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Sertraline for anxiety in adults with a diagnosis of autism

Submission date
02/02/2021

Recruitment status
No longer recruiting

Registration date
08/02/2021

Overall study status
Completed

Last Edited
10/03/2025

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Current plain English summary:
Background and study aims
The study is being done as many autistic adults experience anxiety and many find it very difficult to deal with. Medications like sertraline are often prescribed for anxiety in autistic adults but whether they work, and what their side effects are in the autistic population is not well known. By taking part in this study, participants will be helping to inform whether autistic adults who experience anxiety should be prescribed sertraline.
This study has been designed by experienced researchers and clinicians, with the help of an advisory group of autistic adults. The study will recruit 306 participants over 2 years from the UK (and also the University of Western Australia). Participants can take part entirely remotely (for example using email, telephone, and video-calling), with medication sent out by post, so participants can take part wherever they live in the UK.

Who can participate?
To be potentially eligible, participants need to:
1. Be aged 18 years or over and have a diagnosis of autism (including autism spectrum disorder /condition or other variations, Asperger syndrome, or pervasive developmental disorder)
2. Experience anxiety for which they are willing to try treatment with medication
3. Be able to complete online or paper-based questionnaires about things such as anxiety, other symptoms, and healthcare usage
4. Be able to provide informed consent to take part
The study may not be suitable for participants to take part in if they:
1. Are currently taking medication(s) for depression and/or anxiety at antidepressant doses, or have taken them regularly in the past 8 weeks, or are using St John's Wort
2. Have a moderate or severe learning disability which means they may not be able to provide informed consent and/or understand and complete the study questionnaires
3. Have/had other mental health conditions with currently valid diagnosis such as bipolar disorder or psychosis
4. Have epilepsy that is not well controlled
5. Have current problematic use of alcohol or illicit drugs
6. Have allergies to sertraline or placebo
7. Have/had severe liver problems, bleeding disorders, some heart problems

8. Have swallowing difficulties or are unable to take medication in capsule form
9. Are taking part in another clinical trial
10. Are pregnant, planning pregnancy during the study period, or breastfeeding
Please note that a full list of all exclusion criteria are available on the Participant Information Leaflet here: https://strata.blogs.bristol.ac.uk/information-about-the-study/
Once they have read the information above, as well as the Participant Information Leaflet/s, and discussed the study with family/friends/carers/others if they wish, potential participants can express an interest in taking part by completing a quick form at: https://www.tinyurl.com/STRATAEoI
If they would prefer to complete their expression of interest on paper, or over the phone with a member of the team, potential participants can contact the STRATA study team to request a posted paper copy by email: strata-takepart@bristol.ac.uk or telephone: +44 (0)117 428 3001. If there are any parts of the study information that participants do not understand, or if they have any questions or would like further information, they are welcome to contact the STRATA study team using the details above.

What does the study involve?
Participants will receive either sertraline, or a placebo (inactive) medication which they will be asked to take for up to one year. Participants will be contacted briefly via video call, telephone, text, or email (whichever they prefer) 4 times in the first 4 months, and again after 9 months to see how they are getting on with the medication.
Participants will also complete questionnaires about their anxiety and other symptoms at the start of the study, and after 4 months, 6 months, and 1 year, and will be offered a £10 gift voucher for completing these.
If participants were to take part, they can withdraw from the study at any time, without giving a reason, and without it affecting their medical care or legal rights.

What are the possible benefits and risks of participating?
Participants' anxiety symptoms may improve, but there is no guarantee. They may also benefit from the extra contact from being part of the study. However, please note that taking part in this study does not replace other services participants may be receiving for any physical or mental health problems and they should continue to seek support from their GP and any other services as they would usually do. Participating will help to improve future treatment recommendations for autistic adults who experience anxiety. Participants who agree to the recording of study discussions and an interview will be helping to contribute evidence on the best way of explaining research studies to potential participants.
The first study appointment may last 1 to 2 hours. Participants may find it tiring to complete the questionnaires. The researchers will try to ensure that participants are comfortable and they can take one or more breaks as needed. It may take about an hour to complete each of the other study questionnaires, but this time will vary for each person. Some people will take less time, and others may take longer. Participants will be able to complete these at a time, and by a method, convenient to them. There are no physical risks to having discussions with study staff recorded or being interviewed to understand their views of being invited and taking part in this study. As part of the interview, the researchers may ask about anxiety and its impacts and for some people, this may cause distress or anxiety. The researchers will try to ensure that participants are comfortable. Participants can pause or stop the interview and/or the recording of discussions at any time.

Where is the study run from?
The Bristol Randomised Trials Collaboration, as part of the Bristol Trials Centre (UK)

When is the study starting and how long is it expected to run for?
October 2019 to March 2025

Who is funding the study?
1. National Institute for Health Research Health Technology Assessment programme (NIHR HTA) (UK)
2. National Health and Medical Research Council (NHMRC) (Australia)

Who is the main contact?
STRATA Trial Manager
strata-rct@bristol.ac.uk

Previous plain English summary:
Background and study aims
Anxiety is common in autistic adults and can be more disabling than the core features of autism. Medications for anxiety are often prescribed for autistic adults but their effectiveness or side effects in this population are not well known. Research findings in non-autistic populations may not apply to autistic adults. This study aims to find out whether the drug sertraline is an effective treatment for anxiety in adults with a diagnosis of autism. Sertraline is a commonly prescribed antidepressant and is also recommended for the treatment of anxiety problems. This study will compare the use of sertraline in autistic people with placebo, a non-active identical capsule. The researchers are interested to see whether the treatment improves symptoms of anxiety, enhances quality of life, and is effective in the longer term. They are also interested in understanding the side effects of the treatment.

Who can participate?
Adults with a diagnosis of autism who experience anxiety

What does the study involve?
People who take part will be randomly allocated to receive either sertraline or a placebo (inactive) medication in capsule form. They will be asked to take it for up to 1 year. Please note that the medication capsules may contain gelatine which may not be suitable for vegans. Participants will be contacted briefly by trained study staff by video call, telephone, text or email at 1 to 2, 4, 8, 12 and 36 weeks after they join the study to see how they are getting on with the medication. Participants will be asked to complete questionnaires at the start of the study and 16, 24 and 52 weeks after they join the study. The questionnaires will ask about anxiety, other symptoms, and healthcare usage. To thank them for your time, participants will be offered a £10 gift voucher on receiving each completed questionnaire. In addition, the researchers plan to record conversations where the study is discussed with participants to see how well it is explained. They will also speak with some participants to understand their views on being invited to the study and/or their experiences of taking part in it. These aspects are optional.

What are the possible benefits and risks of participating?
Participants' anxiety symptoms may improve, but there is no guarantee. They may also benefit from the extra contact from being part of the study. However, please note that taking part in this study does not replace other services participants may be receiving for any physical or mental health problems and they should continue to seek support from their GP and any other services as they would usually do. Participating will help to improve future treatment recommendations for autistic adults who experience anxiety. Participants who agree to the recording of study discussions and an interview will be helping to contribute to evidence on the best way of explaining research studies to potential participants.
The first study appointment may last 1 to 2 hours. Participants may find it tiring to complete the

questionnaires. The researchers will try to ensure that participants are comfortable and they can take one or more breaks as needed. It may take about an hour to complete each of the other study questionnaires, but this time will vary for each person. Some people will take less time, and others may take longer. Participants will be able to complete these at a time, and by a method, convenient to them. There are no physical risks to having discussions with study staff recorded or being interviewed to understand their views of being invited and taking part in this study. As part of the interview, the researchers may ask about anxiety and its impacts and for some people this may cause distress or anxiety. The researchers will try to ensure that participants are comfortable. Participants can pause or stop the interview and/or the recording of discussions at any time.

Where is the study run from?
The Bristol Randomised Trials Collaboration, as part of the Bristol Trials Centre (UK)

When is the study starting and how long is it expected to run for?
October 2019 to April 2023

Who is funding the study?
1. National Institute for Health Research Health Technology Assessment programme (NIHR HTA) (UK)
2. National Health and Medical Research Council (NHMRC) (Australia)

Who is the main contact?
STRATA Trial Manager
strata-rct@bristol.ac.uk

Contact information

Type(s)
Public

Contact name
Ms Leonora Cotton

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Bristol Trials Centre
Bristol Medical School
University of Bristol
1-5 Whiteladies Road
Bristol
United Kingdom
BS8 1NU
+44 117 455 5738
strata-rct@bristol.ac.uk

Type(s)
Scientific

Contact name
Dr Dheeraj Rai

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Chief Investigator
Population Health Sciences
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Oakfield House
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BS8 2BN
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Dheeraj.Rai@bristol.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
2019-004312-66

Integrated Research Application System (IRAS)
270727

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 46047, IRAS 270727, HTA - NIHR127337

Study information

Scientific Title
A multicentre double-blind placebo-controlled randomised trial of SerTRaline for AnxieTy in adults with a diagnosis of Autism (STRATA)

Acronym
STRATA

Study objectives
The null hypothesis is that there is no difference in the Generalised Anxiety Disorder Assessment (GAD-7) anxiety scores at 16-weeks between adults with a diagnosis of autism treated with sertraline and those treated with placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 22/07/2022, South Central - Oxford B (Meeting held by video-conference via Zoom; +44 (0)207 104 8178, (0)207104 8360, (0)2071048181; oxfordb.rec@hra.nhs.uk), ref: 22/SC/0296
2. Approved 02/02/2021, Fast-Track REC (no address provided; +44 (0)207 104 8012; fasttrack.rec@hra.nhs.uk), REC ref: 21/FT/0008

Study design

Randomized interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Autism

Interventions
Participants will be randomized to one of two treatment groups: either sertraline (intervention arm) or placebo (control arm). Participants will receive a daily dose of 25 mg encapsulated sertraline or placebo for 2 weeks followed by 2 x 25 mg for 4 weeks. Depending upon tolerability, the prescriber will flexibly increase the dose by 50 mg every 4 weeks to reach the optimal dose. The dose will only be increased if the participant is tolerating it and agrees to try an increased dose, and the prescriber is satisfied that it is appropriate to do so. For example, the dose may go up to a maximum of 200mg by week 14, although it is anticipated that for many participants the optimal dose will be lower (e.g. 50 mg, 100 mg or 150 mg) and reached before this time. Participants will have different treatment schedules depending on their optimal dose. However, in all cases participants shall take medication for up to 52-weeks post-randomisation unless they, or their care team, discontinues medication sooner. After 52-weeks post-randomisation (or if they discontinue medication sooner), participants will complete a downward titration of the study medication for a period of 4 weeks, which involves reduction of medication by 50 mg per week before being returned to standard care. The placebo regimen will be identical.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome(s)
Anxiety measured using Generalised Anxiety Disorder Assessment (GAD-7) anxiety score at baseline and 16 weeks

Key secondary outcome(s))
1. Adverse effects reported using the Modified Toronto side effects scale and open-ended questions (including suicidality item) at baseline, 1, 2, 4, 8, 12, 16, 24, 36 and 52 weeks
2. Response to treatment defined as a 50% reduction in GAD-7 score at baseline, 1, 2, 4, 8, 12, 16, 24, 36 and 52 weeks
3. Patient reported effect of medication on symptoms measured using study-specific questionnaire at 1, 2, 4, 8, 12, 16, 24, 36 and 52 weeks
4. Social anxiety measured using Social Phobia Inventory (SPIN) at baseline, 16, 24 and 52 weeks
5. Obsessive compulsive symptoms measured using Obsessive Compulsory Inventory Revised (OCI-R) at baseline, 16, 24 and 52 weeks

6. Panic attacks measured using Brief Patient Health Questionnaire (PHQ) from Primary Care Evaluation of Mental Disorders (PRIME-MD) at baseline, 16, 24 and 52 weeks
7. Repetitive behaviours measured using Adult Repetitive Behaviours Questionnaire-2 (RBQ-2A) at baseline, 16, 24 and 52 weeks
8. Depressive symptoms measured using Patient Health Questionnaire-9 (PHQ-9) at baseline, 16, 24 and 52 weeks
9. Functioning and disability measured using World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) at baseline, 16, 24 and 52 weeks
10. Health-related quality of life measured using EQ-5D-5L questionnaire at baseline, 12, 16, 24 and 52 weeks
11. Carer burden and health-related quality of life measured using Caregiver Burden Scale, Carer Experience Scale (CES) and EQ-5D-5L questionnaire at baseline, 16, and 52 weeks
12. Adherence to the study medication measured using study-specific questionnaire (adapted from GENPOD and PANDA trials) at 1, 2, 4, 8, 12, 16, 24, 36 and 52 weeks
13. The cost-effectiveness of sertraline treatment for anxiety in adults with a diagnosis of autism measured using EQ-5D-5L (to calculate QALYs) and study-specific patient resource use questionnaire at 24 and 52 weeks
14. Participants' acceptability, experiences of, and adherence to, study processes and treatment, measured using qualitative interviews with participants between 8 and 52 weeks

Completion date
31/03/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 31/03/2022:
1. Aged ≥18 years and have a diagnosis of autism (including autism spectrum disorder/condition or other variations, Asperger syndrome, or pervasive developmental disorder)
2. Experience anxiety for which participants are willing to try treatment with medication
3. Able to complete online or paper-based questionnaires about things such as anxiety, other symptoms, and healthcare usage
4. Able to provide informed consent to take part

Previous participant inclusion criteria:
1. Adults aged ≥18 years
2. A diagnosis of autism made by a specialist including those with a co-occurring mild intellectual disability (autism diagnostic terms may include autism/autistic spectrum disorder or other variations, Asperger syndrome/disorder or pervasive developmental disorder)
3. Anxiety as measured by GAD-7 score ≥10

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 years

Sex
All

Total final enrolment
318

Key exclusion criteria
Current participant exclusion criteria as of 24/02/2023:
1. Currently taking medication(s) for depression and/or anxiety at antidepressant doses, or have taken them regularly in the past 8 weeks, or are using St John's Wort
2. Have a moderate or severe learning disability which means they may not be able to provide informed consent and/or understand and complete the study questionnaires
3. Have/had other mental health conditions with a currently valid diagnosis such as bipolar disorder or psychosis
4. Have epilepsy that is not well controlled
5. Have current problematic use of alcohol or illicit drugs
6. Have allergies to sertraline or placebo
7. Have/had severe liver problems, bleeding disorders, some heart problems
8. Have swallowing difficulties or are unable to take medication in capsule form
9. Taking part in another clinical trial
10. Are pregnant, planning pregnancy during the study period, or breastfeeding

Previous participant exclusion criteria as of 31/03/2022 to 24/02/2023:
1. Currently taking medication(s) for depression and/or anxiety, or have taken them in the past 8 weeks, or are using St John's Wort
2. Have a moderate or severe learning disability which means they may not be able to provide informed consent and/or understand and complete the study questionnaires
3. Have/had other mental health conditions such as bipolar disorder or psychosis
4. Have epilepsy that is not well controlled
5. Have current problematic use of alcohol or illicit drugs
6. Have allergies to sertraline or placebo
7. Have/had severe liver problems, bleeding disorders, some heart problems
8. Have swallowing difficulties or are unable to take medication in capsule form
9. Taking part in another clinical trial
10. Are pregnant, planning pregnancy during the study period, or breastfeeding

Previous participant exclusion criteria:
1. Prescribed a serotonergic antidepressant/anxiolytic in preceding 8 weeks - these include SSRI and non-SSRI antidepressants including tricyclic antidepressants. Individuals prescribed these medications wishing to participate could do so after a washout period of 8 weeks
2. Prescribed an irreversible monoamine oxidase inhibitor (phenelzine, isocarboxazid or tranylcypromine) or pimozide in the preceding 8 weeks
3. Diagnosis of moderate-severe intellectual disability (ID). People who have up to mild ID will be eligible. For the purpose of this study, a person with known intellectual disability will be considered as having a mild ID if they are able to provide written informed consent, and the ability to understand and answer the study questionnaires with the help of reasonable adjustments, if necessary.
4. Inability to provide informed consent and complete study assessments/questionnaires
5. History of bipolar disorder, manic or hypomanic episodes, or psychosis

6. Currently uncontrolled epilepsy
7. Known alcohol or drug use problem
8. Known allergies to sertraline or placebo/excipients
9. Currently enrolled in another RCT
10. Women who are pregnant, are planning pregnancy during the trial period, or breastfeeding
11. Severe liver impairment
12. Bleeding disorders such as such as haemophilia, Christmas disease and von Willebrands disease, as well as those with past medical history of bleeding gastric or duodenal ulcers or other significant bleeding disorders
13. History of long QT syndrome or Torsade de Pointes
14. Swallowing difficulties or inability to take medication in capsule form
15. Currently using St John's Wort

Date of first enrolment
01/06/2021

Date of final enrolment
26/10/2023

Locations

Countries of recruitment
United Kingdom

England

Australia

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

Study participating centre
Leicestershire Partnership NHS Trust
Riverside House
Bridge Park Plaza
Bridge Park Road
Leicester
United Kingdom
LE4 8PQ

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

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

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
Surrey and Borders Partnership NHS Foundation Trust
18 Mole Business Park
Randalls Road
Leatherhead
United Kingdom
KT22 7AD

Study participating centre
Norfolk Community Health and Care NHS Trust
Norwich Community Hospital
Bowthorpe Road
Norwich
United Kingdom
NR2 3TU

Study participating centre
Hertfordshire Partnership University NHS Foundation Trust
The Colonnades
Beaconsfield Close
Hatfield
United Kingdom
AL10 8YE

Study participating centre
Black Country Healthcare NHS Foundation Trust
Trafalgar House
47-49 King Street
Dudley
United Kingdom
DY2 8PS

Study participating centre
Leeds and York Partnership NHS Foundation Trust
2150 Century Way
Thorpe Park
Leeds
United Kingdom
LS15 8ZB

Study participating centre
Fremantle Hospital
Alma St
Fremantle WA
Australia
6160

Study participating centre
Camden and Islington NHS Foundation Trust
St Pancras Hospital
4 St Pancras Way
London
United Kingdom
NW1 0PE

Sponsor information

Organisation
University of Bristol

ROR
https://ror.org/0524sp257

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

Funder Name
National Health and Medical Research Council

Alternative Name(s)
National Health and Medical Research Council, Australian Government, NHMRC National Health and Medical Research Council, NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

Results and Publications

Individual participant data (IPD) sharing plan

The final trial data set will be stored as restricted data on the data.bris research data repository. Data will be made available to approved bona fide researchers only, after their host institution has signed a data access agreement. Details of how to request access are available at the University of Bristol's data repository website (https://data.bris.ac.uk/data/).

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		22/01/2024	12/01/2024	Yes	No
HRA research summary			28/06/2023	No	No
Other files	Health Economics Analysis Plan version 1.0	28/10/2024	24/01/2025	No	No
Participant information sheet	version 2.0	28/01/2021	31/03/2022	No	Yes
Participant information sheet	version 3.0	15/11/2022	10/03/2025	No	Yes
Statistical Analysis Plan	version 1	21/10/2024	24/01/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes