REviewing long term anti-Depressant Use by Careful monitoring in Everyday practice (REDUCE) programme

Results of Work Stream 4 (WS4): Feasibility Randomised Controlled Trial

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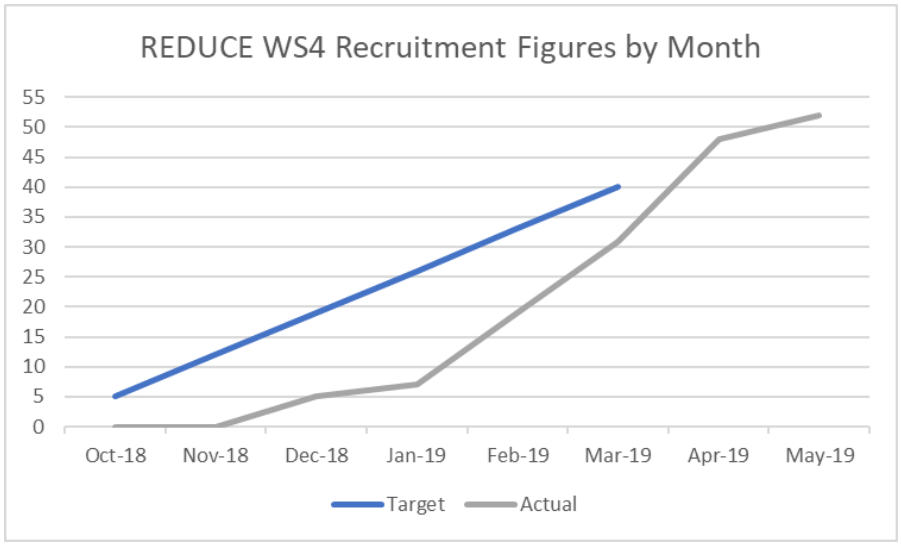
WS4 started in October 2018. We aimed to recruit 40 patients (20 intervention, 20 control) from 14 general practices over 6 months between October 2018 and March 2019 inclusive, and follow them up for 6 months.

Practice recruitment:
Twenty-four GP practices expressed an interest in taking part in the study; 3 were excluded because they had previously taken part in REDUCE WS3 and had seen the digital intervention which would result in contamination if they were randomised to the control arm; 4 later withdrew their expression of interest, and 1 did not respond to emails to arrange a site initiation visit; 1 was not within the Wessex region and was therefore excluded and 1 was excluded due to its remote location, making patient visits difficult and costly. We therefore met our target recruitment of 14 practices.

Patient recruitment:
Recruitment of the first patient was delayed by two months until December 2018, due to delays in arranging site initiation visits and obtaining documents from practices. However we completed recruitment of our target of 40 patients by 10th April, 10 days later than planned. We stopped screening patients after we had consented our 40th, but there were an additional 12 screened patients who had been told they were eligible to take part. We honoured those expressions of interest and therefore ***recruited over our target of 40***. Baseline assessments continued to mid-May, on a total of 52 patients (27 intervention and 25 control). Three have since withdrawn from the study, leaving 49 (26 intervention, 23 control). The graph below shows our monthly recruitment against target.



Patient follow-up:
Patients were either emailed or posted their three-month follow-up questionnaires (depending on what they requested at baseline) and then followed up by email or telephone. Our completion rate for three-month follow-ups was 41 of the 52 patients (78.8%, close to our target of 80%). Due to the initial delays in recruitment, our final six-month follow-ups are expected to continue into early November. As of the end of October we have completed successful follow-up of 40 (81.6%) of the 49 patients who have reached the six-month follow-up point. Three patients have withdrawn, one was excluded after baseline assessment, and five are currently being 'chased'. (See section 5 below for the Consort diagram for the WS4 feasibility trial, up to the end of October).

Qualitative interviews
We also completed 10 qualitative interviews with healthcare practitioners (we wanted to interview 15-20 practitioners but only 10 consented in the event), and 18 qualitative interviews with patients (within our target range of 15-20).

Healthcare practitioner (HP) interviews showed overall:

- A positive response to the study: keen to take part due to topic and good patient response
- Recruitment methods both worked well: mail-out and opportunistic
- Facilitators to recruitment: funding from CRN, receptionist training, patients arriving at first GP appointment 'well prepped by study team', manageable number of patients, good contact from study team, more than one GP per practice working on the study.
- Barriers to recruitment: GP lack of time and appointment waiting times, difficult to maintain continuity with patients, difficulties with record database searches, a negative experience with the first recruit impacting on future recruitment, inability to get more than one GP involved

Patient interviews showed overall:

- Experience of taking part in study mostly positive: improved motivation and confidence to stop, provided opportunity to 'think about' medication, improved self-awareness, reported experiencing a fuller range of emotions.
- Shopping vouchers welcomed, extra support invaluable, pleased to help themselves and others; study was clear/easy/straightforward, with friendly researchers.
- 'Wasn't expecting how easy it was to reduce'
- 'Got me off some pills in a safe and guided way'
- 'Amazed what it's done for my life […] it has turned my life around'
- Negative feedback: Would have liked extra support for 'the ones who are left' (a control arm participant, disappointed to be in the control arm).

Specific individual comments made in the qualitative interviews were discussed within the trial management team, and a number of changes were agreed to the procedures and interventions, which are summarised in the tables in section 6. The changes are largely to the standard operating procedures for the practice site initiation visits, induction of practitioners, consenting of patients, and patient assessments at baseline and follow-up. We need to emphasise the potential help on offer through the on-line interventions, at all of these contacts with the practitioner and patient participants.

However, the tables in sections 6 and 7 below show that none of these proposed refinements to our procedures requires a substantial amendment to the protocol.

Provision of telephone support in intervention arm:
Of the 27 patients in the intervention arm, 24 were referred for telephone support from a psychological wellbeing practitioner (PWP). Three were not referred because they and their GP or Nurse practitioner decided they would not be tapering their medication after all. Two of these patients decided to withdraw from the study altogether and four withdrew from just the telephone support: one before having any calls, one after their first call, and two after their second call.

Of the 21 first telephone calls completed, 19 were audio-recorded and analysed for fidelity against the written telephone support guide provided to the PWPs. This showed a high level of adherence to the protocol. The sections of the written guidance used to measure fidelity were the core parts, and ones that could easily be defined and quantified (consent for the recording; whether tapering had been discussed; whether tapering had started; issues/concerns/barriers/resistance; reference to GP; confidence in tapering; motivation; use of ADvisor; arranging second call).The overall fidelity of the calls was very good (89%). Confidence in tapering was rated lowest at 47% but this was difficult to measure, as the PWPs did not usually ask outright if the patients were confident.

There was however some delay in patients receiving their first telephone support call. The first call is expected to take place around two weeks after the patient's initial GP consultation. Of the 21 patients who had a first call, 13 took longer than two weeks (62%). The second and third calls were to be scheduled at an interval agreed between the psychologist and the patient (for example a patient may have preferred to have their telephone calls nearer the end of their tapering plan). We therefore cannot provide any data about the timeliness of these second and third calls. However, an initial reading of the

telephone call transcripts suggests the psychologists had limited availability and patients did not get the level of choice of appointment times we were hoping for.

In addition to participants being scheduled later than requested, three patients were not in the event called by the psychologist when scheduled, and the patients were not notified (this happened on two occasions to one patient). While three of the four missed calls were rescheduled, one of these patients then did not respond to any further contact about rearranging his calls after his second call was missed. One further patient was called twice for their first call by two different PWPs and therefore had a total of four calls.

As a result of the delays in patients receiving their calls, we concluded that the Solent Health PWPs were only just able to provide telephone support for the 24 WS4 patients alongside their usual NHS commitments, and they will not be able to provide the support required for the many more intervention arm patients in the main trial, WS5 (either 174 or 201 in total, depending on whether the 27 WS4 feasibility trial patients can be included in WS5, see below). We are therefore changing provider for the WS5 telephone support. We have negotiated an agreement with Dr Julian Medical Group Ltd. to provide the telephone support needed for the up to 201 WS5 patients. Dr Julian Medical Group Ltd. is a private provider, but has provided psychological therapy services to Southern Health NHS Foundation Trust patients (Southern Health put us in touch with the CEO Dr Julian Nesbitt). We have gained approval from the North of Scotland Research Ethics Committee to use this provider for WS5, we have just signed the contract for the provision of telephone support, and we are now finalising the standard operating procedures, including risk management procedures, to be followed for this.

The change in service provider for the PWP telephone support calls is the single biggest change from the WS4 feasibility trial that we are making for the WS5 main randomised controlled trial. We are happy, having analysed the audio-recordings of the support calls, that the practitioners did provide the intervention as planned. The delays in arranging calls, and occasional missed calls, were due to the difficulty the PWPs faced in fitting the calls in around their busy NHS psychological service appointments. The PWPs working for Dr Julian Medical Group Ltd. will have greater capacity and flexibility to offer calls at times suitable for participating patients, including evenings and weekends.

In our application we proposed indicative criteria for moving to the main trial which were:

- recruitment of sufficient practices in the feasibility trial, aiming for 14 (7 intervention and 7 control)
- recruitment of sufficient patients, aiming for a participation rate of 9% of patients identified through screening, and at least 3 patients per practice
- evidence that the interventions were acceptable and engaging to the participants
- at least 70% of the sample were followed up – and assuming there were reasonable plans to modify follow-up measures if retention was less than 80%.

In WS4 we have demonstrated:

- ***recruitment of sufficient practices: our target of 14 practices was quickly achieved***
- ***recruitment of sufficient patients: this was also achieved (211 responses were received from 791 letters given out or sent to patients (26.6%); of these 100 (12.6%) were positive, slightly lower than the 15% expected; of 80 patients screened, 53 (66%) were eligible, and so we recruited 13 more than the WS4 target of 40***
- ***evidence that the interventions were acceptable and engaging, from the GP, nurse and patient interviews, and the audio-recordings of the PWP support calls***
- ***at least 70% follow-up: our follow-up rate at 3 months was 78.8%; at six months it is currently (at the end of October) 81.6% (see Consort diagram, below)***

References

1. Maund, E., Leydon, G., Williams, S., Geraghty, A., Bowers, H., May, C., Kendrick, T. (2019). Barriers and facilitators to discontinuing antidepressant use: a systematic review and thematic synthesis. Journal of Affective Disorders, 245, 38-62. DOI: 10.1016/j.jad.2018.10.107
2. Maund, E., Stuart, B., Moore, M., Dowrick, C., Geraghty, A., Dawson, S., & Kendrick, T. (2019). Managing antidepressant discontinuation: a systematic review. Annals of Family Medicine, 17(1), 52-60. DOI: 10.1370/afm.2336

3. Bowers, H. M., Williams, S. J., Geraghty, A. W. A., Maund, E., O'brien, W., Leydon, G., May, C.R., Kendrick, T. (2019). Helping people discontinue long-term antidepressants: views of health professionals in UK primary care. BMJ Open, 9(7), 1-8. [e027837]. DOI: 10.1136/bmjopen-2018-027837
4. Charlesworth G, Burnell K, Hoe J, Orrell M, Russell I. Acceptance checklist for clinical effectiveness pilot trials: a systematic approach. BMC Medical Research Methodology 2013, 13:78. http://www.biomedcentral.com/1471-2288/13/78

Consort diagram for WS4 feasibility trial