## Principal Investigator

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## General Information

**Key Personnel (in addition to PI):** **First Name:** Mousumi
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**Are external grants or funds being used to support this research?:** External grants or funds are being used to support this research.
**Project Funding Source:** The National Institute for Health Research (Health Technology Assessment programme (UK))
ypp-06012016.pdf

## Certification

**Certification:** All information is complete; I (PI) am responsible for the research; data will not be used to support litigious/commercial aims.
**Data Use Agreement Training:** As the Principal Investigator of this study, I certify that I have completed the YODA Project Data Use Agreement Training

**Associated Trial(s):** NCT01009086 - A Study of the Safety and Effectiveness of Ustekinumab in Patients With Psoriatic Arthritis
NCT01077362 - A Study of the Safety and Efficacy of Ustekinumab in Patients With Psoriatic Arthritis With and Without Prior Exposure to Anti-TNF Agents
**What type of data are you looking for?:** Individual Participant-Level Data, which includes Full CSR and all supporting documentation

## Research Proposal

## Project Title

A systematic review and economic evaluation of certolizumab pegol and secukinumab for treating active psoriatic arthritis

**Narrative Summary:**
The purpose of this project is to assess the benefits and adverse effects of two of the newer biologic therapies - certolizumab pegol and secukinumab - for treating active and progressive psoriatic arthritis in patients who have an inadequate response to conventional treatment. This will be done by identifying and analysing data from relevant clinical trials. This study will also evaluate whether these two biologic therapies are a cost-effective use of NHS resources when compared with the other therapies currently recommended by NICE for treating psoriatic arthritis.

**Scientific Abstract:**
Background: Conventional treatment for severe active psoriatic arthritis usually begins with non-steroidal anti-inflammatory drugs, followed by disease-modifying anti-rheumatic drugs. Where necessary these may then be followed by one of several available biologic therapies.
Objective: To determine the clinical effectiveness and cost effectiveness of certolizumab pegol and secukinumab within their marketing authorisations for treating active psoriatic arthritis in adults for whom disease-modifying anti-rheumatic drugs have been inadequately effective.
Study design: Systemtaic review, network meta-analysis and economic evaluation
Participants: Adults with active psoriatic arthritis for whom disease-modifying anti-rheumatic drugs have been inadequately effective.
Main outcome measures: Measures of disease activity - PsARC, ACR 20/50/70, Functional capacity (assessed using HAQ), Radiographic assessment of disease progression, Response of psoriatic skin lesions (assessed using PASI).
Statistical analysis: Network meta-analyses using Bayesian statistical methods will be performed for the outcomes required to populate the economic model. This will provide information on the benefits of the active treatments relative to each other (as few head-to-head trials exist). Clinical and methodological heterogeneity will be evaluated, with sensitivity or subgroup analyses performed where appropriate, and where available data permit. Studies judged to be at high risk of bias will be removed in sensitivity analyses.

**Brief Project Background and Statement of Project Significance:**
We are currently undertaking a multiple technology appraisal (MTA) for NICE. We have so far extracted data which are to be used in network meta-analyses and in modelling of cost-effectiveness. However, the only data published for the two ustekinumab trials (PSUMMIT 1 and PSUMMIT 2) relate to the 24 week time point. The main problems with the 24 week data are a reduction in the preservation of blinding (even though there may still be some level of blinding) and that data imputations have to be made for placebo patients who have entered 'early escape' and crossed over to receive an active treatment. For all the other treatments included in our systematic review we have 12 to 16 week data before patients could enter 'early escape' and cross-over to active treatment. To enable a more robust comparison across treatments we therefore seek 12 week data for these two ustekinumab trials.

**Specific Aims of the Project:**
The purpose of this project is to assess the benefits and adverse effects of two of the newer biologic therapies - certolizumab pegol and secukinumab - for treating active and progressive psoriatic arthritis in patients who have an inadequate response to conventional treatment. This study will also evaluate whether these two biologic therapies are a cost-effective use of NHS resources when compared with the other therapies currently recommended by NICE for treating psoriatic arthritis.

**What is the purpose of the analysis being proposed? Please select all that apply.** Summary-level data meta-analysis
Summary-level data meta-analysis will pool data from YODA Project with other additional data sources
Other

## Research Methods

**Data Source and Inclusion/Exclusion Criteria to be used to define the patient sample for your study:**
Eligible studies will be of adults with active psoriatic arthritis for whom disease-modifying anti-rheumatic drugs have been inadequately effective. Searches of electronic databases have been carried out to identify relevant randomised controlled trials of secukinumab, certolizumab pegol, ustekinumab, etanercept, infliximab, golimumab, adalimumab and apremilast (used at their licensed doses) versus placebo or each other.

**Main Outcome Measure and how it will be categorized/defined for your study:**
For both trials at the 12 week time point, and for the 45mg and placebo arms we seek the following outcome data:
HAQ-DI score (or HAQ-DI change from baseline)
PsARC responder Y/N
ACR 20 responder Y/N
ACR 50 responder Y/N
ACR 70 responder Y/N
In subgroup of patients evaluated for PASI:
PASI 75 responder Y/N
and, if available:
PASI 50 responder Y/N
PASI 90 responder Y/N

**Main Predictor/Independent Variable and how it will be categorized/defined for your study:**
Secukinumab, certolizumab pegol, ustekinumab, etanercept, infliximab, golimumab, adalimumab and apremilast.

**Other Variables of Interest that will be used in your analysis and how they will be categorized/defined for your study:**
For the PSUMMIT 2 trial only we need to know the patient anti-TNF status at baseline: naïve or experienced.

**Statistical Analysis Plan:**
Bayesian network meta analyses will be conducted using WinBUGS software. Intention-to-treat datasets will be used which relate to time points before patients have crossed-over to other trial treatments (typically across trials, these time points range between 12-16 weeks ). The common comparator will be placebo. The results will provide information on the benefits of these agents relative to placebo and to each other.

**Project Timeline:**
The deadline for submitting our final report is 2nd August 2016.

**Dissemination Plan:**
The study will be published as an NIHR HTA report (open access) and publicised on the NICE, CRD and CHE websites.

**Bibliography:**
https://www.nice.org.uk/guidance/GID-TAG521/documents/final-protocol-2