COLLaBORATE) will be done by the patients alone, with the completed forms collected by study staff so that they are not seen by the physicians as this could affect the way that patients respond.

12. DATA MANAGEMENT

The plan for the data management of the study is outlined below. A separate Data Management document will be produced for the study which will contain details of the procedures to be followed.

12.1. Source Data

Source documents are where data are first recorded, and from which participants' CRF data are obtained. These include, but are not limited to, hospital records (from which medical history and previous and concurrent medication may be summarised into the CRF), clinical and office charts, laboratory and pharmacy records, diaries, microfiches, radiographs, and correspondence.

CRF entries will be considered source data if the CRF is the site of the original recording (e.g. there is no other written or electronic record of data). All documents will be stored safely in confidential conditions. On all study-specific documents, other than the signed consent, the participant will be referred to by the study participant number/code, not by name.

12.2. Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations.

12.3. Data Recording and Record Keeping

All trial data will be entered on to paper CRFs at the study sites except for the PsAID-12 which will be recorded on a tablet within the GRAPPA app. A screenshot of this will be saved alongside the paper CRF.

Data from the CRFs and the GRAPPA app will be entered into an electronic database (e.g. Excel file) by staff at Springer Healthcare. Any queries on data e.g. illegible entries, will be relayed back to the relevant study site for clarification. The database will then be updated accordingly. All such data clarifications will be logged to provide an audit trail. Occasional data checks will be run by the study statistician to monitor the accruing data e.g. validity of score ranges and extent of missing data. Any consistent findings will be addressed and raised with the centres concerned to try and rectify any problems as early as possible.

The final database will be imported into SAS ® Version 9.4 for Windows, or later, for analysis.

The participants will be identified by a unique trial specific number and/or code in the database. The name and any other identifying detail (e.g. address, date of birth) will NOT be included in any trial data electronic file.

All paper documents containing personal data (e.g. informed consent forms) will be stored securely and only accessible by study staff and authorised personnel. The study investigator is responsible for keeping these documents securely to ensure that in case of an emergency, participants can be identified and contacted.

All study data will be stored for a minimum of five years after the end of the study in line with the university policy.

13. QUALITY ASSURANCE PROCEDURES

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures.

13.1. Risk assessment

A formal risk assessment and monitoring plan will not be undertaken as the procedures involved are routine and risks are minimal.

13.2. Study monitoring

The study may be monitored, or audited in accordance with the current approved protocol, GCP, relevant regulations and standard operating procedures. A Monitoring Plan has been developed based on a risk assessment. This study has been found to be low risk as it is observational with minimal interventions (just MRI scans). The monitoring activities, based on this risk assessment will therefore only involve central monitoring to ensure that consent forms are completed, that scores are within the defined range for the instrument concerned, and that there are no significant issues with missing data.

13.3. Study Committees

Study Management Group

The study management group will meet at least every 2 months to monitor recruitment and retention and to ensure that the study is being run according to GCP. There are no further specific oversight committees for this small observational study. A DMEC is not required.

14. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file.

15. SERIOUS BREACHES

A “serious breach” is a breach of the protocol or of the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree –

(a) the safety or physical or mental integrity of the trial subjects; or

(b) the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within 1 working day. In collaboration with the C.I., the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and the relevant NHS host organisation within seven calendar days.

16. ETHICAL AND REGULATORY CONSIDERATIONS

16.1. Declaration of Helsinki

The Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

16.2. Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in accordance with relevant regulations and with Good Clinical Practice.

16.3. Approvals

Following Sponsor approval the protocol, informed consent form, participant information sheet will be submitted to an appropriate Research Ethics Committee (REC), and HRA (where required) and host institutions for written approval.

The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

16.4. Other Ethical Considerations

No additional ethical considerations have been identified.

16.5. Reporting

The CI shall submit once a year throughout the study, or on request, an Annual Progress report to the REC Committee, HRA (where required) host organisation, Sponsor and funder (where required). In addition, an End of Study notification and final report will be submitted to the same parties.

16.6. Transparency in Research

Not applicable as the research is non-interventional.

16.7. Participant Confidentiality

The study will comply with the General Data Protection Regulation (GDPR) and Data Protection Act 2018, which require data to be de-identified as soon as it is practical to do so. The processing of the personal data of participants will be minimised by making use of a unique participant study number only on all study documents and any electronic database(s). All documents will be stored securely and only accessible by study staff and authorised personnel. The study staff will safeguard the privacy of participants' personal data.

16.8. Expenses and Benefits

As research appointments will be alongside standard care, reimbursement of expenses will not be provided.

17. FINANCE AND INSURANCE

17.1. Funding

Funding has been provided by Amgen to cover the costs associated with this study.

17.2. Insurance

The University has a specialist insurance policy in place which would operate in the event of any participant suffering harm as a result of their involvement in the research (Newline Underwriting Management Ltd, at Lloyd's of London).

17.3. Contractual arrangements

Appropriate contractual arrangements will be put in place with all third parties.

18. PUBLICATION POLICY

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by Amgen. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

19. DEVELOPMENT OF A NEW PRODUCT/ PROCESS OR THE GENERATION OF INTELLECTUAL PROPERTY

Ownership of IP generated by employees of the University vests in the University. The University will ensure appropriate arrangements are in place as regards any new IP arising from the trial.

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19. ARCHIVING

Paper CRFs will be stored securely at each local site or archived to an approved secure site.

20. REFERENCES

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21. APPENDIX A: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee and HRA (where required).