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What are the indications for prescribing antidepressants that will lead to a clinical benefit?

Submission date
20/03/2014

Recruitment status
No longer recruiting

Registration date
20/03/2014

Overall study status
Completed

Last Edited
02/12/2019

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Depression is a common condition that affects between 2% and 3% of the population at any one time. Depression is commonly treated with antidepressant medication. In England and Wales there were 47 million prescriptions for antidepressants in 2011. Selective serotonin reuptake inhibitors (SSRIs) are the first-line antidepressant recommended by the NICE guidelines. Some people with depression will recover spontaneously and it is not clear at present which people will benefit from a course of antidepressants. Depression is also difficult to assess accurately during a short primary care consultation. As a result, general practitioners often have to make a difficult decision about whether an individual will benefit from an SSRI. This study is designed to refine the indications for the use of antidepressants in people with depression. The aim of this study is to investigate the response to sertraline in people with depression by assessing the severity and duration of their depressive symptoms using a self-administered computerised assessment that could be used in primary care.

Who can participate?
Patients aged 18-74 with depressive symptoms

What does the study involve?
Participants are randomly allocated to take either sertraline or placebo (dummy) capsules for 12 weeks, with assessments at 2, 6 and 12 weeks.

What are the possible benefits and risks of participating?
Some people find it rewarding to take part in medical research, and appreciate the additional monitoring and contact with the researchers. Taking the study medication may improve symptoms of depression, but this cannot be guaranteed, and half of the participants take a dummy pill or placebo. The long-term benefits of the study are improved guidance/treatment recommendations for primary care clinicians, thereby increasing the likelihood that a prescription will lead to clinical benefit, while reducing prescriptions that are not needed.

Where is the study run from?
UCL Division of Psychiatry (UK)

When is the study starting and how long is it expected to run for?
May 2014 to May 2018

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

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2013-003440-22

Protocol serial number
16264

Study information

Scientific Title
A phase IV, double-blind randomised placebo-controlled, parallel group multi-site trial of sertraline compared to placebo in patients presenting with depressive symptoms in primary care where treatment with SSRIs is uncertain. What are the indications for Prescribing ANtiDepressants that will leAd to a clinical benefit? (PANDA RCT)

Acronym
PANDA

Study objectives
Depression is a common condition that affects between 2% and 3% of the population at any one time. Depression is commonly treated with antidepressant medication. In England and Wales there were 47m prescriptions for antidepressants in 2011. Selective serotonin reuptake inhibitors (SSRIs) are the first line antidepressant recommended by NICE guidelines. Some people with depression will recover spontaneously and it is not clear at present which people will benefit from a course of antidepressants. Furthermore it is not known whether the current diagnostic criteria for depression as described in ICD10 or DSM5 indicate benefit from antidepressants. Depression is also difficult to assess accurately during a short primary care consultation. As a result, general practitioners often have to make a difficult decision about whether an individual will benefit from an SSRI. This study is designed to refine the indications for the use of antidepressants in people with depression. The aim of this study is to carry out a randomised controlled trial in order to investigate the severity and duration of depressive symptoms that are associated with a clinically important response to sertraline in people with depression. The trialists plan to assess severity and duration using a standardised assessment that can then be used to guide prescription in primary care. The trialists will include patients presenting in primary care aged 18-74 with depressive symptoms and both the GP and patient are unsure whether there will be significant clinical benefit from taking SSRI antidepressants. Sertraline will be provided in 50mg capsules. The usual dose in primary care is 100mg and the trialists will recommend that all participants take 2 capsules (100mg) unless they cannot tolerate that dose. The participants can increase to 3 capsules if they have not responded and with the agreement of the PI.

Ethics approval required
Old ethics approval format

Ethics approval(s)
13/EE/0418

Study design
Randomised; Interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Mental Health Research Network, Primary Care Research Network for England; Subtopic: Depression, Not Assigned; Disease: Depression, All Diseases

Interventions
Sertraline vs Placebo: The sertraline will be encapsulated and matching placebo capsules produced in order to maintain the blind during the study. Trial treatment will be for 12 weeks with assessments at 2, 6 and 12 weeks. The main treatment response compared to placebo occurs within about 6 weeks. The trialists also want to obtain an early account of adverse events and clinical response at 2 weeks as the first signs of improvement can occur at that point. The 12-week assessment will provide evidence for any sustained benefit.

Follow Up Length: 3 month(s)
Study Entry: Single Randomisation only

Intervention Type
Drug

Phase
Phase IV

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

Primary outcome(s)
Depressive symptoms, measured with the PHQ9 questionnaire; Timepoint(s): 6 weeks follow up

Key secondary outcome(s))
Added 11/07/2017:
1. Depressive symptoms, measured with the PHQ-9 at 2 and 12 weeks as a continuous outcome and at 2, 6 and 12 weeks as a binary outcome
2. Depressive symptoms, measured with the BDI-II at 2, 6 and 12 weeks
3. Anxiety symptoms, measured by the GAD-7 at 2, 6 and 12 weeks
4. Quality of life, measured with the EQ-5D-5L and SF-12 at 2, 6 and 12 weeks
5. Emotional processing task scores, measured at baseline, 2 and 6 weeks
6. Costs associated with health care use, time off work and personal costs over the 6 months period and measured at 12 weeks

Completion date
30/11/2017

Eligibility

Key inclusion criteria
Participants presenting in primary care aged 18-74 with depressive symptoms and both the GP and patient are unsure whether there will be significant clinical benefit from taking SSRI antidepressants and not currently on antidepressants (or in previous 8 weeks).

The trialists want to keep the inclusion criteria pragmatic and broad to reflect the current dilemma in clinical practice. They therefore think that the uncertainty of GP and patient about the possible benefits of antidepressants is the key entry criterion for the trial. They have included participants up to 74 years as additional clinical issues concerned with cognitive decline and social care become more common after that age.
There may be situations where people with severe depressions would be included in the study and might receive placebo. The patient will always be free to consult their general practitioner during the study about any of their health concerns. The patient and GP can contact the PI at any time and seek advice about continuing with the study medication to stop the randomised treatment if there was deterioration or any other clinical need to start antidepressants. The trialists would allow hypnotic medication and other non-pharmacological treatment options including low intensity psychosocial treatments as provided by IAPT or counselling. The trialists will record this information and can investigate any impact on the findings in secondary analyses (and also use for the economic analysis).

There is marked comorbidity between depression and anxiety disorders. The trialists are relying upon the GP referring subjects into the study to exclude all anxiety disorders that they have identified and wish to treat with SSRIs. The trialists will assess anxiety disorders at baseline and any influence of comorbid anxiety (that they expect will be quite common) on outcome can be examined in exploratory analyses.

Target Gender: Male & Female; Upper Age Limit 74 years ; Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
74 years

Sex
All

Total final enrolment
655

Key exclusion criteria
1. Anyone who is incapable of completing the questionnaires or who has other psychiatric disorders including psychosis, bipolar disorder, dementia, eating disorder, substance dependence, schizophrenia, mania, hypomania
2. Known allergies to the IMP, placebo or excipients
3. Poorly controlled epilepsy
4. Hepatic impairment
5. Currently on contraindicated medication: monoamine oxidase Inhibitors within 14 days or pimozide
6. Pregnant women

Added 07/07/2017:
7. People with bleeding disorders 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
8. An episode of Torsade's de Pointes

Date of first enrolment
26/01/2015

Date of final enrolment
31/08/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Centre for Academic Mental Health
Oakfield House
Oakfield Grove
Bristol
United Kingdom
BS8 2BN

Study participating centre
UCL Division of Psychiatry
Maple House
149 Tottenham Court Road
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Study participating centre
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Study participating centre
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Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research (UK) - Programme Grants for Applied Research; Grant Codes: RP-PG-0610-10048

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made 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?
Results article	results	01/11/2019	25/09/2019	Yes	No
Results article	cost-effectiveness results	01/09/2020	02/12/2019	Yes	No
HRA research summary			28/06/2023	No	No

Study website	Study website	11/11/2025	11/11/2025	No	Yes