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Antidepressants to prevent relapse in depression

Submission date	Recruitment status
17/09/2015	No longer recruiting
Registration date	**Overall study status**
21/09/2015	Completed
Last Edited	**Condition category**
10/10/2023	Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Depression is one of the most common mental disorders worldwide. The symptoms of depression can vary greatly from person to person, but generally include low mood, problems with sleeping and/or eating, and a general loss of interest in life. Treatment for depression often relies heavily on antidepressant medications. It is thought that antidepressants work by increasing the levels of certain chemicals in the brain called neurotransmitters. In 2013, there were over 53 million prescriptions for antidepressants in the UK, many of which were repeat prescriptions. This is because they are often taken continuously by patients, to prevent future episodes of depression (maintenance treatment). The current NICE guidelines recommend people “at risk of relapse” should remain on maintenance antidepressants for two years, although there is currently little evidence to support this policy. UK surveys have shown that between 5% and 8% of the general public are taking antidepressants, and up to half of these have been taking them long-term. Many of these people no longer show symptoms of depression, and so the benefits of continuing treatment are debatable. The aim of this study is to evaluate the effectiveness of long-term maintenance treatment for depression in the UK.

Who can participate?
Adults with depression who have been taking antidepressants for at least 9 months, and are willing to consider stopping their medication.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in the first group continue to take their medication (citalopram 20mg, sertraline 100mg, fluoxetine 20mg or mirtazapine 30mg) for the entire study period. Those in the second group take half the dose of their current medication for four weeks, and then take a dummy pill (placebo) for the remainder of the study. At the start of the study and then at 6, 12, 26, 39 and 52 weeks, all participants complete a number of questionnaires to find out if there have been any changes in their mood.

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

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

When is the study starting and how long is it expected to run for?
August 2015 to March 2020

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

Who is the main contact?
Mrs Larisa Duffy

Contact information

Type(s)
Public

Contact name
Mrs Larisa Duffy

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-004210-26

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
HTA 13/115/48; 14/0647

Study information

Scientific Title
A Phase IV double blind multi-site, individually randomised parallel group controlled trial investigating the use of citalopram, sertraline, fluoxetine and mirtazapine in preventing relapse in patients in primary care who are taking long term maintenance antidepressants but now feel well enough to consider stopping medication

Acronym

ANTLER

Study objectives
Maintenance antidepressants reduce the rate of relapse in people who have recovered from depression and have been taking maintenance antidepressants for 9 months.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of England - Cambridge South Research Ethics Committee, 29/03/2016, REC ref: 16/EE/0032

Study design
Phase IV double-blind multi-site randomized parallel-group controlled trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current intervention as of 27/09/2018:
At baseline participants will be taking either citalopram (20 mg), sertraline (100 mg), fluoxetine (20 mg) or mirtazapine (30 mg). They will be randomised into one of two groups:

Control Group: Those in the control group remain on their current medication throughout the study period.

Intervention Group: Those in the intervention group take half the dose of their current medication for a period of four weeks (citalopram 10 mg, sertraline 50 mg, fluoxetine 10 mg or mirtazapine 15 mg). The second month they will take half the dose and placebo on alternate days and from the third month until the end of the study they will take placebo. There is no 10 mg capsule for fluoxetine so those taking fluoxetine at baseline who are allocated to the placebo arm will alternate between a 20 mg tablet and placebo tablet for one month. The second month they will take placebo as fluoxetine has a long half-life. All medications are given in pill form.

Previous intervention:
At baseline participants will be taking either citalopram (20mg), sertraline (100mg), fluoxetine (20mg) or mirtazapine (30mg). They will be randomised into one of two groups:

Control Group: Those in the control group remain on their current medication throughout the study period.

Intervention Group: Those in the intervention group take half the dose of their current medication for a period of four weeks (citalopram 10 mg, sertraline, 50 mg, fluoxetine 10 mg or mirtazapine 15 mg), and take a placebo for the remainder of the study period. All medications are given in Pill form.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
1. Citalopram 2. Sertraline 3. Fluoxetine 4. Mirtazapine

Primary outcome(s)
Current primary outcome measure as of 27/09/2018:
Time to depressive relapse measured using the modified shortened clinical interview schedule-revised (CIS-R) at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks and 52 weeks.

