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A clinical trial to investigate how effective a stimulant medication is compared to a non-stimulant medication in patients who have been diagnosed with attention deficit hyperactivity disorder (ADHD) and also have a history of either psychosis or bipolar disorder

Submission date
26/04/2022

Registration date
18/05/2022

Last Edited
07/11/2025

Recruitment status
Recruiting

Overall study status
Ongoing

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 of protocol

Background and study aims
Attention-Deficit/Hyperactivity Disorder (ADHD) is a common mental disorder that involves problems with attention, overactivity, acting impulsively. ADHD starts in childhood and commonly persists into adulthood commonly occurring alongside psychosis or bipolar disorder (bipolar), both severe mental illnesses. ADHD in adulthood is treated with medication of which there are two types: stimulants, (recommended to be used first), or nonstimulants. Doctors are concerned and uncertain about how effective and safe medications for ADHD are in people who also have psychosis or bipolar. Currently, there is not much evidence to help clinicians and patients in deciding which medication can best be prescribed. The study will try to understand which type of medication is most effective in reducing symptoms of ADHD in these patients, how safe the medications are. The design of the study is called a “randomised controlled trial”, which is the best way to find out the answer to this type of scientific problem.

Who can participate?
Adults over 18 years, with a diagnosis of ADHD.

What does the study involve?
Patients will undergo screening to confirm their ADHD and psychosis or bipolar diagnosis, then will be entered into the main trial to receive the randomly allocated medication. Doctors will carefully assess patients at every 1-2 weeks at first to see if the medication is working, whether they are on the right dose and for side effects. After agreeing to take part, and at 6 & 12 months, patients will be asked to complete self-report questionnaires and interviews with the researcher. The questionnaires will measure ADHD symptoms, day-to-day functioning, quality of life, use of health services and whether new symptoms of psychosis or bipolar emerge.

What are the possible benefits and risks of participating?
Benefits:
• If eligible, then patients taking part in the trial may start their treatment sooner than if they did not enter the trial
• All patients will receive either one of the 2 interventions studied as there is no placebo in the study.
• There is usually more time for patients to discuss their health and their condition and patients feel they may play a more active role in their own healthcare
• Patients are monitored more closely by the clinical team than if they did not take part in the trial
• The study provides costs towards the prescription for trial medication
• There are monetary incentives for completing the study assessments
• Travel costs towards each assessment visit are covered for all patients taking part

Risks:
We would not expect any safety issues for participants. The trial medications being used have long established safety profiles, have been used for a long time in treating ADHD in patients with psychosis or bipolar. Participants will be monitored closely and if at any time symptom severity is presented by the participant, their clinical care team will assess them and decide if they need to change the medication dose or stop taking the trial medication. There is no known risk to female partners of patients taking either drugs but the manufacturer's advise is to avoid pregnancy and breast-feeding whilst on medication. As such, we will screen female participants for pregnancy (excluding those confirmed pregnant) and monitor for pregnancies throughout the duration of the trial intervention. Additionally, female patients of child-bearing age will be asked to take appropriate contraceptive measures to avoid pregnancy during trial treatment.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2021 to May 2026

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

Who is the main contact?
Shrushma Loi, snapper@trials.bham.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Prof Steven Marwaha

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Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000302-21

Integrated Research Application System (IRAS)
1003970

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 49907, NIHR129817

Study information

Scientific Title
A randomised controlled trial to evaluate the clinical and cost-effectiveness of Stimulant compared with Non-stimulant medication for adults with Attention-deficit/hyperactivity disorder and a history of Psychosis or biPolar disordER

Acronym
SNAPPER

Study objectives
To evaluate the clinical and cost-effectiveness of stimulant (lisdexamfetamine) compared with non-stimulant (atomoxetine) medication for adults with Attention-Deficit/Hyperactivity Disorder (ADHD) and a history of either psychosis or bipolar disorder.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/01/2022, Central Bristol REC (Temple Quay House, 2 The Square, Bristol Research Ethics Committee Centre, BS1 6PN, UK; +44 207 104 8029; centralbristol.rec@hra.nhs.uk), ref: 21/SW/0172

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Attention-Deficit/Hyperactivity Disorder (ADHD) and a history of either psychosis or bipolar disorder

Interventions
Current interventions as of 06/03/2025:

Patients will randomised to receive either Lisdexamfetamine (stimulant) initiated at 30mg once daily, and increased to a maximum of 70mg once daily for 6 months; OR Atomoxetine (non-stimulant) initiated at 40mg daily, and increased to a maximum of 100mg daily for 6 months
Randomisation will be provided by a secure online randomisation system at the Birmingham Clinical Trials Unit (BCTU)

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Previous interventions:

Patients will randomised to receive either Lisdexamfetamine (stimulant) initiated at 30mg once daily, and increased to a maximum of 70mg once daily for 12 months; OR Atomoxetine (non-stimulant) initiated at 40mg daily, and increased to a maximum of 100mg daily for 12 months (if on Fluoxetine then starting dose should be halved e.g., 20mg if weight > 70kg).
Randomisation will be provided by a secure online randomisation system at the Birmingham Clinical Trials Unit (BCTU)

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Lisdexamfetamine, atomoxetine

Primary outcome(s)
Current primary outcome measure as of 06/03/2025:

ADHD symptoms at 6 months measured using the Conners Adult ADHD Rating Scale-Observer (CAARS-O) total score

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Previous primary outcome measure:

ADHD symptoms at 12 months measured using the Conners Adult ADHD Rating Scale-Observer (CAARS-O) total score

Key secondary outcome(s))
Current secondary outcome measures as of 06/03/2025:

1. Clinical (ADHD symptoms using CAARS-O total score at 12 months, emergence of hypomania /mania symptoms, emergence of psychotic symptoms and depression over 12 months; emotional dysregulation at 6 and 12 months).
2. Quality of life (QOL) (ADHD specific QOL for participants only using the Adult ADHD QOL (AADHD QOL); health-related QOL and capability wellbeing for both the participant and supporter (close person) at 6 and 12 months) using the EQ-5D-5L and ICECAP-A.
3. Occupational and functional outcomes (occupational and daily functioning, employment, education at 6 and 12 months) using the Functioning Assessment Short Test (FAST).
4. Substance misuse (problem drug use, problem drinking at 6 and 12 months).
5. Adherence at 6 months (Medication Adherence Rating Scale (MARS)
6. Process outcomes (all causes for discontinuation of treatment).
7. Resource use (modified Client Service Receipt Inventory (CSRI) and use of acute services at 6 and 12 months).
8. Concomitant medication use (type, dose and duration) at 6 and 12 months.

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3. Occupational and functional outcomes (occupational and daily functioning, employment, education at 6 and 12 months) using the Functioning Assessment Short Test (FAST).
4. Substance misuse (problem drug use, problem drinking at 6 and 12 months).
5. Adherence at 6 and 12 months (Medication Adherence Rating Scale (MARS) and self-reported adherence at, 6, and 12 months; pill counting on prescription review).
6. Process outcomes (all causes for discontinuation of treatment).
7. Resource use (modified Client Service Receipt Inventory (CSRI) and use of acute services at 6 and 12 months).
8. Concomitant medication use (type, dose and duration) at 6 and 12 months.

Completion date
30/05/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 06/03/2025:

1. Diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) based on the Diagnostic Interview for ADHD in Adults-5 (DIVA-5)
2. Psychosis (schizophrenia spectrum disorders) (Strata 1) OR Bipolar disorder (Strata 2) diagnosis according to the DSM-5 based on the Mini International Neuropsychiatric Interview (MINI)
3. Stable in the opinion of the clinical investigator
4. Males and females aged 18 years and over
5. Not currently (or within the last month) on medication for ADHD
6. Able to give written informed consent

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Previous inclusion criteria:

1. Diagnosis of ADHD according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) based on the Diagnostic Interview for ADHD in Adults-5 (DIVA-5)
2. Psychosis (schizophrenia spectrum disorders) (Strata 1) OR Bipolar disorder (Strata 2) diagnosis according to the DSM-5 based on the Mini International Neuropsychiatric Interview (MINI)
3. Stable and on suitable mood stabilisers or antipsychotics
4. Males and females aged 18 years and over
5. Not currently (or within the last month) on medication for ADHD
6. Able to give written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 06/03/2025:

1. ADHD medication contra-indicated
2. Currently in an acute episode of psychosis or bipolar disorder
3. Severe suicide risk or severe risk of violence to others
4. Severe drug seeking behaviour or a current drug/alcohol withdrawal syndrome
5. History of epilepsy or seizures
6. Congenital or acquired long QT syndrome (LQTS); OR family history of QT prolongation; OR on medication associated with increased risk of QT interval prolongation such as class IA and III anti-arrhythmics,moxifloxacin,erythromycin,methadone,mefloquine,tricyclic antidepressants or cisapride.

7. Currently taking CYP2D6 inhibitors (other than Fluoxetine, Doxepin, Duloxetine, Haloperidol, Paroxetine, Promethazine, Risperidone, Trazadone or Venlafaxine) as these are routinely used in the target population, and clinically accounted for in prescribing ADHD medication dosing and scheduling.
8. Participating in another conflicting/incompatible clinical trial
9. Females of child-bearing age only:
10. Pregnant. Note: Spot urine test will be performed at screening and/or randomisation to rule out pregnancy in females of child-bearing age
11. Not willing to take highly effective contraceptive measures to prevent pregnancy during study participation period AND for 30 days following administration of the last trial medication dose.

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1. ADHD medication contra-indicated
2. Currently in an acute episode of psychosis or bipolar disorder
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6. Congenital or acquired long QT syndrome (LQTS); OR family history of QT prolongation; OR on medication associated with increased risk of QT interval prolongation such as class IA and III anti-arrhythmics,moxifloxacin,erythromycin,methadone,mefloquine,tricyclic antidepressants or cisapride.
7. Currently taking CYP2D6 inhibitors e.g.,quinidine,terbinafine.
8. Participating in another interventional or conflicting/incompatible clinical trial
9. Females of child-bearing age only:
10. Pregnant. Note: Spot urine test will be performed at screening and/or randomisation to rule out pregnancy in females of child-bearing age
11. Not willing to take highly effective contraceptive measures to prevent pregnancy during study participation period AND for 30 days following administration of the last trial medication dose.

Date of first enrolment
23/05/2022

Date of final enrolment
30/05/2026

Locations

Countries of recruitment
United Kingdom

England

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
South London & Maudsley NHS Trust Hq
9th Floor
The Tower Building
11 York Road
London
United Kingdom
SE1 7NX

Study participating centre
South West London & St George's Mental Health Trust
Livingstone House
2 Queens Road
Teddington
United Kingdom
TW11 0LB

Study participating centre
Norfolk and Suffolk NHS Foundation Trust
Hellesdon Hospital
Drayton High Road
Norwich
United Kingdom
NR6 5BE

Study participating centre
NHS Lanarkshire
14 Beckford Street
Hamilton
United Kingdom
ML3 0TA

Study participating centre

Forward Thinking Birmingham
Ftb
1 Printing House Street
Birmingham
United Kingdom
B4 6DF

Study participating centre
Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust
St Nicholas Hospital
Jubilee Road
Gosforth
Newcastle upon Tyne
United Kingdom
NE3 3XT

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
Avon and Wiltshire Mental Health Partnership NHS Trust
Bath NHS House
Newbridge Hill
Bath
United Kingdom
BA1 3QE

Study participating centre
Berkshire Healthcare NHS Foundation Trust
London House
London Road
Bracknell
United Kingdom
RG12 2UT

Sponsor information

Organisation
University of Birmingham

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		06/11/2025	07/11/2025	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes