

# 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

<b>Submission date</b> 26/04/2022	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
<b>Registration date</b> 18/05/2022	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 06/03/2025	<b>Condition category</b> Mental and Behavioural Disorders	<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> 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 advice 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](mailto:snapper@trials.bham.ac.uk)

**Study website**

<https://www.birmingham.ac.uk/snapper>

## Contact information

**Type(s)**

Principal Investigator

**Contact name**

Prof Steven Marwaha

**ORCID ID**

<http://orcid.org/0000-0002-0303-9942>

## Contact details

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School of Psychology  
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Birmingham  
United Kingdom  
B15 2TT

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S.Marwaha@bham.ac.uk

## Additional identifiers

### EudraCT/CTIS number

2021-000302-21

### IRAS number

1003970

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

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

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details to request a patient information sheet

**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 measure**

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

### **Secondary outcome measures**

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.

**Overall study start date**

01/01/2021

**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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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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

244

## 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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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

England

United Kingdom

## 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

### **Sponsor details**

Edgbaston  
Birmingham  
England  
United Kingdom  
B15 2TT  
+44 7814 650003  
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)

## **Results and Publications**

### **Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal

## Intention to publish date

31/05/2027

## 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?
<a href="#">HRA research summary</a>			28/06/2023	No	No