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PATIENT REPORTED OUTCOME MEASURES FOR MONITORING PRIMARY CARE PATIENTS WITH DEPRESSION: FEASIBILITY RANDOMISED TRIAL

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ABSTRACT

Objectives: To determine the feasibility of a trial of patient reported outcome measures (PROMs) for monitoring primary care patients with depression

Design: Partly individually randomised, partly cluster randomised controlled trial

Setting: Nine general practices in southern England

Participants: 47 adults with new episodes of depression: 22 intervention, 25 control

Randomisation: remote computerised sequence generation and allocation

Interventions: Patient Health Questionnaire, Distress Thermometer analogue scale, and PSYCHLOPS problem profile for monitoring depression, following diagnosis and at 10-35 days later

Blinding: non-blinded, using self-completed measures

Primary outcome: Beck Depression Inventory (BDI-II)

Secondary outcome measures: Work and Social Adjustment Scale (WSAS); EuroQol EQ-5D-5L scale for quality of life; modified Client Service Receipt Inventory for costs; Medical Informant Satisfaction Scale (MISS); qualitative interviews with 14 patients and 13 practice staff about feasibility and acceptability of trial design

Results: Three practices failed to recruit the target of six patients in 12 months. Follow-up rates were intervention patients: 18 (82%) at 12 weeks and 15 (68%) at 26 weeks; controls: 18 (72%) and 15 (60%) respectively. At 12 weeks mean BDI-II score was lower among intervention group patients than controls by 5.8 points (95% CI -11.1, -0.5), adjusted for baseline differences and clustering. WSAS scores were not significantly different. At 26 weeks there were no significant differences in symptoms, social functioning, quality of life, or costs, but mean satisfaction score was higher among controls by 22.0 points (95% CI -40.7, -3.29). Intervention patients liked completing PROMs, but were disappointed when practitioners did not use the results to inform management.

Conclusions: PROMs may improve depression outcome in the short term, even if PROM scores do not inform practitioners' management. Challenges in recruiting and following up patients need addressing for a definitive trial. Encouraging practitioners to use PROMs requires identifying relatively brief measures which can potentially inform management.

Strengths and limitations

- Pragmatic trial with few exclusion criteria, readily generalisable
- Patients were randomly allocated with concealment of allocation from patients until after informed consent had been obtained and baseline measures completed
- Patients, practitioners and assessors could not be blinded to allocation
- Self-report research outcome measures should have prevented observer rating bias
- Despite the small sample size we did find a difference in the primary outcome
- The sample may have been too small to accurately estimate the ICC for the outcome

Trial registration: International Standard Randomised Controlled Trial Registry ISRCTN 97492541.

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BACKGROUND

Depression is common and costly. The estimated prevalence among adults in the UK is 11.1%, including major depressive disorder in 3.3%, and mixed depression and anxiety in 7.8%[1]. It can lead to chronic disability, poor quality of life, suicide in some cases and high levels of health service use and economic costs. The King's Fund have estimated that 1.45 million people will have depression in England by 2026, and total societal costs will be £12.2 billion per year including health care, social services and lost employment[2].

The National Institute for Health and Care Excellence (NICE) depression guidelines recommend different interventions for moderate to severe depression than for mild depression[3]. However, general practitioner (GP) clinical assessments of the severity of depression vary and are often inaccurate when compared to validated measures[4,5]. Consequently, some GPs do not accurately target treatment to patients most likely to benefit[6-8], reducing the cost-effectiveness of treatment, which needs to be optimised given the impact of depression.

As a result of these findings, NICE recommends that health professionals consider using validated questionnaire measures of severity at diagnosis to help target treatment[3]. Between 2006 and 2013 the UK GP contract Quality and Outcomes Framework (QOF) paid GPs to use symptom questionnaires as part of their assessments of depression severity at the outset of treatment for patients with a new diagnosis[9]. Symptom questionnaire assessments at follow-up of treated patients were also incentivised through the QOF between 2009 and 2013, to promote follow-up reassessment[10].

Some patients value using symptom questionnaires to assess treatment effectiveness and monitor their progress[11,12], and some GPs also value them for monitoring patients' progress. The likelihood of antidepressant treatment and/or referral for psychological therapy is significantly associated with higher symptom questionnaire scores at diagnosis[13], and decisions to change treatment are significantly associated with changes in scores at follow-up[14].

However, the use of symptom questionnaires is disliked by some GPs, who worry they intrude in sensitive consultations and undermine professional autonomy and, doubting their validity, prefer using clinical judgement to assess severity and response to treatment[11,15]. In 2012 a NICE commissioned systematic review concluded that the evidence supporting questionnaires was not strong enough to require their use in QOF depression indicators[16]. Current QOF guidance suggests formal assessment questionnaires can be used to measure

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severity at reviews 10-56 days after diagnosis, but this is optional rather than required to receive payments for the reviews[17].

The QOF depression symptom questionnaires are an example of patient reported outcome measures (PROMs), the use of which has been promoted in recent years to increase patient involvement in their own care[18]. A recent Cochrane systematic review of the use of PROMs in the treatment of common mental health disorders (CMHDs) including depression found some evidence of benefit for patients identified as having a lack of improvement early on in treatment, but the research was generally of low quality[19]. More research is required, particularly in primary care where most CMHDs are treated.

If using symptom questionnaires and other PROMs is beneficial even to a modest extent, they are likely to be cost-effective given their low cost, and the benefits at a population level would be considerable in public health terms, given the high cost to the nation of depression. Randomised trials of using PROMs to monitor patients' progress in primary care are however needed to inform practitioners definitively whether their use is beneficial, given their justifiable doubts about the validity of the approach.

We decided a feasibility study was needed first, to determine whether practices in England would agree to use PROMs with patients during consultations for the assessment of depression at diagnosis and follow-up. It was also needed to determine whether a trial randomised at patient level would be preferable to cluster randomising whole practices, which might need a bigger sample size, depending on the intra-cluster correlation coefficient between practices, which could also be estimated through a feasibility trial.

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AIM

To test the feasibility of conducting a randomised controlled of PROMs for monitoring outcomes for patients with depression in primary care.

Objectives:

(a) To determine key elements of the best design for a trial, including:

(i) The willingness and ability of general practices to:

- recruit patients during consultations at which depression is diagnosed
- recruit through mailouts to patients recorded as having consulted for depression
- be randomised to intervention or control arms as whole practices (cluster design), or
- have patients individually randomised to intervention or control arms

(ii) The willingness of patients with depression to:

- complete PROMs in the intervention arm
- complete measures of symptoms, functioning, quality of life, and service use

(iii) Numbers of eligible patients found per practice

(iv) Rates of recruitment and follow-up.

(b) To test the Patient Health Questionnaire (PHQ-9)[20] for depressive symptoms; Distress Thermometer analogue scale[21]; and PSYCHLOPS individual problem profile[22] as PROMs for depression.

(c) To explore effects of the intervention on depressive symptoms, social functioning, quality of life, satisfaction, and costs.

(d) To estimate the intra-cluster correlation coefficient (ICC) for the primary outcome to use in calculating the necessary increase in sample size for a cluster randomised full trial.

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METHODS

Trial design

Parallel group, partly individually randomised, partly cluster randomised trial, with 1:1 allocation between intervention and control arms.

Participants

Group general practices in and around Southampton, southern England, were recruited through the National Institute for Health Research (NIHR) Clinical Research Network (CRN).

Eligibility criteria were adult patients aged 18 years and above, diagnosed with a new episode of depression. Exclusion criteria were previous treatment for depression within 12 months, comorbid dementia, psychosis, substance misuse, or serious suicidal ideation needing urgent specialist referral.

Where possible, patients who had been diagnosed with a new episode of depression were recruited opportunistically during consultations by general practitioners (GPs) and practice nurses (PNs) and referred to the study team to discuss taking part. Newly diagnosed patients were also identified through medical record searches, designed to be weekly, by practice administrative staff, mailed information about the study, and asked if they wished to discuss taking part. Records were searched for 116 Read codes[23] for depressive diagnoses and symptoms (see Appendix 1 for a list of specific Read codes).

Intervention

The intervention was the administration of the three PROMs, the Patient Health Questionnaire (PHQ-9)[20] for depressive symptoms; the Distress Thermometer analogue scale for distress[21]; and the PSYCHLOPS profile rating of one or two problems individual to the patient[22], administered as soon as possible after diagnosis, reviewed by the GP or PN, and repeated at a follow-up GP or PN consultation 10-35 days later. Table 1 shows what each of the PROMs measures, and the rationale for their inclusion.

Researchers visited patients willing to be contacted, either at home or at their practices, sought informed written consent, carried out baseline assessments and administered the three PROMs to intervention group patients, with a brief explanation of each measure and further discussion of any questions on the PROMs patients were unsure about. Patients completed the PROMs on paper, and were asked to book an appointment with their GP or PN within a week, or as soon as possible, and to take the completed measures along, to discuss the results. Patients were not routinely given feedback on the meaning of the PROM

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scores by the researcher: routine feedback of results was left to the participating practitioners. If patients asked for immediate feedback, the researchers informed them only what their PROM scores were in relation to the possible maximum scores, and advised them to speak to their GP/PN for further information and guidance.

Table 1 Study patient reported outcome measures (PROMs)

Measure	What it measures	Rationale for inclusion
Patient Health Questionnaire, nine item version (PHQ-9)[20]	Severity of depression using nine questions covering diagnostic criteria for major depression. Total scores are categorised as minimal (1–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27).	Validated in UK primary care[24] and the most commonly used symptom questionnaire in UK general practice when incentivised through the quality and outcomes framework[13].
Distress thermometer single-item question screen originally developed for people with cancer[21] but can measure distress coming from any source	Visual analogue scale on which patients indicate how distressed they have been during the past week on a scale of 0 to 10. Scores of 4 or more indicate a significant level of distress that should be investigated further.	A rapid indication of change in distress level. Does not require English skills to complete, unlike questionnaires.
PSYCHLOPS psychological outcomes profile[22], a one-page three item self-report measure	Patient descriptions of their own particular individual problem or two problems, their ratings (0-5) of how their problem(s) affect their daily functioning, and their ratings (0-5) of overall wellbeing	Approved by the Plain English Campaign and carries the 'Crystal Mark' for clarity. Shown to be highly sensitive to change during the course of psychotherapeutic interventions[22].

Participating GPs and PNs were given up to half an hour's instruction on the meaning of the scores on the three PROMs at the start of the study. They were asked to take the PROM scores into account at their consultations with participating patients within days of completion of the first set of PROMs. They were also asked to provide the patients with another set of the three PROMs to complete again immediately prior to follow-up consultations 10-35 days later. Advice was given on the meaning of scores on the PROMs at the consultation following diagnosis and of changes in scores between the first and second follow-up consultations. See Appendix 2 for the advice given about the meaning of PROM scores.

Whether or not feedback on the results of the PROMs was given by the practitioners to the patients, and any treatment and further follow-up provided for depression, was left to the discretion of participating practitioners for patients in both intervention and control groups.

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Control group patients did not complete any PROMs. All patients completed the research outcome measures (below) but were not given feedback on the results of those assessments.

