

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

Submission date 04/08/2017	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 16/08/2017	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 06/10/2022	Condition category 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?

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Additional identifiers

Protocol serial number

N/A

Study information

Scientific Title

Scientific title as of 21/09/2018:
RANdomised 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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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 ($< 400\text{m}$) or short physical performance battery (≤ 10) at baseline and 3 months
8. Fatigue, measured using validated Fatigue Severity Scale at baseline and 3 months

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 20g/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

Healthy volunteers allowed

No

Age group

Senior

Sex

All

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 $> 5\text{Kg}$ in the last 3 months (as a possible marker of occult cancer)
5. Estimated GFR of $< 30\text{ml/min/1.73m}^2$ 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

United Kingdom

Scotland

Study participating centre

NHS Tayside

United Kingdom

DD2 1SP

Sponsor information

Organisation

University of Aberdeen

ROR

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

Organisation

NHS Grampian

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

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?
HRA research summary			28/06/2023	No	No
Protocol file	version 2	14/06/2018	06/10/2022	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes