ISRCTN12682719 https://doi.org/10.1186/ISRCTN12682719

# Antidepressant for the prevention of depression following first-episode psychosis

**Submission date**
11/11/2020

**Recruitment status**
Recruiting

**Registration date**
24/11/2020

**Overall study status**
Ongoing

**Last Edited**
09/04/2025

**Condition category**
Mental and Behavioural Disorders

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

**Plain English Summary**
Background and study aims
First episode of psychosis (FEP) typically begins in the late teens or early 20s and is diagnosed by the presence of hallucinations and delusions. Medication and cognitive behavioural therapy help to treat these symptoms, but young people struggle to return to previous social and work roles, have suicidal thoughts and are at high risk of relapse. These are related to depression experienced after FEP. 40% of people who have experienced FEP will become depressed. Antidepressant medication is effective for treating depression in established schizophrenia, and robust evidence suggests that using antidepressants in young people over the age of 18 along with medication for psychosis is safe. However, researchers want to know whether antidepressant medication can reduce the risk of depression happening at all after FEP, and whether preventing depression can improve recovery and reduce relapse. This study aims to find out if an antidepressant medication (sertraline) can help to prevent depression in people who have experienced a psychotic episode for the first time.

Who can participate?
People aged between 18 and 65 years who have experienced first-episode psychosis within the last 12 months

What does the study involve?
Participants are randomly allocated to one of two groups. One group will be given a highly effective antidepressant medication (sertraline) while the other will receive a placebo ('sugar pill'), to take once a day for 6 months. In all other ways the two groups will receive the same types of support from Early Intervention of Psychosis Services (EIP). It involves completing baseline and follow-up assessments, which involve answering a series of questions in the form of interviews and questionnaires at certain time-points (eight visits in total). Blood samples will also be taken. The main outcome evaluated will be the number of new depression cases at 6 months. A number of other key outcomes such as the acceptability of the intervention, cost effectiveness and side-effects of antidepressant medication, recovery, suicidal thoughts /behaviour, anxiety, and relapse will be assessed. The researchers will monitor people in the study closely and if at any time a participant is thought to have depression, their multi-disciplinary team will assess them and decide if they need to stop taking trial medication and their illness needs to be more actively managed.

What are the possible benefits and risks of participating?
This study will help the researchers to find out if sertraline helps first episode psychosis patients by preventing depression. Whilst there may be no immediate benefits to you, the aim is to improve care for people with psychosis in the long term. It is not known whether sertraline will help participants manage their illness or not, which is why the researchers are doing the study. Sertraline can have side effects but the research team will closely monitor the participants.

Where is the study run from?
Birmingham Clinical Trials Unit at the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
November 2019 to March 2026

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

Who is the main contact?
Mark Pearce
ADEPP@trials.bham.ac.uk

### Study website
https://www.birmingham.ac.uk/adepp

## Contact information

### Type(s)
Scientific

### Contact name
Mr Mark Pearce

### Contact details
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## Additional identifiers

### EudraCT/CTIS number
2020-002787-32

### IRAS number
279574

### ClinicalTrials.gov number
Nil known

### Secondary identifying numbers
CPMS 47000, IRAS 279574

# Study information

### Scientific Title
Antidepressant for the prevention of DEPression following first-episode Psychosis: the ADEPP trial

### Acronym
ADEPP

### Study hypothesis
To establish if, compared with placebo, the addition of sertraline to continuing antipsychotic medication following the first episode of psychosis reduces the likelihood of developing depression over a 6 month intervention period. The study will also investigate whether this intervention reduces the likelihood of developing anxiety or suicidal behaviour, reduces the risk of psychotic relapse, and improves the level of functional recovery achieved.

The researchers will additionally gather evidence as to whether the prescription of antidepressant medication after the first episode of psychosis is cost-effective and whether any clinical benefit and cost-effectiveness continue beyond the 6-month intervention, up to a year.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 29/10/2020, East Midlands - Leicester South Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; +44 (0)207 1048310; leicestersouth.rec@hra.nhs.uk), REC ref: 20/EM/0216

### Study design
Randomized; Both; Design type: Prevention, Drug, Cross-sectional

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Community, Hospital

### Study type(s)
Treatment

### Participant information sheet

https://adepp-study.digitrial.com/

## Condition
First Episode Psychosis

## Interventions
Participants will be individually randomized on a 1:1 basis between sertraline and matched placebo via a secure, online randomisation system based at Birmingham Clinical Trials Unit. A minimisation algorithm will be used within the randomisation system to ensure equal distribution of the most commonly prescribed antipsychotics in this population and gender.

Screening visit: At a screening visit, the research team will take screening consent and assess eligibility. Participants will be asked to provide answers for the research team to complete the CDSS and PANSS. An electrocardiogram will be performed if not already done so as standard care in the last 12 months.

Baseline visit: If the patient is eligible to take part, the research team will take informed consent, and complete outcome assessments and questionnaires with them at a baseline visit. The research team will record participants' personal details, medical history and current medication for randomization. After randomization, trial medication will be prescribed as per allocation.

Follow up: Participants will have a follow-up visit every month for 6 months and then once at 12 months either at the hospital or at home. During these visits, participants will be asked to repeat some (and at 1/6/12 months all) of the questionnaires and outcome assessments completed at the baseline visit. The visits at 1, 6 and 12 months may take around 2 hours to complete and the visits at 2-5 months may take around 1 hour to complete. At the 1-month visit, in addition to the outcome assessments and questionnaires, a blood sample (1 x 9 ml) will be taken and sent to the University of Birmingham (later analysed at the University of Cardiff) to confirm the level of sertraline in the body. If the participant consents to it, an additional blood sample (2 x 9 ml) will be taken, sent and stored at the University of Birmingham for future use in other ethically approved studies. At the 6-month visit, in addition to the outcome assessments and questionnaires, treatment allocation will be revealed and the participant and the treating psychiatrist will decide whether to start (if in the placebo group) or continue (if in the sertraline group) with sertraline. Study participation will end at the 12-month visit, after completing the final outcome assessments and questionnaires.

Added 08/04/2025:
For participants randomised after 31st March 2025, study participation will end after the 6-month assessment.

## Intervention Type
Drug

## Phase
Phase IV

## Drug/device/biological/vaccine name(s)
Sertraline

## Primary outcome measure

The number of new cases of depression as indicated by a Calgary Depression for Schizophrenia Scale (CDSS) score < 5 and confirmed by Mini International Neuropsychiatric Interview (MINI) in each treatment arm over the 6-month intervention phase. Measured at baseline, monthly for 6 months and at 12 months.

## Secondary outcome measures

Current secondary outcome measures as of 09/04/2025:
1. The presence and change in symptoms of psychosis is assessed using the Positive and Negative Syndrome Scale (PANSS) at baseline, every month for 6 months, and again at 12 months
2. The presence of suicidal ideation and attempts in lifetime ever and preceding 12 months, together with current suicidal ideation and beliefs about future risk, assessed using the Suicidal Behaviours Questionnaire-Revised (SBQ-R) at baseline, 1, 6 and 12 months after randomisation
3. Generalised anxiety is assessed using the Generalised Anxiety Disorder Assessment (GAD-7) at baseline, every month for 6 months, and again at 12 months
4. Relapse of psychosis is assessed, defined by a hospital admission or acute community care provided by a Home Treatment/Crisis Intervention team.
5. Social and occupational functioning is assessed using the Functioning: Social and Occupational Functioning Assessment Scale (SOFAS) at baseline, 1, 6 and 12 months after randomisation
6. Quality of life is assessed using the Quality of Life: EQ-5D-5L and ICEpop CAPability measure for Adults (ICECAP-A) at baseline, 1, 6 and 12 months after randomisation
7. Side effects of antipsychotic medication and SSRI medication are measured using the Antipsychotic Non-Neurological Side Effects Rating Scale-extended (ANNSERS-e) Healthcare Resource Usage (Client Service Receipt Inventory – CSRI) at baseline, 1, 6 and 12 months after randomisation

Previous secondary outcome measures:
1. Psychosis symptoms measured using the Positive and Negative Syndrome Scale (PANSS) at screening, monthly for 6 months and at 12 months
2. Suicidal ideation and attempts in lifetime together with current suicidal ideation and beliefs about future risk, measured using Suicidal Behaviours Questionnaire- Revised (SBQ-R) at baseline, 1 month, 6 months and 12 months
3. Trait and current (state) anxiety assessed using State-Trait Anxiety Inventory (STAI) at baseline, months 1, 6 and 12
4. Generalised anxiety assessed using General Anxiety Disorder (GAD7) at baseline and then monthly for 6 months and at 12 months
5. Relapse of psychosis, as defined by a hospital admission or acute community care provided by Home Treatment/Crisis Intervention team at 6 and 12 months.
6. Depression symptoms measured using Quick Inventory of Depressive Symptomatology (Self-Report) (QIDS-SR) at baseline, monthly for 6 months and at 12 months
7. Functioning measured using the Social and Occupational Functioning Scale (SOFAS) and the Functional Remission of General Schizophrenia (FROGS) at baseline and at 6 and 12 months
8. Quality of life measured using EQ-5D-5L and ICECAP-A at baseline and at 6 and 12 months
9. Side effects measured using Barnes Akathisia Scale (BARS), Antipsychotic Non-Neurological Side Effects Rating Scale - compiled (ANNSERS-c) and Simpson Angus Scale (SAS) at baseline and at 6 and 12 months

## Overall study start date

01/11/2019

## Overall study end date

31/03/2026

# Eligibility

### Participant inclusion criteria
Current inclusion criteria as of 20/03/2023:

1. Diagnosis of first-episode psychosis (FEP)
2. Within 12 months of initial treatment for FEP (as defined by onset of care provision by an Early Intervention Team)
3. Positive and Negative Syndrome Scale (PANSS) individual positive item scores all ≤4
4. Sufficiently recovered from acute psychotic episode with capacity to consent
5. Males and females aged 18-65 years
6. Currently prescribed antipsychotic medication at stable dose.
7. Female participants must be willing to use one form of highly effective contraception

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Previous inclusion criteria:

1. Diagnosis of first-episode psychosis (FEP)
2. Within 3 months of initial treatment for FEP (as defined by onset of care provision by an Early Intervention Team)
3. Positive and Negative Syndrome Scale (PANSS) individual positive item scores all ≤4
4. Sufficiently recovered from acute psychotic episode with capacity to consent
5. Males and females aged 18-35 years
6. Currently prescribed antipsychotic medication at stable dose.
7. Female participants must be willing to use one form of highly effective contraception

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Upper age limit
65 Years

### Sex
Both

### Target number of participants
Planned Sample Size: 338; UK Sample Size: 338

### Participant exclusion criteria
Current exclusion criteria as of 20/03/2023:

1. Current moderate or severe depression (as indicated by a Calgary Depression for Schizophrenia Scale (CDSS) score of > 7)
2. Currently prescribed antidepressant medication (or within 2 weeks of stopping if a Monoamine Oxidase Inhibitor)
3. Previous history of mania
4. Contraindications to selective serotonin reuptake inhibitors (SSRI) antidepressant treatment (e.g. recurrent thrombotic illness, previous adverse reaction, confirmed pregnancy, although risk in pregnancy is low, prescribed pimozide)
5. Serious medical or neurological illness (as identified by the treating consultant psychiatrist)
6. Hypersensitivity to the active substance or any of the excipients or placebo
7. Concomitant treatment with irreversible monoamine oxidase inhibitors (MAOIs)
8. Patient with any other systemic dysfunction (e.g. gastrointestinal, renal, respiratory, cardiovascular, neurological or psychiatric) or significant disorder which, in the opinion of the investigator would jeopardize the safety of the patient by taking part in the trial
9. Electrocardiogram (ECG): QTc interval >450 as measured in the last 12 months
10. Aged below 18 years
11. Aged over 65 years
12. Female participants that do not agree to follow the protocol contraception requirements

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Previous exclusion criteria:

1. Current moderate or severe depression (as indicated by a Calgary Depression for Schizophrenia Scale (CDSS) score of > 7)
2. Currently prescribed antidepressant medication (or within 2 weeks of stopping if a Monoamine Oxidase Inhibitor)
3. Previous history of mania
4. Contraindications to selective serotonin reuptake inhibitors (SSRI) antidepressant treatment (e.g. recurrent thrombotic illness, previous adverse reaction, confirmed pregnancy, although risk in pregnancy is low, prescribed pimozide)
5. Serious medical or neurological illness (as identified by the treating consultant psychiatrist)
6. Hypersensitivity to the active substance or any of the excipients or placebo
7. Concomitant treatment with irreversible monoamine oxidase inhibitors (MAOIs)
8. Patient with any other systemic dysfunction (e.g. gastrointestinal, renal, respiratory, cardiovascular, neurological or psychiatric) or significant disorder which, in the opinion of the investigator would jeopardize the safety of the patient by taking part in the trial
9. Electrocardiogram (ECG): QTc interval >450 as measured in the last 12 months
10. Aged below 18 years
11. Aged over 35 years
12. Female participants that do not agree to follow the protocol contraception requirements

### Recruitment start date
01/02/2021

### Recruitment end date
30/09/2025

## Locations

### Countries of recruitment

England

United Kingdom

Wales

**Study participating centre**
**Birmingham and Solihull Mental Health NHS Foundation Trust**
Unit 1
50 Summer Hill Road
Birmingham
United Kingdom
B1 3RB

**Study participating centre**
**Coventry and Warwickshire Partnership NHS Trust**
Wayside House
Wilsons Lane
Coventry
United Kingdom
CV6 6NY

**Study participating centre**
**Lancashire Care NHS Foundation Trust**
Sceptre Point
Sceptre Way
Bamber Bridge
Preston
United Kingdom
PR5 6AW

**Study participating centre**
**Aneurin Bevan University LHB**
Headquarters - St Cadoc's Hospital
Lodge Road
Caerleon
Newport
United Kingdom
NP18 3XQ