Assessments

Patients were recruited over a 12 month period and followed-up for 26 weeks each, with assessments at baseline, 12 weeks and 26 weeks follow-up. Baseline measures included sociodemographic details (age, gender, length of education, employment, cohabitation); duration of symptoms; previous history of depression; previous treatment; and the Generalised Anxiety Disorder (GAD-7) questionnaire for anxiety symptoms[25].

Outcomes

The primary outcome measured at 12 and 26 weeks follow-up was depressive symptoms on the Beck Depression Inventory 2nd edition (BDI-II)[26]. Social functioning on the Work and Social Adjustment Scale (WSAS)[27], and quality of life on the EuroQol five item, five level scale (EQ-5D-5L)[28] were also measured at 12 and 26 weeks follow-up. At 26 weeks follow up use of services was determined using a modified version of the Client Services Receipt Inventory[29] to allow calculation of NHS service costs, and patient satisfaction was determined using the Medical Informant Satisfaction Scale (MISS)[30].

Sample size

A formal sample size calculation was not performed, as the aim was to explore effectiveness, not to determine it accurately. We aimed to obtain primary outcome data on 40 patients, 20 in each arm, which we judged would be sufficient to allow estimation of rates of recruitment and follow-up, and of the variance in the primary outcome measure the BDI-II, together with its intracluster correlation coefficient (ICC) between practices, to inform a sample size calculation for the main trial if a cluster randomised design were to be chosen.

We estimated an average group practice could recruit six patients in 12 months. This was based on the mean number of patients per practice of 23 per year found to have been assessed using the QOF-incentivised PHQ-9 in a previous observational study[14] and an assumption that around 25% of diagnosed patients would consent to participate. We further anticipated 15% would drop out of follow up based on a previous trial of antidepressants[31] in primary care which meant we would need to recruit 48 patients from eight practices to obtain primary outcome data on around 40 patients at follow-up.

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Randomisation

Four of the practices were cluster randomised to intervention or control arms, while in the remaining practices patients were individually randomised, in order to explore the feasibility and acceptability of both methods. Randomisation was carried by the study statistician (BS) using computerised sequence generation. The researchers were aware of randomisation status for patients of cluster randomised practices. For individually randomised patients researchers telephoned the statistician for allocation to intervention or control after obtaining informed consent and carrying out baseline assessments.

Blinding

Patients, practitioners and researchers could not be blinded to allocation given the nature of the intervention. Self-report outcome measures were used to prevent observer rating bias.

Analysis

Feasibility and acceptability were assessed through analysis of rates of recruitment, drop-out and follow-up. Patients rated the ease of completion of the measures and time taken using 5-point Likert scales.

Differences at 12 and 26 weeks follow-up between intervention and control patients in depressive symptoms and social functioning were explored using a linear mixed model adjusting for sociodemographic characteristics, baseline depressive and anxiety symptoms, and for clustering by practice by including practice as a random effect. Patient satisfaction, quality of life (in QALYs) and costs over 26 weeks were also compared between arms. The analysis included only patients for whom we had outcome data (i.e. complete cases).

The acceptability of trial procedures and chosen PROMs were also explored through semi-structured qualitative interviews with samples of participating patients and health professionals, aiming to interview 15-20 of each. Interviews were transcribed verbatim and analysed using an inductive thematic analysis approach[32].

The study was sponsored by the University of Southampton and approved by the NHS Research Ethics Committee (REC) South Central - Oxford A on 28th July 2014 (reference number 14/SC/1067).

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RESULTS

Recruitment

Recruitment of practices and patients took place between September 2014 and February 2016 inclusively, and the 26 week follow-ups ended in September 2016. Eight practices were recruited to the study in the first month as planned. Four of them were cluster randomised to intervention or control arms, and in the remaining practices patients were individually randomised. However two of the original sample of practices failed to recruit any patients within the first three months. We therefore replaced these practices with two which recruited patients more quickly, but due to slower than desired recruitment among some of the other participating practices we also agreed an amendment to our protocol with the REC to recruit from a ninth practice, in order eventually to achieve recruitment of 47 of our target of 48 patients. One of the three replacement practices was cluster randomised to replace a cluster randomised practice which had dropped out, and in the other two patients were individually randomised.

Three practices recruited six patients within eight weeks, while three failed to recruit six in a year, and three were intermediate recruiters. From the nine practices, a total of 78 patients agreed to discuss participation, of whom 47 (60%) were randomised (37 (79%) recruited in consultations and 10 (21%) through mail-outs). Practice logs showed that fewer than 10% of patients identified as eligible and mailed information about the study returned reply slips indicating whether or not they were interested in participating. Of the 31 patients (40%) who were not recruited, 18 (23%) were uncontactable at baseline, and 13 (17%) declined after initial contact. The main reasons for declining were no longer being interested in taking part, or having competing commitments (see Figure 1, CONSORT flow diagram of patient participation).

Baseline characteristics

Of the 47 recruited patients 29 (62%) were female, 46 (98%) were white, and 31 (66%) were in employment. The average age was 44 years and average age of leaving education 19. Study arms were reasonably well balanced at baseline (Table 2), except more intervention group patients were married or cohabiting, and control patients' scores for depression, social functioning and anxiety were all slightly worse on average, and less variable.

Follow-up rates

At 12 weeks, 18 of 22 intervention arm patients (82%) and 18 of 25 controls (72%) completed the outcome measures, and at 26 weeks, 15 (68%) and 15 (60%) respectively (see CONSORT diagram, Figure 1). Of those followed-up, 29 patients (81%) completed

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questionnaires face-to-face at 12 weeks, and 26 (87%) at 26 weeks, the rest completing them only after further follow-up by post (19% at 12 weeks and 13% at 26). No patients proved contactable in order to complete outcome measures over the telephone.

Table 2: Baseline characteristics

Characteristic	Control patients (n=25)	Intervention patients (n=22)
Female	16 (64.0%)	13 (59.0%)
Age (Mean (SD))	43.1 (17.1)	44.7 (18.5)
White ethnic group	24 (96.0%)	22 (100%)
Marital status		
- Married/Cohabiting	6 (24.0%)	12 (54.5%)
- Widowed/separated/divorced	8 (32.0%)	6 (27.3%)
- Single	11 (44.0%)	4 (18.2%)
Any dependents at home	9 (36.0%)	7 (31.8%)
Age left education	18.6 (5.3)	18.8 (3.4)
Economic position		
- Full/part time work	17 (68.0%)	14 (63.6%)
- Sick/disabled	2 (8.0%)	1 (4.6%)
- Unemployed	1 (4.0%)	1 (4.6%)
- Retired/student/homemaker	5 (20.0%)	5 (22.7%)
- Other	0	1 (4.6%)
BDI-II total score Mean(SD)	26.92 (7.93)	23.90 (11.92)
WSAS total score Mean(SD)	21.88 (9.37)	18.13 (10.00)
GAD-7 total score Mean(SD)	14.32 (5.27)	11.64 (5.83)

BDI-II=Beck Depression Inventory, 2nd edition[24], WSAS=Work and Social Adjustment Scale[25], GAD-7=Generalised Anxiety Disorder scale[23]

Outcomes

Outcome scores at baseline, 12 weeks and 26 weeks follow-up are shown in Table 3. At 12 weeks the intervention group adjusted mean score for depressive symptoms on the BDI-II was significantly lower than the control group by 5.8 points (95% confidence interval (CI) -11.1, -0.5) after adjusting for baseline depression scores, anxiety, sociodemographics, psychotropic medication use, and clustering by practice. Adjusted mean score on the WSAS at 12 weeks was lower (better) in the intervention group than the controls by a mean of 3.0 points, which was not statistically significant (95% CI -7.3, 1.3).

At 26 weeks, there were no significant differences between the groups in symptoms or social functioning (adjusted mean BDI-II was slightly worse in intervention arm by 2.5 points (95% CI -1.7, 6.7); adjusted mean WSAS was lower by 0.3 points (95% CI -5.2, 4.6)). However, the adjusted mean MISS satisfaction score was 22.0 points higher in the control group (95% CI -40.7, -3.29).

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Baseline EQ-5D-5L quality of life scores were similar among intervention and control group patients (Table 3). Scores were improved at 12 weeks for both groups although slightly higher among intervention patients than controls, and scores went down again at 26 weeks among controls.

Table 3: Outcome measures at baseline and follow-up

Measures		Control group			Intervention group		
		Baseline (n=25)	12 weeks (n=18)	26 weeks (n=15)	Baseline (n=22)	12 weeks (n=18)	26 weeks (n=15)
Depression (BDI-II)	Mean (SD)	26.92 (7.93)	19.22 (11.62)	15.53 (10.04)	23.90 (11.92)	12.00 (8.93)	14.13 (12.54)
Social functioning (WSAS)	Mean (SD)	21.88 (9.37)	14.89 (9.30)	14.93 (10.79)	18.13 (10.00)	10.94 (8.12)	12.07 (11.35)
Anxiety (GAD-7)	Mean (SD)	14.32 (5.27)	–	–	11.64 (5.83)	–	–
Quality of life (EQ-5D-5L)	Mean (SD)	0.624 (0.284)	0.698 (0.246)	0.674 (0.299)	0.633 (0.242)	0.759 (0.105)	0.764 (0.158)
Satisfaction (MISS)	Mean (SD)	–	–	148.93 (34.19)	–	–	137.93 (34.74)

BDI-II=Beck Depression Inventory, 2nd edition[24], WSAS=Work and Social Adjustment Scale[25], GAD-7=Generalised Anxiety Disorder scale[23], EQ-5D-5L=EuroQol quality of life scale[26], MISS=Medical Informant Satisfaction Scale[28]

The mean QALY gain over 26 weeks was 0.382 (SD 0.046) for intervention patients, and 0.336 (0.132) for controls, giving a non-significant difference of 0.047 (95% CI -0.036, 0.129). Mean depression related NHS service costs per patient over 26 weeks were similar: control arm £216 (95% CI £135, £297), intervention arm £231 (£129, £332), including £16 per patient for an estimated five minutes GPs or PNs spent dealing with PROM results.

Intra-cluster correlation coefficients

There was no evidence in this sample of clustering by practice for the BDI-II or WSAS: the ICC was zero at baseline for both. After controlling for baseline and randomisation group, the ICC for the BDI-II at 12 weeks was 0.03.

Ease of completion of outcome measures

On average participants rated the BDI-II, WSAS and GAD-7 as easy to use and the time taken was under five minutes for each. Ease of completion scores: mean (s.d) where 1=not

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at all easy and 5=very easy: BDI-II 4.29 (0.94); WSAS 4.38 (0.88) and GAD-7 4.38 (0.83). Time taken (minutes): median (interquartile range): BDI-II 4 (3,5); WSAS 1.5 (1,3); and GAD-7 2 (1,2).

Qualitative interviews with patients and practice staff

The full qualitative analysis and illustrative quotes from participants will be published separately. We present a brief summary only in this paper.

Fourteen patients were interviewed. Overall, in relation to the feasibility of the study, patients were happy to be randomised (even when randomised to the control arm), were supportive of the use of PROMS (seeing potential benefits for understanding their illness) and reported them relatively easy and quick to complete. There were some difficulties found in discussing the results of PROMS with their practitioners which would need attention in a definitive trial. Some were unable to see the same practitioner for follow up, and some expressed disappointment at not having feedback on the PROM scores from participating practitioners. Some would have liked a record of changes in scores over time to show their progress.

Interviews were carried out with 10 GPs, one PN and two practice managers. In relation to feasibility practitioners overall considered the use of PROMS to be feasible. Some felt PROMs could facilitate the consultation but others thought they could hinder it, and the interviews highlighted important areas that would need to be improved to smooth their use in practice including further clarification of patient inclusion criteria, choosing measures that are easy for patients to complete, and more guidance on what to do with the PROM results once completed.

Methodological changes

Several changes were needed to overcome difficulties in recruiting and following-up patients. Because response rates to the practice mail-outs were lower than 10%, we obtained ethics approval to send a revised patient information leaflet which used varied font sizes and coloured text to be more eye-catching, and for practice nurses to telephone non-responding participants two weeks after mail-outs to follow them up more actively (this did not apply to those who had responded to say they were not interested, only those who had not responded at all). However in the event the telephone calls did not yield any more participants.

The follow-up research assessments were originally intended to be completed face to face, but we obtained ethics approval to send the research assessment questionnaires by post if

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patients failed to attend follow-up after two requests. We also obtained approval to send patients a £10 high street shopping gift voucher with the follow up questionnaires sent by post. These changes between them helped improve follow-up rates by around 10%.

Another change was approved to facilitate active follow-up of non-responding patients. If they did not complete follow up questionnaires in person or by post, the study team was permitted to try to contact them and complete the primary outcome measure (BDI-II), and two other key outcome measures (WSAS and EQ-5D-5L), over the telephone. However in the event no non-responders could be reached by telephone.

Finally, approval was given for an additional practice administrative staff review of the medical records of recruited participants at the end of their participation, as we were able to gather only limited information on service use through the patient questionnaires. These record reviews provided extra information on prescribed medication, number of visits to GPs, PNs and community based staff, secondary care contacts, hospital admissions, and length of hospitalisation where appropriate.

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Discussion

Principal findings

It is feasible to carry out a randomised trial of PROMs for the assessment and follow-up of depression in primary care in England. Practices recruited patients both in GP/PN consultations and through staff mailouts to patients, although recruitment rates and follow-up rates, particularly in the control arm, would need improving for a larger, definitive trial. Intervention arm patients were happy to complete the PROMs and research outcome questionnaires and valued seeing the results. Differences between arms suggest PROMs may reduce depressive symptoms, yet also reduce patient satisfaction, perhaps because GPs appeared not to value using PROM results to influence management.

Strengths and limitations

The trial was pragmatic, with few exclusion criteria, and readily generalisable to UK primary care. Patients were randomly allocated to intervention or control, with concealment of allocation from patients until after informed consent had been obtained and baseline measures had been completed. However patients, practitioners and assessors could not be blinded to allocation during the trial given the nature of the intervention, although the use of self-report research outcome measures should have prevented observer rating bias.

The study was necessarily small in keeping with testing feasibility, but in spite of this we did find a difference in the primary outcome measure between arms at 12 weeks follow-up, favouring the intervention. The adjusted difference between arms at 12 weeks as a percentage of the score in the control group was 5.8/19.22 = 30.1%, which is greater than the minimal clinically important difference (MCID) of a 17.5% reduction in scores from baseline found to correspond to patients' global reports of significant improvement[33]. However, the sample may have been too small to accurately estimate the ICC for the outcome measures at baseline.

Comparison with other studies

The results are in keeping with a US primary care based controlled trial of feeding back PHQ-9 scores to family practitioners at diagnosis and follow-up, which demonstrated significantly improved patient outcomes over six months[34]. The difference in outcome could not be explained in terms of any significant differences in management, but the benefits of feeding back scores seemed to arise from increasing patients' awareness of their symptoms and their ability to report relevant changes[35]. That may explain why our patients may have derived benefit from using PROMs even when their GPs did not seem to use the results to inform their care.

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Implications for clinicians, policymakers, and research

The implications are mainly for the design of a definitive trial rather than for practice at this stage, although clinicians and policymakers might be persuaded of the need for a more definitive trial on the basis that short-term differences in outcome favouring the use of PROMs were identified even in this small sample.

Follow-up at 12 weeks of 82% was sufficient in the intervention arm, but needs to be improved from 72% in the control arm, and follow-up at 26 weeks needs to be improved from 68% and 60% respectively, through taking steps to maintain better contact with patients, obtaining mobile phone numbers, postal and email addresses, and permission to post, text, telephone or email them, as a significant proportion failed to meet face-to-face or complete and return the measures sent by post.

Current demands on practices, and the expansion of less than full time working, make it increasingly difficult to provide continuity of care, which may explain why participating patients sometimes found it difficult to get follow-up appointments with the same GP. Therefore it will be important to recruit practices where all GPs and PNs in the practice agree to be involved in the study and to be trained in recruiting, consenting, and following-up all eligible patients, and looking at the results of PROMs for all those in the intervention arm. In a definitive trial practices should be cluster randomised to streamline recruitment and follow-up so all patients in each are treated the same, by whichever GP or PN they see.

Cluster randomisation tends to require a larger sample due to clustering by practice (the design effect), although the increase in sample size necessary appears likely to be small based on this study. There was no evidence of clustering at baseline, but the study may not have been large enough to permit an accurate estimation of the true value of the ICC and it would be sensible in a larger trial to make an allowance for clustering. After controlling for baseline and randomisation group, the ICC for the BDI-II at 12 weeks was 0.03. The ICC for the BDI-II from a previous trial of antidepressants for mild to moderate depression in primary care was 0.02[31], therefore an ICC of 0.03 might be appropriate to use to calculate the design effect if the definitive trial is cluster randomised.

Practice logs and recruitment rates in the better recruiting practices show the numbers of eligible patients per group practice will allow for more than six patients to be recruited per year, given greater commitment. Having a relatively smaller number of practices recruit more patients each will be more efficient in terms of travel to practices by the research team, and

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allow greater contact to be maintained with participating staff in each, to optimise practice commitment.

Administration of PROMs needs to be streamlined, and GPs provided with more guidance on how to assess the results, to avoid disappointing patients by not using the PROMs to inform care. Patients may benefit from being provided with a record of their PROM scores so they can monitor their progress.

The study team needs to spend more time at participating practices training them in the recruitment process, and assisting them with setting up database searches. Practices should complete a trial recruiting period to assess their commitment, and practice research costs should be reimbursed on a per-patient/per-mailout basis rather than paying them a lump sum at the beginning of the trial, to incentivise recruitment.

Conclusions

Even in this small sample, the findings suggest that the use of PROMs may be beneficial in the short term, although maybe not in the longer term. It provides support for our plan to take forward a larger, definitive trial. Before we proceed however, we need to do some more work with potential participants, to identify the most promising PROM. Encouraging practitioners to use PROMs requires identifying relatively brief measures which can potentially change management.

[Word count 4966 including tables]

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Contributorship statement

Tony Kendrick, Beth Stuart, Geraldine Leydon, Adam Geraghty, Lily Yao, Christopher Dowrick, Glyn Lewis and Michael Moore[made substantial contributions to the conception or design of the work.

Rachel Ryves, Samantha Williams and Shihua Zhu made substantial contributions to the acquisition, analysis, and interpretation of data.

All authors contributed to drafting the work and revising it critically for important intellectual content, and all approved the final version submitted.

We agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: all authors had financial support from the NIHR Research for Patient Benefit Programme for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Data sharing statement

We agree to make the relevant anonymised patient level data available on reasonable request.

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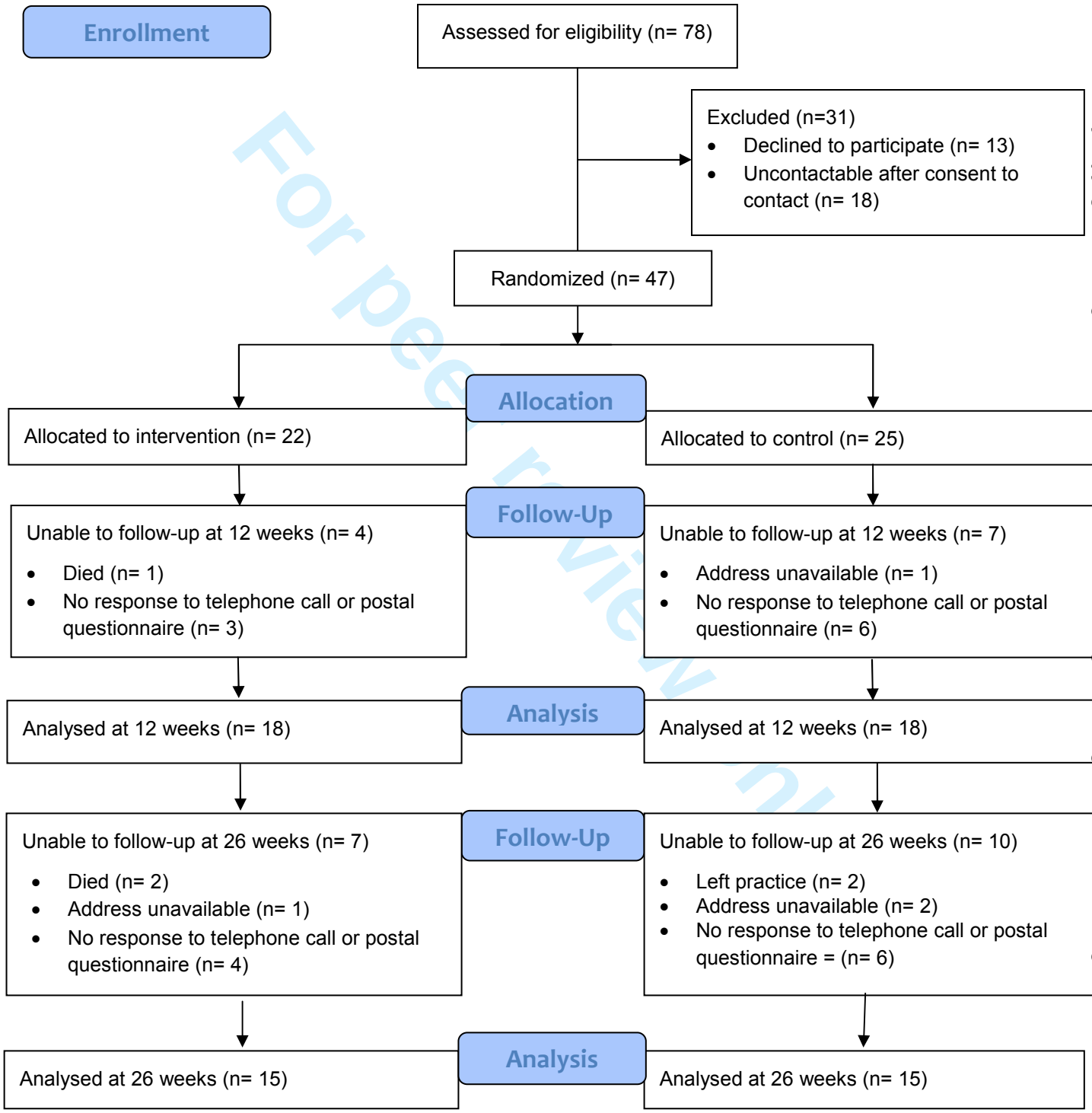

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Appendix 1 List of read codes used by GP practices to search records for potential participants

Read code	Read term
E2B..00	Depressive disorder NEC
1BT..11	Low mood
E200300	Anxiety with depression
Eu32z11	[X]Depression NOS
1B17.00	Depressed
1465	H/O: depression
1B17.11	C/O - feeling depressed
Eu32.00	[X]Depressive episode
E204.00	Neurotic depression reactive type
1BT..00	Depressed mood
1B1U.00	Symptoms of depression
E204.11	Postnatal depression
2257	O/E - depressed
Eu32100	[X]Moderate depressive episode
E113.11	Endogenous depression - recurrent
Eu32z00	[X]Depressive episode, unspecified
1BO..00	Mood swings
Eu32z14	[X] Reactive depression NOS
E112.13	Endogenous depression first episode
E112.14	Endogenous depression
1B1J.11	Emotional upset
E2B1.00	Chronic depression
E112.11	Agitated depression
E112.00	Single major depressive episode
E135.00	Agitated depression
E113700	Recurrent depression
Eu32000	[X]Mild depressive episode
Eu33.00	[X]Recurrent depressive disorder
Eu41200	[X]Mixed anxiety and depressive disorder
Eu32200	[X]Severe depressive episode without psychotic symptoms
1B1U.11	Depressive symptoms
E113.00	Recurrent major depressive episode
Eu32z12	[X]Depressive disorder NOS
Eu3..00	[X]Mood - affective disorders
E112.12	Endogenous depression first episode
Eu32400	[X]Mild depression
Eu32.11	[X]Single episode of depressive reaction
E113200	Recurrent major depressive episodes, moderate
Eu34100	[X]Dysthymia
E112200	Single major depressive episode, moderate
Eu32.13	[X]Single episode of reactive depression
E112100	Single major depressive episode, mild
Eu33100	[X]Recurrent depressive disorder, current episode moderate
Eu34114	[X]Persistant anxiety depression
Eu41211	[X]Mild anxiety depression
E290.00	Brief depressive reaction
Eu53011	[X]Postnatal depression NOS

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Eu33.13	[X]Recurrent episodes of reactive depression
1BQ..00	Loss of capacity for enjoyment
E11z200	Masked depression
Eu33z00	[X]Recurrent depressive disorder, unspecified
Eu34113	[X]Neurotic depression
Eu33.11	[X]Recurrent episodes of depressive reaction
E112z00	Single major depressive episode NOS
E291.00	Prolonged depressive reaction
Eu43012	[X]Acute reaction to stress
Eu32y00	[X]Other depressive episodes
E113z00	Recurrent major depressive episode NOS
Eu43z00	[X]Reaction to severe stress, unspecified
E112300	Single major depressive episode, severe, without psychosis
1BT..12	Sad mood
Eu33200	[X]Recurr depress disorder cur epi severe without psyc sympt
Eu33000	[X]Recurrent depressive disorder, current episode mild
1JJ..00	Suspected depression
E113100	Recurrent major depressive episodes, mild
Eu32212	[X]Single episode major depression w'out psychotic symptoms
Eu34111	[X]Depressive neurosis
Eu32700	[X]Major depression, severe without psychotic symptoms
E113300	Recurrent major depressive episodes, severe, no psychosis
E112000	Single major depressive episode, unspecified
Eu32600	[X]Major depression, moderately severe
Eu33211	[X]Endogenous depression without psychotic symptoms
1BP0.00	Loss of interest in previously enjoyable activity
Eu33.12	[X]Recurrent episodes of psychogenic depression
Eu4..00	[X]Neurotic, stress - related and somoform disorders
E113600	Recurrent major depressive episodes, in full remission
Eu33400	[X]Recurrent depressive disorder, currently in remission
Eu3z.00	[X]Unspecified mood affective disorder
Eu32.12	[X]Single episode of psychogenic depression
Eu32z13	[X]Prolonged single episode of reactive depression
1BU..00	Loss of hope for the future
E113000	Recurrent major depressive episodes, unspecified
Eu32500	[X]Major depression, mild
Eu32y11	[X]Atypical depression
E112500	Single major depressive episode, partial or unspec remission
Eu33212	[X]Major depression, recurrent without psychotic symptoms
Eu53012	[X]Postpartum depression NOS
1S40.00	Dysphoric mood
E284.00	Stress reaction causing mixed disturbance of emotion/conduct
ZV11100	[V]Personal history of affective disorder
E113500	Recurrent major depressive episodes,partial/unspec remission
E11y200	Atypical depressive disorder
Eu3y111	[X]Recurrent brief depressive episodes
Eu33y00	[X]Other recurrent depressive disorders
Eu43y00	[X]Other reactions to severe stress
E112600	Single major depressive episode, in full remission
Eu32211	[X]Single episode agitated depressn w'out psychotic symptoms

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Eu34.00	[X]Persistent mood affective disorders
E290z00	Brief depressive reaction NOS
E292.00	Adjustment reaction, predominant disturbance other emotions
E283z00	Other acute stress reaction NOS
Eu92.11	[X]Emotional behavioural problems
Eu3y.00	[X]Other mood affective disorders
Eu3y000	[X]Other single mood affective disorders
E292400	Adjustment reaction with anxious mood
Eu32y12	[X]Single episode of masked depression NOS
Eu3y100	[X]Other recurrent mood affective disorders
E292z00	Adjustment reaction with disturbance of other emotion NOS
Eu34z00	[X]Persistent mood affective disorder, unspecified
E2C4z00	Mixed disturbance of conduct and emotion NOS
Eu32213	[X]Single episode vital depression w'out psychotic symptoms
Eu33z11	[X]Monopolar depression NOS
Eu3yy00	[X]Other specified mood affective disorders
Eu32B00	[X]Antenatal depression
Eu33214	[X]Vital depression, recurrent without psychotic symptoms
Eu34y00	[X]Other persistent mood affective disorders

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Appendix 2. Advice given to GPs about the meaning of PROM scores.

PHQ-9 Scores and Proposed Treatment Actions

(Adapted from Kroenke K, Spitzer RL, Psychiatric Annals 2002;32:509-521)

PHQ-9 scores at diagnosis

PHQ-9 Score	Depression Severity	Proposed Treatment Actions
0 – 4	None-minimal	None
5 – 9	Mild	Watchful waiting; repeat PHQ-9 at follow-up
10 – 14*	Moderate	Psychological Treatment and follow-up/Antidepressants
15 – 19	Moderately Severe	Antidepressants and Psychological Treatment
20 – 27	Severe	Referral to mental health

* Question B must be answered positively, i.e. the symptoms have made it at least somewhat difficult for the patient to do their work, take care of their home, or get along with other people.

Changes in PHQ-9 Scores at Follow-up and Proposed Treatment Actions

Change in PHQ-9 score	Response	Treatment actions
Drop of 5 or more points from baseline	Adequate	No treatment change needed. Continue treatment and follow-up as planned.
Drop of 2-4 points from baseline.	Probably Inadequate	Often warrants an increase in antidepressant dose; follow-up as planned
Drop of 1-point, or no change, or increase in score, first follow-up	Inadequate	Increase dose or switch drug Refer for psychological treatment Follow-up sooner
Drop of 1-point, or no change, or increase in score, subsequent follow-up	Inadequate	Increase dose or switch drug Refer for psychological treatment Refer to mental health

Distress Thermometer

The patient marks the thermometer to indicate how much distress they have that week, from 0 to 10. Scores above 4 indicate significant distress needing further exploration and possible action.

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PSYCHLOPS

All of the responses in PSYCHLOPS are scored on a six point scale ranging from zero to five. A score of zero indicates the least psychological difficulty whereas a score of five indicates the most psychological difficulty.

The questions which are scored are those relating to Problems (Questions 1b and 2b), Functioning (Question 3b) and Wellbeing (Question 4). Other questions provide useful information but do not contribute to the total score or change score.

The initial score for PSYCHLOPS is unique to each individual. The main purpose of the score is to measure within-person change, i.e. the change in score for the items chosen by the patient.

High scores at diagnosis indicate significant problem areas for the individual patient, and should direct questioning to those areas. Similarly, persistently high scores, or increased scores, at follow-up should direct questioning to those areas of particular concern to the individual patient.

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3-4
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	13-14
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	8
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	8
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

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		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	9
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10-11 plus CONSORT diagram
	13b	For each group, losses and exclusions after randomisation, together with reasons	10-11 plus CONSORT diagram
Recruitment	14a	Dates defining the periods of recruitment and follow-up	10
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	11
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	12
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	11-12
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	11-12
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	16
Other information			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	2

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*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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PATIENT REPORTED OUTCOME MEASURES FOR MONITORING PRIMARY CARE PATIENTS WITH DEPRESSION: PROMDEP FEASIBILITY RANDOMISED TRIAL

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PATIENT REPORTED OUTCOME MEASURES FOR MONITORING PRIMARY CARE PATIENTS WITH DEPRESSION: PROMDEP FEASIBILITY RANDOMISED TRIAL

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ABSTRACT

Objectives: To determine the feasibility of a trial of patient reported outcome measures (PROMs) for monitoring primary care patients with depression

Design: Partly individually randomised, partly cluster randomised controlled trial

Setting: Nine general practices in southern England

Participants: 47 adults with new episodes of depression: 22 intervention, 25 control

Randomisation: remote computerised sequence generation and allocation

Interventions: Patient Health Questionnaire, Distress Thermometer analogue scale, and PSYCHLOPS problem profile for monitoring depression, following diagnosis and at 10-35 days later. Feedback of scores to patients was determined by practitioners.

Blinding: non-blinded, using self-completed measures

Primary outcome: Beck Depression Inventory (BDI-II)

Secondary outcome measures: Work and Social Adjustment Scale (WSAS); EuroQol EQ-5D-5L scale for quality of life; modified Client Service Receipt Inventory for costs; Medical Informant Satisfaction Scale (MISS); qualitative interviews with 14 patients and 13 practice staff about feasibility and acceptability of trial design

Results: Three practices failed to recruit the target of six patients in 12 months. Follow-up rates were intervention patients: 18 (82%) at 12 weeks and 15 (68%) at 26 weeks; controls: 18 (72%) and 15 (60%) respectively. At 12 weeks mean BDI-II score was lower among intervention group patients than controls by 5.8 points (95% CI -11.1, -0.5), adjusted for baseline differences and clustering. WSAS scores were not significantly different. At 26 weeks there were no significant differences in symptoms, social functioning, quality of life, or costs, but mean satisfaction score was higher among controls by 22.0 points (95% CI -40.7, -3.29). Intervention patients liked completing PROMs, but were disappointed when practitioners did not use the results to inform management.

Conclusions: PROMs may improve depression outcome in the short term, even if PROM scores do not inform practitioners' management. Challenges in recruiting and following up patients need addressing for a definitive trial of relatively brief measures which can potentially inform management.

Strengths and limitations

- Pragmatic trial with few exclusion criteria, readily generalisable
- Patients were randomly allocated with concealment of allocation from patients until after informed consent had been obtained and baseline measures completed
- Patients, practitioners and assessors could not be blinded to allocation
- Self-report research outcome measures should have prevented observer rating bias
- Despite the small sample size we did find a difference in the primary outcome
- The sample may have been too small to accurately estimate the ICC for the outcome

Trial registration: International Standard Randomised Controlled Trial Registry ISRCTN 97492541.

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BACKGROUND

Depression is common and costly. The estimated prevalence among adults in the UK is 11.1%, including major depressive disorder in 3.3%, and mixed depression and anxiety in 7.8%[1]. It can lead to chronic disability, poor quality of life, suicide in some cases and high levels of health service use and economic costs. The King's Fund have estimated that 1.45 million people will have depression in England by 2026, and total societal costs will be £12.2 billion per year including health care, social services and lost employment[2].

The National Institute for Health and Care Excellence (NICE) depression guidelines recommend different interventions for moderate to severe depression than for mild depression[3]. However, general practitioner (GP) clinical assessments of the severity of depression vary and are often inaccurate when compared to validated measures[4,5]. Consequently, some GPs do not accurately target treatment to patients most likely to benefit[6-8], reducing the cost-effectiveness of treatment, which needs to be optimised given the impact of depression.

As a result of these findings, NICE recommends that health professionals consider using validated questionnaire measures of severity at diagnosis to help target treatment[3]. Between 2006 and 2013 the UK GP contract Quality and Outcomes Framework (QOF) paid GPs to use symptom questionnaires as part of their assessments of depression severity at the outset of treatment for patients with a new diagnosis[9]. Symptom questionnaire assessments at follow-up of treated patients were also incentivised through the QOF between 2009 and 2013, to promote follow-up reassessment[10].

Some patients value using symptom questionnaires to assess treatment effectiveness and monitor their progress[11,12], and some GPs also value them for monitoring patients' progress. The likelihood of antidepressant treatment and/or referral for psychological therapy is significantly associated with higher symptom questionnaire scores at diagnosis[13], and decisions to change treatment are significantly associated with changes in scores at follow-up[14].

However, the use of symptom questionnaires is disliked by some GPs, who worry they intrude in sensitive consultations and undermine professional autonomy and, doubting their validity, prefer using clinical judgement to assess severity and response to treatment[11,15]. In 2012 a NICE commissioned systematic review concluded that the evidence supporting questionnaires was not strong enough to require their use in QOF depression indicators[16]. Current QOF guidance suggests formal assessment questionnaires can be used to measure

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severity at reviews 10-56 days after diagnosis, but this is optional rather than required to receive payments for the reviews[17].

The QOF depression symptom questionnaires are an example of patient reported outcome measures (PROMs), the use of which has been promoted in recent years to increase patient involvement in their own care[18]. A recent Cochrane systematic review of the use of PROMs in the treatment of common mental health disorders (CMHDs) including depression found some evidence of benefit for patients identified as having a lack of improvement early on in treatment, but the research was generally of low quality[19]. More research is required, particularly in primary care where most CMHDs are treated.

If using symptom questionnaires and other PROMs is beneficial even to a modest extent, they are likely to be cost-effective given their low cost, and the benefits at a population level would be considerable in public health terms, given the high cost to the nation of depression. Randomised trials of using PROMs to monitor patients' progress in primary care are however needed to inform practitioners definitively whether their use is beneficial, given their justifiable doubts about the validity of the approach.

We decided a feasibility study was needed first, to determine whether practices in England would agree to use PROMs with patients during consultations for the assessment of depression at diagnosis and follow-up. It was also needed to determine whether a trial randomised at patient level would be preferable to cluster randomising whole practices, which might need a bigger sample size, depending on the intra-cluster correlation coefficient between practices, which could also be estimated through a feasibility trial.

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AIM

To test the feasibility of conducting a randomised controlled of PROMs for monitoring outcomes for patients with depression in primary care.

Objectives:

(a) To determine key elements of the best design for a trial, including:

(i) The willingness and ability of general practices to:

- recruit patients during consultations at which depression is diagnosed
- recruit through mailouts to patients recorded as having consulted for depression
- be randomised to intervention or control arms as whole practices (cluster design), or
- have patients individually randomised to intervention or control arms

(ii) The willingness of patients with depression to:

- complete PROMs in the intervention arm
- complete measures of symptoms, functioning, quality of life, and service use

(iii) Numbers of eligible patients found per practice

(iv) Rates of recruitment and follow-up.

(b) To test the feasibility and acceptability of administering the Patient Health Questionnaire (PHQ-9)[20] for depressive symptoms; Distress Thermometer analogue scale[21]; and PSYCHLOPS individual problem profile[22] as PROMs for depression.

(c) To explore effects of the intervention on depressive symptoms, social functioning, quality of life, satisfaction, and costs.

(d) To estimate the intra-cluster correlation coefficient (ICC) for the primary outcome to use in calculating the necessary increase in sample size for a cluster randomised full trial.

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METHODS

Trial design

Parallel group, partly individually randomised, partly cluster randomised trial, with 1:1 allocation between intervention and control arms.

Participants

Group general practices in and around Southampton, southern England, were recruited through the National Institute for Health Research (NIHR) Clinical Research Network (CRN).

Eligibility criteria were adult patients aged 18 years and above, diagnosed with a new episode of depression. Exclusion criteria were previous treatment for depression within 12 months, comorbid dementia, psychosis, substance misuse, or serious suicidal ideation needing urgent specialist referral. The diagnosis of a new episode of depression, and previous treatment for depression, were both defined by the participating GPs rather than assessed independently, in keeping with the pragmatic nature of the trial.
Where possible, patients who had been diagnosed with a new episode of depression were recruited opportunistically during consultations by general practitioners (GPs) and practice nurses (PNs) and referred to the study team to discuss taking part. Newly diagnosed patients were also identified through medical record searches, designed to be weekly, by practice administrative staff, mailed information about the study, and asked if they wished to discuss taking part. Records were searched for 116 Read codes[23] for depressive diagnoses and symptoms (see Appendix 1 for a list of specific Read codes).

Intervention

The intervention was the administration of the three PROMs, the Patient Health Questionnaire (PHQ-9)[20] for depressive symptoms; the Distress Thermometer analogue scale for distress[21]; and the PSYCHLOPS profile rating of one or two problems individual to the patient[22], administered as soon as possible after diagnosis, reviewed by the GP or PN, and repeated at a follow-up GP or PN consultation 10-35 days later. Table 1 shows what each of the PROMs measures, and the rationale for their inclusion.

Researchers visited patients willing to be contacted, either at home or at their practices, sought informed written consent, carried out baseline assessments and administered the three PROMs to intervention group patients, with a brief explanation of each measure and further discussion of any questions on the PROMs patients were unsure about. Patients completed the PROMs on paper, and were asked to book an appointment with their GP or PN within a week, or as soon as possible, and to take the completed measures along, to

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discuss the results. Patients were not routinely given feedback on the meaning of the PROM scores by the researcher: routine feedback of results was left to the participating practitioners. If patients asked for immediate feedback, the researchers informed them only what their PROM scores were in relation to the possible maximum scores, and advised them to speak to their GP/PN for further information and guidance.

Table 1 Study patient reported outcome measures (PROMs)

Measure	What it measures	Rationale for inclusion
Patient Health Questionnaire, nine item version (PHQ-9)[20]	Severity of depression using nine questions covering diagnostic criteria for major depression. Total scores are categorised as minimal (1–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27).	Validated in UK primary care[24] and the most commonly used symptom questionnaire in UK general practice when incentivised through the quality and outcomes framework[13].
Distress thermometer single-item question screen originally developed for people with cancer[21] but can measure distress coming from any source	Visual analogue scale on which patients indicate how distressed they have been during the past week on a scale of 0 to 10. Scores of 4 or more indicate a significant level of distress that should be investigated further.	A rapid indication of change in distress level. Does not require English skills to complete, unlike questionnaires.
PSYCHLOPS psychological outcomes profile[22], a one-page three item self-report measure	Patient descriptions of their own particular individual problem or two problems, their ratings (0-5) of how their problem(s) affect their daily functioning, and their ratings (0-5) of overall wellbeing	Approved by the Plain English Campaign and carries the 'Crystal Mark' for clarity. Shown to be highly sensitive to change during the course of psychotherapeutic interventions[22].

Participating GPs and PNs were given up to half an hour's instruction on the meaning of the scores on the three PROMs at the start of the study. They were asked to take the PROM scores into account at their consultations with participating patients within days of completion of the first set of PROMs. They were also asked to provide the patients with another set of the three PROMs to complete again immediately prior to follow-up consultations 10-35 days later. Advice was given on the meaning of scores on the PROMs at the consultation following diagnosis and of changes in scores between the first and second follow-up consultations. See Appendix 2 for the advice given about the meaning of PROM scores.

Whether or not feedback on the results of the PROMs was given by the practitioners to the patients, and any treatment and further follow-up provided for depression, was left to the discretion of participating practitioners for patients in both intervention and control groups.

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Control group patients did not complete any PROMs. All patients completed the research outcome measures (below) but were not given feedback on the results of those assessments, (see Appendix 3 for an overview of study intervention and control procedures).

Assessments

Patients were recruited over a 12 month period and followed-up for 26 weeks each, with assessments at baseline, 12 weeks and 26 weeks follow-up. Baseline measures included sociodemographic details (age, gender, length of education, employment, cohabitation); duration of symptoms; previous history of depression; previous treatment; and the Generalised Anxiety Disorder (GAD-7) questionnaire for anxiety symptoms[25].

Outcomes

The primary outcome measured at 12 and 26 weeks follow-up was depressive symptoms on the Beck Depression Inventory 2nd edition (BDI-II)[26]. Social functioning on the Work and Social Adjustment Scale (WSAS)[27], and quality of life on the EuroQol five item, five level scale (EQ-5D-5L)[28] were also measured at 12 and 26 weeks follow-up. At 26 weeks follow up use of services was determined using a modified version of the Client Services Receipt Inventory[29] to allow calculation of NHS service costs, and patient satisfaction was determined using the Medical Informant Satisfaction Scale (MISS)[30].

Sample size

A formal sample size calculation was not performed, as the aim was to explore effectiveness, not to determine it accurately. We aimed to obtain primary outcome data on 40 patients, 20 in each arm, which we judged would be sufficient to allow estimation of rates of recruitment and follow-up, and of the variance in the primary outcome measure the BDI-II, together with its intracluster correlation coefficient (ICC) between practices, to inform a sample size calculation for the main trial if a cluster randomised design were to be chosen.

We estimated an average group practice could recruit six patients in 12 months. This was based on the mean number of patients per practice of 23 per year with a new episode of depression found to have been assessed using the QOF-incentivised PHQ-9 in a previous observational study[14] and an assumption that around 25% of diagnosed patients would consent to participate. (The prevalence of depression is considerably higher[1], but we aimed to recruit only patients with an incident episode rather than all patients currently suffering from depression). We further anticipated 15% would drop out of follow up based on a previous trial of antidepressants[31] in primary care which meant we would need to

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recruit 48 patients from eight practices to obtain primary outcome data on around 40 patients at follow-up.

Randomisation

Four of the practices were cluster randomised to intervention or control arms, while in the remaining practices patients were individually randomised, in order to explore the feasibility and acceptability of both methods. Randomisation was carried by the study statistician (BS) using computerised sequence generation. The researchers were aware of randomisation status for patients of cluster randomised practices. For individually randomised patients researchers telephoned the statistician for allocation to intervention or control after obtaining informed consent and carrying out baseline assessments.

Blinding

Patients, practitioners and researchers could not be blinded to allocation given the nature of the intervention. Self-report outcome measures were used to prevent observer rating bias.

Analysis

Feasibility and acceptability were assessed through analysis of rates of recruitment, drop-out and follow-up. Patients rated the ease of completion of the measures and time taken using 5-point Likert scales.

Differences at 12 and 26 weeks follow-up between intervention and control patients in depressive symptoms and social functioning were explored using a linear mixed model adjusting for sociodemographic characteristics, baseline depressive and anxiety symptoms, and for clustering by practice by including practice as a random effect. Patient satisfaction, quality of life (in QALYs) and costs over 26 weeks were also compared between arms. The analysis included only patients for whom we had outcome data (i.e. complete cases).

The acceptability of trial procedures and chosen PROMs were also explored through semi-structured qualitative interviews with samples of participating patients and health professionals, aiming to interview 15-20 of each. Interviews were transcribed verbatim and analysed using an inductive thematic analysis approach[32].

The study was sponsored by the University of Southampton and approved by the NHS Research Ethics Committee (REC) South Central - Oxford A on 28th July 2014 (reference number 14/SC/1067).

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RESULTS

Recruitment

Recruitment of practices and patients took place between September 2014 and February 2016 inclusively, and the 26 week follow-ups ended in September 2016. Eight practices were recruited to the study in the first month as planned. Four of them were cluster randomised to intervention or control arms, and in the remaining practices patients were individually randomised. However two of the original sample of practices failed to recruit any patients within the first three months. We therefore replaced these practices with two which recruited patients more quickly, but due to slower than desired recruitment among some of the other participating practices we also agreed an amendment to our protocol with the REC to recruit from a ninth practice, in order eventually to achieve recruitment of 47 of our target of 48 patients. One of the three replacement practices was cluster randomised to replace a cluster randomised practice which had dropped out, and in the other two patients were individually randomised.

Three practices recruited six patients within eight weeks, while three failed to recruit six in a year, and three were intermediate recruiters. Two of the three practices that failed to recruit had individual mitigating circumstances. One was recruited to the study late, with only a one-month time frame, so did well to recruit three patients. Another decided to stop actively taking part in all research, and did not continue to recruit patients. Feedback from the third practice suggested that greater clarity on study eligibility criteria and guidance to promote the study during consultations was needed to prompt recruitment.

From the nine practices, a total of 78 patients agreed to discuss participation, of whom 47 (60%) were randomised (37 (79%) recruited in consultations and 10 (21%) through mail-outs). Practice logs showed that fewer than 10% of patients identified as eligible and mailed information about the study returned reply slips indicating whether or not they were interested in participating. Of the 31 patients (40%) who were not recruited, 18 (23%) were uncontactable at baseline, and 13 (17%) declined after initial contact. The main reasons for declining were no longer being interested in taking part, or having competing commitments (see Figure 1, CONSORT flow diagram of patient participation).

Baseline characteristics

Of the 47 recruited patients 29 (62%) were female, 46 (98%) were white, and 31 (66%) were in employment. The average age was 44 years and average age of leaving education 19. Study arms were reasonably well balanced at baseline (Table 2), except more intervention

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group patients were married or cohabiting, and control patients' scores for depression, social functioning and anxiety were all slightly worse on average, and less variable.

Follow-up rates

At 12 weeks, 18 of 22 intervention arm patients (82%) and 18 of 25 controls (72%) completed the outcome measures, and at 26 weeks, 15 (68%) and 15 (60%) respectively (see CONSORT diagram, Figure 1). Of those followed-up, 29 patients (81%) completed questionnaires face-to-face at 12 weeks, and 26 (87%) at 26 weeks, the rest completing them only after further follow-up by post (19% at 12 weeks and 13% at 26). No patients proved contactable in order to complete outcome measures over the telephone.

Table 2: Baseline characteristics

Characteristic	Control patients (n=25)	Intervention patients (n=22)
Female	16 (64.0%)	13 (59.0%)
Age (Mean (SD))	43.1 (17.1)	44.7 (18.5)
White ethnic group	24 (96.0%)	22 (100%)
Marital status		
- Married/Cohabiting	6 (24.0%)	12 (54.5%)
- Widowed/separated/divorced	8 (32.0%)	6 (27.3%)
- Single	11 (44.0%)	4 (18.2%)
Any dependents at home	9 (36.0%)	7 (31.8%)
Age left education	18.6 (5.3)	18.8 (3.4)
Economic position		
- Full/part time work	17 (68.0%)	14 (63.6%)
- Sick/disabled	2 (8.0%)	1 (4.6%)
- Unemployed	1 (4.0%)	1 (4.6%)
- Retired/student/homemaker	5 (20.0%)	5 (22.7%)
- Other	0	1 (4.6%)
BDI-II total score Mean(SD)	26.92 (7.93)	23.90 (11.92)
WSAS total score Mean(SD)	21.88 (9.37)	18.13 (10.00)
GAD-7 total score Mean(SD)	14.32 (5.27)	11.64 (5.83)

BDI-II=Beck Depression Inventory, 2nd edition[24], WSAS=Work and Social Adjustment Scale[25], GAD-7=Generalised Anxiety Disorder scale[23]

Outcomes

Outcome scores at baseline, 12 weeks and 26 weeks follow-up are shown in Table 3. At 12 weeks the intervention group adjusted mean score for depressive symptoms on the BDI-II was significantly lower than the control group by 5.8 points (95% confidence interval (CI) -11.1, -0.5) after adjusting for baseline depression scores, anxiety, sociodemographics, psychotropic medication use, and clustering by practice. Adjusted mean score on the WSAS

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at 12 weeks was lower (better) in the intervention group than the controls by a mean of 3.0 points, which was not statistically significant (95% CI -7.3, 1.3).

At 26 weeks, there were no significant differences between the groups in symptoms or social functioning (adjusted mean BDI-II was slightly worse in intervention arm by 2.5 points (95% CI -1.7, 6.7); adjusted mean WSAS was lower by 0.3 points (95% CI -5.2, 4.6)). However, the adjusted mean MISS satisfaction score was 22.0 points higher in the control group (95% CI -40.7, -3.29).

Baseline EQ-5D-5L quality of life scores were similar among intervention and control group patients (Table 3). Scores were improved at 12 weeks for both groups although slightly higher among intervention patients than controls, and scores went down again at 26 weeks among controls.

Table 3: Outcome measures at baseline and follow-up

Measures		Control group			Intervention group		
		Baseline (n=25)	12 weeks (n=18)	26 weeks (n=15)	Baseline (n=22)	12 weeks (n=18)	26 weeks (n=15)
Depression (BDI-II)	Mean (SD)	26.92 (7.93)	19.22 (11.62)	15.53 (10.04)	23.90 (11.92)	12.00 (8.93)	14.13 (12.54)
Social functioning (WSAS)	Mean (SD)	21.88 (9.37)	14.89 (9.30)	14.93 (10.79)	18.13 (10.00)	10.94 (8.12)	12.07 (11.35)
Anxiety (GAD-7)	Mean (SD)	14.32 (5.27)	–	–	11.64 (5.83)	–	–
Quality of life (EQ-5D-5L)	Mean (SD)	0.624 (0.284)	0.698 (0.246)	0.674 (0.299)	0.633 (0.242)	0.759 (0.105)	0.764 (0.158)
Satisfaction (MISS)	Mean (SD)	–	–	148.93 (34.19)	–	–	137.93 (34.74)

BDI-II=Beck Depression Inventory, 2nd edition[24], WSAS=Work and Social Adjustment Scale[25], GAD-7=Generalised Anxiety Disorder scale[23], EQ-5D-5L=EuroQol quality of life scale[26], MISS=Medical Informant Satisfaction Scale[28]

The mean QALY gain over 26 weeks was 0.382 (SD 0.046) for intervention patients, and 0.336 (0.132) for controls, giving a non-significant difference of 0.047 (95% CI -0.036, 0.129). Mean depression related NHS service costs per patient over 26 weeks were similar: control arm £216 (95% CI £135, £297), intervention arm £231 (£129, £332), including £16 per patient for an estimated five minutes GPs or PNs spent dealing with PROM results.

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Intra-cluster correlation coefficients

There was no evidence in this sample of clustering by practice for the BDI-II or WSAS: the ICC was zero at baseline for both. After controlling for baseline and randomisation group, the ICC for the BDI-II at 12 weeks was 0.03.

Ease of completion of outcome measures

On average participants rated the BDI-II, WSAS and GAD-7 as easy to use and the time taken was under five minutes for each. Ease of completion scores: mean (s.d) where 1=not at all easy and 5=very easy: BDI-II 4.29 (0.94); WSAS 4.38 (0.88) and GAD-7 4.38 (0.83). Time taken (minutes): median (interquartile range): BDI-II 4 (3,5); WSAS 1.5 (1,3); and GAD-7 2 (1,2).

Qualitative interviews with patients and practice staff

The full qualitative analysis and illustrative quotes from participants will be published separately. We present a brief summary only in this paper.

Fourteen patients were interviewed. Overall, in relation to the feasibility of the study, patients were happy to be randomised (even when randomised to the control arm), were supportive of the use of PROMS (seeing potential benefits for understanding their illness) and reported them relatively easy and quick to complete. There were some difficulties found in discussing the results of PROMS with their practitioners which would need attention in a definitive trial. Some were unable to see the same practitioner for follow up, and some expressed disappointment at not having feedback on the PROM scores from participating practitioners. Some would have liked a record of changes in scores over time to show their progress.

Interviews were carried out with 10 GPs, one PN and two practice managers. In relation to feasibility practitioners overall considered the use of PROMS to be feasible. Positive feedback on using PROMs included: help with communication, encouraging patients to feed back on symptoms, feel listened to and taken seriously (particularly the PSYCHLOPS); help with treatment planning, confirming decisions, and measuring progress; providing structure in a consultation which could save time; and not missing anything (especially the PHQ-9) . Negative feedback included: PROMS are too simplistic (especially the Distress Thermometer); could be difficult for patients to complete (due to insufficient health literacy, sensitive questions, or wanting to give the 'correct' answer); take time to complete in consultations; and may depersonalise interactions. Important areas that would need to be improved to smooth their use in practice included further clarification of patient inclusion

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criteria, choosing measures that are easy for patients to complete, and more guidance on what to do with the PROM results once completed.

Methodological changes

Several changes were needed to overcome difficulties in recruiting and following-up patients. Because response rates to the practice mail-outs were lower than 10%, we obtained ethics approval to send a revised patient information leaflet which used varied font sizes and coloured text to be more eye-catching, and for practice nurses to telephone non-responding participants two weeks after mail-outs to follow them up more actively (this did not apply to those who had responded to say they were not interested, only those who had not responded at all). However in the event the telephone calls did not yield any more participants.

The follow-up research assessments were originally intended to be completed face to face, but we obtained ethics approval to send the research assessment questionnaires by post if patients failed to attend follow-up after two requests. We also obtained approval to send patients a £10 high street shopping gift voucher with the follow up questionnaires sent by post. These changes between them helped improve follow-up rates by around 10%.

Another change was approved to facilitate active follow-up of non-responding patients. If they did not complete follow up questionnaires in person or by post, the study team was permitted to try to contact them and complete the primary outcome measure (BDI-II), and two other key outcome measures (WSAS and EQ-5D-5L), over the telephone. However in the event no non-responders could be reached by telephone.

Finally, approval was given for an additional practice administrative staff review of the medical records of recruited participants at the end of their participation, as we were able to gather only limited information on service use through the patient questionnaires. These record reviews provided extra information on prescribed medication, number of visits to GPs, PNs and community based staff, secondary care contacts, hospital admissions, and length of hospitalisation where appropriate.

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Discussion

Principal findings

It is feasible to carry out a randomised trial of PROMs for the assessment and follow-up of depression in primary care in England, although recruitment rates and follow-up rates, particularly in the control arm, would need improving significantly for a larger, definitive trial. Intervention arm patients were happy to complete the PROMs and research outcome questionnaires and valued seeing the results. Differences between arms suggest PROMs may reduce depressive symptoms, yet also reduce patient satisfaction, perhaps because GPs appeared not to value using PROM results to influence management.

Strengths and limitations

The trial was pragmatic, with few exclusion criteria, and readily generalisable to UK primary care, although the small number of patients recruited in some of the practices raises the question of how representative the sample was of all patients with new episodes of depression. Practices were able to recruit patients both in GP/PN consultations and through staff mailouts to patients, but two practices had to be dropped because of non-recruitment after several months, and difficulties in recruitment in other practices meant we recruited only 47 of the target of 48 patients.

Patients were randomly allocated to intervention or control, with concealment of allocation from patients until after informed consent had been obtained and baseline measures had been completed. However patients, practitioners and assessors could not be blinded to allocation during the trial given the nature of the intervention, although the use of self-report research outcome measures should have prevented observer rating bias.

The study was necessarily small in keeping with testing feasibility, but in spite of this we did find a difference in the primary outcome measure between arms at 12 weeks follow-up, favouring the intervention. The adjusted difference between arms at 12 weeks as a percentage of the score in the control group was 5.8/19.22 = 30.1%, which is greater than the minimal clinically important difference (MCID) of a 17.5% reduction in scores from baseline found to correspond to patients' global reports of significant improvement[33]. We did not determine how many practitioners actually gave feedback on the PROMs to their patients, but our patient interviews suggest not all practitioners did. This might have influenced the clinical outcome of the study, yet some benefit was identified nevertheless.

Comparison with other studies

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The results are in keeping with a US primary care based controlled trial of feeding back PHQ-9 scores to family practitioners at diagnosis and follow-up, which demonstrated significantly improved patient outcomes over six months[34]. The difference in outcome could not be explained in terms of any significant differences in management, but the benefits of feeding back scores seemed to arise from increasing patients' awareness of their symptoms and their ability to report relevant changes[35]. That may explain why our patients may have derived benefit from using PROMs even when their GPs did not seem to use the results to inform their care.

Implications for clinicians, policymakers, and research

The implications are mainly for the design of a definitive trial rather than for practice at this stage, although clinicians, policymakers and research funders might be persuaded of the need for a more definitive trial on the basis that short-term differences in outcome favouring the use of PROMs were identified even in this small sample.

To facilitate recruitment, and ensure as representative a sample of patients as possible, a definitive trial should aim to recruit more patients per practice from a smaller number of more committed practices, rather than fewer patients each from a larger number of practices. Depressed patients are often viewed as in need of protection by GPs, who may feel introducing research is intrusive[36]. A lack of skills in introducing research could be addressed through more training in a smaller group of practices.

Follow-up at 12 weeks of 82% was sufficient in the intervention arm, but needs to be improved from 72% in the control arm, and follow-up at 26 weeks needs to be improved from 68% and 60% respectively, through taking steps to maintain better contact with patients, obtaining mobile phone numbers, postal and email addresses, and permission to post, text, telephone or email them, as a significant proportion failed to meet face-to-face or complete and return the measures sent by post. Participating practitioners should also be trained to remind patients of their involvement in the study when they attend review appointments. It is possible that some of the apparent benefit of the intervention was due to the extra attention patients received so it is important to have similar follow-up rates in the two arms.

Current demands on practices, and the expansion of less than full time working, make it increasingly difficult to provide continuity of care, which may explain why participating patients sometimes found it difficult to get follow-up appointments with the same GP. Therefore it will be important to recruit practices where all GPs and PNs in the practice agree to be involved in the study and to be trained in recruiting, consenting, and following-up all

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eligible patients, and looking at the results of PROMs for all those in the intervention arm. In a definitive trial practices should be cluster randomised to streamline recruitment and follow-up so all patients in each are treated the same, by whichever GP or PN they see.

Cluster randomisation tends to require a larger sample due to clustering by practice (the design effect), although the increase in sample size necessary appears likely to be small based on this study. There was no evidence of clustering at baseline, but the study may not have been large enough to permit an accurate estimation of the true value of the ICC and it would be sensible in a larger trial to make an allowance for clustering. After controlling for baseline and randomisation group, the ICC for the BDI-II at 12 weeks was 0.03. The ICC for the BDI-II from a previous trial of antidepressants for mild to moderate depression in primary care was 0.02[31], therefore an ICC of 0.03 might be appropriate to use to calculate the design effect if the definitive trial is cluster randomised. This is a relatively small ICC, but if a smaller number of practices each recruiting more patients is recruited, the design effect will be greater as it increases with increasing cluster size.

Practice logs and recruitment rates in the better recruiting practices show the numbers of eligible patients per group practice will allow for more than six patients to be recruited per year, given greater commitment. Having a relatively smaller number of practices recruit more patients each will be more efficient in terms of travel to practices by the research team, and allow greater contact to be maintained with participating staff in each, to optimise practice commitment.

Administration of PROMs needs to be streamlined, and GPs provided with more guidance on how to assess the results, to avoid disappointing patients by not using the PROMs to inform care. Patients may benefit from being provided with a record of their PROM scores so they can monitor their progress.

The study team needs to spend more time at participating practices training them in the recruitment process, and assisting them with setting up database searches. Practices should complete a trial recruiting period to assess their commitment, and practice research costs should be reimbursed on a per-patient/per-mailout basis rather than paying them a lump sum at the beginning of the trial, to incentivise recruitment.

Conclusions

Even in this small sample, the findings suggest that the use of PROMs may be beneficial in the short term, although maybe not in the longer term. It provides support for our plan to take

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forward a larger, definitive trial. Before we proceed however, we need to do some more work with potential participants, to identify the most promising PROM. Given that some practitioners found them time consuming and wanted more guidance on how to take account of the results in their treatment decisions, encouraging more practitioners to use PROMs requires identifying relatively brief measures which can potentially change management.

[Word count 4984 not including tables]

Figure 1 CONSORT flow diagram of patient participation

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Contributorship statement

Tony Kendrick, Beth Stuart, Geraldine Leydon, Adam Geraghty, Lily Yao, Christopher Dowrick, Glyn Lewis and Michael Moore[made substantial contributions to the conception or design of the work.

Rachel Ryves, Samantha Williams and Shihua Zhu made substantial contributions to the acquisition, analysis, and interpretation of data.

All authors contributed to drafting the work and revising it critically for important intellectual content, and all approved the final version submitted.

We agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Competing interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: all authors had financial support from the NIHR Research for Patient Benefit Programme for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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Data sharing statement

We agree to make the relevant anonymised patient level data available on reasonable request.

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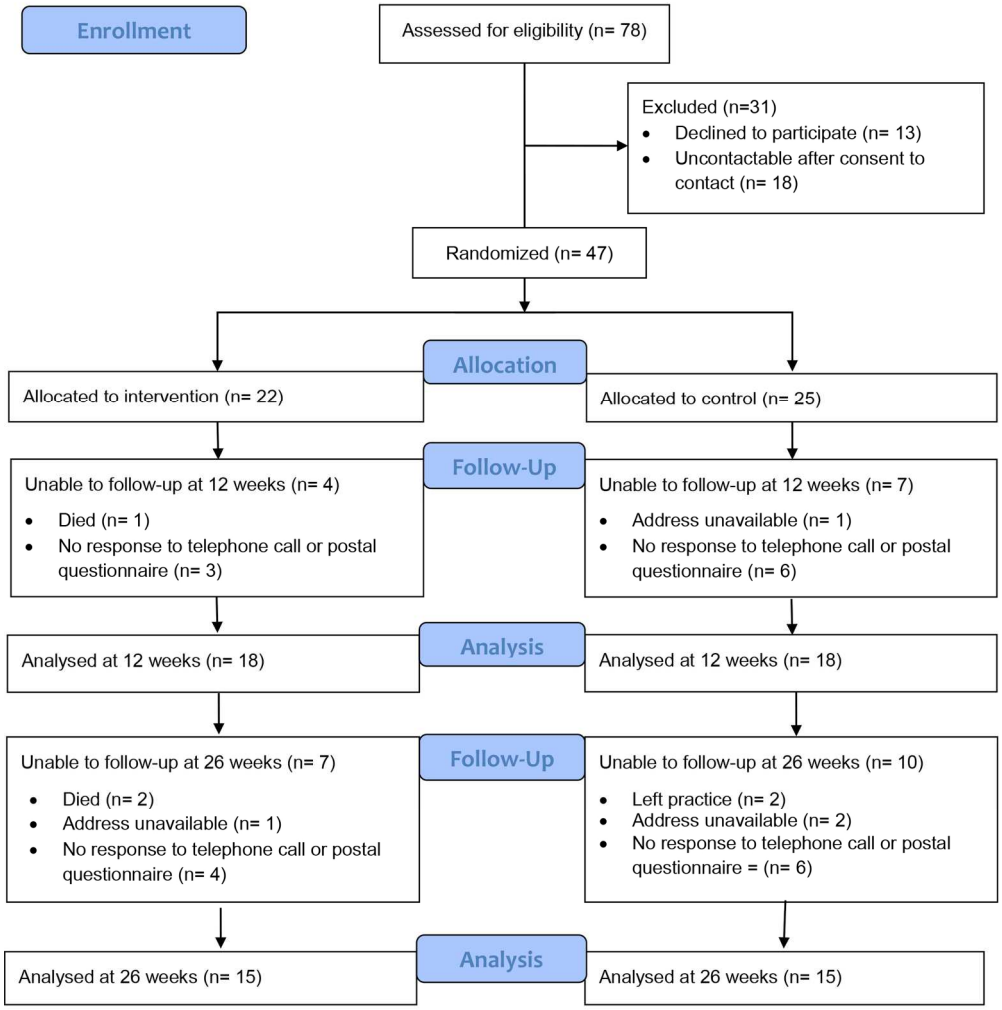

Figure 1 CONSORT flow diagram of patient participation

177x180mm (300 x 300 DPI)

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Appendix 1: List of read codes used by GP practices to search records for potential participants

Read code	Read term
E2B..00	Depressive disorder NEC
1BT..11	Low mood
E200300	Anxiety with depression
Eu32z11	[X]Depression NOS
1B17.00	Depressed
1465	H/O: depression
1B17.11	C/O - feeling depressed
Eu32.00	[X]Depressive episode
E204.00	Neurotic depression reactive type
1BT..00	Depressed mood
1B1U.00	Symptoms of depression
E204.11	Postnatal depression
2257	O/E - depressed
Eu32100	[X]Moderate depressive episode
E113.11	Endogenous depression - recurrent
Eu32z00	[X]Depressive episode, unspecified
1BO..00	Mood swings
Eu32z14	[X] Reactive depression NOS
E112.13	Endogenous depression first episode
E112.14	Endogenous depression
1B1J.11	Emotional upset
E2B1.00	Chronic depression
E112.11	Agitated depression
E112.00	Single major depressive episode
E135.00	Agitated depression
E113700	Recurrent depression
Eu32000	[X]Mild depressive episode
Eu33.00	[X]Recurrent depressive disorder
Eu41200	[X]Mixed anxiety and depressive disorder
Eu32200	[X]Severe depressive episode without psychotic symptoms
1B1U.11	Depressive symptoms
E113.00	Recurrent major depressive episode
Eu32z12	[X]Depressive disorder NOS
Eu3..00	[X]Mood - affective disorders
E112.12	Endogenous depression first episode
Eu32400	[X]Mild depression
Eu32.11	[X]Single episode of depressive reaction
E113200	Recurrent major depressive episodes, moderate
Eu34100	[X]Dysthymia
E112200	Single major depressive episode, moderate
Eu32.13	[X]Single episode of reactive depression
E112100	Single major depressive episode, mild
Eu33100	[X]Recurrent depressive disorder, current episode moderate
Eu34114	[X]Persistant anxiety depression
Eu41211	[X]Mild anxiety depression
E290.00	Brief depressive reaction
Eu53011	[X]Postnatal depression NOS

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Eu33.13	[X]Recurrent episodes of reactive depression
1BQ..00	Loss of capacity for enjoyment
E11z200	Masked depression
Eu33z00	[X]Recurrent depressive disorder, unspecified
Eu34113	[X]Neurotic depression
Eu33.11	[X]Recurrent episodes of depressive reaction
E112z00	Single major depressive episode NOS
E291.00	Prolonged depressive reaction
Eu43012	[X]Acute reaction to stress
Eu32y00	[X]Other depressive episodes
E113z00	Recurrent major depressive episode NOS
Eu43z00	[X]Reaction to severe stress, unspecified
E112300	Single major depressive episode, severe, without psychosis
1BT..12	Sad mood
Eu33200	[X]Recurr depress disorder cur epi severe without psyc sympt
Eu33000	[X]Recurrent depressive disorder, current episode mild
1JJ..00	Suspected depression
E113100	Recurrent major depressive episodes, mild
Eu32212	[X]Single episode major depression w'out psychotic symptoms
Eu34111	[X]Depressive neurosis
Eu32700	[X]Major depression, severe without psychotic symptoms
E113300	Recurrent major depressive episodes, severe, no psychosis
E112000	Single major depressive episode, unspecified
Eu32600	[X]Major depression, moderately severe
Eu33211	[X]Endogenous depression without psychotic symptoms
1BP0.00	Loss of interest in previously enjoyable activity
Eu33.12	[X]Recurrent episodes of psychogenic depression
Eu4..00	[X]Neurotic, stress - related and somoform disorders
E113600	Recurrent major depressive episodes, in full remission
Eu33400	[X]Recurrent depressive disorder, currently in remission
Eu3z.00	[X]Unspecified mood affective disorder
Eu32.12	[X]Single episode of psychogenic depression
Eu32z13	[X]Prolonged single episode of reactive depression
1BU..00	Loss of hope for the future
E113000	Recurrent major depressive episodes, unspecified
Eu32500	[X]Major depression, mild
Eu32y11	[X]Atypical depression
E112500	Single major depressive episode, partial or unspec remission
Eu33212	[X]Major depression, recurrent without psychotic symptoms
Eu53012	[X]Postpartum depression NOS
1S40.00	Dysphoric mood
E284.00	Stress reaction causing mixed disturbance of emotion/conduct
ZV11100	[V]Personal history of affective disorder
E113500	Recurrent major depressive episodes,partial/unspec remission
E11y200	Atypical depressive disorder
Eu3y111	[X]Recurrent brief depressive episodes
Eu33y00	[X]Other recurrent depressive disorders
Eu43y00	[X]Other reactions to severe stress
E112600	Single major depressive episode, in full remission
Eu32211	[X]Single episode agitated depressn w'out psychotic symptoms

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Eu34.00	[X]Persistent mood affective disorders
E290z00	Brief depressive reaction NOS
E292.00	Adjustment reaction, predominant disturbance other emotions
E283z00	Other acute stress reaction NOS
Eu92.11	[X]Emotional behavioural problems
Eu3y.00	[X]Other mood affective disorders
Eu3y000	[X]Other single mood affective disorders
E292400	Adjustment reaction with anxious mood
Eu32y12	[X]Single episode of masked depression NOS
Eu3y100	[X]Other recurrent mood affective disorders
E292z00	Adjustment reaction with disturbance of other emotion NOS
Eu34z00	[X]Persistent mood affective disorder, unspecified
E2C4z00	Mixed disturbance of conduct and emotion NOS
Eu32213	[X]Single episode vital depression w'out psychotic symptoms
Eu33z11	[X]Monopolar depression NOS
Eu3yy00	[X]Other specified mood affective disorders
Eu32B00	[X]Antenatal depression
Eu33214	[X]Vital depression, recurrent without psychotic symptoms
Eu34y00	[X]Other persistent mood affective disorders

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Appendix 2: Advice given to GPs about the meaning of PROM scores

PHQ-9 Scores and Proposed Treatment Actions

(Adapted from Kroenke K, Spitzer RL, Psychiatric Annals 2002;32:509-521)

PHQ-9 scores at diagnosis

PHQ-9 Score	Depression Severity	Proposed Treatment Actions
0 – 4	None-minimal	None
5 – 9	Mild	Watchful waiting; repeat PHQ-9 at follow-up
10 – 14*	Moderate	Psychological Treatment and follow-up/Antidepressants
15 – 19	Moderately Severe	Antidepressants and Psychological Treatment
20 – 27	Severe	Referral to mental health

* Question B must be answered positively, i.e. the symptoms have made it at least somewhat difficult for the patient to do their work, take care of their home, or get along with other people.

Changes in PHQ-9 Scores at Follow-up and Proposed Treatment Actions

Change in PHQ-9 score	Response	Treatment actions
Drop of 5 or more points from baseline	Adequate	No treatment change needed. Continue treatment and follow-up as planned.
Drop of 2-4 points from baseline.	Probably Inadequate	Often warrants an increase in antidepressant dose; follow-up as planned
Drop of 1-point, or no change, or increase in score, first follow-up	Inadequate	Increase dose or switch drug Refer for psychological treatment Follow-up sooner
Drop of 1-point, or no change, or increase in score, subsequent follow-up	Inadequate	Increase dose or switch drug Refer for psychological treatment Refer to mental health

Distress Thermometer

The patient marks the thermometer to indicate how much distress they have that week, from 0 to 10. Scores above 4 indicate significant distress needing further exploration and possible action.

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PSYCHLOPS

All of the responses in PSYCHLOPS are scored on a six point scale ranging from zero to five. A score of zero indicates the least psychological difficulty whereas a score of five indicates the most psychological difficulty.

The questions which are scored are those relating to Problems (Questions 1b and 2b), Functioning (Question 3b) and Wellbeing (Question 4). Other questions provide useful information but do not contribute to the total score or change score.

The initial score for PSYCHLOPS is unique to each individual. The main purpose of the score is to measure within-person change, i.e. the change in score for the items chosen by the patient.

High scores at diagnosis indicate significant problem areas for the individual patient, and should direct questioning to those areas. Similarly, persistently high scores, or increased scores, at follow-up should direct questioning to those areas of particular concern to the individual patient.

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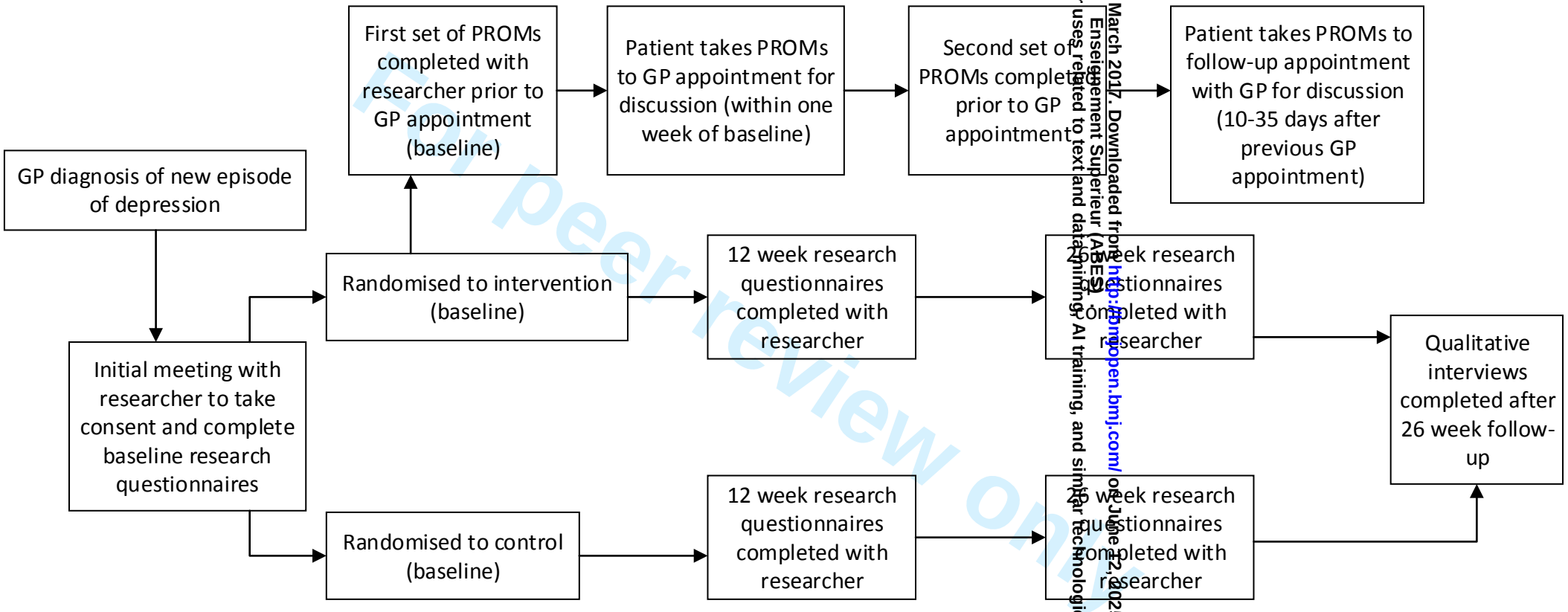
Appendix 3: Study intervention and control procedures



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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3-4
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	13-14
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	8
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	8
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

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		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	9
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10-11 plus CONSORT diagram
	13b	For each group, losses and exclusions after randomisation, together with reasons	10-11 plus CONSORT diagram
Recruitment	14a	Dates defining the periods of recruitment and follow-up	10
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	11
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	12
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	11-12
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	11-12
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	15
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	16
Other information			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	2

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*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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