Previous primary outcome measure:
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Key secondary outcome(s))
Current secondary outcome measures as of 01/10/2018:
1. Depressive symptoms will be measured using the PHQ9 at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks, 52 weeks
2. Anxiety symptoms will be measured using the GAD7 questionnaire at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks, 52 weeks
3. Quality of life will be measured using the EQ5D-5L questionnaire for quality adjusted life years (QALYs) at baseline, 12 weeks, 26 weeks, 39 weeks, 52 weeks
4. Adverse effects of antidepressants will be measured using a modified Toronto Side Effects scale at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks, 52 weeks
5. Adherence to study medication will be measured using the same criteria as used in the COBALT trial to define adherence using a 5-item self-report measure of compliance at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks, 52 weeks
6. Quality of life will be measured using the Health related quality of life questionnaire (SF12) at baseline, 12 weeks, 26 weeks, 39 weeks and 52 weeks
7. Withdrawal symptoms based on DESS will be measures at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks and 52 weeks
8. Healthcare resource use collected from GP electronic records
9. Patient's overall impression of their wellbeing assessed using a global rating question with 5 points ranging from 'I feel a lot better' to 'I feel a lot worse' asked at baseline, 6 weeks, 12 weeks, 26 weeks, 39 weeks and 52 weeks follow-up

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3. Quality of life will be measured using the EQ5D-5L questionnaire for quality adjusted life years (QALYs) at baseline, 12 weeks, 26 weeks, 39 weeks, 52 weeks
4. Adverse effects of antidepressants will be measured using a modified Toronto Side Effects scale at baseline, 12 weeks, 26 weeks, 39 weeks, 52 weeks
5. Adherence to study medication will be measured using the modified Morisky scale at baseline, 12 weeks, 26 weeks, 39 weeks, 52 weeks
6. Quality of life will be measured using the Health related quality of life questionnaire (SF12) at baseline, 12 weeks, 26 weeks, 39 weeks, 52 weeks

Completion date
08/03/2020

Eligibility

Key inclusion criteria
1. Aged between 18 and 74 years
2. Have experienced at least two episodes of depression
3. Have been taking antidepressants for at least 9 months (citalopram 20mg, sertraline 100mg, fluoxetine 20mg or mirtazapine 30mg)
4. Be well enough to consider stopping their antidepressant medication

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
74 years

Sex
All

Total final enrolment
478

Key exclusion criteria
Current exclusion criteria as of 27/09/2018:
1. Meet internationally agreed (ICD10) criteria for a depressive illness
2. Have bipolar disorder, psychotic illness, dementia or a terminal illness
3. Are not able to complete self-administered questionnaires in English
4. Have contraindications for any of the prescribed medication
5. Women who are currently pregnant or planning pregnancy or lactating
6. Concurrently enrolled in another investigational medicinal product (IMP) trial

Previous exclusion criteria:
1. Meet internationally agreed (ICD10) criteria for a depressive illness
2. Score above 10 on the depressive symptom questionnaire (PHQ9)
3. Have bipolar disorder, psychotic illness, dementia or a terminal illness
4. Are not able to complete self-administered questionnaires in English
5. Have contraindications for any of the prescribed medication

Date of first enrolment
01/03/2017

Date of final enrolment
28/02/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University College London
149 Maple House
Tottenham Court Road
London
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Sponsor information

Organisation
PRIMENT CTU, University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will not be made widely available as the researchers do not have the consent of the participants.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	30/09/2021	30/09/2021	Yes	No
Results article	Cost-Utility Analysis protocol	08/11/2021	10/11/2021	Yes	No

Protocol article		03/06/2019	05/06/2019	Yes	No
Funder report results		25/11/2021	30/11/2021	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Substudy results	16/03/2023	10/10/2023	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes