ISRCTN26190474 https://doi.org/10.1186/ISRCTN26190474

Antidepressants to prevent relapse in depression in older people aged 75 years and over

Submission date
05/07/2024

Recruitment status
Recruiting

Registration date
22/08/2024

Overall study status
Ongoing

Last Edited
10/09/2024

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Depression is common in older adults and 1 in 7 will become depressed enough to need treatment. Although psychological (talking) therapies can be helpful, many people are treated with antidepressant medication by their general practitioner. Once depression has improved, it is unclear for how long antidepressant treatment should be continued. When patients ask "When can I stop my antidepressant?" their doctors do not have an answer that is based on evidence. Antidepressant drugs can have side effects that can contribute to memory and concentration difficulties and affect the control of blood pressure or the healthy rhythm of the heart. Many people are keen to stop their antidepressants as soon as they can. There is good evidence from studies involving younger people and a small amount of information from older people, that continuing antidepressants for at least 6 months after recovery can help to reduce the risk of depressed mood returning. Some people who have taken an antidepressant will experience withdrawal symptoms in the days and weeks whilst reducing and after stopping treatment. These withdrawal symptoms can sometimes resemble the symptoms of a recurrence of depression and it is important to be able to identify them so that they can be distinguished from each other. The ANTLER clinical trial (https://www.isrctn.com/ISRCTN15969819) showed in people aged 18 to 74 years, that continuing antidepressants for 12 months after they had recovered halved the risk they would become depressed again. Depression in people over the age of 75 and the response to treatment are often different from those in younger people. Risk factors for developing depression and continuing to be depressed are different, and older adults are also more likely to have additional physical illnesses as well as diseases affecting the blood supply to the brain that can reduce the effectiveness of depression treatment and increase the side effects of antidepressants. This study is a very similar clinical trial to ANTLER, involving people aged 75 years or older.

Who can participate?
Patients aged 75 years or older, who are taking antidepressants

What does the study involve?
Participation in the trial will involve a 50% chance of continuing the antidepressant for 12

months and a 50% chance of reducing and stopping the antidepressant to take a dummy pill (placebo). All trial medication will appear identical so that participants and trial staff remain unaware of what treatment is being taken by an individual in the trial. The most important measure from the trial will be the time at which depression returns during the 12 months of the study, should this occur. The study will also investigate differences in the experience of symptoms of antidepressant withdrawal, anxiety, memory and concentration and side effects of antidepressant medications. From information collected on the quality of life of participants in continuation and discontinuation groups, their use of health and social services and the impact of their depression on their activities and family life, the study will also investigate whether any benefits of continuing treatment also impact on the financial costs of illness. Some participants will be interviewed about their experiences of reducing and stopping treatment.

What are the possible benefits and risks of participating?
Benefits and risks not provided at time of registration

Where is the study run from?
University College London CCTU (UK)

When is the study starting and how long is it expected to run for?
December 2023 to February 2028

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Sue Philpott (Trial Manager), s.philpott@ucl.ac.uk

Contact information

Type(s)
Principal Investigator

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Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1009793

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
149926, IRAS 1009793, CPMS 63558

Study information

Scientific Title
Antidepressants to prevent relapse in depression in older people (ANTLER 75+ Trial) – a double blind randomised controlled trial to evaluate the effectiveness and cost-effectiveness of continuing antidepressants

Acronym
ANTLER 75+

Study objectives
To estimate the effectiveness and cost-effectiveness of continuing antidepressant medication for one year compared to discontinuation, in preventing depression relapse in UK primary care in people aged 75 years and older who have had two or more episodes of depression or have been taking antidepressants for at least 2 years, have taken citalopram, mirtazapine or sertraline for at least nine months and are now well enough to consider stopping the antidepressant. This study will compare maintenance antidepressants with discontinuation following a taper period.

To estimate the difference in depression and anxiety symptoms between randomised groups.
To estimate the difference in adverse effects of antidepressants by randomised groups.
To determine the difference in withdrawal symptoms between randomised groups.
To estimate the difference in health-related quality of life between randomised groups.
To compare the relative cost-effectiveness of the two arms of the trial.
To understand older adults' decision-making about antidepressants, their experiences of reducing and stopping antidepressants and withdrawal symptoms.
To understand the perspectives of general practitioners about the diagnosis and management of depression in older adults, prescribing, monitoring and deprescribing antidepressants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/08/2024, South Central - Hampshire B Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)207 104 8088; hampshireb.rec@hra.nhs.uk); ref: 24/SC/0247

Study design
Multicentre interventional double-blinded randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice, Home, Telephone

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
Depression

Interventions
The Intervention will be a continuation of the antidepressant medication that the participants are already taking compared to tapering and discontinuing the antidepressant medication to estimate the effectiveness and cost-effectiveness in preventing depression relapse in people aged 75 and over.

Participants who meet the eligibility criteria and sign the informed consent form will be randomised (using a Sealed Envelope method).

Participants will be randomised into 2 groups: Arm A (Continue with their usual antidepressant) or Arm B (taper off and discontinue usual antidepressants)

Comparator (Arm A): Continued treatment with citalopram 20mg, sertraline 50mg or mirtazapine 30mg using identical appearing study IMP.

Intervention (Arm B): 12 months' discontinuation after tapering in patients receiving treatment with citalopram 20mg, sertraline 50mg or mirtazapine 30mg. Using identical appearing tapering doses of antidepressants and placebos.

For weeks 1-6 participants will be instructed to take 1 capsule a day from a single bottle:
Arm A: (continuation of current antidepressant): usual dose
Arm B: (tapering and discontinuation): half of the usual dose

Weeks 7-12 participants will receive 2 bottles of medication and instructed to take one capsule a day from alternate bottles:
Arm A: usual dose in each bottle
Arm B: half dose in bottle 1 and placebo in bottle 2

Weeks 13-52 participants will be instructed to take 1 capsule a day from a single bottle:
Arm A: usual dose
Arm B: placebo only

All trial IMP will be posted to the participant's home address.

Participants will be followed up during the 12 months with regular telephone assessments and questionnaires.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacoeconomic, Therapy

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Citalopram 10mg film-coated tablets [Citalopram hydrobromide] , Citalopram 20mg film-coated tablets [Citalopram hydrobromide] , Mirtazapine 15 mg tablets [Mirtazapine] , Mirtazapine Aurobindo 15mg film-coated tablets [Mirtazapine] , Mirtazapine 30mg tablets [Mirtazapine] , Mirtazapine Aurobindo 30mg film-coated tablets [Mirtazapine] , Sertraline 50mg film-coated tablets [Sertraline hydrochloride] , Sertrone 25mg film-coated tablets [Sertraline hydrochloride]

Primary outcome measure
The time to first relapse of depression during the 52-week follow-up, as determined in a time-to-event analysis. This will be determined using the Clinician Interview Schedule-Revised (rCIS-R)

Secondary outcome measures
1. Depression measured using the Geriatric Depression Scale (GDS-15) at baseline and weeks 8, 16, 24, 32, 40, 48 and 52
2. Symptoms of anxiety measured using the Generalised Anxiety Disorder Assessment 7-item version (GAD7) at baseline and weeks 8, 16, 24, 32, 40, 48 and 52
3. Physical symptoms of side effects of antidepressants measured using the Toronto Side Effect Scale at baseline and weeks 8, 16, 32 and 48 weeks
4. Antidepressant withdrawal effects measured using a modified 17-item version of the Discontinuation-Emergent Signs and Symptoms (DESS) checklist at baseline and weeks 4, 8, 12, 14, 16 and 18
5. Quality of Life Scores for Physical and Mental Health measured using the 12-item Short-Form Survey (SF-12) at baseline and weeks 24 and 52
6. Cognitive Functioning measured using the Montreal Cognitive Assessment (MOCA) at baseline

and weeks 24 and 52
7. Adherence to study medication measured using a single question at each follow-up
8. Levels of Fitness-Frailty, polypharmacy and multimorbidity measured using the Pictorial Fit-Frail Scale (PFFS) at baseline and weeks 24 and 52
9. Resource for health and social care measured using a modified version of the Client Service Receipt Inventory (CSRI) at baseline and weeks 24 and 52
10. Health Quality of life measured using the EQ-5D-5L (a five-item, five-level questionnaire) at baseline and weeks 24 and 52
11. Understanding older adults' decision-making about antidepressants and their experience of reducing and stopping measured using qualitative follow-up interviews after collection of primary endpoint data
12. Understanding the perspective of GPs on the diagnosis and management of depression in older adults measured using qualitative interviews after collection of primary endpoint data

Overall study start date
01/12/2023

Completion date
28/02/2028

Eligibility

Key inclusion criteria
1. Aged 75 years old and over
2. Either 2 or more previous episodes of depression treated with antidepressants (any antidepressant for any length of time) OR taking any antidepressant for at least 2 years at any time
3. Currently has been taking either citalopram, sertraline or mirtazapine for at least 9 months, of which the last 3 months should be at the following doses: 20mg citalopram, 50 mg sertraline or 30mg mirtazapine. These 9 months can be included in the 2 years stated in inclusion 2
4. Currently not depressed (scores <5 on 15-item Geriatric Depression Scale) and are now well enough to consider stopping the antidepressant
5. Presence of a Study Partner (a family member, friend or formal caregiver) who sees or speaks to the participant at least once a week and is prepared to support the completion of outcome measures that involve recall of the previous 8 weeks
6. Provides Informed Consent

Participant type(s)
Patient

Age group
Senior

Lower age limit
75 Years

Upper age limit
100 Years

Sex

Both

Target number of participants
430

Key exclusion criteria
1. Diagnosis of Bipolar Disorder
2. Diagnosis of Dementia (although people with mild cognitive impairment will be eligible for the trial)
3. Currently prescribed a combination of antidepressants or an antidepressant and a mood stabiliser or an antipsychotic as this would indicate individuals with a history of more severe depression who would be at higher risk of relapse of depression
4. Participation in another interventional study
5. Participated in a CTIMP or a trial of psychological intervention in the preceding 3 months

Date of first enrolment
01/11/2024

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University College London, Division of Psychiatry
6th Floor, Wings A and B, Maple House, 149 Tottenham Ct Rd
London
United Kingdom
W1T 7NF

Study participating centre
-
Manchester
United Kingdom
-

Study participating centre

-
Nottingham
United Kingdom
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Study participating centre
-
Newcastle
United Kingdom
-

Study participating centre
-
Oxford
United Kingdom
-

Study participating centre
-
Keele
United Kingdom
-

Sponsor information

Organisation
University College London

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Sponsor type
University/education

Website

https://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care 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

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website

Anonymised data will be available for sharing after publication of the trial results. Researchers wishing to access ANTLER 75+ data should contact the Trial Management Group in the first instance, clearly outlining the purposes. Any researchers would be expected to collaborate with the ANTLER 75+ research team and any requests will need to be approved by the TSC and Sponsor.

Intention to publish date
28/02/2029

Individual participant data (IPD) sharing plan
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