

# Improving outcomes for patients with rheumatoid arthritis with intermediate disease - is intensive management more effective than standard care?

<b>Submission date</b> 16/01/2014	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 16/01/2014	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 26/09/2023	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Rheumatoid arthritis is a major health problem that affects one adult in a hundred. Its NHS costs exceed £500 million yearly. The main problem in rheumatoid arthritis is swollen (inflamed) joints. If persistent these cause disability and reduce quality of life. It is accepted that patients with active early rheumatoid arthritis need intensive care. This type of care results in reduction in one third of patients. Such reductions minimise disability and maximise quality of life. However, two thirds of active patients fail to achieve this reduction. Their ongoing grumbling arthritis - neither active nor in remission - means most of them are likely to become very disabled in the fullness of time with current treatment approaches. This study focuses on these patients. It is designed to find out whether intensive care results in more reduction of disease in patients with intermediate disease activity. It will also see whether intensive management reduces disability, enhances quality of life and is acceptable to patients.

### Who can participate?

The study will involve men and women aged over 18 years who have a diagnosis of Rheumatoid Arthritis.

### What does the study involve?

Participants will be randomly chosen to receive intensive management or standard care. Patients receiving intensive management will have monthly sessions with a specialist nurse /health practitioner, drug treatment will be optimised and treatment support regarding pain management, exercise and adherence will be given. The other group will receive standard care. All participants will be in the trial for 12 months. Patients will be assessed initially and at six and 12 months through self-completed questionnaires and clinical evaluation.

### What are the possible benefits and risks of participating?

There may not be any direct benefit to participants taking part in the study; however, their arthritis will be monitored very closely by the research team, and it is hoped that this research

will help improve the treatment and management of rheumatoid arthritis for all patients in the future. The risks involved in taking part in the study are small. Patients receiving intensive management are likely to receive more drug therapy. While it is possible that this will result in more side effects, there is little evidence that this will occur. This is because close monitoring and adjustment of treatment is more likely to limit the risk of side effects.

Where is the study run from?

The study will be recruiting through rheumatology departments across England. The study will be run from King's College London (UK).

When is the study starting and how long is it expected to run for?

Recruitment will begin around April 2014. Each participant is expected to be enrolled in the trial for a period of 12 months. The study is due to end in July 2017.

Who is funding the study?

The study is funded by a National Institute for Health Research (NIHR), UK.

Who is the main contact?

Dr Fowzia Ibrahim  
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### **Study website**

<http://www.titrate.org.uk>

## **Contact information**

### **Type(s)**

Scientific

### **Contact name**

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### **Contact details**

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# Additional identifiers

## EudraCT/CTIS number

Nil known

## IRAS number

## ClinicalTrials.gov number

Nil known

## Secondary identifying numbers

15762

# Study information

## Scientific Title

A pragmatic randomised controlled open trial of the effect of intensive management (IM) compared with standard care (SC) on remission rates at 12 months in rheumatoid arthritis patients with intermediate disease activity

## Acronym

TITRATE

## Study objectives

TITRATE will formally test the hypothesis that patients with established RA who currently have intermediate disease activity (defined as DAS28-ESR 3.2-5.1 with at least 3 active joints) and are currently receiving at least one DMARD, are more likely to achieve remission at 12 months if they receive intensive management than if they continue to have standard care.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

West London Research Ethics Committee, 28/10/2013, ref: 13/LO/1308

## Study design

Randomized controlled open interventional multicentre trial

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## **Participant information sheet**

Not currently available in web format. Please use the contact details to request a patient information sheet.

## **Health condition(s) or problem(s) studied**

Rheumatoid arthritis

## **Interventions**

The study will compare standard care with intensive management over a period of 12 months. Intensive management will involve monthly sessions with a trained specialist nurse or health practitioner. A management algorithm will be used to optimise drug treatment and treatment support spanning pain management, exercise and adherence will be given. Drugs will be used within their licensed indications.

The control group will receive standard care according to local and national pathways, which normally involves six-monthly clinical reviews.

## **Intervention Type**

Other

## **Phase**

Not Applicable

## **Primary outcome measure**

Disease remission at 12 months (final assessment) measured by the Disease Activity Score-28 (DAS28) criterion (DAS28-ESR<2.6)

## **Secondary outcome measures**

1. Alternative assessments of remission: Remission measured by the DAS28-CRP and the Simplified Disease Activity Index (SDAI) (remission defined as  $SDAI \leq 3.3$ ) at 12 months; remission assessed by all measures at six months.
2. Assessment of Individual Components of Remission: Tender joint counts (68 joints), swollen joint counts (66 joints), patient global assessments on 100mm visual analogue scales (VAS), physician global assessments on 100mm VAS, C-Reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) at baseline, 6 months and 12 months.
3. Disability: Health Assessment Questionnaire (HAQ) at baseline, 6 months and 12 months.
4. Joint Imaging (Predictor of future disability): Plain X-rays of the hands and feet read by a modified Larsen's score at baseline and 12 months.
5. Quality Of Life: EuroQOL 5 Dimensional score (EQ5D-5L) and patient-rated fatigue scale on 100mm VAS at baseline, six and 12 months.
6. Patient Acceptability: Modified version of the Measuring Actual Patient-led Expectations in Rheumatoid Arthritis (MAPLe-RA) questionnaire at baseline and 12 months, Medication Adherence Rating Scale (MARS) and adverse events at baseline, six and 12 months.
7. Economic Assessments: Modified Client Service Receipt Inventory (CSRI) at baseline, six and 12 months.

## **Overall study start date**

01/04/2014

**Completion date**

14/07/2018

## **Eligibility**

**Key inclusion criteria**

Current inclusion criteria as of 11/06/2015:

1. Diagnosis of Rheumatoid Arthritis (by ACR, 2010 criteria)
2. Have received at least one DMARD for at least six months, and currently receiving at least one DMARD
3. Have intermediate disease activity, defined by:
  - 3.1. DAS28-ESR 3.2-5.1.
  - 3.2. At least three active joints (defined as swollen and/or tender) on 66/68 joint count, to include at least one swollen joint
4. Willing and able to follow an intensive management programme
5. Able and willing to give informed consent

Previous inclusion criteria:

1. Diagnosis of Rheumatoid Arthritis (by ACR, 2010 criteria); duration six months to 10 years
2. Have received at least one DMARD for at least six months, and currently receiving at least one DMARD
3. Have intermediate disease activity, defined by:
  - 3.1. DAS28-ESR 3.2-5.1.
  - 3.2. At least three swollen joints and three tender joints on 66/68 joint count
4. Willing and able to follow an intensive management programme
5. Able and willing to give informed consent

**Participant type(s)**

Patient

**Age group**

Adult

**Sex**

Both

**Target number of participants**

398

**Total final enrolment**

335

**Key exclusion criteria**

1. Major co-morbidities making intensive treatment inadvisable (e.g. heart failure)
2. Previously failed multiple DMARDs (more than or equal to 5 treatments) or having received biologics
3. Irreversible disability from extensive joint damage (for example, replacement of three or more major joints)

4. Women who are pregnant, breastfeeding or planning to conceive
5. Currently in early RA pathway
6. Current or recent (within the previous 12 weeks) participation in another interventional trial

**Date of first enrolment**

01/04/2014

**Date of final enrolment**

30/06/2017

## Locations

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**King's College London**

London

United Kingdom

SE5 9RJ

## Sponsor information

**Organisation**

King's College London

**Sponsor details**

Strand

London

England

United Kingdom

WC2R 2LS

**Sponsor type**

University/education

**Website**

<http://www.kcl.ac.uk/index.aspx>

**ROR**

<https://ror.org/0220mzb33>

**Organisation**

King's College Hospital NHS Foundation Trust

**Sponsor details**

Research & Development  
161 Denmark Hill  
London  
England  
United Kingdom  
SE5 8EF

**Sponsor type**

Hospital/treatment centre

**Website**

<https://www.kch.nhs.uk/>

**ROR**

<https://ror.org/01n0k5m85>

**Funder(s)****Funder type**

Government

**Funder Name**

National Institute for Health Research (NIHR) (UK) - Programme Grant for Applied Research, Ref: RP-PG-0610-10066

**Results and Publications****Publication and dissemination plan**

To be confirmed at a later date

**Intention to publish date**

30/09/2020

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are not expected to be made available as there is no consent to make this data available in the public domain. However, the researchers will be able to provide an appropriate request i.e. summary participant data after review by the TITRATE team.

**IPD sharing plan summary**

Not expected to be made available

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/10/2020	06/10/2020	Yes	No
<a href="#">HRA research summary</a>	Secondary analysis	25/09/2023	28/06/2023	No	No
<a href="#">Other publications</a>			26/09/2023	Yes	No