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# Tackling statin intolerance with N-of-1 trials (TASINI)

**Submission date**
02/04/2019

**Recruitment status**
No longer recruiting

**Registration date**
27/06/2019

**Overall study status**
Completed

**Last Edited**
16/06/2022

**Condition category**
Circulatory System

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

## Plain English summary of protocol

Background and study aims
Statins reduce deaths from heart problems by 25%. Treatment is cheap, effective, safe, and randomised trials show that it is well-tolerated causing few side effects. However, half of all patients prescribed statins have stopped them one year later, primarily due to the perceived side-effects. One explanation for this is that people are experiencing adverse events that they misattribute to the statin and stop the medication.
We propose to harness individuals' tendency to experiment with medication and create a coalition between doctor and patient that legitimizes and affirms experimentation in a way that will allow both to make inferences about the cause of adverse events that are more likely to be correct than currently is the case.

Who can participate?
Anyone living in the trial area over the age of 18, who is recommended by their GP to be on a statin can take part.

What does the study involve?
Participants will be placed into 3 groups. The open-label group will receive atorvastatin on and off in 4-week blocks. The closed-label group will receive atorvastatin and placebo in alternating 4-week blocks (but the capsules will look the same). The control group will receive treatment as usual. Participants will be supported to monitor adverse events and draw sound inferences about their cause using symptom diaries, 4-week on-off periods of medication use, and a review from their GP.

What are the possible benefits and risks of participating?
The benefits of taking part for participants is the opportunity to speak to the GP about the best way to reduce cholesterol and try a new approach to test whether the medicine (i.e. atorvastatin) is suitable to take long-term.
Taking part in the trial involves giving up some time to attend up to four study visits, and if randomised to one of the treatment groups, to complete a daily diary (taking about 5 minutes) for a week each month for the next six months. Taking part involves having a blood sample (requiring up to 8ml of blood). All blood tests come with a risk of bruising and pain.

Where is the study run from?
South Oxford Health Centre (UK)

When is the study starting and how long is it expected to run for?
May 2019 to April 2020

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Prof Paul Aveyard, paul.aveyard@phc.ox.ac.uk

# Contact information

### Type(s)
Public

### Contact name
Prof Paul Aveyard

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# Additional identifiers

### EudraCT/CTIS number
Nil known

### IRAS number

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
41074

# Study information

### Scientific Title

Tackling Statin Intolerance with N-of-1 trials in primary care (TASINI): testing the feasibility of a GP delivered behavioural intervention to increase statin adherence.

## Acronym
TASINI

## Study objectives
This is a feasibility trial. The principal question is whether a GP led intervention can improve adherence to statin medication (using an n-of-1-trial)

## Ethics approval required
Old ethics approval format

## Ethics approval(s)
Approved 22/02/2019, North of Scotland Research Ethics Committee (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE; Tel: +44 (0)1224 558458; Email: nosres@nhs.net), ref: 19/NS/0014

## Study design
Individual randomised multi-centred trial

## Primary study design
Interventional

## Secondary study design
n-of-1 trial

## Study setting(s)
GP practice

## Study type(s)
Prevention

## Participant information sheet
See additional files

## Health condition(s) or problem(s) studied
Cardiovascular disease - preventing heart attack and stroke

## Interventions
Participants will be randomised using an online randomization generator (http://www.randomization.com) to one of three arms: usual care, blinded n-of-1 experiment, and open-label n-of-1 experiment.

Participants in the open-label arm will receive atorvastatin 20mg on and off in 4 week blocks. Participants in the closed label arm will receive encapsulated atorvastatin 20mg and placebo in 4 week blocks (the order of statin/placebo will be randomised for the final 16 weeks of the study). Participants in the control group will receive usual care.

Participants will be supported to monitor adverse events and draw sound inferences about their cause using symptom diaries, 4-week on-off periods of medication use, and a review from their

GP. We will then test the feasibility of this approach to assess whether GPs deliver the intervention as planned, whether patients engage with this, and whether it improves adherence to statins.

### Intervention Type
Mixed

### Primary outcome measure
1. The proportion of invited patients who enrol in the trial.
2. The proportion of enrolled participants who accept GPs behavioural intervention.
3. Proportion of patients in the treatment conditions who decide to continue statin therapy compared to the proportion who decide to continue statin therapy in the usual care control arm.

### Secondary outcome measures
1. Difference in the proportion of participants who decide to continue statin therapy in the 'open-label' (unblinded) treatment arm (i.e. alternating between medication and no treatment) compared to the proportion of participants who decide to continue statin therapy in the 'closed-label' (blinded) treatment arm (i.e. alternating between statin and placebo) and compared to the proportion of participants receiving usual care (control arm). Timepoint: 24 week follow up; decision to persist with statin therapy treatment full time.
2. Count of the number of adverse events by system class and preferred term level (according to MedDRA) in the blinded arm compared to the unblinded arm. Timepoint: 24 week follow up. Analysis of the symptom diary.
3. Count of the number of times that participant attributes side effects to statin medication in blinded arm compared to the unblinded arm. Timepoint: 24 week follow up; analysis of symptom diary.
4. The difference in mean pain severity (taken from Brief Pain Inventory) scores between statin therapy and placebo in the open label arm compared to the closed label arm. Timepoint: 24-week follow up; analysis of symptom diary.
5. The difference in mean pain interference scores (taken from the brief pain inventory) between statin therapy and placebo in the open-label arm compared to the closed label arm. Timepoint: 24-week follow up; analysis of symptom diary.
6. If applicable, focus groups with patients who declined to participate in the main study on the reasons for this decision. Timepoint: focus groups after recruitment period ends.
7. Compare participant BMQ scores before and after the intervention. Compare BMQ score changes between study groups. Timepoint: 24 week follow up.

### Overall study start date
01/05/2019

### Completion date
01/04/2020

## Eligibility

### Key inclusion criteria
Any patient that:
1. Is 18 years of age or older
2. Requiring statin therapy according to NICE guidelines and the GP thinks statins are indicated
3. Has previously been prescribed/recommended statin treatment
4. Has stopped/is considering stopping statin treatment/ or has not started statin treatment due

to concerns about or experience of side-effects
5. Is willing and able to give informed consent for participation in the study and comply with study procedures
6. If on ezetimibe or another alternative to atrovstatin, willing to potentially cease said medication if randomised to one of the intervention arms

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants
95

### Total final enrolment
93

### Key exclusion criteria
Any patient that:
1. The GP thinks it is not indicated to recommence statins or the previous intolerance was severe enough to mean that recommencing statins may comprise a significant risk to health
2. Is unable to adhere to study procedures through illness or infirmity
3. Has any contraindications listed in the Summary of Product Characteristics (SmPC) for atorvastatin 20mg or placebo drug, including pregnancy
4. Is participating in any research project that may interact with the current study

### Date of first enrolment
01/06/2019

### Date of final enrolment
06/09/2019

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**South Oxford Health Centre**
Lake St

Oxford
United Kingdom
OX1 4RP

# Sponsor information

### Organisation
University of Oxford

### Sponsor details
Joint Research Office
1st floor, Boundary Brook House
Churchill Drive, Headington
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### Sponsor type
Research organisation

### Website
www.admin.ox.ac.uk/researchsupport/ctrg/

### ROR
https://ror.org/052gg0110

# Funder(s)

### Funder type
Government

### Funder Name
NIHR BRC Oxford Chronic Disease Cluster

### Funder Name
National Institute for Health Research

### Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

### Funding Body Type
Government organisation

### Funding Body Subtype
National government

### Location
United Kingdom

### Funder Name
NIHR CLAHRC Oxford

## Results and Publications

### Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

### Intention to publish date
01/04/2022

### Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

### IPD sharing plan summary
Other

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | | 28/02/2019 | 27/06/2019 | No | Yes |
| Protocol article | | 12/02/2020 | 22/09/2021 | Yes | No |
| Results article | | 14/06/2022 | 16/06/2022 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |