ISRCTN15036829 https://doi.org/10.1186/ISRCTN15036829

REDUCE Programme WS4: REviewing long term anti-DEpressant Use by Careful monitoring in Everyday practice

Submission date
10/09/2018

Recruitment status
No longer recruiting

Registration date
12/09/2018

Overall study status
Completed

Last Edited
09/10/2024

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
There is concern about increasing antidepressant use. In England. GPs are writing more than 60 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, many patients 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. Therefore, people often restart their antidepressant quickly.
Common side effects of antidepressants include changes in weight, changes in sleep, and changes in sexual functions. Less commonly, some patients suffer bleeding from the stomach or intestine, falls, seizures, and strokes. However, studies show that when GPs review patients on long-term antidepressants and recommend that they could begin to stop taking them, only 1-in-14 is able to stop.
The REDUCE (REviewing long term antiDepressant Use by Careful monitoring in Everyday practice) study aims to identify safe, effective, and cost-effective ways of helping patients taking long-term antidepressants taper off and stop treatment, when appropriate. This study in particular, part of the REDUCE programme, aims to determine the feasibility of a randomised controlled trial of online (Internet) interventions to support practitioners and guide patients on coming off antidepressants.
We aim to assess the acceptability of the Internet interventions, recruitment of practitioners and patients, and acceptability of planned outcome measures.

Who can participate?
Patients from primary care practices recruiting to the study can take part that have been taking antidepressants for longer than a year for a first episode of depression, or longer than two years for repeated episodes of depression, and are feeling well and would like to consider coming off the antidepressants by reducing the dose in stages.

What does the study involve?
Participants will be assessed for eligibility over the telephone. If eligible, participants will be required to meet with the researcher at 3 time points (baseline, 3 months, and 6 months) to complete a set of questionnaires. The questionnaires ask participants about their symptoms, social circumstances, and use of health services.
Participants randomised to the intervention arm will have access to an internet programme designed to help with antidepressant withdrawal. They will also receive three telephone calls from a psychological practitioner to offer support.
Participants randomised to the control arm will receive usual care.
After the baseline visit, all participants will be required to make appointments with their GP for a review of their antidepressant medication.
Some participants will also be asked to take part in an interview with a researcher to find out about their experiences of taking part in the study. This is optional and participants do not have to do this part of the study if they do not want to.

What are the possible benefits and risks of participating?
The main benefit will be that participants will have a review of their medication and a discussion with their GP or nurse prescriber about whether they should reduce and stop their long-term antidepressants.
The possible risks of taking part are that participants may experience withdrawal symptoms or a recurrence of depression or anxiety. The participants will have their GP or nurse prescriber on hand to offer support if this happens.

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

When is the study starting and how long is it expected to run for?
September 2018 to October 2019

Who is funding the study?
NIHR Central Commissioning Facility (CCF) (UK)

Who is the main contact?
Dr Hannah Bowers, Research Fellow
reduce@soton.ac.uk

Study website
http://www.southampton.ac.uk/medicine/academic_units/projects/reduce.page

Contact information

Type(s)
Scientific

Contact name
Prof Anthony Kendrick

ORCID ID
http://orcid.org/0000-0003-1618-9381

Contact details

University of Southampton,
Aldermoor Health Centre
Southampton
United Kingdom
SO16 5ST

Type(s)
Public

Contact name
Ms Wendy O'Brien

Contact details
University of Southampton,
Aldermoor Health Centre
Southampton
United Kingdom
SO16 5ST
023 8059 1754
W.O'brien@soton.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
39509

Study information

Scientific Title
REviewing long term anti-DEpressant Use by Careful monitoring in Everyday practice (REDUCE) programme. WS4: Pilot Feasibility Randomised Controlled Trial

Acronym
REDUCE

Study objectives
The REDUCE (REviewing long term anti-Depressant Use by Careful monitoring in Everyday practice) study aims to identify safe, effective, and cost-effective ways of helping patients taking long-term antidepressants taper off and stop treatment, when appropriate. This Work Stream 4 (WS4) of the REDUCE programme aims to determine the feasibility of a randomised controlled trial of online (Internet) interventions to support practitioners and guide patients on coming off antidepressants.
WS4 aims to assess the acceptability of the Internet interventions, recruitment of practitioners and patients, and acceptability of planned outcome measures.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/09/2018, West of Scotland REC 5 (West of Scotland Research Ethics Service, West Glasgow Ambulatory Care Hospital, Dalnair Street, Glasgow, G3 8SJ; 0141 232 1809; WoSREC5@ggc.scot.nhs.uk), ref: 18/WS/0143

Study design
Randomised; Both; Design type: Treatment, Drug, Education or Self-Management, Psychological & Behavioural, Complex Intervention, Management of Care, Active Monitoring, Qualitative

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

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

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

Interventions
The trial is cluster randomised by participating general practices. Whole practices will be randomised to the intervention or control arms, rather than randomising individual patients, in order to avoid contamination between arms (the inadvertent application of the intervention to control patients). 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).
In the intervention arm, practitioners will receive education and advice on best practice in the supervision of antidepressant withdrawal. They will be given access to web-based practitioner support modules and information and advice on patient monitoring during antidepressant withdrawal. The practitioner web-based intervention (called 'ADvisor' as it gives advice about Anti-Depressants) includes modules on:
1.Why reduce?
2. Broaching the subject
3. When to start tapering
4. Reduction schedules for individual antidepressants
5. Dealing with withdrawal symptoms
6. Dealing with relapse

7. ADvisor for patients (a summary)
8. Printable pages on antidepressant reduction regimes and sections of ADvisor for patients to recommend patients consult
The number and timing of GP consultations during tapering will be left to the participating GPs to agree with the patients on an individual basis.
Participating patients will be contacted by the research team, and given advice and support to log on and engage with their web-based patient support. After looking at the web-based support, patients will arrange to see their GP to discuss coming off antidepressants, including agreeing a time to start tapering the dose, and a first follow-up appointment for review.
The patient intervention (also called 'ADvisor') includes Internet modules on:
1. Reducing and stopping (introduction to website)
2. How to reduce antidepressants
3. Thinking about antidepressants (their effects and why lifelong treatment may not be necessary)
4. Dealing with withdrawal symptoms
5. I'm worried about stopping
6. Keeping well
7. Thinking about what you value in life
8. Moving forward.
In addition to the Internet modules, three telephone support calls from a psychological wellbeing practitioner (PWP) will be provided to patients in the intervention arm.
In the control arm participating practices will be informed that participating patients are eligible for withdrawal from antidepressants. Their electronic medical records will be flagged and as part of usual care their GPs/NPs will be asked to review treatment, but they will not be prompted to withdraw treatment, or trained in best practice in withdrawal, unlike practitioners in the intervention arm.
Alerting the control arm practices to the eligibility of patients for withdrawal from antidepressants might result in some patients being withdrawn from treatment, as part of usual care in the absence of practice participation in the trial. This will be permitted though not encouraged within the trial.
Participants will be in the study for a total of 6 months. In both arms, participants will complete research assessments at baseline, 3 months, and 6 months. All participants will be required to visit their GP to discuss discontinuation of their antidepressants within the first 2 weeks of their involvement in the study. In the intervention arm, participants will have access to the ADvisor website from the end of the baseline visit, for the duration of the study. In the intervention arm, participants will receive 3 telephone calls from psychological practitioners at roughly week 2, week 5, and between weeks 8-12. Participants that take part in the qualitative interviews will complete them at any point between weeks 6 and 24.

Intervention Type
Other

Primary outcome measure
1. Patient follow-up rate, assessed by the percentage of patients recruited who complete the Patient Health Questionnaire (PHQ-9) at the 6 month follow-up:
1.1. If this is less than 70% the main trial will not proceed
1.2. If it is greater than 80% the main trial will proceed
1.3. If it is between 70% and 80% it will proceed provided measures can be put in place to reassure the funder that follow-up can be increased to 80%
2. The willingness of general practices to be recruited to the study based on the number of expressions of interest and subsequent recruitment - the percentage of practices approached

who complete participation in the study, assessed at the end of the patient follow-up
3. The willingness of practices to be randomised to intervention or control arms of the study as whole practices, in a cluster randomised design - the percentage of practices which withdraw from the study, assessed after randomisation and before the end of the patient follow-up
4. The willingness and ability of general practitioners (GPs) and nurse practitioners (NPs) to recruit and randomise patients to the two arms of the study in consultations for the follow-up of patients taking antidepressants for depression, based on recruitment rates and feedback in qualitative interviews at the end of the patient follow-up
5. The mean number of eligible patients found per practice through the database searches at the end of the patient follow-up
6. Recruitment rates among eligible patients identified through the searches and contacted by post at the end of the patient follow-up
7. The willingness of patients to engage with the Internet intervention and telephone support in the intervention arm based on intervention use data and qualitative interviews at the end of the patient follow-up
8. The willingness of patients to have their PP telephone support calls based on PP support call uptake and qualitative interviews at the end of the patient follow-up
9. The acceptability of the proposed research outcome measures to patients, in both intervention and control arms, measured using a Likert rating scale during researcher visits at the end of the patient follow-up
10. Response rates to research outcome measures administered by post and followed up by face-to-face or telephone administration where necessary at the end of the patient follow-up
11. The intra-cluster correlation coefficient (ICC) between practices for depressive symptoms on the PHQ-9 (to help inform the sample size calculation for the main trial, along with published ICCs from other trials), assessed at the end of data analysis, following the end of patient follow-up

Secondary outcome measures

The following will be collected using postal questionnaires, followed up by telephone calls and face-to-face visits where necessary:
1. Depression, assessed using the Patient Health Questionnaire (PHQ-9) at the baseline and after 3, 9 and 12 months
2. Anxiety, assessed using the 7-item Generalised Anxiety Disorder questionnaire (GAD-7) at the baseline and after 3, 6, 9 and 12 months
3. Discontinuation of anti-depressants, defined as no use for 2 months from results of the Patient Use of Antidepressant Questionnaire, assessed at the baseline and after 6 months
4. Dose of antidepressant (if not discontinued), assessed using the Patient Use of Antidepressant Questionnaire at the baseline and after after 6 months
5. Quality of life, assessed at the baseline and after 3, 6, 9 and 12 months using:
5.1. EuroQol questionnaire (EQ-5D-5L)
5.2. Medical Outcomes Study Short Form (SF-12)
6. Wellbeing, assessed using the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) at the baseline and after 3 months
7. Withdrawal symptoms, assessed using the Discontinuation Emergent Signs and Symptoms Scale (DESS) at the baseline and after 3 months
8. Antidepressant side effects, assessed at the baseline and after 3, 6 and 12 months:
8.1. Antidepressant side effects checklist (ASEC)
8.2. Changes in Sexual Functioning Questionnaire (CSFQ-C)
9. Patient satisfaction, assessed using the Medical Interview Satisfaction Scale (MISS-29) at the baseline and after 6 months:
10. Enablement, assessed using the Patient Enablement Instrument at the baseline and after 6

months
11. Costs, assessed using a bespoke questionnaire at the baseline and after 3, 6, 9 and 12 months

Overall study start date
01/09/2018

Completion date
31/10/2019

Eligibility

Key inclusion criteria
1. Aged 18 years and over
2. On antidepressant treatment for more than 1 year for a first episode
3. Treated for more than 2 years for a recurrent episode
4. No longer depressed or judged to be at significant risk of relapse

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 70; UK Sample Size: 70

Total final enrolment
52

Key exclusion criteria
1. Significant risk factors for relapse, including:
1.1. Current significant depressive symptoms on the PHQ-9 (score 12+) despite antidepressant treatment
1.2. Current significant anxiety symptoms on the GAD-7 (score 10+)
1.3. Current suicidal ideas
1.4. Depression needing current psychiatric outpatient or inpatient treatment
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
01/10/2018

Date of final enrolment
31/05/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Southampton
Primary Care & Population Sciences
Aldermoor Health Centre
Aldermoor Close
Southampton
United Kingdom
SO16 5ST

Sponsor information

Organisation
University of Southampton

Sponsor details
University Road,
Highfield
Southampton
England
United Kingdom
SO17 1BJ
023 8059 5000
rginfo@soton.ac.uk

Sponsor type
Hospital/treatment centre

Website
https://www.southampton.ac.uk/about/departments/faculties.page

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

Publication and dissemination plan
The findings will be disseminated to patients, clinicians, academics and the media as follows:
1. Patients: With assistance from our PPI representatives, we will disseminate study reports in plain English to people with depression through Depression Alliance, MIND, and other patient groups. Tony Kendrick will report back on the Southampton based feasibility study to our PPI reference group at a local meeting of Depression Alliance.
2. Clinicians: We will publish the findings in short articles in GP trade journals (Pulse, Doctor, and the Practitioner) as well as peer reviewed academic journals such as Annals of Family Medicine, the British Medical Journal, British Journal of General Practice, Family Practice etc. In addition, we will submit abstracts to the Royal College of General Practitioners' annual conference aiming to publicise the findings through oral or poster presentations.
3. Academics: In addition to publishing the findings in academic journal papers as above, we will submit abstracts to the Society for Academic Primary Care, and North American Primary Care Research Group, aiming to publicise the findings through oral or poster presentations.
4. Media: We will send press releases to local and national papers and media organisations.

Intention to publish date
30/04/2020

Individual participant data (IPD) sharing plan
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
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other unpublished results			09/11/2021	No	No
Protocol article		24/05/2020	04/10/2022	Yes	No
HRA research summary			28/06/2023	No	No
Results article		24/06/2024	09/10/2024	Yes	No