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Evaluating Diuretics in Normal Care (EVIDENCE) - a cluster randomised evaluation of hypertension prescribing policy

Submission date 09/08/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 11/08/2017	**Overall study status** Ongoing	
Last Edited 20/01/2025	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Having high blood pressure increases the chances that a person will suffer a heart attack or stroke in the future. The aim of treating high blood pressure with medication is to reduce this risk. A number of different types of medication are known to be effective in reducing blood pressure and in reducing the risk of heart attack and stroke. One of these medication types is the diuretics, often referred to as “water-tablets”. There are two diuretics commonly used in the UK for the treatment of high blood pressure but we do not know which is better. We know that they both work but one may be more effective than the other in the long term. The EVIDENCE (Evaluating Diuretics in Normal Care) study aims to find out if one of these medications is better than the other at preventing heart attacks and strokes. In everyday practice, GP's and hospital doctors are guided by agreed policies, based upon the best available evidence, in deciding which medications are likely to be the most effective. This study aims to compare the effectiveness of two different prescribing policies for diuretics in preventing heart attacks and strokes.

Who can participate?
Patients aged 18 and older who are diagnosed with a thiazide, or thiazide-like diuretic to treat hypertension.

What does the study involve?
Participating GPs are randomly assigned to one of these two prescribing policies. The doctors within that practice then use that policy to guide their prescribing decisions. As already happens in the NHS, mechanisms for switching from one medication to another is used to help practices adhere to their prescribing policy. GP's and their patients are free to choose what they think is the most appropriate treatment in each individual case. People who are registered in practices taking part in the study have their blood pressure medication managed by their GP in the usual way. If the practice policy requires a change to a patient’s usual diuretic prescription, participants are sent a letter advising them that this will take effect on their next requested prescription. All such patients will be given the opportunity to decline the switch. Participants are followed up with for the cardiovascular outcomes.

What are the possible benefits and risks of participating?
As the two medications in question are currently thought to be effectively the same in terms of benefits and side effects, there will be no direct risk or benefit to a person whose GP practice is taking part in the study.

Where is the study run from?
Medicines Monitoring Unit, University of Dundee (UK)

When is the study starting and how long is it expected to run for?
October 2017 to December 2025

Who is funding the study?
University of Dundee (UK)

Who is the main contact?
Dr Amy Rogers
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Study website
https://www.memoresearch.com/evidence

Contact information

Type(s)
Public

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
219202

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Protocol number: 2016CV12

Study information

Scientific Title
EValuatIng DiurEtics in Normal CarE (EVIDENCE) - a cluster randomised evaluation of hypertension prescribing policy

Acronym
EVIDENCE

Study objectives
The aim of this study is to formally evaluate the effectiveness of a policy of prescribing bendroflumethiazide versus a policy of prescribing indapamide as first-line choice of thiazide /thiazide-like diuretic in the treatment of hypertension.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 04/01/2017, East of Scotland Research Ethics Service (EoSRES) (Tayside Medical Science Centre (TASC), Ninewells Hospital and Medical School, Dundee, DD1 9SY, United Kingdom; 01382 383878; tay.eosres@nhs.scot), ref: 219202 17/ES/0016

Study design
Two-arm cluster randomized study of prescribing policy

Primary study design
Interventional

Secondary study design
Cluster randomised trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Hypertension and cardiovascular risk

Interventions

Current interventions as of 27/02/2020:
There are two study arms. Practices are randomly assigned on a 1:1 basis (using a computer algorithm) to either of two prescribing policies:

1. A policy of using Bendroflumethiazide (2.5mg, oral, once daily) as first choice when a diuretic is required for the treatment of hypertension

2. A policy of using Indapamide (2.5mg, immediate release, oral, once daily) as first choice when a diuretic is required for the treatment of hypertension

Practices agreed to adopt the assigned policy for future prescribing and existing routine prescriptions are been switched accordingly. Doctors remain free to select the most appropriate medication for their patients.
All patients eligible for a potential medication switch are informed by letter of the policy change. The letter explains the reason for any medication changes and directs patients to visit the study website or contact the study team (by telephone or email) to find out more about the study or to opt-out of the proposed medication change.

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Previous interventions:
There are two study arms. Practices are randomly assigned on a 1:1 basis (using a computer algorithm) to either of two prescribing policies:

1. A policy of using Bendroflumethiazide (2.5mg, oral, once daily) as first choice when a diuretic is required for the treatment of hypertension

2. A policy of using Indapamide (2.5mg, immediate release, oral, once daily) as first choice when a diuretic is required for the treatment of hypertension

Individual treatment decisions regarding drug choice, dosage, method and frequency of administration for patients will be left up to the treating GPs.

Where patients are already taking thiazide, or thiazide-like, diuretics at the time a practice joins the study, routine repeat prescriptions will be switched to the policy preferred drug, unless clinically indicated.

Intervention Type
Other

Primary outcome measure
The composite cardiovascular outcome (comprising non-fatal MI, non-fatal stroke, hospitalization for congestive heart failure, and vascular death) is measured using electronic record-linkage to national datasets of routinely collected data and supported by information from medical records.

Secondary outcome measures
1. Each individual component of the composite primary outcome will be included as a secondary outcome
2. All-cause mortality is measured using record-linkage to national datasets of routinely collected data

The study is primary outcome driven so the outcomes are counted as they occur rather than at defined time periods. We expect that the follow-up process will take around 3 years to accrue sufficient events to power the study.

Overall study start date
21/03/2017

Completion date
31/12/2025

Eligibility

Key inclusion criteria
1. Registered patients with a documented diagnosis of hypertension and prescribed a thiazide, or thiazide-like, diuretic in a participating practice
2. Aged 18 years and older

Participant type(s)
Other

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
100 GP practices of typical size (including approximately 240 individuals prescribed diuretics for hypertension)

Total final enrolment
98

Key exclusion criteria
Does not meet the inclusion criteria

Date of first enrolment
01/10/2017

Date of final enrolment
31/07/2023

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Medicines Monitoring Unit
University of Dundee
Ninewells Hospital and Medical School
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United Kingdom
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Sponsor information

Organisation
University of Dundee/NHS Tayside

Sponsor details
TASC (Tayside Medical Science Centre)
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Sponsor type
University/education

Website
http://www.ahspartnership.org.uk/ahsp

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Research council

Funder Name

Results and Publications

Publication and dissemination plan
We will publish the study protocol (where possible) and will undertake to make public the study results. The major form of publication will be articles in scientific journals but presentations and press releases may also be made. Protocol and statistical analysis plan will be made available at a later date.

Intention to publish date
30/06/2026

Individual participant data (IPD) sharing plan
Current IPD sharing statement as of 11/11/2022:
The datasets generated during and/or analysed during the current study are not expected to be made available because these are anonymised clinical data sets that must be analysed in a secure SAFE HAVEN accessed only by Public Benefit and Privacy Panel (PBPP)-approved individuals and therefore cannot be made publicly available. Only summary statistics (in a publication) will be presented.

Previous IPD:
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	feasibility report	17/11/2021	31/01/2022	Yes	No
Interim results article		11/03/2022	14/03/2022	Yes	No
HRA research summary			28/06/2023	No	No