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Trial of Internet and telephone support to people coming off long-term antidepressants

Submission date
07/10/2019

Recruitment status
No longer recruiting

Registration date
07/10/2019

Overall study status
Completed

Last Edited
25/06/2024

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
There is considerable concern about increasing antidepressant use in England. GPs are writing more than 70 million prescriptions a year, to around 1-in-10 adults. Some people need long-term antidepressants to stop them getting depressed, but a third-to-a-half could possibly stop them without relapsing. However, stopping is not always easy. Some patients may experience withdrawal symptoms, while others may be fearful that they will experience them. Withdrawal symptoms can include anxiety and depression, which are usually temporary, but can feel similar to the reasons why patients first started antidepressants. So understandably, some people restart their antidepressant quickly. Others are reluctant to try stopping because they feel well on medication, they are afraid their symptoms may come back, and they feel that there is too much at stake to take the risk of stopping.

Taking antidepressants long-term exposes patients to the risks of side-effects. Common side effects of antidepressants include changes in weight, changes in sleep, and changes in libido or sexual functions. Less commonly, some patients develop bleeding from the stomach or intestine, and the use of antidepressants in people over 65 is associated with an increase in the risks of falls, seizures, and strokes. Some patients also complain that they feel emotionally numb on antidepressants. These are all good reasons for proposing that the drugs should not be continued long-term unless there is a good reason for taking them. People taking antidepressants have told us their GPs rarely review them and just give repeat prescriptions. Studies show that when GPs do review patients on long-term antidepressants and recommend that they could begin to stop taking them, only 1-in-14 is able to stop. Patients can be fearful and cessation can be tricky, so GPs and Nurse Practitioners (NPs) who prescribe antidepressants need to develop individual cessation strategies for each patient, and be able to offer them sustained support, especially in the first few weeks or months.

The NHS funded six-year REDUCE (REviewing long term antiDepressant Use by Careful monitoring in Everyday practice) research programme aims to identify feasible, safe, effective, and cost-effective ways of helping patients taking long-term antidepressants taper off and stop treatment, when appropriate.

Who can participate?
Adults registered with participating practices who taking long-term antidepressants for more than one year for a first episode, or more than two years for a recurrent episode, are no longer depressed or anxious, and not under psychiatric care

What does the study involve?
This Work Stream 5 (WS5) of the REDUCE programme aims to determine the effectiveness of online (Internet) interventions which support practitioners and guide patients on coming off antidepressants, together with psychological practitioner telephone calls to support the patients.

We will assess the effectiveness of the interventions in terms of reductions in antidepressant use in the absence of worsening of depression, and assess patients' and practitioners' use of the interventions (automatically recorded by the Southampton 'LifeGuide' software used for the Internet guidance)

Through open-ended interviews with 15-20 patients and 15-20 practitioners in each arm, we will explore why the interventions were effective or not, depending on the results. We will also look at the use of the telephone support provided by psychological practitioners (PWPs), and any technical support needed for patients to be able to use the internet intervention. The interviews will be recorded and typed out (transcribed) for 'thematic analysis', which is line by line examination of the interview transcripts to identify themes among the reactions of the patients and practitioner involved in the trial

What are the possible benefits and risks of participating?
A possible benefit to patients is having their antidepressant treatment reviewed and discontinued where possible. There are risks of side effects of withdrawal, and of recurrence of depression, in a minority of patients

Where is the study run from?
The Universities of Southampton, Liverpool, Hull, York, and University College London

When is the study starting and how long is it expected to run for?
It starts 1st November 2019 and will run for three years.

Who is funding the study?
The NHS National Institute for Health Research

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)
Nil known

Integrated Research Application System (IRAS)
266517

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 43140, IRAS 266517

Study information

Scientific Title
REviewing long term anti-DEpressant Use by Careful monitoring in Everyday practice (REDUCE) programme. Workstream 5 (WS5): Randomised Controlled Trial

Acronym
REDUCE WS5

Study objectives
Providing Internet and telephone support to people coming off long-term antidepressants is effective and cost-effective

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 10/09/2019, North of Scotland Research Ethics Committee 1 (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE; +44 (0)1224 558458; nosres@nhs.net), ref: 19/NS/0144

Study design
Randomized; Interventional; Design type: Treatment, Education or Self-Management, Psychological & Behavioural

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
Mood [affective] disorders

Interventions
The NHS funded six-year REDUCE (REviewing long term antiDepressant Use by Careful monitoring in Everyday practice) research programme aims to identify feasible, safe, effective, and cost-effective ways of helping patients taking long-term antidepressants taper off and stop treatment, when appropriate. This Work Stream 5 (WS5) of the REDUCE programme aims to determine the effectiveness of online (Internet) interventions which support practitioners and guide patients on coming off antidepressants, together with psychological practitioner telephone calls to support the patients. This work stream draws on a previous systematic review and qualitative synthesis of the existing literature on antidepressant cessation carried out in work stream 1; analyses of qualitative interviews and focus groups carried out with patients and practitioners respectively on the difficulties of antidepressant cessation in work stream 2; the development of the intervention using 'think-aloud' interviews with patients and practitioners in work stream 3; a feasibility randomised trial in work stream 4; the lived experience of our patient and public involvement (PPI) advisors; and our team's research and development expertise.

WS5 is a fully powered randomised controlled trial (RCT), which aims to assess the effectiveness of the Internet and telephone interventions. It will take 36 months to complete, starting in October 2018. We will recruit 402 patients (201 randomly allocated to the intervention arm and 201 controls), from 134 general practices over 15-18 months, and follow them up for 12 months. We will assess the effectiveness of the interventions in terms of reductions in antidepressant use in the absence of worsening of depression, and assess patients' and practitioners' use of the interventions (automatically recorded by the Southampton 'LifeGuide' software used for the Internet guidance).

A qualitative process evaluation will be conducted through open-ended interviews with 15-20 patients and 15-20 practitioners in each arm. We will explore why the interventions were effective or not, depending on the results. We will also look at the use of the telephone support provided by psychological practitioners (PWPs), and any technical support needed for patients to be able to use the internet intervention. The interviews will be recorded and typed out (transcribed) for 'thematic analysis', which is line by line examination of the interview transcripts to identify themes among the reactions of the patients and practitioner involved in the trial.

Patient recruitment
Potential patient participants will be approached in two ways:
(i) through practice records database searches, and
(ii) opportunistically in general practitioner (GP) or nurse practitioner (NP) consultations

All eligible patients identified by searches will be actively approached in both intervention and control arms, to avoid the risk of selection bias inherent in relying only on opportunistic recruitment by practitioners.

Practice computerised medical records databases will be searched using 'Read' diagnostic and symptom codes for depressive diagnoses and symptoms, together with British National Formulary chapter codes for antidepressants taken over the previous two years. Standardised searches were developed during the WS4 feasibility RCT, for the two main practice computer systems SystmOne and EMIS, which can be given to participating practices. Participating GPs will

check the lists of potential participants against the inclusion and exclusion criteria, to ensure all are suitable to be invited to take part.

Mail-out packs to patients will include an invitation letter from the GP, the Participant Information Leaflet (PIL), and a reply slip for the patients to complete indicating whether they are interested in taking part. We will use the Docmail digital mail-out facility where possible. Interested patients will be asked to contact the REDUCE team directly using the reply slips (in Freepost envelopes) or by email. If patients do not contact the research team then the team will have no knowledge of their names or addresses, thus maintaining patient confidentiality.

Eligible patients may also be invited to consider taking part within a GP or NP consultation for depression. Patients will be provided by the practitioner with a pack including the GP invitation Letter, PIL and reply slip to be returned directly to the research team using a Freepost envelope if the patient is interested in discussing possible involvement in the trial. Again, there will be no contact between the research team and potential patients unless the patients initiate it.

Those patients who return reply slips to the research team indicating a willingness to discuss possible participation will be contacted by a member of the research team by telephone and screened for the exclusion criteria. This will involve asking a standard set of yes/no questions and administration of the PHQ-9 for depressive symptoms and the GAD-7 for anxiety symptoms (see below). Patients will be reminded of the information provided to them in the PIL sent with the GP invitation letter, and if they have no exclusion criteria they will be asked for a convenient time to meet with a member of the research team.

We will ask the participating general practice if they would like to send a reminder invitation to participate letter, to participants who do not respond to the first invitation to participate. We think that some participants may not be ready to taper their anti-depressants when they receive the first invitation, for reasons that may be transient, for example too close to Christmas. As people's situations and personal circumstances fluctuate, a follow up letter may be received at a time that the participant considers more appropriate for tapering.

Consent procedure
The researcher will arrange to meet the patient, either at their GP practice or at their home if they prefer, to go over the consent procedure. If the patient gives written consent to take part at that point, the researcher will conduct a baseline assessment. Information given at the point of consent will be the same in both arms. All patients will be told we are recruiting people who have been taking antidepressants for more than a year for a first episode, or more than two years for a recurrent episode, with a view to working out how to help them reduce their medication if appropriate, with the advice of their practice GP or nurse (see patient information leaflet and consent form).The information leaflet will outline the two different approaches but not in detail and potential participants will not know to which arm their general practice has been randomised. This is to avoid differential rates of consent to the two arms based on patients' opinions of the intervention or procedures involved in each.

Patients who do not wish to consent to take part at that point for reasons which may be temporary (i.e. they do wish to try to reduce and stop taking their antidepressant, but not at that time due to current life stresses, recent life events, or the timing of upcoming events etc.), will have the option of consenting to be re-contacted after three months, to be asked again if they wish to participate at that later point.

Having once consented to take part in writing on this initial basis, and having undergone baseline assessment, patients will then be given further information about the details of the

procedures in the arm to which their practice has been randomised. In the intervention arm, patients will be given advice and support to log on and engage with their web-based support (see below). After looking at the on-line ADvisor for patients, they will be asked to arrange to see their GP/NP to discuss coming off antidepressants, including agreeing a time to start tapering the dose, and a first follow-up appointment for review.

After they have seen their GP and agreed a start date for tapering, a psychological practitioner will arrange to telephone them for their first support call, timed within the first two weeks of their GP appointment (see below). In the control arm, patients will be asked to arrange to see their GP/NP to discuss whether or not they should try coming off their antidepressants. Whether or not they start to taper will be a matter for them to agree with their GP or prescribing nurse.

Intervention arm
The practitioner intervention (called 'ADvisor for Health Professionals' as it gives advice about AntiDepressants) includes Internet modules on: Why reduce; Broaching the subject; When to start tapering; Reduction schedules for individual antidepressants; Dealing with withdrawal symptoms; Dealing with relapse; ADvisor for patients (a summary); and printable pages on antidepressant reduction regimes and sections of ADvisor for patients to recommend patients consult.

The patient intervention (called 'ADvisor for Patients') includes Internet modules on: Reducing and stopping (introduction to website); How to reduce antidepressants; Thinking about antidepressants (their effects and why lifelong treatment may not be necessary); Dealing with withdrawal symptoms; I'm worried about stopping; Keeping well; Thinking about what you value in life; and Moving forward.

In the intervention arm practices, the GPs/NPs will be given access to the on-line ADvisor for practitioners, and induction to the study, which will be either practice-based or on-line. They will receive an introduction to ADvisor, and education on best practice in the supervision of antidepressant tapering and cessation, focussing on the differences between withdrawal symptoms and relapse, and the management of withdrawal symptoms.

The number and timing of subsequent GP/NP consultations during tapering and following drug cessation will be left to the participating GPs/NPs to agree with the patients on an individual basis.

In addition to the ADvisor Internet modules and GP/NP consultations, the following telephone support will be provided
to patients in the intervention arm by a trained psychological practitioner (PP):
- Call 1 (0-2 weeks), for 30 minutes: to check the patient's understanding of the ADvisor intervention and encourage confidence in going through the tapering and cessation process
- Call 2 (4-6 weeks), for 15 minutes: to ask the patient how tapering is going and whether they are following the schedule, and where necessary, to advise the patient to discuss any issues with tapering with their GP
- Call 3 (timing agreed with patient), for 15 minutes: to ask the patient about any residual withdrawal symptoms and go over techniques to help with relapse prevention.

Control arm
In the control arm, participating practices will be informed that the recruited patients are potentially eligible for tapering off antidepressants. Their electronic medical records will be

flagged and patients will be asked to make an appointment as part of usual care to see their GPs /NPs for a review, but they will not be trained in best practice in tapering, unlike practitioners in the intervention arm.

Alerting the control arm practices to the potential eligibility of patients for tapering off antidepressants, will result in some patients tapering and ceasing treatment. Some patients would have discontinued treatment anyway, as part of usual care. This will be permitted within the trial. Our power calculation for the secondary outcome of antidepressant discontinuation in the main trial assumes a 7% discontinuation rate in the control practices, which is the rate found in previous studies of simply prompting GPs to review patients potentially eligible for discontinuation.

Randomisation
Randomisation will be computerised and carried out independently by the Southampton Clinical Trials Unit (SCTU). We will use the statistical technique of 'minimisation' to balance practice size (large/small), location (urban/rural), and social deprivation (dichotomised around the median Index of Multiple Deprivation (IMD) score). There is a random element to the minimisation algorithm, and so we might not expect perfect balance to the randomisation

(added 14/07/2022)
The sample size assumptions were monitored by the Independent Data Monitoring Committee. A check in April 2022 suggested that based on the original sample size assumptions but allowing for the correlation between baseline and follow up values for the primary outcome of 0.48, a sample size of 309 would be required. Therefore, the study team and IDMC were confident that the recruited sample size of 330 would be sufficient to meet the trial objectives, assuming the target follow up rate of 80% was achieved.

Intervention Type
Other

Primary outcome(s)
Depression measured by PHQ-9 score at baseline and 6 months

Key secondary outcome(s))
1. Depression measured by PHQ-9 score at baseline and 12 months
2. Discontinuation of antidepressants (for at least 2 months) measured at 6 months
3. Mental wellbeing measured using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) at baseline, 6 and 12 months
4. Antidepressant withdrawal symptoms measured using the Discontinuation Emergent Signs and Symptoms Scale (DESS) at baseline, 3 and 6 months
5. Antidepressant side effects measured using the Antidepressant Side-Effects Check-list (ASEC) and Changes in Sexual Functioning Questionnaire (CSFQ-C) at baseline, 6 and 12 months
6. Patient satisfaction measured using a modified version of the 'Medical Interview Satisfaction Scale' (MISS-29) at 6 and 12 months
7. Enablement measured using the Patient Enablement Instrument (PEI) at 6 and 12 months
8. Quality of life measured using the EuroQol-5D-5L and Medical Outcomes Study Short Form SF-12 at baseline, 6 and 12 months
9. Use of services (to calculate costs) using a bespoke questionnaire at baseline, 6 and 12 months

Completion date
30/03/2023

Eligibility

Key inclusion criteria
1. Patients who are taking long-term antidepressant treatment, which is not indicated according to the NICE depression guideline (NICE, 2009):
1.1 Treated for more than 1 year for a first episode, and
1.2 Treated for more than 2 years for a recurrent episode, who are:
1.3 No longer depressed or judged to be at significant risk of relapse
2. Adults over 18 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
330

Key exclusion criteria
1. At risk for relapse:
1.1 Current significant depressive symptoms on the PHQ-9 (see below) despite antidepressant treatment
1.2 Current significant anxiety symptoms on the GAD-7
1.3 Current suicidal ideas
1.4 Current psychiatric outpatient or inpatient treatment for depression
2. Bipolar disorder, comorbid psychosis, substance use, or dementia as a primary diagnosis
3. Spoken or written English language inadequate to take part in interviews or complete questionnaires
4. Another indication for taking antidepressants, e.g. neuropathic pain

Date of first enrolment
01/01/2020

Date of final enrolment
31/03/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Primary Care, Population Sciences and Medical Education, University of Southampton
Aldermoor Health Centre
Aldermoor Close
Southampton
United Kingdom
SO16 5ST

Study participating centre
Primary Medical Care, University of Liverpool
B121 Waterhouse Buildings
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Study participating centre
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Study participating centre
Department of Health Sciences, University of York
Seebohm Rowntree Building
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Sponsor information

Organisation
University of Southampton

ROR
https://ror.org/01ryk1543

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: RP-PG-1214-20004

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. We shall not make qualitative data available to the scientific community, due to the difficulty in anonymising it. We shall make quantitative data available with as few restrictions as feasible, while retaining exclusive use until the publication of major outputs. Anonymised data will be deposited in a data repository to encourage wider use. Further details will be made available at a later date.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		03/06/2024	25/06/2024	Yes	No
Protocol article	protocol	24/05/2020	26/05/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Statistical Analysis Plan	version 1	21/04/2022	19/06/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes