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Stimulant medication for ADHD and tics - understanding response versus non-stimulants

Submission date
26/08/2022

Recruitment status
Recruiting

Registration date
30/11/2022

Overall study status
Ongoing

Last Edited
28/04/2025

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
In the UK, 3-5% of children and young people (CYP) have attention deficit hyperactivity disorder (ADHD). Out of those, 1 in 5 also experiences tics. Stimulant medication is effective for ADHD, however, there is concern among doctors that it may worsen children/young people's tics. As a result, they prefer to prescribe non-stimulants which may be less effective for ADHD to CYP who suffer from both ADHD and tics.
The aim of the SATURN trial is to understand whether stimulant or non-stimulant medication is the most effective in children and young people (6-16 years old) with ADHD and tics.
The medications that are being studied are:
1) modified-release (MR) methylphenidate (stimulant). Methylphenidate is the first-line treatment recommended by the National Institute for Health and Care Excellence (NICE) for ADHD and the most commonly prescribed medication in this population.
2) guanfacine extended-release (non-stimulant). Guanfacine is the first-line treatment recommended by NICE for tic disorders and second-line for ADHD.

Who can participate?
Children and young people (6-16 years old) with ADHD and tics will be recruited in England.

What does the study involve?
Parents/carers who express an interest in their children/young people taking part will be asked to complete a pre-screening questionnaire - the Development and Wellbeing Assessment (DAWBA). Eligible families will undergo a screening call with a researcher and those who are eligible and would like to take part, will have their baseline visit scheduled.
During this visit, which is face-to-face, eligibility will be confirmed, consent will be taken (parent and 16-year-old) and assent where applicable (children/young people 6-15 years old) and baseline questionnaire data and measurements will be collected. Participants will be randomly allocated to one of the two medications and will be seen weekly (mainly remotely) for 12 weeks and again at approximately six months and 12 months from randomisation (end of participation).

What are the possible benefits and risks of participating?
The researchers cannot promise that taking part in this study will benefit the participants personally. The main benefit of this research is that the researchers will learn more about which

medication is best to help children and young people with ADHD and tics, which may mean getting the right help is easier for children and young people in the future.
Both groups will receive a treatment (medication) that has been approved for this use in this age group. Both treatments are commonly prescribed in our target population and are recommended by NICE (methylphenidate as first-line treatment for ADHD while guanfacine as the first-line treatment for tics and second-line treatment for ADHD). The inclusion/exclusion criteria exclude participants with contraindications to either of the trial medications and concomitant medications and treatments are closely monitored while in the trial. Baseline measures include a cardiovascular exam and participants with increased cardiovascular risk based on the exam and the relevant EAGG guidance will be considered for exclusion. Those that are included in the trial will be allocated to the 'enhanced monitoring group' and will be asked to provide Blood Pressure (BP) and pulse measurements frequently (frequency to be determined by the research clinician). The trial has undergone a risk assessment by the Nottingham Clinical Trials Unit (NCTU) and the overall risk categorisation is low.
The trial will employ at least one research clinician and research assistant (they may be referred to as researcher or research support officer elsewhere) per regional hub who will be appropriately trained and will have frequent contact with the trial participants (weekly during the titration phase and then at approximately 6- and 12- months following randomisation). The research clinicians and research assistants will be supervised by the regional hub leads who are experienced child and adolescent psychiatrists. The hub leads are experienced clinical leads who have been involved in the grant application and protocol development as co-applicants and have an in-depth knowledge of the trial as well as the target population.
As both medications have marketing authorisation for this use in this population, side effects are known and well documented. Adverse event data will be collected until the end of the participant's involvement in the trial (approx. 12 months). Any serious adverse events will be reported timely (within 24 hours of becoming aware) and monitored until the event is resolved.
Risk of inconvenience or discomfort: Families who travel to attend their Baseline Visit will be reimbursed for any travel costs, even if they are not enrolled in the trial. Apart from Visit 1, participants will be able to complete other measures and questionnaires at their home in their own time (as close to the agreed timepoint as possible) when it is most convenient to them. Where questionnaire data need to be obtained by a researcher a phone call/Teams call will be arranged at a time that suits.
Additionally, families will receive a total of £30 in vouchers and will be entered in up to six prize draws as a small token of appreciation for their time to complete baseline and follow-up measures.
Risk of breach of confidentiality: All members of the research team will have undergone GCP training. No personal information will be sent to the research team prior to receiving a 'consent to contact' form from the parent/carer. The REDCap database is designed so only relevant members of the research team can see the outcome measures of their participants. It is a validated secure web-based platform which allows for data tracking via date-stamped audit logs. Participant data will be identified only by their unique trial ID number to protect from bias and ensure confidentiality.

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

When is the study starting and how long is it expected to run for?
August 2022 to November 2025

Who is funding the study?
NIHR Health Technology Assessment Programme (UK)

Who is the main contact?
Dr Chris Hollis, chris.hollis@nottingham.ac.uk

Study website
https://www.institutemh.org.uk/research/projects-and-studies/current-studies/saturn

Contact information

Type(s)
Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
2022-002425-10

IRAS number

1005480

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
22031, IRAS 1005480, CPMS 53869

Study information

Scientific Title
Stimulant Medication for ADHD and Tics - Understanding Response versus Non-stimulants (SATURN): a randomised trial of the clinical and cost-effectiveness of methylphenidate versus guanfacine for ADHD in children and young people with a co-existing tic disorder

Acronym
SATURN

Study objectives
Primary objectives:
To evaluate the clinical and cost-effectiveness of MR-MPH compared with guanfacine XR medication for children and young people (CYP) with ADHD and co-existing tics.
ADHD symptoms and tics at 12 weeks post-randomisation are designated joint primary outcomes. The trial aim is to test whether, in CYP with ADHD and co-existing tics, stimulant (MR-MPH) compared with non-stimulant (Guanfacine XR) medication is:
1. superior for ADHD symptoms: MR-MPH should result in a clinically important improvement in ADHD symptoms.
2. non-inferior for tics: MR-MPH should not result in a clinically important worsening with respect to tics.

The secondary objectives are:
1. To determine the effect of MR-MPH compared with Guanfacine XR on ADHD symptoms and tics at 24 and 52 weeks post-randomisation
2. To assess the relative effectiveness of MR-MPH compared with Guanfacine XR on the global measure of clinical functioning and physical measures
3. To compare the relative cost-effectiveness of the two medications
4. To assess adherence to the interventions
5. To compare the safety of the interventions

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/11/2022, North West - Haydock Research Ethics Committee (Health Research Authority, Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0) 2071048032; haydock.rec@hra.nhs.uk), ref: 22/NW/0283

Study design
Interventional open randomized parallel-group controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Other

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Attention Deficit Hyperactivity Disorder (ADHD) and tics

Interventions
Participants will be randomised to either the intervention arm in which they will be prescribed a stimulant medication (Modified-Release Methylphenidate) to be taken orally, once daily or the comparator arm in which they will be prescribed a non-stimulant medication (Guanfacine Extended-Release) to be taken orally, once daily. Treatment will be assigned randomly using a probabilistic minimisation algorithm. Allocation will be concealed using a web-based randomisation system. Randomisation results will be disclosed to participants at the baseline visit during which the first prescription will be issued and the 12-week titration period will begin. The optimal dose for each participant will be established during this 12-week period when there will be weekly (face-to-face or virtual) follow-up assessments. Subsequent follow-up assessments will take place at 24 and 52 weeks post-baseline. The research team will be responsible for prescribing during the 12 weeks period after which point it will be handed over to the participants' usual care team. (Please note, the processes are the same for both arms).

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Methylphenidate hydrochloride, guanfacine hydrochloride

Primary outcome measure
1. ADHD symptoms measured using Swanson, Nolan, and Pelham Rating Scale (SNAP-IV) at 12 weeks post-randomisation
2. Tics severity measured by Yale Global Tic Severity Scale (YGTSS) Total Tic Severity Score (TTSS) at 12 weeks post-randomisation

Secondary outcome measures
1. Clinical:
1.1 ADHD symptoms measured using SNAP-IV at 24 and 52 weeks

1.2 Tics severity measured by YGTSS (TTSS) at 24 and 52 weeks
1.3 Global measure of clinical functioning: Clinical Global Impressions (CGI-I) at 1–12, 24 and 52 weeks

2. Safety:
2.1 Medication adverse events at 1–12, 24 and 52 weeks. Adverse events will be recorded throughout the 52-week follow-up period on a modified version of the side effects scale developed by Hill and Taylor. Serious adverse events will be recorded and reported in a timely fashion (within 24 hours of awareness of the event) following the procedure outlined in the protocol submitted with this application. Cardiovascular examination (blood pressure and pulse) will be conducted as part of routine safety monitoring as required. Physical measures and monitoring will be adjusted depending on treatment route; a decision based on individual risk factors and the baseline examination.

3. Health Economics:
3.1 Child health-related quality of life: Child Health Utility – Nine Dimensions (CHU-9D), EQ-5DY at Baseline, 12, 24 and 52 weeks
3.2 Parent health-related quality of life: EQ5D-5I at Baseline, 12, 24 and 52 weeks

Overall study start date
01/08/2022

Completion date
30/11/2025

Eligibility

Key inclusion criteria
Inclusion criteria for the young person:
1. Aged ≥6 years up to <17 years at randomisation
2. Diagnosis of ADHD by clinical team (ADHD DSM-5) confirmed by the research clinician (following review of all available information including the DAWBA)
3. Mild-moderate tics: Score >5 on the Yale Global Tic Severity Scale (YGTSS) Total Tic Severity Score (TTSS)
4. Any ICD-10 Tic Disorder F95 (F95.0-F95.9)
5. Referred to CAMHS or community paediatrics taking part in the trial
6. Parent/carer and CYP seeking medication for ADHD (either ADHD medication naïve or seeking medication change)
7. Willing to adhere to the trial procedures=
8. If currently or recently on a different medication for ADHD or tics willing to go through or complete the appropriate wash-out period (as per standard care) to be able to receive the allocated trial IMP
9. Able to give valid, informed assent (aged <16 years) or consent (aged 16 years)
10. Able to understand and complete assessments in English
11. Eligible parent/carer willing and able to participate alongside the CYP

Inclusion criteria for the parent/carer:
1. Individual with parental responsibility
2. Individual with sufficient knowledge of CYP's medical history to be able to complete the relevant assessment tools
3. Access to reliable internet connection and email

4. Able to give valid, informed consent
5. Able to speak, understand and complete assessments in English

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Years

Upper age limit
17 Years

Sex
Both

Target number of participants
314

Key exclusion criteria
Exclusion criteria for the young person:
1. Current pharmacotherapy for tics
2. Current pharmacotherapy for ADHD
3. Abnormal cardiovascular examination (e.g., BP >95th percentile, tachycardia)
4. Diagnoses of alcohol/substance dependence, psychosis or mania (as per clinician judgement)
5. Intellectual disability (clinical estimate of IQ <70) (confirmed by Child and Adolescent Intellectual Disability Screening Questionnaire; CAIDS-Q)
6. Contraindications to MR-MPH and guanfacine
7. Immediate risk to self or others
8. Individual who is pregnant or plans to get pregnant while in the trial
9. Individual who is breastfeeding

Exclusion criteria for the parent/carer:
1. Local authority representative

Date of first enrolment
07/03/2023

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nottinghamshire Healthcare NHS Foundation Trust
The Resource, Trust Hq
Duncan Macmillan House
Porchester Road
Nottingham
United Kingdom
NG3 6AA

Sponsor information

Organisation
University of Nottingham

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NG8 1BB
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Sponsor type
University/education

Website
http://www.nottingham.ac.uk/

ROR
https://ror.org/01ee9ar58

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

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

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Conference presentation
3. Publication on website
4. Submission to regulatory authorities

Intention to publish date
30/11/2026

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date. Study data will be collected with the knowledge and consent/assent of the participant and consent of their parent/carer and held in the secure, encrypted trial database. Only members of the research team will have access to the participant's trial data. Consent for use of data in future studies is not sought in this trial. Anonymised participant data may be shared with researchers external to the trial research team in accordance with the NCTU's data-sharing procedure.

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?
HRA research summary			28/06/2023	No	No