

# Oral iron, intravenous iron or discontinuation of therapy for older adults with treatment unresponsive iron deficiency anaemia

<b>Submission date</b> 04/08/2017	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 16/08/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 06/10/2022	<b>Condition category</b> Haematological Disorders	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Anaemia due to low iron levels is common in older people and can cause tiredness and breathlessness. It is commonly treated with iron tablets. However, iron tablets do not improve anaemia in many people and they have side effects. It is not known what strategy of care is best for patients who do not respond to iron tablets: should treatment stop, continue with tablets (which is current practice), or switch to iron given by a drip (intravenous iron)? Before a large study is run to find the answers to these questions, a smaller study is needed to make sure that the study processes can be run properly, to test that people can be recruited to the large study, and to work out how many people must be recruited to the large study. This is why this smaller study is being run first.

### Who can participate?

Patients aged 65 and over with anaemia due to low iron levels who have not improved after at least 8 weeks of iron tablets

### What does the study involve?

Participants are randomly allocated to either continue the iron tablets they are already taking, stop their iron tablets and receive iron in a drip on one or two occasions, or to stop their iron tablets and have no further iron. Before the start and 3 months later, all participants are asked a series of questions about how tired or breathless they feel; undergo a walking test and other measures of fitness and balance; and are asked questions about how well they are taking their medicines, their quality of life, and what contact they have had recently with health services. The trialists compare how easy it is to find eligible people through GP practices, adverts and hospital clinics, and measure levels of haemoglobin in the blood (a measure of anaemia) at the start and 3 months later.

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

If one treatment is better than another, participants may feel less tired and breathless, or not have the side effects that their usual iron tablets give them. Iron tablets can cause constipation and indigestion. These are the standard treatment that all participants will already be taking

before entering the study. Intravenous iron (through a drip) can rarely cause allergic reactions or damage skin if the drip leaks from the vein.

Where is the study run from?

The University of Aberdeen is leading the study, assisted by Tayside Clinical Trials Unit.

Participants are recruited from Tayside, Grampian and Fife regions of Scotland, and through the Norfolk and Norwich NHS Trust area in England.

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

August 2017 to December 2019

Who is funding the study?

The Chief Scientist Office of the Scottish Government (UK)

Who is the main contact?

1. Prof. Phyo Myint

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2. Dr Miles Witham

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**Study website**

<https://raindrop.org.uk/>

## Contact information

**Type(s)**

Public

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## **Additional identifiers**

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**

**Secondary identifying numbers**

N/A

## **Study information**

### **Scientific Title**

Scientific title as of 21/09/2018:

RArandomised Iron Deficiency anaemia management Pilot

Previous scientific title:

Oral iron, intravenous iron or discontinuation of therapy for older adults with treatment unresponsive iron deficiency anaemia: a pilot randomised controlled trial

### **Acronym**

RAINDroP

### **Study objectives**

The primary objective of this pilot trial is to estimate the recruitment rates and examine recruitment strategies at pilot sites across different settings and different NHS providers. The secondary objectives are to examine the change in a key surrogate outcome (haemoglobin levels) and to obtain preliminary data on the proposed patient outcomes (quality of life, symptoms and physical function) to inform the sample size calculation for a future definitive trial.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

North of Scotland research ethics committee, approval date 05/06/2018, approval number 18/NS/0064

### **Study design**

Three-arm parallel-group randomised controlled trial

**Primary study design**

Interventional

**Secondary study design**

Randomised parallel trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format; please use contact details to request a participant information sheet

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

Iron deficiency anaemia

**Interventions**

Participants will be randomised on a 1:1:1 allocation ratio via a web-based randomisation system run by a third party. A minimisation algorithm with a small random element will be used to ensure balance across recruitment centres and key baseline measures. Randomisation will be stratified by site, and further balanced using minimisation. Haemoglobin after minimum 8 weeks of oral iron ( $\geq 100\text{g/L}$  vs  $< 100\text{g/L}$ ), ferritin prior to commencement of oral iron ( $\geq 50\text{ug/L}$  vs  $< 50\text{ug/L}$ ) and six minute walk distance ( $\geq 300\text{m}$  vs  $< 300\text{m}$ ) will be the minimisation variables.

Participants are randomised to either:

1. Continue the iron tablets they are already taking
2. Stop their iron tablets and receive intravenous iron on one or two occasions
3. Stop their iron tablets and have no further iron

Before the start and 3 months later, participants are asked a series of questions about how tired or breathless they feel; undergo tests to see how quickly they can walk and other measures of fitness and balance; complete questionnaires about how well they are taking their medicines, their quality of life, and what contact they have had recently with health services. The trialists will compare how easy it is to find eligible people through GP practices, adverts and hospital clinics, and will measure haemoglobin in the blood (a measure of anaemia) at the start and 3 months later.

**Intervention Type**

Other

**Primary outcome measure**

Co-primary outcomes, measured from recruitment records at the end of recruitment:

1. The rate of randomisation per month across the pilot sites
2. The proportion recruited from each route of recruitment

**Secondary outcome measures**

Measured between baseline and 3 months:

1. Hemoglobin levels, measured by blood sample at baseline and 3 months
2. Eligible patients per site, measured from recruitment records at end of recruitment
3. Proportion of eligible patients agreeing to take part and passing screening, measured from recruitment records at end of recruitment
4. Feasibility of collecting primary (physical functioning and health-related and general quality of life) and secondary outcomes for main trial:
  - 4.1. Six minute walk distance, measured by walk test at baseline and 3 months
  - 4.2. Short physical performance battery (SPPB), measured at baseline and 3 months
  - 4.3. Health-related quality of life, measured using EQ-5D, 15D
  - 4.4. Anemia-related symptoms (e.g. breathlessness, tiredness, fatigue), measured by symptom questionnaire at baseline and 3 months
  - 4.5. Healthcare use including use of blood transfusions and hospitalisation, measured by questionnaire at 3 months
  - 4.6. Mortality, measured by death certificate records at 3 months
5. Dropout and crossover rate, measured from recruitment and follow up records at 3 months
6. Side effects and adverse events (GI symptoms, headache, dizziness, rash), measured from case record form at 3 months
7. Functional limitation, measured using six-minute walk (<400m) or short physical performance battery ( $\leq 10$ ) at baseline and 3 months
8. Fatigue, measured using validated Fatigue Severity Scale at baseline and 3 months

**Overall study start date**

01/08/2017

**Completion date**

31/12/2019

## **Eligibility**

**Key inclusion criteria**

1. Age 65 years or over
2. Haemoglobin of  $\geq 85\text{g/L}$  and  $\leq 110\text{g/L}$  prior to commencing oral iron
3. Ferritin  $< 100\mu\text{g/L}$  prior to commencing oral iron
4. Currently taking oral iron at any dose with a minimum of 8 weeks therapy
5. Insufficient response to oral iron therapy (sufficient response defined as improvement in Hb of  $20\text{g/L}$  after a minimum of 8 weeks of oral iron therapy)
6. Relevant investigations (including upper and lower GI endoscopies) either already conducted, offered but declined by the patient, or deemed not appropriate by the treating clinician

**Participant type(s)**

Patient

**Age group**

Senior

**Sex**

Both

**Target number of participants**

## **Total final enrolment**

5

## **Key exclusion criteria**

1. Active GI cancers
2. Active (unhealed) peptic ulcer disease
3. No ferritin level performed prior to commencing oral iron
3. Bleeding disorders (including being on oral anticoagulants; antiplatelet agents are permitted)
4. Weight loss of >5Kg in the last 3 months (as a possible marker of occult cancer)
5. Estimated GFR of <30ml/min/1.73m<sup>2</sup> by CKD-EPI equation
6. Symptomatic chronic heart failure (defined according to the European Society of Cardiology guidelines; note asymptomatic left ventricular systolic dysfunction is not classed as heart failure)
7. Terminal illness (with life expectancy less than 3 months as deemed by the local investigator)
8. Severe cognitive impairment precluding written informed consent
9. Unable to mobilise without human assistance (walking aids are allowed)
10. Previous reaction to intravenous iron
11. Currently participating in, or within 30 days of completion of, another clinical trial

## **Date of first enrolment**

01/09/2018

## **Date of final enrolment**

31/12/2019

## **Locations**

### **Countries of recruitment**

Scotland

United Kingdom

### **Study participating centre**

**NHS Tayside**

United Kingdom

DD2 1SP

## **Sponsor information**

### **Organisation**

University of Aberdeen

### **Sponsor details**

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King's College, Aberdeen  
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**Sponsor type**

University/education

**Website**

<http://www.abdn.ac.uk/>

**ROR**

<https://ror.org/016476m91>

**Organisation**

NHS Grampian

**Sponsor details**

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**Sponsor type**

Hospital/treatment centre

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

Government

**Funder Name**

Chief Scientist Office

**Alternative Name(s)**

CSO

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Local government

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

Results will be posted on ISRCTN, published in peer-reviewed journals and presented to both participants and scientific conferences after the end of 2019.

**Intention to publish date**

01/10/2022

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

At the end of the trial, deidentified trial data will be made available on request to other bona fide academic investigators via data sharing agreements overseen by the University of Aberdeen.

**IPD sharing plan summary**

Available on request

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol file</a>	version 2	14/06/2018	06/10/2022	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No