

# Antidepressants to prevent relapse in depression

<b>Submission date</b>	<b>Recruitment status</b>	<input checked="" type="checkbox"/> Prospectively registered
17/09/2015	No longer recruiting	<input checked="" type="checkbox"/> Protocol
<b>Registration date</b>	<b>Overall study status</b>	<input type="checkbox"/> Statistical analysis plan
21/09/2015	Completed	<input checked="" type="checkbox"/> Results
<b>Last Edited</b>	<b>Condition category</b>	<input type="checkbox"/> Individual participant data
10/10/2023	Mental and Behavioural Disorders	

## 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

**Contact details**  
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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**

**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:

Time to depressive relapse measured using the modified shortened clinical interview schedule-revised (CIS-R) at baseline, 12 weeks, 26 weeks, 39 weeks and 52 weeks.

**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

Previous secondary outcome measures as of 27/09/2018:

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
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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. Global rating question

Previous secondary outcome measures:

1. Depressive symptoms will be measured using the PHQ9 at baseline, 12 weeks, 26 weeks, 39 weeks, 52 weeks
2. Anxiety symptoms will be measured using the GAD7 questionnaire at baseline, 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, 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

United Kingdom

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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?
<a href="#">Results article</a>	results	30/09/2021	30/09/2021	Yes	No
<a href="#">Results article</a>	Cost-Utility Analysis protocol	08/11/2021	10/11/2021	Yes	No

<a href="#"><u>Protocol article</u></a>		03/06/2019	05/06/2019	Yes	No
<a href="#"><u>Funder report results</u></a>		25/11/2021	30/11/2021	Yes	No
<a href="#"><u>HRA research summary</u></a>			28/06/2023	No	No
<a href="#"><u>Other publications</u></a>	Substudy results	16/03/2023	10/10/2023	Yes	No
<a href="#"><u>Participant information sheet</u></a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#"><u>Study website</u></a>	Study website	11/11/2025	11/11/2025	No	Yes