**Study participating centre**

**Worcestershire Health and Care NHS Trust**
Isaac Maddox House
Shrub Hill Industrial Estate
Worcester
United Kingdom
WR4 9RW

**Study participating centre**
**Midlands Partnership NHS Foundation Trust**
Trust Headquarters
St. Georges Hospital
Corporation Street
Stafford
United Kingdom
ST16 3SR

**Study participating centre**
**Black Country Partnership NHS Foundation Trust**
Delta Point
Greets Green Road
West Bromwich
United Kingdom
B70 9PL

**Study participating centre**
**Birmingham Women's and Children's NHS Foundation Trust**
Finch Road Primary Care Centre
2nd floor (early intervention)
2 Finch Road
Birmingham
United Kingdom
B19 1HS

**Study participating centre**
**North London NHS Foundation Trust**
4th Floor, East Wing
St. Pancras Hospital
4 St. Pancras Way
London
United Kingdom
NW1 0PE

**Study participating centre**
**Central & North West London NHS Foundation Trust Headquarters**
Greater London House
Hampstead Road
London
United Kingdom
NW1 7QY

**Study participating centre**
**Cardiff and Vale NHS Trust**
Cardigan House
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

**Study participating centre**
**Derbyshire Healthcare NHS Foundation Trust**
Trust Headquarters
Kingsway Hospital
Kingsway
Derby
United Kingdom
DE22 3LZ

**Study participating centre**
**Gloucestershire Health and Care NHS Foundation Trust**
Edward Jenner Court
1010 Pioneer Avenue
Gloucester Business Park
Gloucester
United Kingdom
GL3 4AW

**Study participating centre**
**Leicestershire Partnership NHS Trust Mental Health Services**
George Hine House
Gipsy Lane
Humberstone

Leicester
United Kingdom
LE5 0TD

**Study participating centre**
**Merseycare NHS Trust**
V7 Building
Kings Business Park
Prescot
United Kingdom
L34 1PJ

**Study participating centre**
**Nottinghamshire Healthcare NHS Trust Headquarters**
Duncan Macmillan House
Porchester Road
Nottingham
United Kingdom
NG3 6AA

**Study participating centre**
**Oxford Health NHS Foundation Trust**
Littlemore Mental Health Centre
Sandford Road
Littlemore
Oxford
United Kingdom
OX4 4XN

**Study participating centre**
**Hampshire and Isle of Wight Healthcare NHS Foundation Trust**
Tatchbury Mount Hospital
Calmore
Southampton
United Kingdom
SO40 2RZ

**Study participating centre**
**Cornwall Partnership NHS Foundation Trust**
Carew House
Beacon Technology Park

Dunmere Road
Bodmin
United Kingdom
PL31 2QN

**Study participating centre**
**Cheshire and Wirral Partnership NHS Foundation Trust**
Trust Headquarters Redesmere
The Countess of Chester Health Park
Liverpool Road
Chester
United Kingdom
CH2 1BQ

**Study participating centre**
**Somerset NHS Foundation Trust**
Trust Management
Lydeard House
Musgrove Park Hospital
Taunton
United Kingdom
TA1 5DA

# Sponsor information

**Organisation**
University of Birmingham

**Sponsor details**
c/o Dr Birgit Whitman
Room 117, Aston Webb Building
University of Birmingham
Birmingham
England
United Kingdom
B15 2TT
+44 (0)1214158011
researchgovernance@contacts.bham.ac.uk

**Sponsor type**
University/education

**Website**

http://www.birmingham.ac.uk/index.aspx

**ROR**
https://ror.org/03angcq70

# Funder(s)

**Funder type**
Government

**Funder Name**
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR127700

# Results and Publications

**Publication and dissemination plan**
1. The protocol and other documents will be on the public trial website https://www.birmingham.ac.uk/adepp
2. Planned publication in a high-impact peer reviewed journal 1 year after the overall trial end date

**Intention to publish date**
31/12/2024

**Individual participant data (IPD) sharing plan**
Requests for data generated during this study will be considered by BCTU (via bctudatashare@contacts.bham.ac.uk). Data will typically be available within 6 months after the primary publication unless it is not possible to share the data (for example the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data).
Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BCTU Data Sharing Committee in discussion with the Chief Investigator and, where appropriate (or in absence of the Chief Investigator) any of the following: the Trial Sponsor, the relevant Trial Management Group (TMG), and independent Trial Steering Committee (TSC).
A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers transfer of patient identifiable information. Any data transfer will use a secure and encrypted method.

**IPD sharing plan summary**
Available on request

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| HRA research summary | | 28/06/2023 | No | No |
| Protocol article | 06/10/2023 | 10/10/2023 | Yes | No |