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CollAborative care for Screen-Positive ElderRs with major depression (CASPER plus): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness

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Abstract

CollAborative care for Screen-Positive ElderRs with major depression (CASPER plus): a multicentred randomised controlled trial of clinical effectiveness and cost-effectiveness

Katharine Bosanquet,[1] Joy Adamson,[1] Katie Atherton,[2] Della Bailey,[1] Catherine Baxter,[2] Jules Beresford-Dent,[2] Jacqueline Birtwistle,[3] Carolyn Chew-Graham,[4] Emily Clare,[5] Jaime Delgadillo,[1,6] David Ekers,[7,8] Deborah Foster,[1] Rhian Gabe,[1,9] Samantha Gascoyne,[1] Lesley Haley,[8] Jahnese Hamilton,[5] Rebecca Hargate,[2] Catherine Hewitt,[1] John Holmes,[3] Ada Keding,[1] Helen Lewis,[1] Dean McMillan,[1,9] Shaista Meer,[3] Natasha Mitchell,[1] Sarah Nutbrown,[1] Karen Overend,[1] Steve Parrott,[1] Jodi Pervin,[1] David A Richards,[10] Karen Spilsbury,[1] David Torgerson,[1] Gemma Traviss-Turner,[3] Dominic Trépel,[1] Rebecca Woodhouse[1] and Simon Gilbody[1,9]*

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Background: Depression in older adults is common and is associated with poor quality of life, increased morbidity and early mortality, and increased health and social care use. Collaborative care, a low-intensity intervention for depression that is shown to be effective in working-age adults, has not yet been evaluated in older people with depression who are managed in UK primary care. The CollAborative care for Screen-Positive ElderRs (CASPER) plus trial fills the evidence gap identified by the most recent guidelines on depression management.

Objectives: To establish the clinical effectiveness and cost-effectiveness of collaborative care for older adults with major depressive disorder in primary care.

Design: A pragmatic, multicentred, two-arm, parallel, individually randomised controlled trial with embedded qualitative study. Participants were automatically randomised by computer, by the York Trials Unit Randomisation Service, on a 1 : 1 basis using simple unstratified randomisation after informed consent and baseline measures were collected. Blinding was not possible.

Setting: Sixty-nine general practices in the north of England.

Participants: A total of 485 participants aged ≥ 65 years with major depressive disorder.

Interventions: A low-intensity intervention of collaborative care, including behavioural activation, delivered by a case manager for an average of six sessions over 7–8 weeks, alongside usual general practitioner (GP) care. The control arm received only usual GP care.

Main outcome measures: The primary outcome measure was Patient Health Questionnaire-9 items score at 4 months post randomisation. Secondary outcome measures included depression severity and caseness at 12 and 18 months, the EuroQol-5 Dimensions, Short Form questionnaire-12 items, Patient Health Questionnaire-15 items, Generalised Anxiety Disorder-7 items, Connor–Davidson Resilience Scale-2 items, a medication questionnaire, objective data and adverse events. Participants were followed up at 12 and 18 months.

Results: In total, 485 participants were randomised (collaborative care, $n = 249$; usual care, $n = 236$), with 390 participants (80%: collaborative care, 75%; usual care, 86%) followed up at 4 months, 358 participants (74%: collaborative care, 70%; usual care, 78%) followed up at 12 months and 344 participants (71%: collaborative care, 67%; usual care, 75%) followed up at 18 months. A total of 415 participants were included in primary analysis (collaborative care, $n = 198$; usual care, $n = 217$), which revealed a statistically significant effect in favour of collaborative care at the primary end point at 4 months [8.98 vs. 10.90 score points, mean difference 1.92 score points, 95% confidence interval (CI) 0.85 to 2.99 score points; $p < 0.001$], equivalent to a standard effect size of 0.34. However, treatment differences were not maintained in the longer term (at 12 months: 0.19 score points, 95% CI –0.92 to 1.29 score points; $p = 0.741$; at 18 months: < 0.01 score points, 95% CI –1.12 to 1.12 score points; $p = 0.997$). The study recorded details of all serious adverse events (SAEs), which consisted of 'unscheduled hospitalisation', 'other medically important condition' and 'death'. No SAEs were related to the intervention. Collaborative care showed a small but non-significant increase in quality-adjusted life-years (QALYs) over the 18-month period, with a higher cost. Overall, the mean cost per incremental QALY for collaborative care compared with usual care was £26,016; however, for participants attending six or more sessions, collaborative care appears to represent better value for money (£9876/QALY).

Limitations: Study limitations are identified at different stages: design (blinding unfeasible, potential contamination), process (relatively low overall consent rate, differential attrition/retention rates) and analysis (no baseline health-care resource cost or secondary/social care data).

Conclusion: Collaborative care was effective for older people with case-level depression across a range of outcomes in the short term though the reduction in depression severity was not maintained over the longer term of 12 or 18 months. Participants who received six or more sessions of collaborative care did benefit substantially more than those who received fewer treatment sessions but this difference was not statistically significant.

Future work recommendations: Recommendations for future research include investigating the longer-term effect of the intervention. Depression is a recurrent disorder and it would be useful to assess its impact on relapse and the prevention of future case-level depression.

Trial registration: Current Controlled Trials ISRCTN45842879.

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List of abbreviations

CADET	CollAborative DEpression Trial
CASPER	CollAborative care for Screen-Positive ElderRs with major depression
CD-RISC2	Connor–Davidson Resilience Scale-2 items
CEAC	cost-effectiveness acceptability curve
CI	confidence interval
CM	case manager
CRN	Clinical Research Network
EQ-5D-3L	EuroQol-5 Dimensions, 3 levels
GAD-7	Generalised Anxiety Disorder-7 items
GP	general practitioner
IAPT	Improving Access to Psychological Therapies
ICC	intracluster correlation coefficient
ICER	incremental cost-effectiveness ratio
IMPACT	Improving Mood-Promoting Access to Collaborative Treatment
MCS	mental component summary
MINI	Mini International Neuropsychiatric Interview
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
ONS	Office for National Statistics
PC-MIS	Patient Case-Management Information System
PCS	physical component summary
PHQ-9	Patient Health Questionnaire-9 items
PHQ-15	Patient Health Questionnaire-15 items
PT	participant
PTW	withdrawn participant
PWP	psychological well-being practitioner
QALY	quality-adjusted life-year
RCT	randomised controlled trial
REC	Research Ethics Committee
SAE	serious adverse event
SD	standard deviation
SES	socioeconomic status
SF-12	Short Form questionnaire-12 items
SF-6D	Short Form questionnaire-6 Dimensions
SHARD	Self Help At Risk Depression

Plain English summary

The ageing process increases the risk of depression in older people and, although depression is relatively common, it often goes unrecognised and untreated. Traditionally, feeling low was considered an inevitable part of growing old about which nothing could be done.

The CollAborative care for Screen-Positive ElderRs with major depression (CASPER) plus trial aimed to see if collaborative care, a new type of care involving a case manager who co-ordinates different aspects of a participant's care, could help to reduce depression severity. Case managers worked with participants for an average of six sessions over 7–8 weeks, mainly over the telephone. In order to test whether or not collaborative care worked, it was compared with usual general practitioner care. Each person taking part was given one type of care, which was decided by chance, similar to the roll of a dice, to make sure it was fair.

The trial took place in the north of England. In total, 485 older adults took part for up to 18 months. After 4 months, the results showed a statistically significant benefit for collaborative care relating to the primary outcome of depression severity. However, this improvement in people's mental well-being was not maintained in the longer term at 12 or 18 months. Collaborative care was more expensive than usual general practitioner care but, as it may have improved the quality of people's lives, particularly for people who had six or more sessions, it might be value for money.

Scientific summary

Background

Depression is one of the most common reasons for consulting with a general practitioner (GP), and its associated personal and economic burden is considerable. Depression is often associated with long-term medical conditions but is commonly unrecognised or suboptimally treated. Older people are disproportionately affected by depression, which is associated with poor function and poor outcomes. Strategies to encourage the recognition and management of depression among older people and those with long-term conditions have been proposed. Guidance often encourages GPs to screen for depression, and evidence-supported treatments include the prescription of antidepressants and/or the provision of brief psychological treatments.

Collaborative care involves the provision of low-intensity psychosocial treatment by a case manager working in collaboration with the primary care team. Psychological interventions form part of care and are delivered over the telephone. Collaborative care has a strong evidence base among people with depression. The majority of trials have been conducted in the USA, although evidence from UK trials on the effectiveness of this approach is now accumulating. There are no large-scale trials that focus on older adults, who often have long-term physical health problems. In this trial, we adapted collaborative care for a population of older people whereby an evidence-supported treatment (including behavioural activation and medication management) was delivered by primary care psychological well-being practitioners over the telephone.

Objectives

The CollAborative care for Screen-Positive ElderRs with major depression (CASPER) plus trial was a randomised controlled trial (RCT) of usual GP care compared with the addition of collaborative care for the treatment of clinical depression in older adults. This included concurrent qualitative and economic evaluations. We first conducted an internal pilot trial, the objectives of which were to:

1. establish the clinical effectiveness of a low-intensity intervention of collaborative care for older adults with screen-positive major depression disorder.
2. examine the cost-effectiveness of a low-intensity intervention of collaborative care for older adults with screen-positive major depression disorder across a range of health and social care costs.
3. explore the views and experiences of the CASPER plus intervention within the collaborative care framework for the management of depression in older people from the perspectives of participants, case managers and GPs.

Method

Design

We conducted a pragmatic, multicentred, two-arm, parallel, open RCT. Participants with major depression disorder were individually randomised (1 : 1) to receive either collaborative care in addition to usual GP care, or just usual GP care.

Setting

Participants were recruited from general practices in four centres in the north of England: (1) York centre (the core centre) covering the city of York, Harrogate, Hull and the surrounding areas; (2) Leeds centre and the surrounding area; (3) Durham centre and the surrounding area; and, (4) Newcastle upon Tyne centre, including Northumberland and North Tyneside.

Participants

Potential participants were identified by postal questionnaire and were eligible if they reported depressive symptoms ('screened positive') to the Whooley questions, and were then found to have major depressive disorder according to standardised diagnostic criteria using the Mini International Neuropsychiatric Interview. Respondents with less severe depression ('subthreshold depression') were offered the opportunity to partake in a related Health Technology Assessment-funded trial (CASPER ISRCTN02202951) that is not reported in this monograph. We excluded people with known alcohol dependency, psychotic symptoms, recent evidence of suicidal risk or self-harm, significant cognitive impairment or other factors that would make an invitation to participate in the trial inappropriate, such as recent bereavement or terminal illness.

Interventions

Participants in the intervention group were allocated to receive a manualised low-intensity programme of collaborative care using behavioural activation, designed specifically for those aged ≥ 65 years with depression. Collaborative care was delivered by a case manager [a primary care mental health worker/Improving Access to Psychological Therapies (IAPT) worker]. Participants received on average six sessions over 8–9 weeks, of which, on average, one was delivered face to face and five were delivered over the telephone. Collaborative care in the CASPER plus trial consisted of telephone support, medication management, symptom monitoring and active surveillance, facilitated by a computerised case management. The first session was delivered face to face and subsequent sessions via the telephone.

Participants in the control group were allocated to receive usual GP care; therefore, they received no care additional to the usual primary care management of subthreshold depression offered by their GP. Participants who were allocated to collaborative care received the intervention as well as usual GP care.

Main outcome measures

The primary outcome was self-reported symptoms of depression, assessed by the Patient Health Questionnaire-9 items (PHQ-9) at 4 months post randomisation and also at 12 months and 18 months. Secondary outcomes were, at 4, 12 and 18 months, a dichotomised measure of depression according to 'caseness' (PHQ-9 score of ≥ 10), anxiety [measured by the Generalised Anxiety Disorder-7 item (GAD-7) scale], somatoform complaints [measured by the Patient Health Questionnaire-15 items (PHQ-15)] and health-related quality of life [measured by the Short Form questionnaire-12 items (SF-12)]. We also measured resilience (using the Connor–Davidson Resilience Scale-2 items) and antidepressant use. The economic evaluation resource use was ascertained from administrative primary care records and health-state utility was measured using the Short Form questionnaire-6 Dimensions.

Results

A total of 485 patients (mean age 72 years) were recruited to the trial between May 2012 and August 2014, with 249 participants randomised to collaborative care and 236 to usual GP care. Of these, 390 participants (80%: collaborative care, 75%; usual care, 86%) were followed up at 4 months, 358 participants (74%: collaborative care, 70%; usual care, 78%) were followed up at 12 months and 344 participants (71%: collaborative care, 67%; usual care, 75%) were followed up at 18 months. For those allocated to collaborative care, 83% engaged with the intervention and the average number of sessions completed was six out of the planned eight sessions.

Clinical effectiveness

Adjusted PHQ-9 score means and group differences for the primary analysis model revealed significant differences between trial arms at the 4-month primary outcome in favour of collaborative care [1.92 score points; 95% confidence interval (CI) 0.85 to 2.99 score points; $p < 0.001$]. This represented a standard effect size of 0.34. However, this difference in depression severity was not maintained at the long-term follow-up at 12 months ($p = 0.741$) or 18 months ($p = 0.997$). The results were robust to a number of sensitivity analyses, including adjustment for clustering at the level of the case manager. The proportion of participants with case-level depression at 4 months was reduced in the collaborative care group (odds ratio at 4 months 2.18, 95% CI 1.36 to 3.51; $p = 0.001$), but there was no clear advantage for collaborative care at 12 months (odds ratio 1.40, 95% CI 0.72 to 2.72; $p = 0.319$) or 18 months (odds ratio 0.72, 95% CI 0.31 to 1.71; $p = 0.461$).

Between-group differences were observed in favour of collaborative care for a range of secondary outcomes including anxiety and somatoform complaints. Anxiety was measured using the GAD-7 and was reduced at 4 months (GAD-7 mean score difference 1.68, 95% CI 0.77 to 2.59; $p < 0.001$) and at 12 months (mean score difference 1.09, 95% CI 0.14 to 2.03; $p = 0.024$), but not at 18 months ($p = 0.511$). Somatoform complaints as measured using the PHQ-15 were reduced at 4 months (PHQ-15 mean score difference 1.67, 95% CI 0.98 to 2.36; $p < 0.001$) and 12 months (PHQ-15 mean score difference 1.19, 95% CI 0.47 to 1.90; $p = 0.001$), but not at 18 months ($p = 0.423$). Health-related quality of life was improved in mental domains at 4 months (SF-12 mental component summary score mean score difference 3.02, 95% CI –5.04 to –0.99; $p = 0.004$) but not at 12 months ($p = 0.125$) or 18 months ($p = 0.273$), and there was no difference in physical domains (SF-12 physical component summary score $p = 0.583$ at 4 months; $p = 0.769$ at 12 months; and $p = 0.514$ at 18 months).

Cost-effectiveness analysis

Providing collaborative care was estimated to cost an average of £495 per participant (accounting for costs of training case managers, their expected rate of patient contacts and a standardised agenda case manager). Analysis of routinely collected data collected during the delivery of collaborative care (i.e. as may be provided within a typical IAPT service) suggests the expected cost of collaborative care is £198 per patient and, therefore, lower than assumptions based on the treatment manual. The number of quality-adjusted life-years (QALYs) gained was higher among articipants who were allocated to collaborative care than in the control group (difference in adjusted QALY gains = 0.019; $p = 0.338$). In the base-case analysis, the incremental cost-effectiveness ratio for collaborative care was £26,010 per QALY. The probability that the incremental cost-effectiveness of collaborative care was < £20,000 per QALY was 39%, and the probability that it fell below the £30,000 per QALY willingness-to-pay threshold was 55%. When only participants who engaged with six or more sessions were included in the analysis, the cost per QALY estimate fell to £9876.

Qualitative evaluation

The qualitative study suggests that the intervention was acceptable to a large proportion of participants but that others did not engage. The main reasons for non-engagement were explored and were found to be related to the misgivings of participants about the potential benefits of behavioural-based programmes. The importance of the adaptation of treatment to those with long-term conditions or limitations was underlined. The positive aspects of treatment included the fact that people saw the benefits of behavioural activation and engaged well with their case managers, even if there were initial misgivings. The qualitative evaluation also highlighted the paucity of psychosocial interventions that are available for older people in primary care, and the potential role for collaborative care in 'plugging these gaps'. The role of the case manager was valued by participants in ensuring good communication with the GP and in the co-ordination of care, as well as providing them with the opportunity to talk outside the clinical setting of the primary care consultation room.

Conclusions

This is the first large-scale trial in the UK to test the clinical effectiveness and cost-effectiveness of using collaborative care to treat older people with depression. Collaborative care has been shown to be clinically effective at reducing depression severity in the short term, at 4-month follow-up, but benefits were not sustained at 12 or 18 months, so longer-term efficacy was not demonstrated. The effectiveness of collaborative care for older people with depression was greater for those people who had six or more treatment sessions. This intervention might be delivered as part of the IAPT services in the NHS at an acceptable ratio of benefits to cost – if it were highlighted that a minimum of six sessions were needed for it to be cost-effective.

Implications for health care

- Collaborative care was acceptable for the majority of older people with depression and could readily be delivered by low-intensity IAPT workers over the telephone, following a first face-to-face meeting.
- In this large-scale trial for older people with depression, collaborative care was clinically effective in improving the primary outcome of depression and across a range of secondary outcomes.
- The cost-effectiveness of collaborative care for depression has been robustly estimated within the CASPER plus trial and this could be viewed as cost-effective under conventional willingness-to-pay thresholds.

Recommendations for research

- A significant proportion of older people in the CASPER plus trial had a long-term health problem, and there were some improvements in quality of life across the trial population. Future adaptations and trials of collaborative care could focus on its use in populations with serious physical comorbidities and its impact on physical outcomes.
- More patients in the collaborative care arm discontinued treatment or dropped out of the trial. Further qualitative and quantitative work should explore the reasons for this, how to maximise the acceptability and effectiveness of collaborative care for this population and how to identify the most appropriate target population for the intervention.
- Depression is a recurrent disorder and it would be useful to judge longer-term impact on relapse and the prevention of future depression.
- This was a brief intervention and its benefits disappeared after 12 months. Future research should be conducted to establish how minimal interventions may be offered to ensure that early gains from treatment are sustained. Trials of 12-month top-up sessions for collaborative care (delivered by telephone) are needed.

Trial registration

This trial is registered as ISRCTN45842879.

Funding

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Chapter 1 Introduction

Depression in older adults

Depression accounts for the greatest burden of disease among all mental health conditions, and is expected to become the second highest among all general health problems by 2020.[1] It is currently estimated that in the UK around 10–20% of people aged ≥ 65 years have depression.[2] Projected demographic changes mean that population strategies to tackle depression will increasingly have to address the specific needs of older adults.[3] Depression often occurs alongside long-term physical health conditions[4] and/or cognitive impairment and it is more prevalent among people who live alone in social isolation. All these factors tend to disproportionately affect the older adult population. Among older adults, a clinical diagnosis of a major depressive disorder is the strongest predictor for impaired quality of life.[5] Indeed, beyond personal suffering and family disruption, depression worsens the outcomes of many medical disorders and promotes disability.[6] In 2009, the National Institute for Health and Care Excellence (NICE) published guidelines that acknowledged the coexistence of physical health problems and depression.[7,8] Furthermore, it was recognised that the impairments in quality of life associated with depression are comparable to those of major physical illness.[5]

Rationale for the CollAborative care for Screen-Positive EldeRs plus trial

Depression in older people is relatively common.[9] The effects on the individual include poor quality of life, increased morbidity and early mortality,[10] and increased health and social care use.[11] Depression is often under-recognised and undertreated in primary care.[12,13] At present, the management of depression tends to be limited to the prescription of antidepressants, with poor adherance an associated problem.[12] In particular, older adults seem to be less likely than working-age adults to be offered psychological treatments.[14,15] So far, the evidence for psychological interventions relates to higher-intensity models of care that cannot feasibly be delivered at scale in primary care. Collaborative care is a framework model for organising and delivering psychosocial interventions at scale.[16] It represents a brief, patient-centred, psychosocial package of care delivered by a case manager who works to a defined protocol and co-ordinates the patient's medication management with their general practitioner (GP). The case manager is supervised by a specialist who facilitates liaison across the primary care–secondary care interface.[17] In the USA, collaborative care has shown promising trial results among older people;[16] however, the transferability of this model of service to the UK NHS cannot be assumed. Consequently, the CollAborative care for Screen-Positive EldeRs with major depression (CASPER) plus trial will substantially enhance the randomised evidence base in the care of older people with depression and inform future service provision.

Collaborative care: an organisational model of providing care

The vast majority of depression in older adults is managed entirely in primary care without recourse to specialist mental health services.[3,18] Although a range of individual treatments have been shown to be effective in the management of clinical depression in older adults, including antidepressants and psychosocial interventions,[18] a repeated observation among those with depression has been the failure to integrate these effective elements of care into routine primary care services.[19] In addition, the implementation of any form of care will require a strategy that is low intensity and can be offered within primary care.[20]

In recent years, an organisational model of care has been introduced called collaborative care.[21] Collaborative care borrows much from chronic disease management and ensures the delivery of effective forms of treatment (such as pharmacotherapy and/or brief psychological therapy) through augmenting

the role of non-medical specialists in primary care. Collaborative care is a model whereby the non-medical specialists, or case managers, form a close collaboration with the person with depression and others involved in their care. The case manager acts as a conduit for the passage of information between all individuals involved and supports the participant to enable effective discussion of important problems. Case managers provide information and help participants to access appropriate services, such as social care and voluntary sector services.

The ubiquity of depression in primary care settings, along with the poor integration and co-ordination of care, has led to the development of, and increased use of, this model of care. In a 2012 Cochrane review[22] of 79 randomised controlled trials (RCTs) (24,308 participants), clear and robust evidence of the effectiveness of collaborative care was shown. It improved depression outcomes in both the short and medium term. Moreover, there was evidence to suggest that collaborative care can be cost-effective by reducing health-care utilisation and improving overall quality of life.[23,24] However, the greater proportion of studies related to working-age adults. A relative lack of any evidence for older adults was identified, which led to calls for further research on collaborative care among that age group. One important exception was the evidence provided by the US Improving Mood-Promoting Access to Collaborative Treatment (IMPACT) study of the effectiveness of collaborative care for older adults.

The IMPACT study was conducted by Unützer *et al.*[16] for those aged > 60 years with case-level clinical depression. The main finding was that, at 12 months, depression severity was at least 50% improved from baseline in almost half the participants in the intervention group, but only one in five of those receiving usual care. In 2007, a UK feasibility trial[9] of collaborative care in older adults showed some positive results. In recent years, the evidence base has expanded, although not with direct reference to older adults. The CollAborative DEpression Trial (CADET)[11] showed that collaborative care was effective at improving depression outcomes in a UK primary care population, and the Collaborative Interventions for Circulation and Depression: study protocol for a cluster randomized controlled trial of collaborative care for depression in people with diabetes and/or coronary heart disease (COINCIDE) trial[10] showed a modest effect at reducing depression and improving self-management of chronic disease.

In addition to the provision of collaborative care, the studies also provide information and support to enable participants to undertake brief psychological therapies, in this case behavioural activation. Behavioural activation for the CASPER plus trial was adapted from the behavioural activation intervention delivered in CADET.[11] Manualised psychological interventions, such as behavioural activation, may benefit individuals experiencing depressive symptoms. It focuses on addressing the behavioural deficits common among those with depression by reintroducing positive reinforcement and reducing avoidance. Such interventions aim to manipulate the behavioural consequence of a trigger (environmental or cognitive) rather than directly interpret or restructure cognitions.[25] Behavioural activation is about helping patients to 'act their way out' of depression rather than wait until they are ready to 'think their way out'. Helping people to identify and reintroduce valued activities that they have stopped doing, or to introduce ones they would like to take up, is an important component. The effectiveness of this psychological approach is now well demonstrated.[26,27] Behavioural activation can be readily delivered by a trained case manager either over the telephone or face to face (for those who experience difficulty using or accessing telephone-based therapy).[28]

Limitations of previous trials

The major limitation of previous trials was an absence of a definitive UK trial of collaborative care in older adults with depression. The absence of UK trials of collaborative care was highlighted in 2009 guidance for depression issued by NICE, and the need for such trials was highlighted as a research priority.[7] We proposed to measure the clinical effectiveness and cost-effectiveness of using collaborative care on older adults with major depression in response to a lack of evidence of its benefit to the older population in UK primary care.

Chapter 2 Research objectives

The research objectives of this trial were to:

1. establish the clinical effectiveness of a collaborative care intervention for older people with screen-positive above-threshold ('major depressive episode') depression within a definitive RCT
2. examine the cost-effectiveness of a collaborative care intervention for older people with screen-positive above-threshold ('major depressive episode') depression across a range of health and social care costs within a definitive RCT.

The definitive RCT was preceded by a developmental phase to produce a manualised collaborative care intervention for older people and an internal pilot trial to optimise recruitment, randomisation and retention, and we report these preparatory objectives within the body of this report.

Chapter 3 Methods

For CASPER plus, those patients identified at the screening phase as having above-threshold, case-level depression will be eligible to enter the CASPER plus substudy.

Trial design

We conducted a pragmatic, multicentred, two-arm, parallel, open RCT. Participants with major depression were individually randomised (1 : 1) to receive either collaborative care in addition to usual GP care, or just usual GP care.

Approvals obtained

This study was approved by NHS Leeds East Research Ethics Committee (REC) on 28 September 2010 (REC reference number 10/H1306/61). Research management and governance approval was obtained for each trial centre thereafter (see *Appendix 1*). This trial was assigned the International Standard Randomised Controlled Trial Number of ISRCTN45842879.

Trial centres

Four centres in the north of England were selected as trial sites: (1) York centre (the core study centre) covering the city of York, Harrogate, Hull and the surrounding areas; (2) Leeds centre and the surrounding area; (3) Durham centre and the surrounding area; and (4) Newcastle upon Tyne centre, including Northumberland and North Tyneside. Each centre was responsible for co-ordinating the recruitment of participants into the study (trial and epidemiological cohort).

Duration of follow-up

All participants were followed up by questionnaire at 4, 12 and 18 months (see *Chapter 4*).

Participant eligibility

Inclusion criteria

People for whom both of the following criteria applied:

- aged $\geq$ 65 years
- identified by GP practice as being able to take part in collaborative care.

Exclusion criteria

Potential participants were excluded if identified by primary care clinicians as meeting one of the following criteria:

- known alcohol dependency (as recorded on GP records)
- known to be experiencing psychotic symptoms (as recorded on GP records)
- any known comorbidity that would, in the GP's opinion, make entry to the trial inadvisable (e.g. recent evidence of suicidal risk or self-harm, significant cognitive impairment)
- other factors that would make an invitation to participate in the trial inappropriate (e.g. recent bereavement, terminal malignancy).

Sample size

To detect a minimum standard effect size of 0.35 (aligning with the US IMPACT study[16] and our previous CASPER trial[29,30]) with 80% power and a two-sided 5% significance level, 260 patients (130 per arm) would be required. Although this is an individually randomised trial, there may be potential clustering at the level of each collaborative care case manager, and hence the sample size was inflated to account for this.

Based upon an estimated intracluster correlation coefficient (ICC) of 0.02 and a case load size of 20, the design effect would be 1.38 {1 + [(20 – 1) × 0.02]} and 360 patients (180 in each arm) would be required. Allowing for 20% loss to follow-up, the final sample size needed was 450 patients (225 per arm).

Epidemiological cohort

During the first year of the CASPER plus trial, an epidemiological cohort was assembled. This consisted of people who had consented to participate in the trial but who were not depressed. Through our broad inclusion criteria we successfully recruited a total of 4668 patients aged ≥ 65 years into the CASPER cohort, from who we identified those with major depression who were eligible to participate in the CASPER plus trial. The reasons for this strategy were twofold: first, to recruit an adequate number of potential participants who would subsequently be identified as having depression, as we believed this would not always be recorded on GP records; and, second, to establish an epidemiological cohort of older adults who could be followed up and who would help inform the knowledge base around the health and well-being of older adults. This type of study design is termed a cohort multiple RCT.[31]

Recruitment into the trial

Recruitment of all participants into the trial took place through primary care. GP practices agreed to participate after a member of the study team had introduced it to them with written information, followed by a face-to-face visit to explain the study and what participation would involve. Patients were identified by a computer search and then invited to participate in the CASPER study by their general practice, which posted an invitation pack to all eligible patients. The packs comprised an invitation letter (see *Appendix 2*) signed from the general practice, a consent form (see *Appendix 3*), a decline form (see *Appendix 4*), a participant information sheet (see *Appendix 5*), a background information sheet (see *Appendix 6*) and a prepaid return envelope addressed to the core study centre. No patient-identifiable data were available to the study teams until patients returned their consent form.

Consenting participants

During the consent stage, potential participants were asked to complete the Whooley questions,[32] a two-item depression-screening/case-finding tool. These questions were asked at two different time points – on the background information sheet at invitation and in the baseline questionnaire – both times as self-reports. At the consent stage, participants were informed about the opportunity of participating in other related studies (e.g. qualitative studies) and were asked to indicate if they agreed to be approached in the future by ticking a box on the consent form. All participants who consented to take part in the CASPER study at this stage became part of the CASPER cohort. Participants did not become part of the CASPER plus trial until they had been subsequently assessed for suitability by completing a standardised diagnostic interview and randomisation.

Baseline assessment

On receipt of written consent from participants by the return of their consent form via post, baseline data were collected through a self-report questionnaire. All participants who returned completed consent forms to the core study centre were sent a baseline questionnaire (see *Appendix 7*). Participants were asked to respond to the Whooley questions[32] for a second time and to provide self-report medication data. They were also asked to complete a range of health surveys, which consisted of the Patient Health Questionnaire-9 items (PHQ-9)[33] – a measure of depression severity using a nine-item depression scale in reference to how a respondent has been feeling over the past 2 weeks; the Short Form questionnaire-12 items (SF-12)[34] – a measure of health-related quality of life to obtain health-state utility by estimating the Short Form questionnaire-6 Dimensions (SF-6D); the EuroQol-5 Dimensions, 3 levels (EQ-5D-3L)[35] – a standardised measure of health-state utility, designed primarily for self-completion by respondents; the Generalised Anxiety Disorder-7 item (GAD-7)[36] scale – a severity measure of generalised anxiety used to gauge the past 2 weeks; the Patient Health Questionnaire-15 items (PHQ-15)[37] – a measure of somatic complaints using a 15-item scale in reference to the last month; and the Connor–Davidson Resilience Scale-2 items (CD-RISC2)[38] – used to measure an individual's resilience and ability to bounce back.

Randomisation

Randomisation was carried out by the York Trials Unit Randomisation Service [www.yorkrand.com (accessed 23 June 2016)], accessed by a trained researcher from the study team. Participants were automatically randomised by a computer on a 1 : 1 basis by simple unstratified randomisation to either the intervention group or control group, following the completion of a diagnostic interview. All diagnostic interviews were conducted over the telephone by a trained researcher from the study team. The major depressive episode module of the Mini International Neuropsychiatric Interview (MINI) was used to ascertain the presence or absence of core depressive symptoms.[39] The MINI shows good agreement with other semistructured diagnostic interviews conducted to internationally recognised standards.[40–42] This allowed potential recruits to be identified as having major depressive disorder (five or more symptoms), subthreshold depression (two to four symptoms) or no depression (one symptom) (*Table 1*).[39,43,44] All participants diagnosed with major depressive disorder were randomised to either the intervention or the control arm.

Once participants had been randomised, they were sent a letter informing them of the outcome of their diagnostic interview. If their MINI outcome was major depression, they were informed of their group allocation, either collaborative care or usual care. The participant's GP was also sent a letter informing them that the named patient was eligible to take part in the CASPER plus trial owing to the major depression outcome of their diagnostic interview. It also specified which arm of the trial they had been randomised to.

Ineligible participants

All participants whose outcome was not major depression (either non-depressed or subthreshold) were sent a letter informing them that they were ineligible for the CASPER plus trial but that they would remain in the CASPER epidemiological cohort and continue to be followed up via questionnaires. Their GPs were also informed of this. This process of following up non-trial participants was discontinued once the original CASPER trial completed (see *Chapter 4*).

Trial interventions

Control group

Participants in the control group were allocated to receive usual GP care. They received no care additional to the usual primary care management of major depression offered by their GP in line with NICE depression guidance as implemented by their GP and local service provision.[7,8]

Intervention group

Participants in the intervention group were allocated to receive a low-intensity programme of collaborative care using behavioural activation, designed specifically for those aged ≥ 65 years with major depression.

TABLE 1 Symptoms of depression[a]

Key symptoms	Other symptoms
Depressed mood	Substantial changes in weight/appetite
Loss of interest	Change in sleep patterns
	Change in energy levels
	Movement slowing down or speeding up
	Feeling guilty or worthless
	Unable to make decisions
	Thinking of death or suicide

a Based on the *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition.[43]

Collaborative care was delivered by a case manager [a primary care mental health worker/Improving Access to Psychological Therapies (IAPT) worker] for an intended 8–10 weeks. This took place alongside participants' usual GP care. The defining feature of collaborative care is a collaboration of expertise to help support the participant. A case manager works alongside the participant, sharing any relevant information with the GP and a mental health specialist (psychiatrist or psychologist). The case manager is a cohesive link between the participant and other professionals involved in their care. For example, a case manager who deemed a participant's depressive symptoms to have deteriorated would pass this information on to the participant's GP, who would optimise the management of the patient's condition.

Collaborative care in the CASPER plus trial consisted of telephone support, symptom monitoring and active surveillance, facilitated by a computerised Patient Case-Management Information System (PC-MIS) [www.york.ac.uk/healthsciences/pc-mis (accessed 23 June 2016)] and low-intensity psychosocial management (behavioural activation). Participants randomised to the collaborative care intervention group were contacted by a case manager within 1 week of their randomisation to arrange their first collaborative care session. This was carried out face to face, usually at the participant's home unless an alternative venue was preferred. After this initial meeting, subsequent sessions were carried out on a, more or less, weekly basis by telephone unless the participant had sensory impairments or preferred face-to-face visits. Case managers worked collaboratively with the participants, liaising with GPs and other health professionals involved in their care to discuss issues relating to participants' mental and physical health, both during routine updates and when any concerns were identified. This included liaising with GPs as necessary to consider reviews of medication, which could relate to depression but also to comorbid physical health problems. It also included discussing with GPs referrals to other services, such as health services (e.g. pain clinics) or engagement with social services. Case managers worked with the participants to identify problems and agree goals for the intervention. They also worked with participants to identify, and subsequently provide, information about other services that may be useful, such as voluntary and statutory sector organisations and services.

Refinement of collaborative care/behavioural activation

The delivery of collaborative care and behavioural activation had been established in working-age adults for whom an appropriate training package and manual already existed.[28] However, these had not been tailored for use with older adults diagnosed with major depression. Before the study began, necessary changes were made to both the training package and manual (detailed in this section) to account for differences that may exist in the older adult population.

Training occurred over 2 days and involved a combination of brief lectures and role-play. Topics covered were the collaborative care approach as applied to older adults, medication management in older adults, behaviour theory and behavioural activation as adapted for older adults.

Adaptations to language and content

Adaptations were made to the information gathered at the initial assessment. Older adults are more likely to experience long-term health problems and a reduced level of functioning, with their psychological status often closely linked to their physical functioning.[45] Additional questions regarding health conditions and their impact were added to the standard assessment format. However, case managers were reminded to deliver a person-centred approach and not let preconceptions about the level of functioning of older adults influence their information gathering. Liaison with health professionals who were involved in treating the participant's long-term health conditions was encouraged to promote a depth of understanding of these issues. Depression in older adults is associated with impaired social support;[46] therefore, additional questions regarding social contacts and family were added. The risk assessment (see *Appendix 8*) was also adapted to enquire about past passive and past active suicide ideation as well as current plans and preparations, as past suicidality is a risk factor for current suicidal behaviour.[47]

Information in the manual was tailored to meet the needs of older adults. Age-appropriate examples were used, such as bereavement and loss of role, to facilitate engagement and make it easier to relate to.

The psychoeducation material given to participants was also modified to include information about depressive symptoms that occur specifically in older adulthood. As depression is associated with cognitive impairment in older people,[48] a larger font and increased space for writing was introduced. In addition, when individuals displayed mild cognitive impairment, simpler language was used and the number of steps in each session, along with the homework, was reduced. Questions were also added to help the case manager assess the participant's understanding of the treatment principles.

Functional equivalence and keeping well

Case managers were made aware of the importance of helping patients to identify functionally equivalent activities and a section was added to the Keeping Well Plan to prompt participants to identify functionally equivalent activities that may replace enjoyable or rewarding activities they were no longer able to undertake. Further details of the adaptations made can be found in Pasterfield *et al.*[49]

Participant follow-up

All participants in the CASPER plus trial were followed up with questionnaires at 4 months (see *Appendix 9*), 12 months (see *Appendix 10*) and 18 months (see *Appendix 11*). All post-randomisation questionnaires were posted to participants from the York Trials Unit along with a pre-addressed prepaid envelope. Participants could complete the questionnaires manually and return them by post to York Trials Unit or they could complete the questionnaire online; an instruction sheet explaining how to log on to the CASPER study site and complete the process was included with each questionnaire. Reminder letters were sent by post at 2 weeks to any participants who had not returned their questionnaire. Telephone follow-up by one of the study team's researchers was conducted for any participants who did not return the reminder questionnaire in order to complete the primary outcome measure (PHQ-9) at the very least.

Trial completion and exit

Participants were deemed to have exited the trial when they:

- withdrew consent (wished to exit the trial with no further contact for follow-up or objective data)
- had been in the trial for 18 months post randomisation
- had reached the end of the trial
- died
- moved general practice to one not participating in the CASPER study
- had another reason to exit according to clinical judgement from a health professional.

Withdrawals

Withdrawal could occur at any point during the study at the request of the participant. If a participant indicated that he or she wished to withdraw from the study, a researcher would speak to the participant to clarify to what extent they wished to withdraw: from the intervention, from the follow-up or from all aspects of the study. When withdrawal was only from the intervention, then follow-up data continued to be collected. Data were retained for all participants up to the date of withdrawal, unless they specifically requested for their details to be removed.

Objective data

Once the CASPER plus trial participants of a general practice had completed their follow-up, objective data were collected for each trial participant. Objective data consisted of details on each participant's prescribed medication and the number of contacts they had with their general practice during their time in the trial. The only exception was for those participants who had withdrawn in full, thereby withdrawing consent to access their medical records. Objective data were collected from general practices via request from the core study centre. A spreadsheet template was e-mailed to the key contact of each general practice that included the identification codes of each trial participant for the practice with prewritten frozen headings: there were no identifiable data. The search dates for each participant were also listed, from the date they

were randomised until either the date they completed the study 18 months later or the date that they had died, if that was the case. Data were still collected on participants who had withdrawn from treatment or follow-up, as they had provided us with consent to access their health records for the 18 months that they would have been in the study. The transfer of all objective data via e-mail was approved on the basis that no identifiable data were shared either with the general practice at the request stage or with the core study centre at the stage that objective data were returned.

Suicide protocol

A small but elevated risk of suicide and self-harm was inherent in the study population, all members of which had been identified as having major depression. All participants (both usual care and collaborative care) were subject to usual GP care and GPs were responsible for the day-to-day management of major depression. GPs were accountable for all treatment and management decisions including prescribing of medication, referral and assessment of risk. This arrangement was made clear to all clinicians and general practices that agreed to participate in the study. The pragmatic nature of the CASPER plus trial meant that we did not seek to influence this arrangement. However, we did follow good clinical practice by monitoring for suicide risk during all our encounters with participants. When a patient expressed a risk through thoughts of suicide or self-harm, we followed the study-specific procedure for suicide risk (see *Appendix 8*).

Patient and public involvement in research

The CASPER plus trial was informed by the involvement of users of mental health services and carers throughout the research period. An advisory group was established in the early stages of study. This consisted of a number of older adults, some of whom had mental health conditions, along with a carer representative. This group provided valuable insights into the relevance and readability of the study documentation. In the future, we plan to engage patient and public involvement in our dissemination strategies to guide on how best to share the findings.

Further studies

Following completion of the CASPER trial, the Self Help At Risk Depression (SHARD) substudy (not described in this report) was introduced to randomise participants identified with subthreshold depression to receive a self-help workbook or usual GP care. Results from the SHARD study will follow.

Clinical effectiveness

Primary outcome

The primary end point for the trial was patient-reported depression severity, as measured by the PHQ-9[33] at 4 months' follow-up. Each item is scored from 0 to 3; thus, PHQ-9 scores can range from 0 to 27, with higher scores indicating more severe depression. Total scores from 0 (non-depressed) to 27 (severely depressed) were calculated based on the nine PHQ-9 items. These data were collected via self-report on the follow-up questionnaires. Any participants who did not return a completed questionnaire were sent a reminder, and those participants who did not respond were telephoned by one of the study team's researchers to ask them to complete the PHQ-9 over the telephone. Missing items were replaced with the mean of the remaining items if one or two items were missing.

The PHQ-9 data were collected at baseline and randomisation (at the diagnostic interview), as well as at 4, 12 and 18 months' follow-up. Scores at baseline and randomisation are reported in *Chapter 5*, *Baseline characteristics*. When analyses were adjusted for initial PHQ-9 score, the score at randomisation was used. The primary end point for the CASPER plus trial was at 4 months' follow-up. At that point, treatment differences in the magnitude of a standard effect size of 0.35 were sought, which is of moderate size for psychological interventions and in line with collaborative care effects observed in other studies. Cohen[50] classifies a standard effect size of 0.3 as a small to medium effect size, and this is in line with NICE guidelines for depression, which adopts a similar grading of clinical significance. Four months was selected

as the primary end point, because it would occur soon after the end of the planned treatment but allow some additional time in the event that it was not possible to see participants on a weekly basis for practical reasons (e.g. holidays).

Secondary outcomes

The secondary outcome measures used were:

- depression severity and symptomatology at 12 and 18 months (PHQ-9)
- binary depression severity at 4, 12 and 18 months (PHQ-9), using scores of ≥ 10 to designate moderate depression caseness
- quality of life at 4, 12 and 18 months (SF-12 and EQ-5D-3L)
- psychological anxiety at 4, 12 and 18 months (GAD-7)
- mental health medication at 4, 12 and 18 months
- physical health problems at baseline, 4, 12 and 18 months (PHQ-15)
- psychological resilience at baseline, 4, 12 and 18 months (CD-RISC2)
- mortality at 4, 12 and 18 months.

Short Form questionnaire-12 items

The SF-12[34] is a generic health status measure and a short form of the Short Form questionnaire-36 items health survey. It consists of 12 questions measuring eight domains (physical, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health) rated over the past month. Questions have three or five response categories, and responses are summarised into a physical component summary (PCS) score and mental component summary (MCS) score. The PCS and MCS scores range from 0 (the lowest level of health) to 100 (the highest level of health) and were designed to have a mean score of 50 in a representative sample of the US population. Therefore, scores > 50 represent above average health status, and vice versa. The SF-6D was estimated from responses to the SF-12 questionnaire and provided health-state utilities to inform cost–utility analysis.

EuroQol-5 Dimensions, 3 levels

The EQ-5D-3L[35] is a standardised measure of current health status developed by the EuroQol Group for clinical and economic appraisal. The EQ-5D-3L consists of five questions each assessing a different quality-of-life dimension (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension is rated on three levels: no problems (score = 1), some problems (score = 2) and extreme problems (score = 3). A weighted summary index can be derived to give a score between 1 (perfect health) and 0 (death). For the purpose of the clinical effectiveness analysis, only scores of the individual dimensions were utilised. Health-state utilities (along with SF-6D) were estimated to potentially inform the cost–utility analysis; however, the SF-6D was ultimately found to be more sensitive to change in this cohort.

Generalised Anxiety Disorder-7 items scale

The GAD-7[36] is a brief measure of symptoms of anxiety based on diagnostic criteria described in *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition.[43] It consists of seven questions and is calculated by assigning scores of 0, 1, 2 and 3 to the response categories of 'not at all', 'several days', 'more than half the days' and 'nearly every day,' respectively. GAD-7 total score for the seven items ranges from 0 to 21. Scores of 5, 10 and 15 represent cut-off points for mild, moderate and severe anxiety, respectively.

Patient Health Questionnaire-15 items

The PHQ-15[37] is a 15-item physical health problems questionnaire. Each health issue is rated as 0 (not bothered), 1 (bothered a little) or 2 (bothered a lot). Items are added to form a scale from 0 to 30, higher scores indicating worse symptom severity. Scores of 5, 10 and 15 have been used as cut-off points for low, medium and high symptom severity. Item 4 of the PHQ-15 (menstrual problems) was deemed not relevant for the older CASPER patient population and omitted from all questionnaires. Therefore, the total possible PHQ-15 score was 28.

Connor–Davidson Resilience Scale two-items

The CD-RISC2[38] is a two-item short form of the full Connor–Davidson Resilience Scale-25 items. It is a psychological resilience measure with specific items for bounce-back from adversity and adaptability to change. Agreement with the two items is scored from 0 to 4, resulting in a total score of 0 to 8, where a higher score indicates greater resilience.

Mental health medication

Medication data were captured by self-report on the follow-up questionnaires. Participants indicated prescribed medication by selecting from a list of 10 antidepressants, as well as listing any other medications they were prescribed.

Mortality data

A data linkage service was established with the NHS Digital to provide regular updates from the Office for National Statistics (ONS) mortality data on any trial participants who had died while in the study. Members of the research team recorded any identified deaths, date and cause of death on the study management database.

Other collected patient questionnaire data

Adverse events

The CASPER plus study was not a Clinical Trial of an Investigational Medicinal Product and was, therefore, not subject to any additional restrictions. Decisions regarding prescription of medications were made by the participant in conjunction with their GP: participation in the study had no bearing on this process. Any participants who asked a member of the CASPER plus study team for an opinion on medication issues were strongly encouraged to seek advice from their GP.

The study recorded details of all serious adverse events (SAEs). Any judged to have been related to the study were required to be reported to the REC under the terms of the standard operating procedures for RECs.[51] In the context of the older adult population of the CASPER plus study, many of the SAEs were expected: unscheduled hospitalisations, life-threatening conditions, incapacitating illnesses and deaths. These were not perceived as unexpected events; therefore, they would be reported as SAEs only if they appeared to be related to an aspect of taking part in the study (e.g. participation in treatment, completion of follow-up questionnaires, participation in qualitative substudies or telephone contact).

When a SAE was identified, the trial manager was informed by e-mail using a participant's trial identification number, and not by any identifiable data. He or she then informed the chief investigator and two members of the Trial Management Group, who jointly decided if the event should be reported to the REC as a SAE. A SAE form was completed and a copy was filed securely at the core study centre. Any unexpected SAEs that were also judged to have been related should have been reported to the main REC within 15 days of the chief investigator becoming aware of the event. In the CASPER plus study, none of the SAEs were judged to have been related to the trial.

The occurrence of adverse events during the trial was monitored by an independent Data Monitoring Ethics Committee and the Trial Steering Committee. The Data Monitoring Ethics Committee/Trial Steering Committee would have seen immediately all SAEs thought to be treatment related.

Data collection schedule

An overview of the time points at which trial data were collected is presented in *Table 2*.

Statistical assumptions

Participants, care deliverers and the study team were not blinded to treatment allocation. However, allocations were concealed (group A and group B) for interim study reports, for example for the purpose of independent

TABLE 2 Data collection schedule

Data collected	Time point					
	Invitation	Baseline	Diagnostic interview/ randomisation	4 months' follow-up	12 months' follow-up	18 months' follow-up
Consent/decline	✓					
Demographics	✓					
Whooley questions	✓	✓				
Physical health problems	✓					
MINI major depressive module			✓			
PHQ-9		✓	✓	✓	✓	✓
SF-12		✓		✓	✓	✓
EQ-5D-3L		✓		✓	✓	✓
GAD-7		✓		✓	✓	✓
PHQ-15		✓		✓	✓	✓
CD-RISC2		✓		✓	✓	✓
Mental health medication		✓		✓	✓	✓
Mortality				✓	✓	✓
SAEs				✓	✓	✓

data monitoring reporting. The trial statistician who was responsible for the final statistical analysis was kept blind to group allocation until the primary analysis had been completed.

All analyses were conducted on intention-to-treat basis, using a two-sided statistical significance level of 0.05 unless otherwise stated. A full specification of the statistical analyses is documented in the CASPER plus statistical analysis plan (version 1.0). Any additional data assumptions for data, once received from the York Trials Unit data management team and the CASPER plus trial management team, for the purpose of this report, are documented separately.

Statistical analysis

Baseline characteristics

All participant baseline data (demographics from the background information form, outcome data from the baseline questionnaire, PHQ-9 and MINI responses from the diagnostic interview) were summarised descriptively by trial arm for all randomised participants and all participants included in the primary analysis.

The analysis population included all patients in their randomised groups with available outcome data (for the primary analysis: PHQ-9 score at 4, 12 or 18 months' follow-up) as well as complete baseline covariates specified for the analysis.

Primary analysis

Unadjusted descriptives of depression severity (PHQ-9) at all follow-up time points were presented. A covariance pattern linear mixed-effects model was used to compare collaborative care with usual care on PHQ-9 scores at 4 months. Effects of interest and baseline covariates were specified as fixed effects, and the correlation of observations within patients over time was modelled by a covariance structure to describe the random effects. The mixed model provided increased statistical power by utilising all patients with outcomes for at least one follow-up time point.

The outcome modelled was PHQ-9 at 4, 12 and 18 months. The model included time, trial arm and time-by-treatment interaction as fixed effects, adjusting for PHQ-9 score at randomisation and physical/functional limitations (as measured by the baseline SF-12 PCS score). Different covariance structures for the repeated measurements available in the analysis software were explored, and the most appropriate pattern was used for the final model based on the model Akaike information criterion. The primary end point was the estimate of the effect of the intervention at 4 months, which is presented with 95% confidence intervals (CIs) and associated *p*-values.

Secondary analyses

The primary analysis model was repeated (1) including case managers as a random effect to account for clustering within case managers, (2) including additional covariates predictive of PHQ-9 scores at 4 months as identified by univariate regressions, (3) including additional covariates predictive of non-response at 4 months as identified by univariate regressions and (4) using multiply imputed data. Results from the secondary analyses were compared with those from the primary analysis in order to ascertain the robustness of any observed treatment differences.

Secondary outcomes

Patient Health Questionnaire 9-items depression severity estimates at 12 and 18 months were extracted from the primary analysis model and presented with 95% CIs and associated *p*-value. A logistic mixed-effects model was used to compare PHQ-9 depression caseness (scores of ≥ 10), using the same covariates as the primary analysis. Odds ratios and 95% CIs are presented for the effect of the intervention at 4, 12 and 18 months. Analyses of other secondary outcomes were conducted using linear or logistic mixed models, depending on the outcome measure, adjusting for PHQ-9 score at randomisation and baseline SF-12 PCS score as well as the outcome measure at baseline. Treatment effects at each time point were reported. EQ-5D-3L responses were reported descriptively as part of the statistical analysis and analysed fully as part of the economic analysis. Frequencies of adverse events were reported descriptively by treatment arm, including breakdown by type and estimated relatedness to the intervention. The number of deaths occurring in the 18-month trial period was summarised by trial arm and overall. A chi-squared test was used to compare proportions between trial arms if more than five participants died in each arm.

Economic analysis

Economic analysis took the form of a cost-effectiveness analysis and, in line with NICE guidance,[52,53] adopted the perspective of the health and personal social services. The aim of the analysis was to estimate the value for money of providing collaborative care as compared with usual care. The time horizon for the analysis was 18 months from the date of randomisation; therefore, costs and quality-adjusted life-years (QALYs) were discounted at 3% for observations beyond 12 months. The analysis was conducted in Stata® version 13.1 (StataCorp LP, College Station, TX, USA).

Quality-adjusted life-years were estimated from responses to the SF-12 questionnaire to estimate SF-6D health state utilities.[54] This enables comparisons to be made across different health interventions and provides extra information for decision-makers. QALYs were estimated by measuring the area under the curve[55] that joins the baseline and follow-up SF-6D utility scores, which was derived from population-based values.

A base-case cost of collaborative care was estimated, based on the case manager training manual, which describes the treatment protocol (the manual is available from the authors on request). Over the full intended duration of the study (i.e. 18 months), participants' health-care resource use was collected to estimate total cost of health care during treatment and the follow-up period. Various methods of collecting resource use data were initially considered (e.g. self-report questionnaires and medical record checks). Objective data were obtained from general practices giving information on participants' (1) contacts with GPs (appointments, home visits or telephone consultations), (2) contacts with practice nurses (appointments

or telephone consultations) and (3) prescriptions (although we were unable to analyse these data owing to methodological challenges). Given the sample age (≥ 65 years), additional 'self-report questions' were not added in order to limit overall questionnaire burden. National unit costs applied to the quantities of resources utilised.[56]

For decision analysis, costs of the intervention, health-care use and changes in QALYs in the RCT will be combined to calculate the incremental cost-effectiveness ratio (ICER) using the following formula:

$$\text{ICER} = \frac{\Delta C}{\Delta E} = \frac{\bar{C}_{\text{I}} - \bar{C}_{\text{C}}}{\bar{E}_{\text{I}} - \bar{E}_{\text{C}}}, \quad (1)$$

where C is the costs and E is the effects (as QALYs) in the intervention (I) or control (C) arm.

To estimate the joint distributions of cost and QALYs, non-parametric bootstrapping was conducted on the observed data.[57] This non-parametric bootstrap resampling technique allows us to assess uncertainty in the ICER.[58] First, results of the bootstrapped cost and QALYs are presented on the cost-effectiveness plane. The confidence ellipse indicates the incremental costs and QALYs on the 50%, 75% and 95% CIs, indicating the probability space in the cost-effectiveness plane within which we are confident that the true ICER is found.

To further evaluate the joint distributions of costs and benefits, a cost-effectiveness acceptability curve (CEAC) is generated.[59] The CEAC summarises information on uncertainty in cost-effectiveness estimate and illustrates how the probability that collaborative care will be cost-effective as the willingness-to-pay of decision-makers increases. According to NICE, the willingness-to-pay threshold for an additional QALY ranges between £20,000 and £30,000; the CEAC indicates the probability that collaborative care is within this range.

Participants' take-up of collaborative care was recorded during sessions by case managers. This allowed deterministic sensitivity analysis of the potential variation in direct costs of intervention. Over the course of treatment, the case managers recorded information on the duration of the contact and how this took place for each contact with the participants. This information was used to adjust the expected cost of collaborative care when the patient, the case manager and supervisors agreed to deviation from the manualised intervention. The results were expressed on a CEAC and adjusted probabilities of falling within the NICE range of willingness to pay are presented.

Sensitivity analysis was performed to examine the implication to fidelity to intervention sessions and an ex post adjustment of the expected direct cost of collaborative care. The prescription of a programme of collaborative care is based on an assumption that all participants received the full course of treatment (i.e. 8–10 sessions) and this is an ex ante assumption underlying our base-case cost-effectiveness analysis.

Given that a service provider has intention to treat, the resources required to supply all of the intended sessions for collaborative care must be allocated and, therefore, the budget must include the total expected cost. However, after the allocation of a treatment package, individuals will have varying levels of fidelity to the programme and the expected direct cost of collaborative care may be adjusted when non-attendance of sessions is clearly documented.

All case managers were asked to log their activities with patients on PC-MIS (Patient Case Management Information System; www.york.ac.uk/healthsciences/pc-mis/; accessed 29 May 2016), which has been designed for IAPT. As collaborative care involves both assessment and treatment, demand may vary in relation to the specific levels of need of individuals. The number and duration of a participant's contact with the case manager was contemporaneously logged on PC-MIS. It was noted whether or not these occurred face to face or by telephone.

Chapter 4 Protocol changes

The following changes were made to the original protocol, after it was initially approved by the REC on 28 September 2010 and the substantial amendment (number 6 of the CASPER trial) to run CASPER plus was approved on 20 April 2012 (see www.ncbi.nlm.nih.gov/pubmed/25409776; accessed 7 June 2016).

CollAborative care for Screen-Positive ElderRs plus trial

In the original CASPER protocol, the objective was to evaluate the clinical effectiveness and cost-effectiveness of a collaborative care intervention for older adults with subthreshold depression. In order to broaden the reach of CASPER, the CASPER plus trial and qualitative substudy were introduced to run concurrently, using the same recruitment procedure, interventions and measures to evaluate an adapted intervention for case-level depression. A separate CASPER plus protocol and amended study documents were developed and approved on 20 April 2012.

Recruitment methods

Direct referral

In order to maximise recruitment in an often difficult to reach group, an additional method of recruitment was introduced. In addition to the original strategy of sending an invitation pack by post to all patients (aged ≥ 65 years) who were identified by computer search as eligible for invitation by the general practice, this was supplemented with direct GP referral at patient consultation. GPs from participating practices were given a number of patient invitation packs (identical to those currently sent by post) that could be handed to patients aged ≥ 65 years who may be consulting about depression and who did not meet the exclusion criteria.

Targeted search

In order to optimise the search strategy, there was a move from an all-inclusive approach to a more targeted approach. The targeted search strategy was developed to include only patients who had a diagnosis of depression or those who were prescribed depression medication and had other conditions associated with an increased risk of depression (e.g. depression, low mood, antidepressant medication, ischaemic heart disease, diabetes, chronic obstructive pulmonary disease, arthritis or being a carer). This was done using the aforementioned Read codes (a coded thesaurus of clinical terms that have been used in the NHS since 1985), the choice of which was left to the discretion of the participating general practice.

Follow-up

Eighteen-month follow-up questionnaire

An 18-month follow-up questionnaire was introduced to obtain longer-term outcomes.

Cohort

In the original protocol, it was stated that all participants who returned screening questionnaires would be followed up at 4 and 12 months via post or online. This included participants both in the RCT and those in the epidemiological cohort. On completion of the CASPER trial of subthreshold depression, this policy was discontinued in order to maximise recruitment and retention to the CASPER plus trial. For the remainder of the trial, only CASPER plus trial participants were followed up. All potential cohort participants who had consented but did not meet the criteria for major depression at diagnostic interview were not followed up.

Inclusion/exclusion criteria

In the original protocol participants were excluded owing to alcohol dependency, any known comorbidity that would, in the GP's opinion, make entry to the trial inadvisable (e.g. recent evidence of self-harm, known current thoughts of self-harm, significant cognitive impairment) and other factors that would make an invitation to participate in the trial inappropriate (e.g. recent bereavement, terminal malignancy) and/or because they were currently experiencing psychotic symptoms. During the trial there were several withdrawals from CASPER plus collaborative care condition as participants were already undergoing therapies and wished to continue with those therapies. Therefore, a screening question was added at the end of the diagnostic interview. This was not done at the invitation stage, to allow for people who had been referred to psychological services but had either not engaged with the service or who were still on a waiting list to participate in the study. People who answered 'yes' to this question did not proceed with the diagnostic interview and were excluded from the trial.

Recording of sessions

In the original protocol, there was no quality assurance procedure in place. In order to monitor and improve the quality of the collaborative care intervention delivered during the trial, a purposive sample of sessions was to be recorded. The sample was selected to reflect a range of backgrounds and experience of case managers. The allocation letter received by participants following randomisation was adapted from one that simply informed the participant that a case manager would be in touch shortly to a new letter that informed participants that we may wish to record some of their sessions with their case manager as a quality evaluation, stressing that the decision to agree to this was the participant's alone and would not affect the treatment that he or she would receive. They also received an additional participant information sheet and consent form regarding the audio-recording.

Telephone delivery

In the original protocol all collaborative care participants were seen for their first session face to face. In the final stages of recruitment it was necessary to enable initial contacts to also be delivered by telephone to ensure that all participants could begin their collaborative care programme without delay. Some IAPT services deal exclusively with their patients via the telephone and so this mix of contacts reflects current practice in IAPT.

Chapter 5 Clinical results

Recruitment and flow of participants through the trial

Recruitment and follow-up

Participants were randomised into the CASPER plus trial between September 2012 and August 2014 from four UK sites and their surrounding areas in the north of England: York, Leeds, Durham and Newcastle upon Tyne. A total of 74 general practices screened their practice lists and identified patients who met the initial inclusion criteria. Exclusion criteria consisted of any known alcohol dependency and/or psychotic symptoms as recorded on GP records, any known adverse comorbidities or any other factors that GPs deemed made it inadvisable to invite patients, such as recent bereavement.

A total of 64,214 patients were identified by GP practices between 5 May 2012 and 10 June 2014 and invited by letter to take part in the CASPER study. Of 10,686 patients who consented, 3224 patients were assessed for eligibility by diagnostic interview. Based on the diagnostic interview, 485 (15%) patients were identified to have a major depressive episode and were randomised into the CASPER plus trial. Of the 485 participants randomised, 249 were allocated to collaborative care and 236 to usual care. The remaining patients were classified as having either below threshold depression ($n = 1525$) or subthreshold depression ($n = 1214$). They became part of the epidemiological cohort or were entered into the CASPER or CASPER SHARD trials if within the recruitment window for these trials. The randomised number of 485 participants exceeded that of the planned sample size of 450. The flow of participants is illustrated in *Figure 1*.

Trial withdrawals

Participants were able to withdraw from the study at any point. They were offered the options of withdrawing from the intervention only, from questionnaire follow-up (allowing continued collection of objective data) or from all aspects of the study. Data up to the date of withdrawal were retained for all participants, unless they specifically requested for their details to be removed. This happened on one occasion. The total number of trial withdrawals by trial arm is given in *Table 3*. Participants could withdraw from only collaborative care treatment but remain in the trial for follow-up purposes. A total of 83 participants (33%) in the collaborative care arm withdrew from treatment at some point, and the numbers of full or partial withdrawals were greater in this arm ($n = 55$) than in the usual-care group ($n = 24$).

When reasons for withdrawal were provided by the participant, these were documented in the study management database. Following completion of the trial, reasons were grouped into common categories, and these are listed in *Tables 4–6* for the different types of follow-up.

The trial sample size calculation allowed for losses to follow-up of 20% at the primary end point at 4 months. The primary outcome (PHQ-9 depression severity) was available for 390 patients at that point, equating to an actual loss to follow-up of 19.6% (25.3% in the collaborative care arm and 13.6% in the usual-care arm).

The intervention: collaborative care

Collaborative care was offered to all patients in the intervention arm. A total of 21 case managers were trained to deliver the intervention, although only 12 delivered it in practice (a case load of 11.9 randomised patients per case manager). In practice, the intervention was delivered by 20 case managers (a case load of 10.4 patients who completed at least one session). Further details on the case load of each individual case manager are given as part of the practitioner analysis (see *Chapter 3*, *Secondary analyses*).

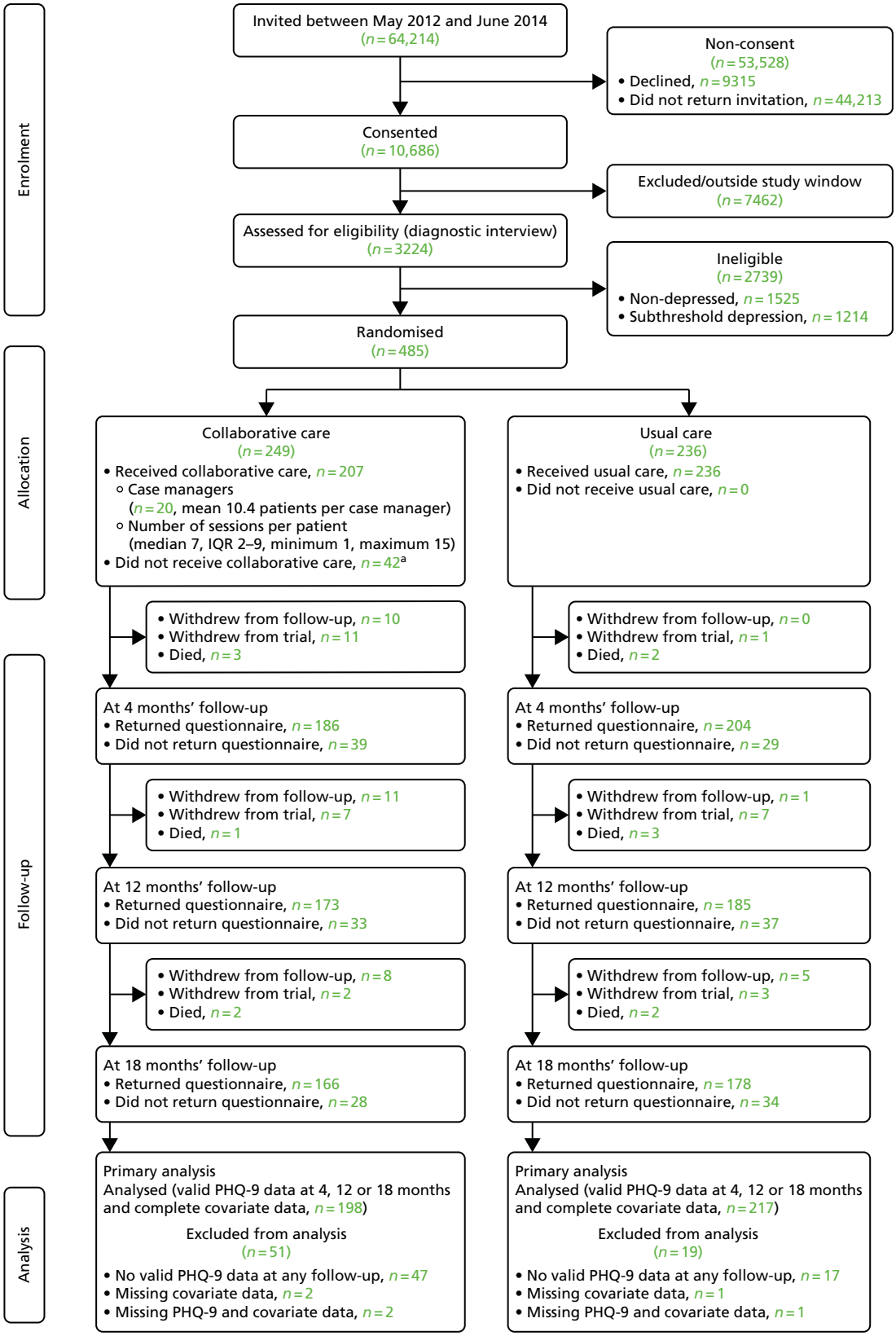

FIGURE 1 Consolidated Standards of Reporting Trials diagram. a, Reasons for not receiving collaborative care: Carer – no time (n=1), causing marital unrest ($n = 2$), cognitive impairment ($n = 1$), did not wish to engage ($n = 10$), died ($n = 2$), invasive ($n = 6$), lost interest ($n = 3$), not low in mood ($n = 1$), physical disability (poor hearing) ($n = 1$), physical ill health ($n = 8$), receiving other counselling ($n = 1$), too busy ($n = 2$), too severely depressed ($n = 1$) and unable to contact ($n = 3$). IQR, interquartile range.

TABLE 3 Participant withdrawal from follow-up or full withdrawal (by each time point)

	Trial arm			
	Collaborative care (*N* = 55 withdrawn)		Usual care (*N* = 24 withdrawn)	
Type of withdrawal	*n*	% of 249	*n*	% of 236
By 4 months' follow-up				
Withdrawal from follow-up	10	4.0	0	0.0
Full withdrawal	11	4.4	1	0.6
Died	3	1.2	2	1.1
By 12 months' follow-up				
Withdrawal from follow-up	21	8.4	1	0.4
Full withdrawal	18	7.2	8	3.4
Died	4	1.6	5	2.1
By 18 months' follow-up				
Withdrawal from follow-up	29	11.7	6	2.5
Full withdrawal	20	8.0	11	4.7
Died	6	2.4	7	3.0

TABLE 4 Reasons for withdrawal from treatment

	Trial arm			
	Collaborative care (*N* = 83 withdrawn)		Usual care (*N* = 0 withdrawn)	
Reason for withdrawal	*n*	%	*n*	%
Carer – no time	4	4.8	–	–
Causing marital unrest	3	3.6	–	–
Cognitive impairment	1	1.2	–	–
Did not wish to engage	23	27.7	–	–
Died	2	2.4	–	–
Does not need further support	2	2.4	–	–
Intervention not useful	1	1.2	–	–
Invasive	7	8.4	–	–
Lost interest	3	3.6	–	–
Not low in mood	5	6.0	–	–
Physical disability (poor hearing)	1	1.2	–	–
Physical ill health	13	15.7	–	–
Receiving other counselling	3	3.6	–	–
Too busy	5	6.0	–	–
Too severely depressed	1	1.2	–	–
Unable to contact	7	8.4	–	–
Unknown	2	2.4	–	–
Total	83	100.0	–	–

TABLE 5 Reasons for withdrawal from follow-up

	Trial arm			
	Collaborative care (*N* = 29 withdrawn)		Usual care (*N* = 6 withdrawn)	
Reason for withdrawal	*n*	%	*n*	%
Carer – no time	1	3.5	0	0.0
Did not wish to engage	1	3.5	0	0.0
Invasive	3	10.3	0	0.0
Lost interest	14	48.3	1	16.7
Moved out of area	1	3.5	2	33.3
Physical disability (poor sight)	1	3.5	1	16.7
Physical ill health	4	13.8	0	0.0
Suffered recent bereavement	1	3.5	0	0.0
Too busy	2	6.9	1	16.7
Too much effort	0	0.0	1	16.7
Too severely depressed	1	3.5	0	0.0
Total	29	100.0	6	100.0

TABLE 6 Reasons for full withdrawal

	Trial arm			
	Collaborative care (*N* = 20 withdrawn)		Usual care (*N* = 11 withdrawn)	
Reason for withdrawal	*n*	%	*n*	%
Carer – no time	0	0.0	1	9.1
Cognitive impairment	1	5.0	1	9.1
Did not wish to engage	5	25.0	0	0.0
Does not need further support	1	5.0	0	0.0
Invasive	2	10.0	3	27.3
Lost interest	2	10.0	2	18.2
Moved out of area	2	10.0	2	18.2
Physical ill health	4	20.0	1	9.1
Too much effort	1	5.0	0	0.0
Unable to contact	1	5.0	1	9.1
Unknown	1	5.0	0	0.0
Total	20	100.0	11	100.0

An overview of received treatments is provided in the Consolidated Standards of Reporting Trials diagram in *Figure 1* and further details are presented in *Tables 7* and *8*. Of 249 randomised patients, 83% had at least one collaborative care session. Participants received on average six sessions over 8–9 weeks, of which, on average, one was delivered face to face and five were delivered over the telephone. The average session duration was 37 minutes. The most frequent reasons for not wanting to receive any collaborative care were not wishing to engage, physical ill health and invasiveness (*Table 9*).

TABLE 7 Collaborative care received

	Patients randomised to collaborative care (*N* = 249)	
Collaborative care status	*n*	%
Did not start treatment	42	16.9
Started treatment	207	83.1

TABLE 8 Average characteristics of collaborative care

	Patients who received some collaborative care (*N* = 207)					
Collaborative care details	*n*	Mean	SD	Median	Minimum	Maximum
Days from referral to first session	207	34.4	25.5	27	7	220
Number of sessions received	207	6.0	3.48	7	1	15
Face to face	207	1.3	1.44	1	0	11
Telephone	207	4.8	3.37	5	0	11
Average length of session (minutes)	207	36.7	8.24	37	0	62
Days from first to last session	207	62.0	50.38	58	0	333

SD, standard deviation.

TABLE 9 Reasons for not receiving any collaborative care

	Patients who received no collaborative care (*N* = 42)	
Reason	*n*	%
Carer – no time	1	2.4
Causing marital unrest	2	4.8
Cognitive impairment	1	2.4
Did not wish to engage	10	23.8
Invasive	6	14.3
Lost interest	3	7.1
Not low in mood	1	2.4
Physical disability (poor hearing)	1	2.4
Physical ill health	8	19.1
Receiving other counselling	1	2.4
Too busy	2	4.8
Too severely depressed	1	2.4
Unable to contact	3	7.1
Died	2	4.8

Baseline characteristics

Characteristics at consent, baseline and diagnostic interview (point of randomisation) for randomised participants and participants included in the primary analysis ('as analysed' population: patients with a valid PHQ-9 score at 4, 12 or 18 months' follow-up) and valid covariate data (PHQ-9 score at randomisation and baseline SF-12 PCS score) are presented in *Tables 10–12*.

TABLE 10 Baseline characteristics (demographics and general health at consent)

Characteristic	As randomised		As analysed[a]	
	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Collaborative care (*N* = 198)	Usual care (*N* = 217)
Age at consent (years)				
n	248	236	198	217
Mean (SD)	72.5 (6.57)	71.8 (6.07)	71.9 (6.03)	71.6 (5.96)
Median (minimum, maximum)	71 (64, 98)	70 (65, 92)	70 (64, 88)	70 (65, 92)
Sex, *n* (%)				
Male	98 (39.4)	85 (36.0)	81 (40.9)	80 (36.9)
Female	150 (60.2)	151 (64.0)	117 (59.1)	137 (63.1)
Educated past 16 years of age, *n* (%)	108 (43.4)	101 (42.8)	88 (44.4)	95 (43.8)
Degree or equivalent professional qualification	57 (22.9)	68 (28.8)	44 (22.2)	62 (28.6)
Smoking (yes), *n* (%)	30 (12.0)	28 (11.9)	25 (12.6)	27 (12.4)
Three or more alcohol units/day, *n* (%)	31 (12.4)	26 (11.0)	23 (11.6)	23 (10.6)
Ethnicity, *n* (%)				
White	241 (96.8)	233 (98.7)	193 (97.5)	215 (99.1)
Asian or Asian British	1 (0.4)	0 (0)	1 (0.5)	0 (0)
Black or black British	1 (0.4)	0 (0)	1 (0.5)	0 (0)
Other	3 (1.2)	2 (0.8)	3 (1.5)	2 (0.9)
Health problems, *n* (%)				
Diabetes	59 (23.7)	47 (19.9)	49 (24.7)	42 (19.4)
Osteoporosis	36 (14.5)	25 (10.6)	28 (14.1)	22 (10.1)
High blood pressure	120 (48.2)	111 (47.0)	96 (48.5)	103 (47.5)
Rheumatoid arthritis	50 (20.1)	36 (15.3)	38 (19.2)	31 (14.3)
Osteoarthritis	81 (32.5)	75 (31.8)	60 (30.3)	71 (32.7)
Stroke	21 (8.4)	22 (9.3)	18 (9.1)	18 (8.3)
Cancer	31 (12.4)	21 (8.9)	23 (11.3)	20 (9.2)
Respiratory conditions	71 (28.5)	68 (28.8)	52 (26.3)	64 (29.5)
Eye condition	84 (33.7)	67 (28.4)	64 (32.3)	62 (28.6)
Heart disease	55 (22.1)	71 (30.1)	42 (21.2)	64 (29.5)
Other	63 (25.3)	50 (21.2)	54 (27.3)	47 (21.7)

TABLE 10 Baseline characteristics (demographics and general health at consent) (*continued*)

Characteristic	As randomised		As analysed[a]	
	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Collaborative care (*N* = 198)	Usual care (*N* = 217)
Whooley: Over the past month have you been bothered by feeling down, depressed or hopeless?, *n* (%)				
Yes	227 (91.2)	202 (85.6)	178 (89.9)	186 (85.7)
No	21 (8.4)	34 (14.4)	20 (10.1)	31 (14.3)
Whooley: Over the past month have you been bothered by having little or no interest or pleasure in doing things?, *n* (%)				
Yes	210 (84.3)	186 (78.8)	164 (82.8)	171 (78.8)
No	38 (15.3)	50 (21.2)	34 (17.2)	46 (21.2)

SD, standard deviation.
a All patients who were included in the primary analysis, that is patients with a valid PHQ-9 score at 4, 12 or 18 months' follow-up and valid covariate data (PHQ-9 score at randomisation and baseline SF-12 PCS score).

TABLE 11 Baseline characteristics (outcomes at baseline)

Characteristic	As randomised		As analysed[a]	
	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Collaborative care (*N* = 198)	Usual care (*N* = 217)
PHQ-9				
n	248	236	198	217
Mean score (SD)	12.4 (5.43)	12.1 (5.31)	12.3 (5.43)	12.0 (5.32)
Median score (minimum, maximum)	12 (0, 27)	12 (1, 27)	12 (0, 27)	12 (1, 27)
PHQ-9 grouping,* n *(%)				
No depression	19 (7.6)	15 (6.4)	16 (8.1)	15 (6.9)
Mild depression	64 (25.7)	64 (27.1)	52 (26.3)	59 (27.2)
Moderate depression	79 (31.7)	85 (36.0)	61 (30.8)	77 (35.5)
Moderately severe depression	67 (26.9)	51 (21.6)	53 (26.8)	47 (21.7)
Severe depression	19 (7.6)	21 (8.9)	16 (8.1)	19 (8.8)
PHQ-15				
n	246	234	196	215
Mean score (SD)	12.3 (4.51)	11.9 (4.33)	12.0 (4.46)	11.9 (4.36)
Median score (minimum, maximum)	12 (2, 26)	11 (2, 24)	12 (2, 24)	11 (2, 24)
SF-12 (PCS)				
n	245	234	198	217
Mean score (SD)	35.6 (13.08)	36.8 (13.32)	36.1 (13.16)	36.6 (13.39)
Median score (minimum, maximum)	34.5 (7.1, 66.3)	35.8 (5.9, 69.6)	34.9 (7.1, 66.3)	38.8 (5.9, 69.6)
SF-12 (MCS)				
n	245	234	198	217
Mean score (SD)	35.4 (9.51)	35.7 (10.53)	35.5 (9.66)	36.0 (10.52)
Median score (minimum, maximum)	35.8 (10.3, 60.2)	36.2 (2.2, 62.9)	35.9 (10.3, 60.2)	36.4 (2.2, 62.9)

continued

TABLE 11 Baseline characteristics (outcomes at baseline) (*continued*)

Characteristic	As randomised		As analysed[a]	
	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Collaborative care (*N* = 198)	Usual care (*N* = 217)
GAD-7				
n	247	234	197	215
Mean score (SD)	9.4 (5.03)	9.3 (4.92)	9.4 (5.12)	9.2 (4.95)
Median score (minimum, maximum)	9 (0, 21)	9 (0, 21)	9 (0, 21)	9 (0, 21)
EQ-5D-3L,* n *(%)				
Mobility				
No problems	71 (28.5)	76 (32.2)	61 (30.8)	70 (32.3)
Some problems	176 (70.7)	157 (66.5)	136 (68.7)	144 (66.4)
Confined to bed	0 (0.0)	2 (0.8)	0 (0.0)	2 (0.9)
Self-care				
No problems	163 (65.5)	175 (74.2)	134 (67.7)	160 (73.7)
Some problems	75 (30.1)	55 (23.3)	58 (29.3)	52 (24.0)
Unable to wash/dress	5 (2.0)	4 (1.7)	2 (1.0)	3 (1.4)
Usual activities				
No problems	64 (25.7)	66 (28.0)	52 (26.3)	62 (28.6)
Some problems	159 (63.9)	151 (64.0)	131 (66.2)	138 (63.6)
Unable to perform	24 (9.6)	18 (7.6)	14 (7.1)	16 (7.4)
Pain/discomfort				
No pain	34 (13.7)	27 (11.4)	30 (15.2)	24 (11.1)
Moderate pain	156 (62.7)	152 (64.4)	129 (65.2)	140 (64.5)
Extreme pain	57 (22.9)	54 (22.9)	38 (19.2)	50 (23.0)
Anxiety/depression				
Not anxious/depressed	26 (10.4)	25 (10.6)	21 (10.6)	25 (11.5)
Moderately anxiety/depression	176 (70.7)	178 (75.4)	141 (71.2)	161 (74.2)
Extremely anxiety/depression	44 (17.7)	31 (13.1)	34 (17.2)	29 (13.4)
Prescribed antidepressants	82 (32.9)	79 (33.5)	67 (33.8)	77 (35.5)
Whooley: Over the past month have you been bothered by feeling down, depressed or hopeless?,* n *(%)				
Yes	238 (95.6)	219 (92.8)	190 (96.0)	201 (92.6)
No	10 (4.0)	17 (7.2)	8 (4.0)	16 (7.4)
Whooley: Over the past month have you been bothered by having little or no interest or pleasure in doing things?,* n *(%)				
Yes	220 (88.4)	210 (89.0)	177 (89.4)	195 (89.9)
No	28 (11.2)	26 (11.0)	21 (10.6)	22 (10.1)

SD, standard deviation.

a All patients who were included in the primary analysis, that is patients with a valid PHQ-9 score at 4, 12 or 18 months' follow-up and valid covariate data (PHQ-9 score at randomisation and baseline SF-12 PCS score).

TABLE 12 Baseline characteristics (outcomes at diagnostic interview/randomisation)

Characteristic	As randomised		As analysed[a]	
	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Collaborative care (*N* = 198)	Usual care (*N* = 217)
PHQ-9				
N	248	236	198	217
Mean score (SD)	14.0 (5.37)	14.0 (4.93)	13.9 (5.42)	13.9 (4.80)
Median score (minimum, maximum)	14 (3, 27)	14 (4, 27)	14 (3, 26)	14 (4, 27)
PHQ-9 grouping, *n* (%)				
No depression	2 (0.8)	4 (1.7)	1 (0.5)	4 (1.8)
Mild depression	60 (24.1)	46 (19.5)	51 (25.8)	41 (18.9)
Moderate depression	77 (30.9)	77 (32.6)	57 (28.8)	73 (33.6)
Moderately severe depression	69 (27.7)	76 (32.2)	57 (28.8)	73 (33.6)
Severe depression	40 (16.1)	33 (14.0)	32 (16.2)	26 (12.0)
From MINI: Were you *ever* depressed or down, most of the day, nearly every day for 2 weeks?, *n* (%)				
Yes	213 (85.5)	207 (87.7)	170 (85.9)	191 (88.0)
No	35 (14.1)	29 (12.3)	28 (14.1)	26 (12.0)
From MINI: For the *past 2 weeks*, were you depressed or down, most of the day, nearly every day?, *n* (%)				
Yes	182 (73.1)	172 (72.9)	141 (71.2)	157 (72.4)
No	31 (12.4)	35 (14.8)	29 (14.6)	34 (15.7)
From MINI: Were you *ever* much less interested in most things or much less able to enjoy things you used to enjoy most of the time for 2 weeks?, *n* (%)				
Yes	234 (94.0)	218 (92.4)	190 (96.0)	202 (93.1)
No	14 (5.6)	18 (7.6)	8 (4.0)	15 (16.9)
From MINI: In the *past 2 weeks*, were you much less interested in most things or much less able to enjoy the things you used to enjoy, most of the time?, *n* (%)				
Yes	214 (85.9)	205 (86.9)	178 (89.9)	190 (87.6)
No	20 (8.0)	13 (5.5)	12 (6.1)	12 (5.5)

SD, standard deviation.
a All patients who were included in the primary analysis, that is patients with a valid PHQ-9 score at 4, 12 or 18 months' follow-up and valid covariate data (PHQ-9 score at randomisation and baseline SF-12 PCS score).

Primary outcome

Near-complete PHQ-9 responses were available for participants at diagnostic interview (one participant asked for all data to be destroyed at the point of withdrawal). At follow-up, 300 patients (62%) had valid PHQ-9 scores at all three follow-up times, 118 patients (24%) had a valid PHQ-9 score at 4 months or 12 months only, and for 67 patients (14%) no PHQ-9 scores were available at 18 months' follow-up.

Score distribution

Figure 2 illustrates the distribution of PHQ-9 scores for each trial arm over time. At randomisation, scores were distributed approximately normal with a slight right skew, which became more pronounced over the follow-up period, as patients in both arms improved.

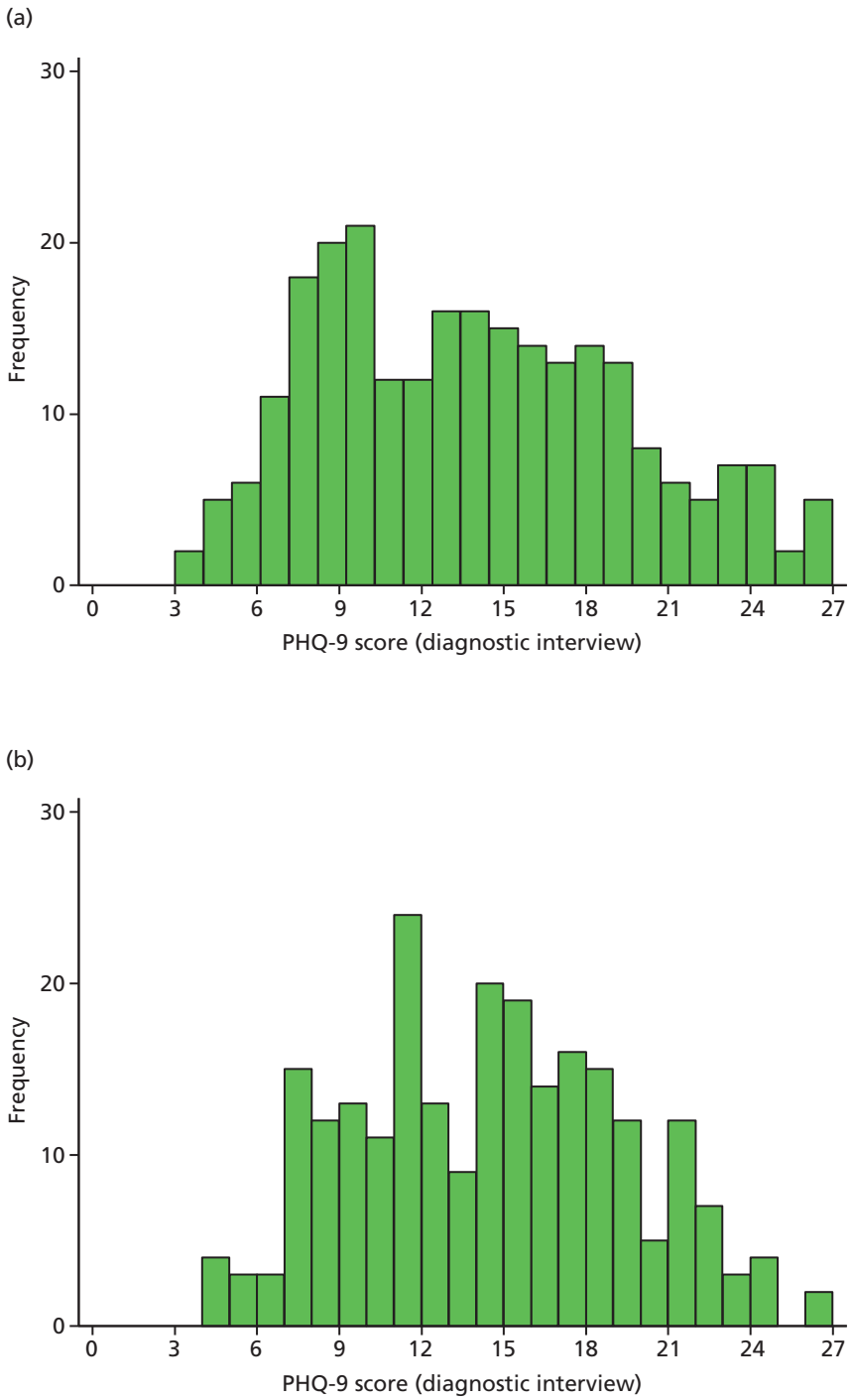

FIGURE 2 Distribution of PHQ-9 scores by trial arm. (a) Randomisation, collaborative care; (b) randomisation, usual care; (c) 4 months' follow-up, collaborative care; (d) 4 months' follow-up, usual care; (e) 12 months' follow-up, collaborative care; (f) 12 months' follow-up, usual care; (g) 18 months' follow-up, collaborative care; and (h) 18 months' follow-up, usual care. (*continued*)

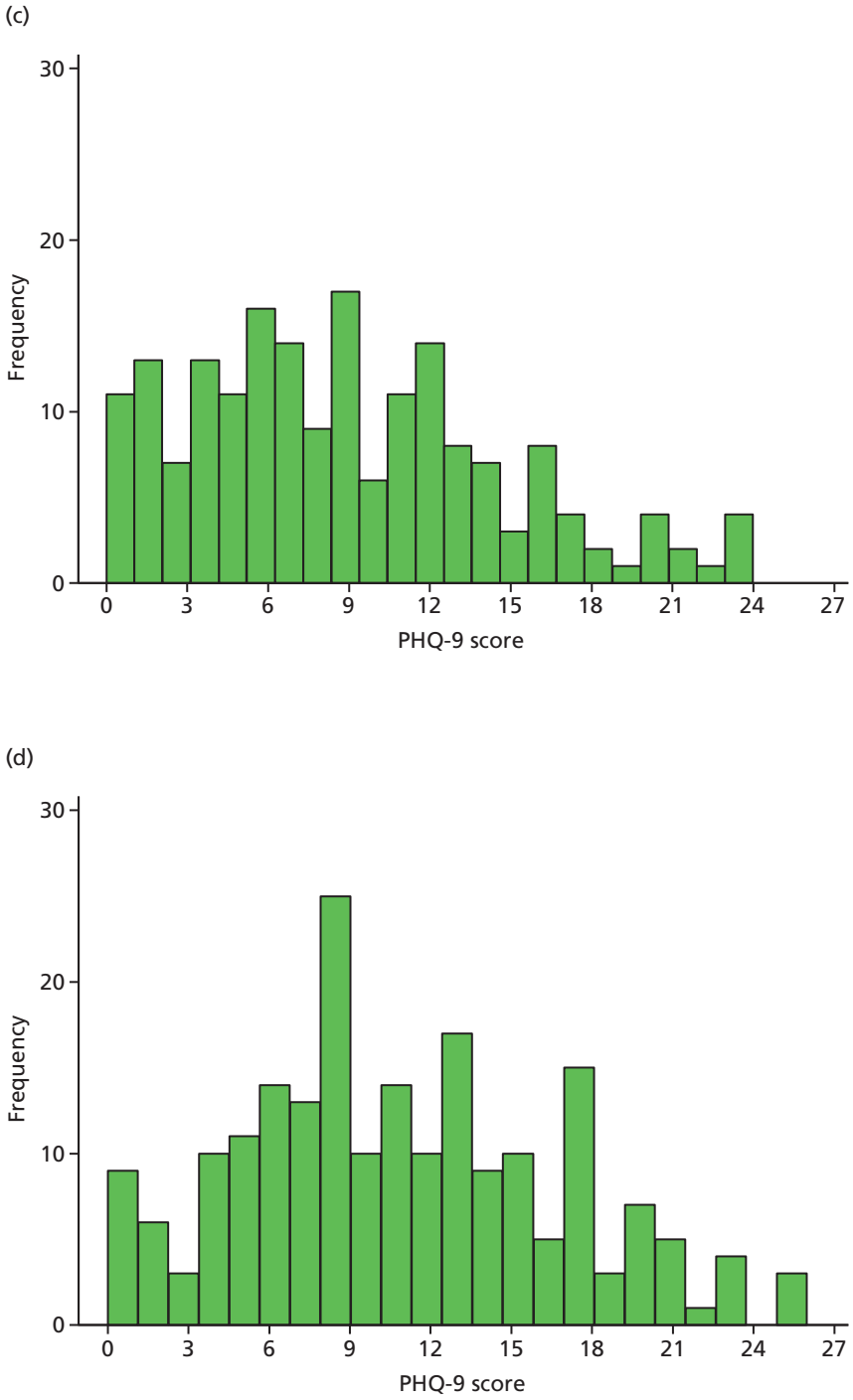

FIGURE 2 Distribution of PHQ-9 scores by trial arm. (a) Randomisation, collaborative care; (b) randomisation, usual care; (c) 4 months' follow-up, collaborative care; (d) 4 months' follow-up, usual care; (e) 12 months' follow-up, collaborative care; (f) 12 months' follow-up, usual care; (g) 18 months' follow-up, collaborative care; and (h) 18 months' follow-up, usual care. (*continued*)

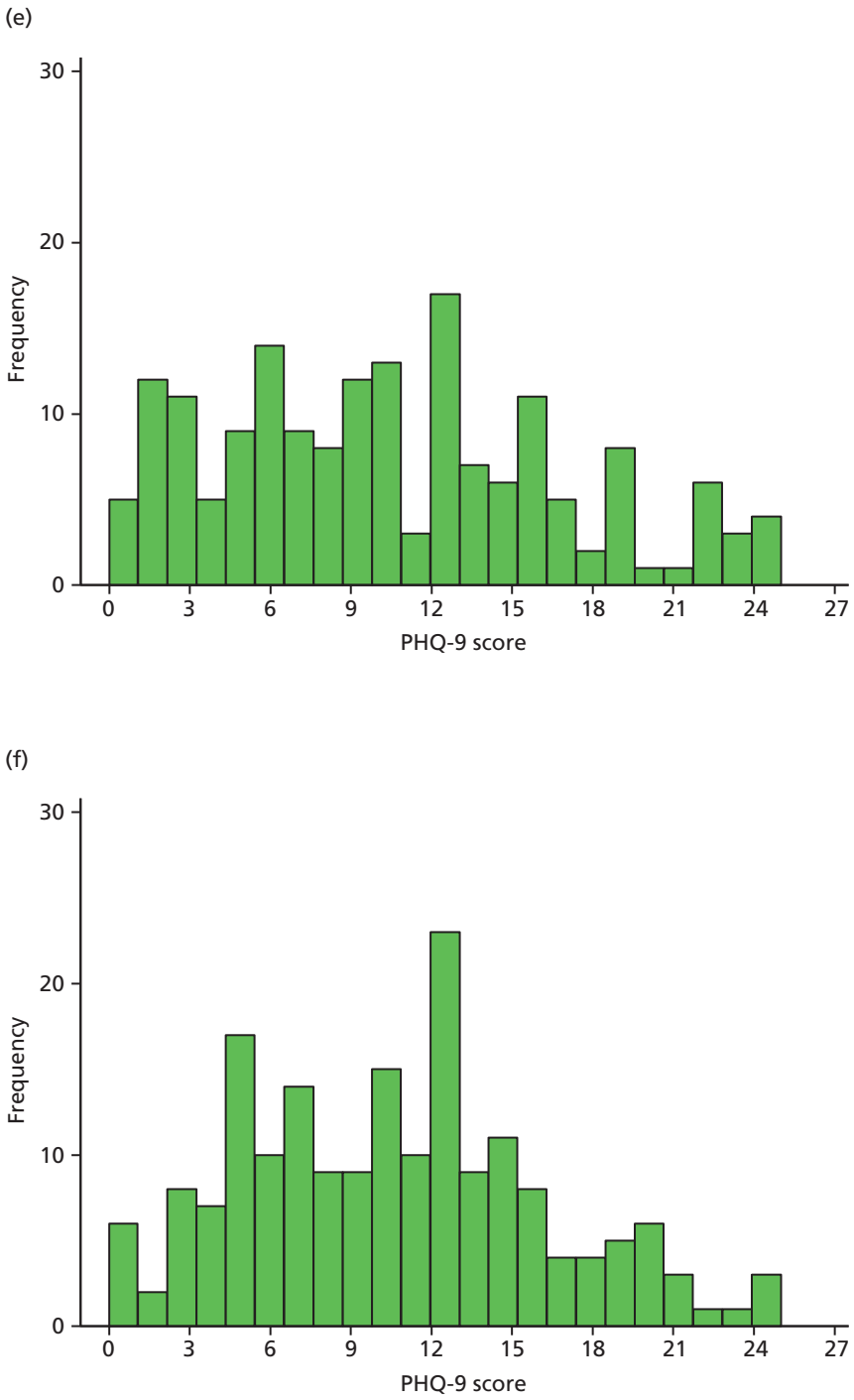

FIGURE 2 Distribution of PHQ-9 scores by trial arm. (a) Randomisation, collaborative care; (b) randomisation, usual care; (c) 4 months' follow-up, collaborative care; (d) 4 months' follow-up, usual care; (e) 12 months' follow-up, collaborative care; (f) 12 months' follow-up, usual care; (g) 18 months' follow-up, collaborative care; and (h) 18 months' follow-up, usual care. (*continued*)

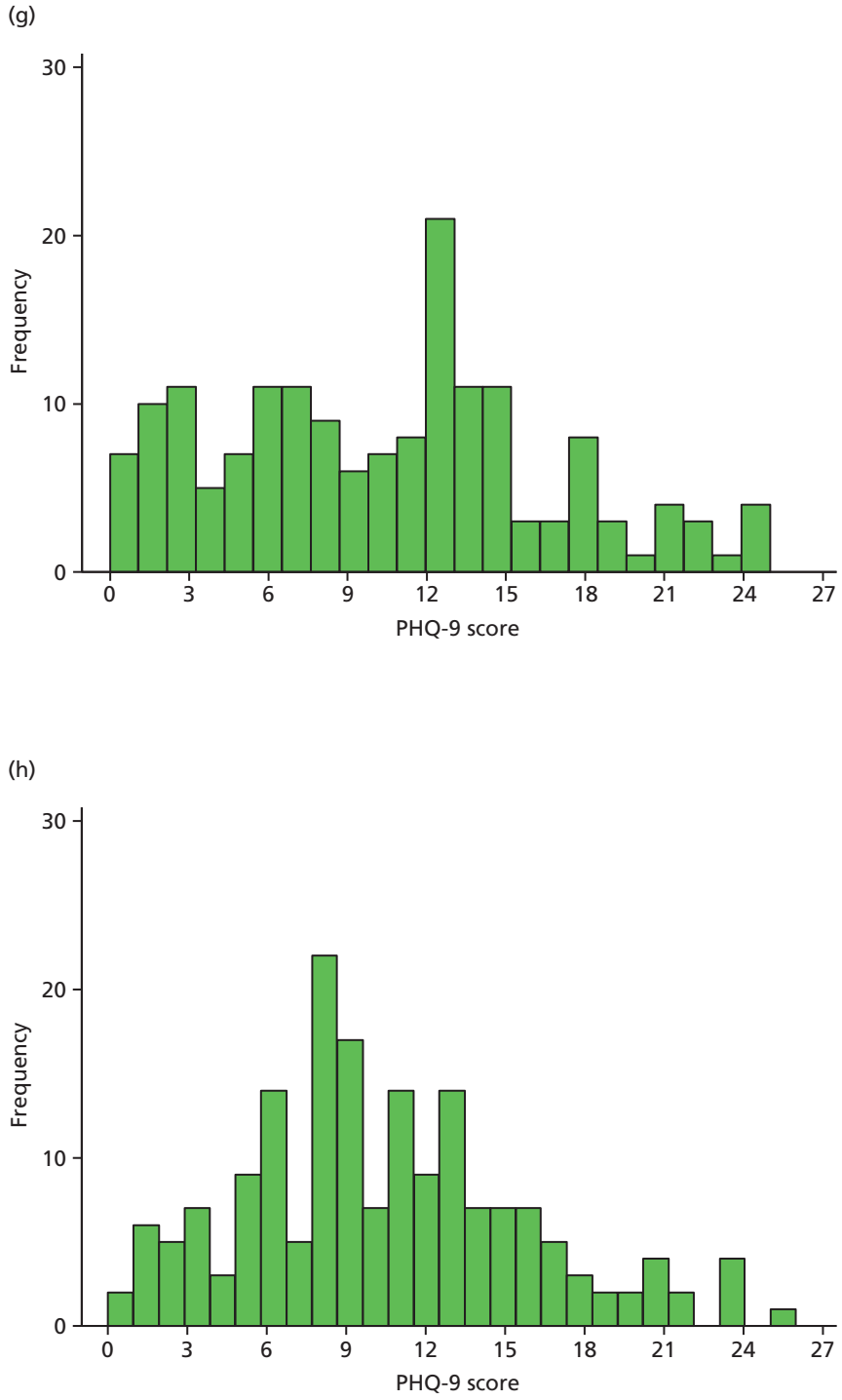

FIGURE 2 Distribution of PHQ-9 scores by trial arm. (a) Randomisation, collaborative care; (b) randomisation, usual care; (c) 4 months' follow-up, collaborative care; (d) 4 months' follow-up, usual care; (e) 12 months' follow-up, collaborative care; (f) 12 months' follow-up, usual care; (g) 18 months' follow-up, collaborative care; and (h) 18 months' follow-up, usual care.

Unadjusted summary statistics

Summary statistics of the raw PHQ-9 scores are given in *Table 13* and are illustrated in *Figure 3*. Average depression severity, as measured by the PHQ-9, was around 14 score points at randomisation. Scores in both treatment arms improved between randomisation and 4 months' follow-up, but to a greater extent in the collaborative care group (to a score of around 9) than in the usual-care group (to a score of around 11). By 12 and 18 months' follow-up, average depression scores continued to improve slightly in the usual-care group, whereas scores in the collaborative care group increased again to similar levels.

TABLE 13 Unadjusted PHQ-9 descriptive statistics

	Trial arm		
Time	Collaborative care ($N = 249$)	Usual care ($N = 236$)	Total ($N = 485$)
Randomisation, *n* (%)	248 (99.6)	236 (100)	484 (99.8)
Mean (SD)	14.0 (5.37)	14.0 (4.93)	14.0 (5.15)
Median (minimum, maximum)	14 (3, 27)	14 (4, 27)	14 (3, 27)
4 months, *n* (%)	186 (75)	204 (86)	390 (80)
Mean (SD)	8.9 (5.53)	10.9 (5.89)	9.9 (5.79)
Median (minimum, maximum)	8 (0, 24)	11 (0, 26)	9 (0, 26)
12 months, *n* (%)	172 (69)	185 (78)	357 (74)
Mean (SD)	10.4 (6.25)	10.6 (5.52)	10.5 (5.87)
Median (minimum, maximum)	10 (0, 25)	10 (0, 25)	10 (0, 25)
18 months, *n* (%)	165 (66)	178 (75)	343 (71)
Mean (SD)	10.4 (6.09)	10.3 (5.50)	10.4 (5.79)
Median (minimum, maximum)	10 (0, 25)	9 (0, 26)	10 (0, 26)

SD, standard deviation.

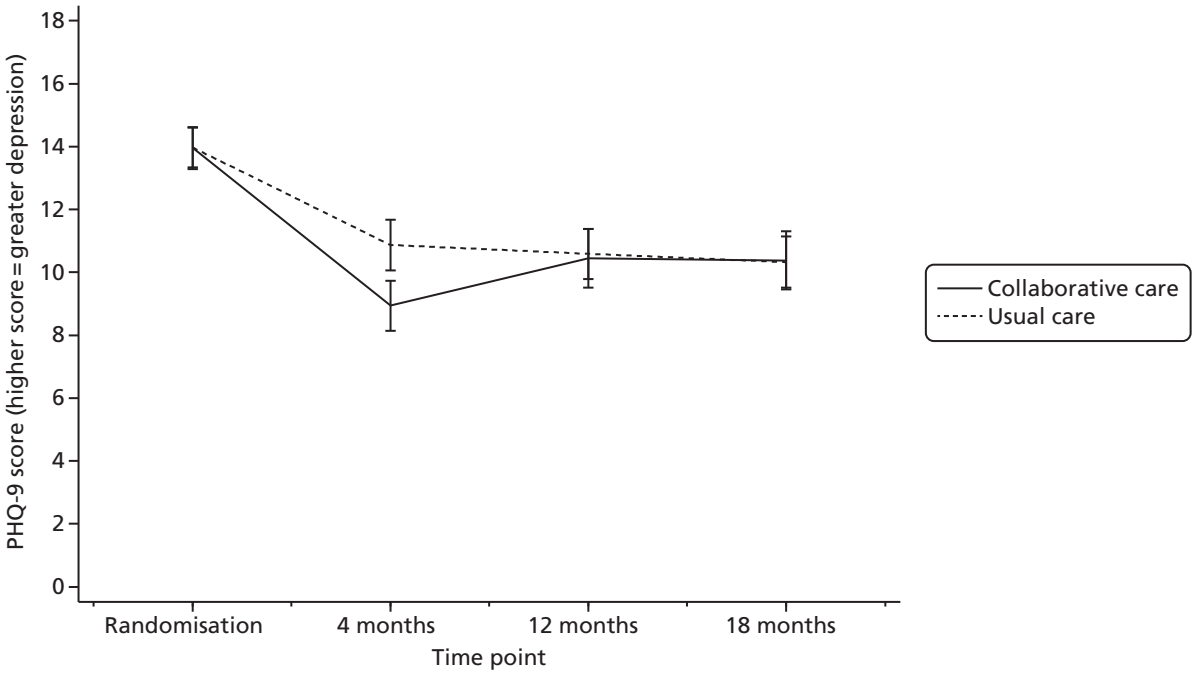

FIGURE 3 Unadjusted mean PHQ-9 scores (with 95% CIs).

Primary analysis

The primary outcome was analysed by a covariance pattern linear mixed model using PHQ-9 score at 4 and 12 months as the outcome. The model included as fixed effects: time, trial arm and time-by-treatment interaction, adjusting for PHQ-9 depression at randomisation and physical/functional limitations as measured by the baseline SF-12 PCS score. Patients were included in the analysis if they had a valid PHQ-9 score at 4, 12 or 18 months' follow-up and complete covariate data. Patients were analysed as part of the group to which they had been randomised (intention to treat).

The correlation of observations within patients over time was modelled by a covariance structure to describe the random effects. Different types of available covariance structures were investigated for this model (unstructured, independent, exchangeable, autoregressive and exponential). The exchangeable covariance structure (estimating one covariance parameter to model the relatedness between any two time points) displayed the lowest and therefore best-fitting log likelihood values, and was not significantly worse fitting than the full-parameter unstructured model when compared using the chi-squared test. Therefore, the exchangeable covariance pattern was selected.

Diagnostics of model fit showed an acceptable distribution of standard residuals with a small number of outliers at the higher end of the distribution. There was uniform variance between predicted and actual residuals, and no transformation of PHQ-9 scores was carried out for the analysis.

Adjusted PHQ-9 score means and group differences for the primary analysis model as specified above are presented in *Table 14*. The analysis revealed significant differences between trial arms at each 4 months' follow-up in favour of collaborative care, but not at 12 or 18 months' follow-up: 1.92 score points (95% CI 0.85 to 2.99 score points; $p < 0.001$) for the primary end point at 4 months; 0.19 score points (95% CI –0.92 to 1.29 score points; $p = 0.741$) at 12 months and 0.002 score points (95% CI –1.12 to 1.12 score points; $p = 0.997$) at 18 months. Using the overall residual standard deviation (SD, 5.72), the score difference at 4 months equates to a standard effect size of 0.34 (the trial was powered for a standard effect size of 0.35).

Secondary outcomes analyses

Adjusting for clustering by case manager

It was expected in the planning and sample size calculation for this trial that collaborative care case managers would work with an average case load of 20 patients, and the clustering of outcomes within case managers was expected to be described by an ICC of 0.02. In total, there were 20 case managers (four in York, four in Leeds, 10 in Durham and two in Newcastle upon Tyne) for a total of 246 participants in the collaborative care arm, that is, an average case load of 12.3 randomised patients per case manager.

TABLE 14 Group difference in mean PHQ-9 score: primary analysis

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months[a]	198	8.98	8.20 to 9.75	217	10.90	10.16 to 11.64	1.92	0.85 to 2.99	< 0.001
12 months	198	10.44	9.65 to 11.24	217	10.63	9.87 to 11.40	0.19	–0.92 to 1.29	0.741
18 months	198	10.53	9.72 to 11.34	217	10.53	9.76 to 11.31	0.002	–1.12 to 1.12	0.997

a Primary end point.
Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation and baseline SF-12 PCS score.

Case loads varied considerably between 1 and 46 patients. Three patients withdrew before they were assigned a case manager.

The average ICC for clustering within case managers was found to negligible: ICC ≤ 0.0001 (95% CI 0 to 0.0757) for PHQ-9 scores at 4 months.

In order to quantify the impact of the grouping by case managers with respect to the primary outcome, case manager identifiers were included as a random effect in the primary linear mixed-analysis model, nested within treatment arm. Participants in the usual-care arm were coded as their own case managers for the purpose of analysis, and the covariance structure was estimated separately for each treatment arm in order to account for the differences in variability for the random effect.

Adjusted PHQ-9 score means and group differences for this analysis are given in *Table 15*. Group differences remained significant in favour of collaborative care at 4 months' follow-up (a difference of 1.92 PHQ-9 score points), and outcomes did not significantly differ between groups at 12 or 18 months. Thus, accounting for the clustering by case manager did not affect the size of the treatment effect compared with the primary analysis.

Adjusting for covariates predictive of Patient Health Questionnaire 9-items at 4 months

The primary analysis was adjusted for PHQ-9 depression at randomisation and baseline physical limitations (SF-12 PCS score). In order to identify any other relevant covariates of depression severity at follow-up, a number of selected demographics and baseline measures were used as predictors of PHQ-9 depression at 4 months in individual regressions followed by a combined regression to avoid issues of multicollinearity, using a non-conservative significance level of $p < 0.10$ at each stage. All analyses adjusted for PHQ-9 scores at randomisation.

Considered predictors were age, sex, an indicator of whether or not any selected antidepressants had been prescribed at baseline, a history of depression [as measured by two questions of the MINI at randomisation: (1) whether or not patients had ever been consistently depressed for a minimum of 2 weeks and (2) whether or not patients had ever experienced a lack of interest or enjoyment for a minimum of 2 weeks], baseline anxiety (as measured by the GAD-7) and baseline physical functioning (as measured by the PHQ-15).

Results of the individual regressions and summary regression are given in *Table 16*. Positive coefficients indicate increased depression at 4 months for higher values of the predictor variable (or for the condition specified in the table for categorical variables). Initial identified predictors following individual regressions were prescribed medication, a history of depression (both indicators) as well as baseline GAD-7 and PHQ-15 scores. Higher levels of anxiety, physical health problems, a greater likelihood of being described antidepressants and having a history of depression were associated with higher PHQ-9 depression severity at 4 months. Of these predictors, all but prescribed antidepressants remained significant in a summary

TABLE 15 Group difference in mean PHQ-9 score: adjusted for clustering by case manager

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	198	8.98	8.20 to 9.76	217	10.90	10.16 to 11.63	1.92	0.85 to 2.99	< 0.001
12 months	198	10.45	9.65 to 11.25	217	10.63	9.87 to 11.39	0.18	–0.92 to 1.29	0.744
18 months	198	10.54	9.73 to 11.35	217	10.53	9.76 to 11.30	–0.01	–1.13 to 1.11	0.991

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation and baseline SF-12 PCS score, including case manager as random effect.

TABLE 16 Predictors of PHQ-9 scores at 4 months, controlling for PHQ-9 at randomisation

Characteristic	Coefficient	Standard error	*p*-value[a]
Individual regressions			
Age	–0.04	0.046	0.363
Sex (being female)	0.70	0.567	0.217
Prescribed antidepressants (any)	1.18	0.578	**0.043**
Ever having been depressed or down for 2 weeks	2.90	0.804	**< 0.001**
Ever having lost interest or enjoyment for 2 weeks	2.78	1.189	**0.020**
Baseline GAD-7 score	0.33	0.056	**< 0.001**
Baseline PHQ-15 score	0.21	0.066	**0.002**
Summary regression			
Prescribed antidepressants (any)	0.63	0.558	0.259
Ever having been depressed or down for 2 weeks	2.65	0.788	**0.001**
Ever having lost interest or enjoyment for 2 weeks	2.20	1.174	**0.062**
Baseline GAD-7 score	0.26	0.058	**< 0.001**
Baseline PHQ-15 score	0.14	0.065	**0.034**

a Bold *p*-values indicate inclusion of the covariate at the next analysis stage, that is a *p*-value of < 0.10.

regression and were included in the primary analysis model. Age and sex were not significant predictors of PHQ-9 scores.

Adjusted PHQ-9 score means and group differences for the primary analysis model [additionally adjusting for history of depression (two questions), GAD-7 and PHQ-15 at baseline] are given in *Table 17*. Group differences remained significant in favour of collaborative care at 4 months' follow-up (a difference of 1.95 PHQ-9 score points), whereas differences at 12 and 18 months remained not statistically significant. Thus, accounting for additional predictors of the primary outcome did not affect treatment differences. An overall comparison of treatment effects for PHQ-9 depression severity from different analyses is presented in *Table 18*.

TABLE 17 Group difference in mean PHQ-9 score: adjusted for predictors of PHQ-9 score at 4 months

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	196	7.68	6.41 to 8.94	214	9.62	8.41 to 10.84	1.95	0.92 to 2.98	< 0.001
12 months	196	9.09	7.81 to 10.37	214	9.35	8.12 to 10.58	0.26	–0.81 to 1.32	0.633
18 months	196	9.21	7.93 to 10.49	214	9.25	8.02 to 10.47	0.04	–1.04 to 1.11	0.945

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score, ever having been depressed or down for 2 weeks, ever having lost interest or enjoyment for 2 weeks, baseline GAD-7 score and baseline PHQ-15 score.

TABLE 18 Summary of PHQ-9 group differences from different analyses

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
Unadjusted means									
4 months	186	8.94	8.14 to 9.74	204	10.87	10.06 to 11.68	1.93	–	–
12 months	172	10.44	9.50 to 11.38	185	10.59	9.79 to 11.39	0.15	–	–
18 months	165	10.38	9.44 to 11.32	178	10.33	9.51 to 11.14	–0.05	–	–
Primary analysis[a]									
4 months[b]	198	8.98	8.20 to 9.75	217	10.90	10.16 to 11.64	1.92	0.85 to 2.99	< 0.001
12 months	198	10.44	9.65 to 11.24	217	10.63	9.87 to 11.40	0.19	–0.92 to 1.29	0.741
18 months	198	10.53	9.72 to 11.34	217	10.53	9.76 to 11.31	0.00	–1.12 to 1.12	0.997
Analysis adjusted for clustering by case manager[c]									
4 months	198	8.98	8.20 to 9.76	217	10.90	10.16 to 11.63	1.92	0.85 to 2.99	< 0.001
12 months	198	10.45	9.65 to 11.25	217	10.63	9.87 to 11.39	0.18	–0.92 to 1.29	0.744
18 months	198	10.54	9.73 to 11.35	217	10.53	9.76 to 11.30	–0.01	–1.13 to 1.11	0.991
Analysis adjusted for additional covariates predictive of PHQ-9 score at 4 months[d]									
4 months	196	7.68	6.41 to 8.94	214	9.62	8.41 to 10.84	1.95	0.92 to 2.98	< 0.001
12 months	196	9.09	7.81 to 10.37	214	9.35	8.12 to 10.58	0.26	–0.81 to 1.32	0.633
18 months	196	9.21	7.93 to 10.49	214	9.25	8.02 to 10.47	0.04	–1.04 to 1.11	0.945
Analysis adjusted for covariates predictive of non-response at 4 months[e]									
4 months	196	8.94	7.77 to 10.11	215	10.91	9.81 to 12.00	1.97	0.93 to 3.00	< 0.001
12 months	196	10.35	9.16 to 11.53	215	10.60	9.49 to 11.72	0.26	–0.81 to 1.33	0.637
18 months	196	10.47	9.28 to 11.66	215	10.54	9.42 to 11.65	0.07	–1.01 to 1.15	0.903
Analysis using multiply imputed data[f]									
4 months	249	9.01	8.21 to 9.81	236	10.94	10.20 to 11.68	1.93	0.89 to 2.96	< 0.001
12 months	249	10.51	9.70 to 11.33	236	10.74	9.96 to 11.52	0.23	–0.86 to 1.32	0.679
18 months	249	10.66	9.82 to 11.51	236	10.57	9.78 to 11.37	–0.09	–1.18 to 1.00	0.869

a Primary analysis: mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation and baseline SF-12 PCS score.
b Primary end point.
c As primary analysis model, additionally including case manager as random effect.
d As primary analysis model, additionally adjusting for ever having been depressed or feeling down for 2 weeks, ever having lost interest or enjoyment for 2 weeks, baseline GAD-7 score and baseline PHQ-15 score.
e As primary analysis model, additionally adjusting for age at consent, baseline SF-12 MCS score, baseline PHQ-15 score, prescription of any antidepressants and ever having lost interest or enjoyment for 2 weeks.
f As primary analysis model, based on complete data obtained by multiple imputation using chained equations (outcomes predicted from available PHQ-9 scores, allocation, baseline SF-12 PCS score and all additional predictors identified in footnotes d and e).

Adjusting for missingness

No valid PHQ-9 response at the primary end point of 4 months' follow-up was available for 25.3% ($n = 63$) of patients in the collaborative care arm and 13.6% ($n = 32$) of patients in the usual-care arm. In order to investigate the impact of missing data on the treatment effect, any baseline predictors of non-response at 4 months' follow-up (no valid PHQ-9 score) were identified by individual and a summary logistic regression using $p < 0.10$ and included as covariates in the primary analysis model.

Considered predictors were age, sex, an indicator of whether or not any selected antidepressants had been prescribed at baseline, a history of depression (as measured by two questions of the MINI at randomisation), depression at randomisation (PHQ-9 score), baseline mental well-being (SF-12 MCS score), baseline anxiety (GAD-7 score) and baseline physical functioning (PHQ-15 score, SF-12 PCS score).

The results of the individual and summary regressions are presented in *Table 19*. Odds ratios > 1 indicate a greater likelihood of non-response at 4 months for higher values of the predictor variable (or for the condition specified in the table for categorical variables). The initial identified predictors were age, GAD-7 score, SF-12 MCS score, PHQ-15 score, prescribed antidepressants and ever having lost interest or enjoyment for ≥ 2 weeks. PHQ-9 response at 4 months was more likely to be missing for older participants, participants with greater anxiety, reduced mental functioning or more physical problems, those not on antidepressants and those who reported ever having lost interest or enjoyment for more than 2 weeks. Of these predictors, age, the SF-12 MCS score, PHQ-15 score, antidepressant use and loss of interest remained significant in a summary regression and were included in the primary analysis model.

TABLE 19 Predictors of non-response (missing PHQ-9 scores) at 4 months

Characteristic	Odds ratio	Standard error	*p*-value[a]
Individual regressions			
Age	1.04	0.018	**0.005**
Sex (being female)	1.09	0.260	0.715
Baseline GAD-7 score	1.04	0.024	**0.074**
Baseline SF-12 MCS score	0.98	0.011	**0.059**
Baseline SF-12 PCS score	0.99	0.009	0.207
Baseline PHQ-15 score	1.07	0.037	**0.011**
Randomisation PHQ-9 score	1.03	0.023	0.164
Prescribed antidepressants (any)	0.63	0.164	**0.078**
Ever having been depressed or down for 2 weeks	1.05	0.361	0.884
Ever having lost interest or enjoyment for 2 weeks	0.50	0.201	**0.085**
Summary regression			
Age	1.05	0.019	**0.007**
Baseline GAD-7 score	1.01	0.030	0.738
Baseline SF-12 MCS score	0.98	0.014	**0.085**
Baseline PHQ-15 score	1.06	0.030	**0.058**
Prescribed antidepressants (any)	0.62	0.171	**0.084**
Ever having lost interest or enjoyment for 2 weeks	0.44	0.186	**0.051**

a Bold *p*-values indicate inclusion of the covariate at the next analysis stage, that is a *p*-value of < 0.10.

Adjusted PHQ-9 score means and group differences for the primary analysis model are given in *Table 20*. Group differences remained significant in favour of collaborative care at 4 months' follow-up (a difference of 1.97 PHQ-9 score points), and remained not statistically significant at 12 and 18 months' follow-up. Thus, accounting for predictors of non-response did not affect the treatment effect. An overall comparison of treatment effects for PHQ-9 depression severity from different analyses is presented in *Table 18*.

In addition, the primary analysis was repeated using complete data derived from multiple imputation by chained equations. Data were imputed from all additional predictors identified in the previous two analyses (age, baseline SF-12, GAD-7 and PHQ-15 scores, antidepressant use and depression history) as well as treatment allocation and available PHQ-9 scores at any time points. Adjusted PHQ-9 score means and group differences for the primary analysis model are given in *Table 21* (results based on 20 imputations). Group differences remained significant in favour of collaborative care at 4 months' follow-up (a difference of 1.93 PHQ-9 score points), and remained not statistically significant at 12 and 18 months' follow-up. Thus, using complete data did not affect the treatment effect. An overall comparison of treatment effects for PHQ-9 depression severity from different analyses is presented in *Table 18*.

Summary of Patient Health Questionnaire-9 items analysis models

Table 18 provides an overview of group means and treatment effect estimates from the primary analysis and secondary analyses of depression severity at 4, 12 and 18 months as measured by PHQ-9 scores. Unadjusted means are presented for reference. Adjusted average estimates of group differences at the primary end point at 4 months ranged from 1.92 to 1.97 PHQ-9 score points in favour of collaborative care.

TABLE 20 Group difference in mean PHQ-9 score: adjusted for predictors of non-response

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	196	8.94	7.77 to 10.11	215	10.91	9.81 to 12.00	1.97	0.93 to 3.00	< 0.001
12 months	196	10.35	9.16 to 11.53	215	10.60	9.49 to 11.72	0.26	–0.81 to 1.33	0.637
18 months	196	10.47	9.28 to 11.66	215	10.54	9.42 to 11.65	0.07	–1.01 to 1.15	0.903

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score, ever having been depressed or down for 2 weeks, ever having lost interest or enjoyment for 2 weeks, baseline GAD-7 score and baseline PHQ-15 score.

TABLE 21 Group difference in mean PHQ-9 score: using imputed data

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	249	9.01	8.21 to 9.81	236	10.94	10.20 to 11.68	1.93	0.89 to 2.96	< 0.001
12 months	249	10.51	9.70 to 11.33	236	10.74	9.96 to 11.52	0.23	–0.86 to 1.32	0.679
18 months	249	10.66	9.82 to 11.51	236	10.57	9.78 to 11.37	–0.09	–1.18 to 1.00	0.869

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score (outcomes derived by multiple imputation).

Binary Patient Health Questionnaire 9-items outcome

Using the cut-off point of ≥ 10 PHQ-9 score points, *Table 22* presents the number and percentage of moderately to severely depressed participants at randomisation and follow-up by treatment arm. The figures are illustrated in *Figure 4*. Approximately 77% of randomised CASPER plus participants were depressed at randomisation. At 4 months' follow-up, this percentage improved to 40% in the collaborative care arm and 55% in the usual-care arm. This difference was not maintained at 12 or 18 months' follow-up.

Data were analysed by logistic mixed-effects modelling, including moderate to severe PHQ-9 depression (yes or no) at 4, 12 and 18 months as the outcome, predicted by trial arm, time (4, 12 or 18 months), group by time interaction, depression severity at randomisation (PHQ-9 score) and baseline physical functioning (SF-12 PCS score). Resulting treatment effect estimates are presented in *Table 23*.

The greater reduction in moderately to severely depressed cases seen in the collaborative care arm compared with the usual-care arm was statistically significant at 4 months' follow-up (odds ratio 2.18, 95% CI 1.36 to 3.51; $p < 0.001$), but was not statistically significant at 12 or 18 months.

Secondary outcomes

Continuous and binary secondary outcomes were analysed by longitudinal linear and logistic mixed models, adjusting for the baseline assessment of the outcome, PHQ-9 score at randomisation and SF-12 PCS score. Estimates of the effect of the intervention were derived and are presented for each follow-up time point. In addition, adverse events are reported descriptively and the number of deaths are compared by chi-squared test.

Antidepressants

Patients indicated on questionnaires whether or not they were currently prescribed any of a list of 10 antidepressants (see *Table 24* for details and the frequencies of prescriptions by trial arm). Citalopram was the most commonly prescribed antidepressant.

A binary variable was created to indicate whether or not patients had been prescribed any of the listed antidepressants. *Table 25* presents the number and percentage of patients on antidepressants at baseline and follow-up by treatment arm. The figures are illustrated in *Figure 5*. Approximately 33% of patients were prescribed antidepressants at baseline. Of the participants remaining in the trial at follow-up, antidepressants were prescribed to a greater percentage at 4, 12 and 18 months than at baseline, around 36% on average. Differences between treatment arms were small.

TABLE 22 Cases of moderate to severe depression (PHQ-9 score of ≥ 10)

	Trial arm								
	Collaborative care			Usual care			Total		
Time point	*n*	Total	%	*n*	Total	%	*n*	Total	%
Randomisation	186	248	75.0	186	236	78.8	372	484	76.9
4 months	75	186	40.3	113	204	55.4	188	390	48.2
12 months	87	172	50.6	103	185	55.7	190	357	53.2
18 months	88	165	53.3	88	178	49.4	176	343	51.3

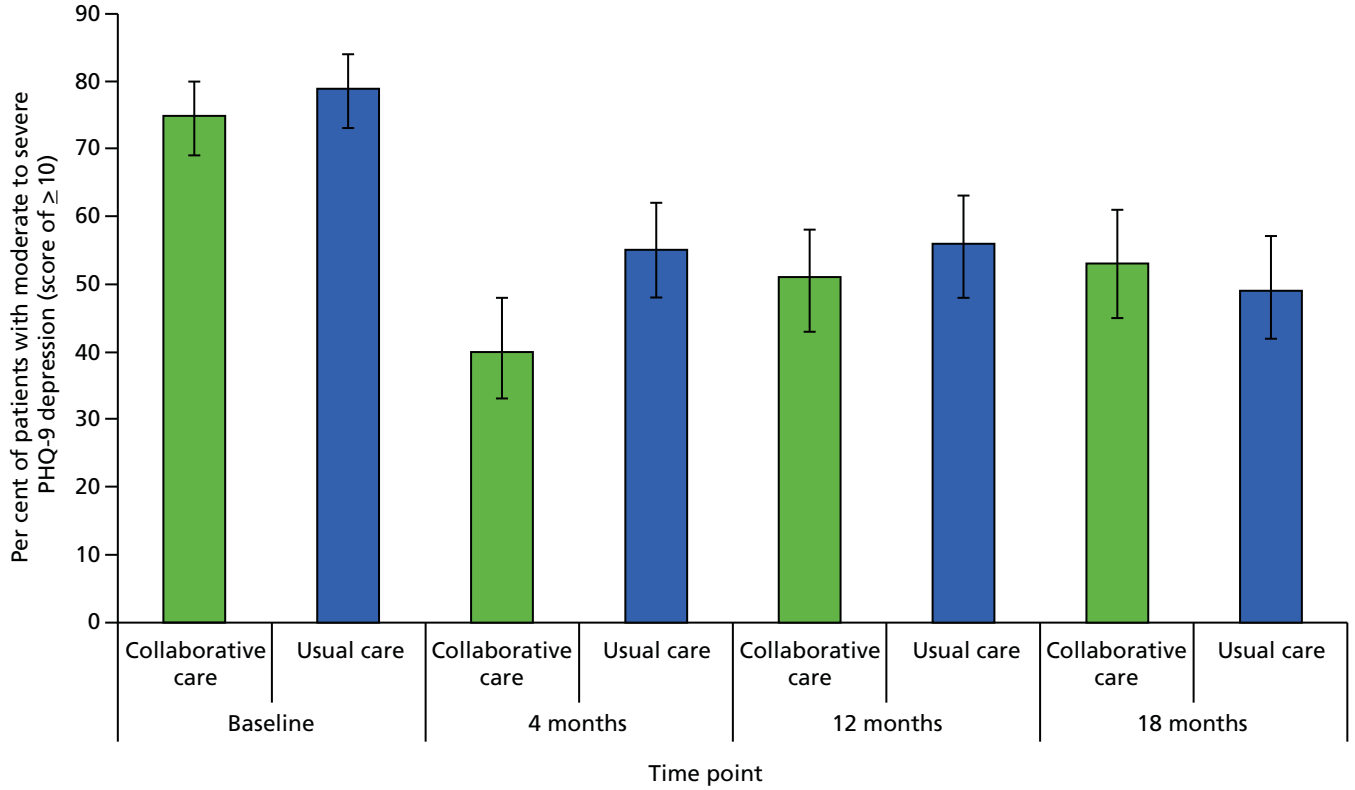

FIGURE 4 Unadjusted per cent of patients (with 95% CIs) with moderate to severe depression.

TABLE 23 Group difference in proportions of moderate to severe PHQ-9 depression

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Odds ratio	95% CI	*n*	Odds ratio	95% CI	Odds ratio	95% CI	*p*-value
4 months	198	0.95	0.58 to 1.33	217	2.08	1.27 to 2.89	2.18	1.36 to 3.51	0.001
12 months	198	1.65	0.79 to 2.52	217	2.31	1.14 to 3.49	1.40	0.72 to 2.72	0.319
18 months	198	2.29	0.76 to 3.81	217	1.66	0.62 to 2.69	0.72	0.31 to 1.71	0.461

Mixed-effects logistic model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation and baseline SF-12 PCS score.

TABLE 24 Number of patients being prescribed specific antidepressants

	Trial arm											
	Collaborative care				Usual care				Total			
	Month				Month				Month			
Antidepressant	0	4	12	18	0	4	12	18	0	4	12	18
Dosulepin	3	3	3	2	8	4	4	3	11	7	7	5
Sertraline	17	18	17	16	13	14	17	16	30	32	34	32
Venlafaxine	10	7	9	8	6	6	4	5	16	13	13	13
Lofepramine	1	1	0	1	4	3	2	1	5	4	2	2
Fluoxetine	14	8	7	7	15	13	9	6	29	21	16	13
Duloxetine	2	1	2	2	1	1	2	1	3	2	4	3
Citalopram	27	19	17	19	24	18	18	19	51	37	35	38
Paroxetine	3	3	4	3	2	3	2	1	5	6	6	4
Trazodone	6	3	1	2	3	4	5	6	9	7	6	8
Mirtazapine	9	9	5	7	11	8	11	10	20	17	16	17

TABLE 25 Number of patients being prescribed any antidepressants

	Trial arm								
	Collaborative care			Usual care			Total		
Time point	*n*	Total	%	*n*	Total	%	*n*	Total	%
Baseline	82	248	33.1	79	236	33.5	161	484	33.3
4 months	70	186	37.6	68	204	33.3	138	390	35.4
12 months	61	173	35.3	68	185	36.8	129	358	36.0
18 months	61	166	36.8	61	178	34.3	122	344	35.5

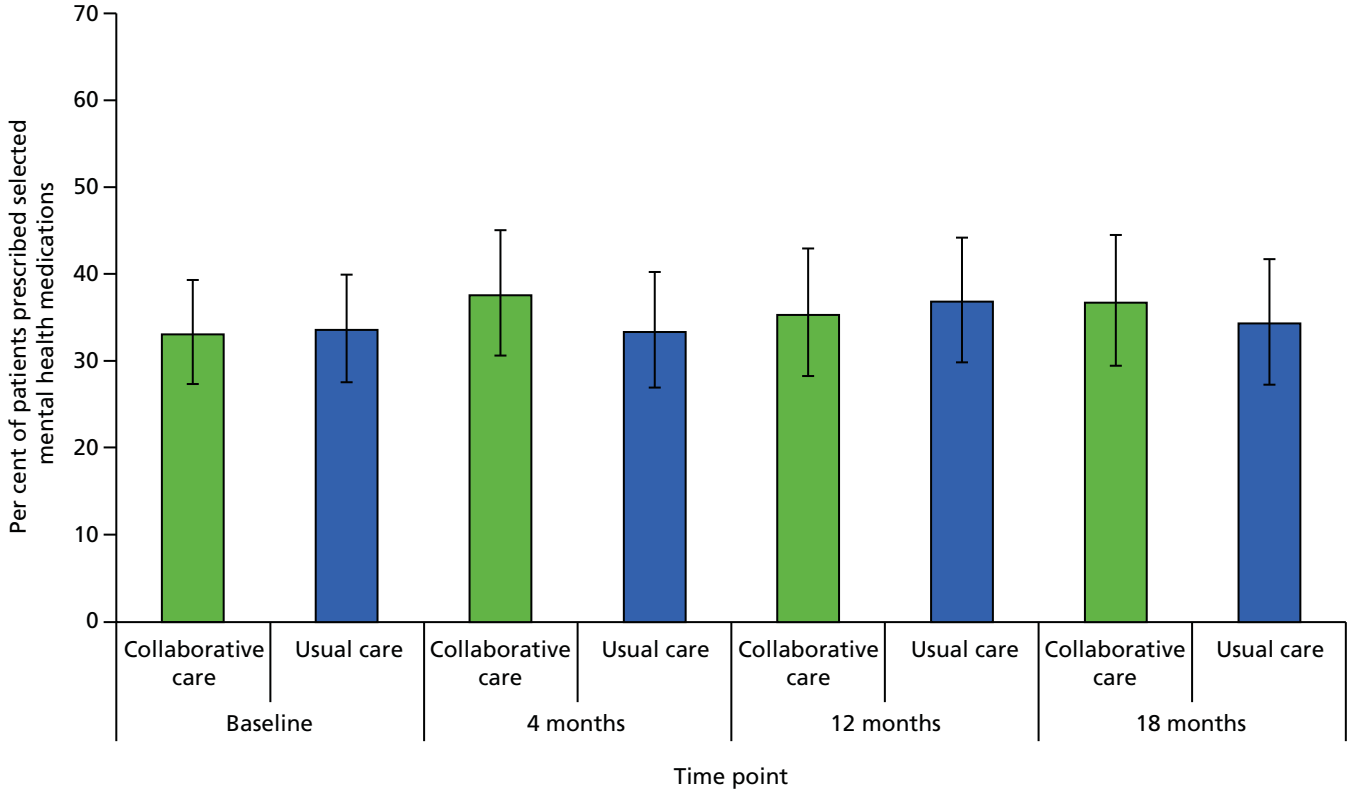

FIGURE 5 Unadjusted per cent of patients (with 95% CIs) who were prescribed antidepressants.

Data were analysed by a logistic mixed-effects model, including prescribed medication (yes or no) at 4, 12 and 18 months as the outcome, and were predicted by trial arm, time (4, 12 and 18 months), group by time interaction and prescribed antidepressants at baseline. Treatment effect estimates are presented in *Table 26*.

The adjusted relative odds of being prescribed antidepressants were higher in the collaborative care arm than the usual-care arm at 4 months (odds ratio 0.39, 95% CI 0.17 to 0.89; $p = 0.025$); however, differences between treatment arms were not statistically significant at 12 or 18 months' follow-up.

Generalised Anxiety Disorder-7 item scale psychological anxiety

The GAD-7 is a brief measure of symptoms of anxiety with a score range of 0–21, with higher scores indicating more severe anxiety. Unadjusted means for psychological anxiety based on the GAD-7 are presented in *Table 27* and *Figure 6*, and the results of the formal statistical analysis by mixed modelling are given in *Table 28*.

TABLE 26 Group difference in proportions of patients with prescribed antidepressants

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Odds ratio	95% CI	*n*	Odds ratio	95% CI	Odds ratio	95% CI	*p*-value
4 months	198	6.86	1.22 to 12.50	217	2.70	0.88 to 4.53	0.39	0.17 to 0.89	0.025
12 months	198	2.77	0.40 to 5.15	217	4.03	0.62 to 7.45	1.45	0.55 to 3.88	0.454
18 months	198	2.28	0.15 to 4.40	217	2.07	0.17 to 3.97	0.91	0.30 to 2.79	0.868

Mixed-effects logistic model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, baseline antidepressant prescriptions, PHQ-9 score at randomisation and SF-12 PCS score.

TABLE 27 Unadjusted GAD-7 descriptive statistics

	Trial arm		
Time	Collaborative care ($N = 249$)	Usual care ($N = 236$)	Total ($N = 485$)
Baseline *n*	247	234	481
Mean (SD)	9.4 (5.03)	9.3 (4.92)	9.4 (4.97)
Median (minimum, maximum)	9 (0, 21)	9 (0, 21)	9 (0, 21)
4 months *n*	181	191	372
Mean (SD)	6.7 (5.07)	8.3 (5.25)	7.5
Median (minimum, maximum)	6 (0, 20)	7 (0, 21)	6 (0, 21)
12 months *n*	166	176	342
Mean (SD)	7.4 (5.71)	8.4 (5.36)	7.9 (5.55)
Median (minimum, maximum)	6 (0, 21)	8 (0, 21)	7 (0, 21)
18 months *n*	161	171	322
Mean (SD)	7.5 (5.22)	7.9 (4.94)	7.7 (5.07)
Median (minimum, maximum)	7 (0, 21)	8 (0, 20)	7 (0, 21)

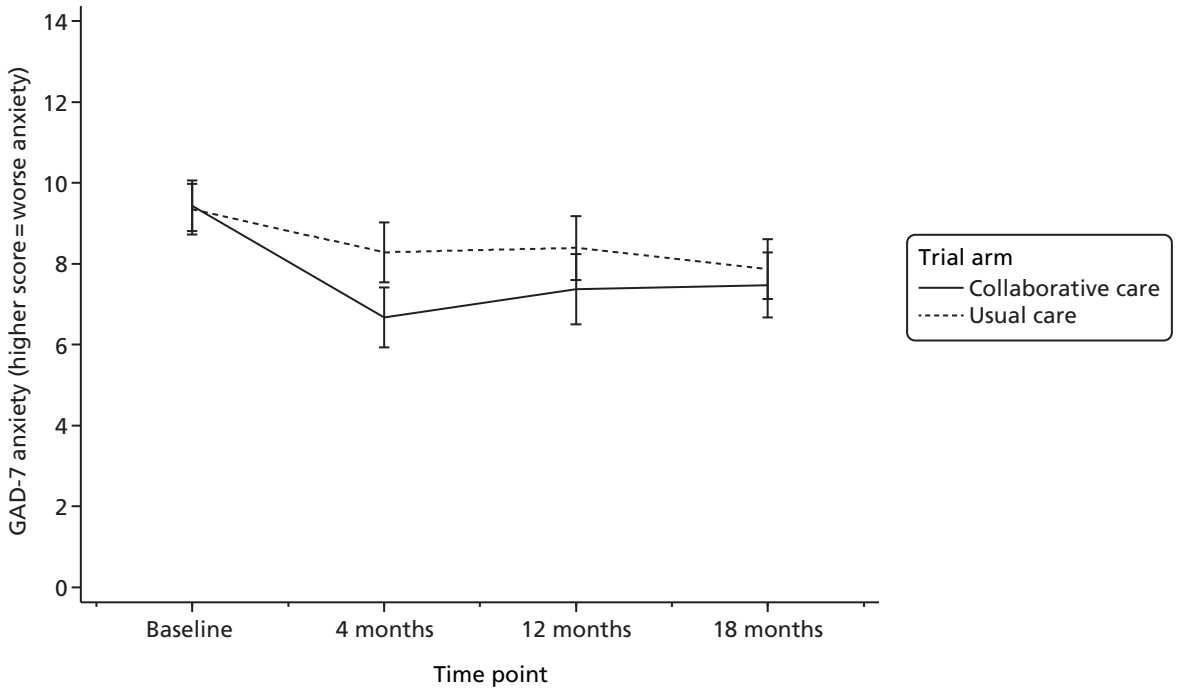

FIGURE 6 Unadjusted mean GAD-7 scores (with 95% CIs).

TABLE 28 Group difference in mean GAD-7 scores

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	195	6.60	5.94 to 7.25	210	8.27	7.64 to 8.91	1.68	0.77 to 2.59	< 0.001
12 months	195	7.33	6.65 to 8.01	210	8.42	7.76 to 9.07	1.09	0.14 to 2.03	0.024
18 months	195	7.59	6.91 to 8.27	210	7.91	7.25 to 8.57	0.32	–0.63 to 1.27	0.511

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score and baseline GAD-7 scores.

The figures indicate that anxiety was on average at around nine score points for all participants at baseline. Both trial arms improved anxiety levels at 4 months' follow-up, significantly more so in the collaborative care arm (mean score difference 1.68, 95% CI 0.77 to 2.59; $p < 0.001$). Group differences decreased in magnitude but remained statistically significant at 12 months' follow-up (mean score difference 1.09, 95% CI 0.14 to 2.03; $p = 0.024$), but not at 18 months.

Short Form questionnaire-12 items physical component summary score

The SF-12 PCS score ranges from 0 to 100, with higher scores indicating better functioning. Unadjusted means for physical functioning are presented in *Table 29* and *Figure 7*, and the results of the formal statistical analysis by mixed modelling are given in *Table 30*.

The figures indicate that physical functioning was below average adult physical health status (scores of < 50) for participants throughout the trial period, as would be expected in an elderly population. Patients maintained similar functioning levels between baseline and 18 months, and group differences in physical functioning were not statistically significant based on the mixed-effects analysis at 4 months (mean score difference –0.44, 95% CI –2.00 to 1.23; $p = 0.583$) or any other follow-up.

TABLE 29 Unadjusted SF-12 PCS score descriptive statistics

Time	Trial arm		
	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Total (*N* = 485)
Baseline *n*	245	234	479
Mean (SD)	35.6 (13.08)	36.8 (13.32)	36.2 (13.20)
Median (minimum, maximum)	34.5 (7.1, 66.3)	35.8 (5.9, 69.6)	35.3 (5.9, 69.6)
4 months *n*	178	188	366
Mean (SD)	35.2 (13.53)	35.8 (12.14)	35.5 (12.82)
Median (minimum, maximum)	33.5 (7.3, 64.0)	34.0 (12.9, 65.5)	33.8 (7.3, 65.5)
12 months *n*	166	171	337
Mean (SD)	34.3 (13.17)	34.3 (12.02)	34.3 (12.58)
Median (minimum, maximum)	33.8 (7.7, 69.6)	33.0 (9.4, 61.0)	33.7 (7.7, 69.6)
18 months *n*	158	167	325
Mean (SD)	34.0 (13.51)	35.1 (12.11)	34.6 (12.80)
Median (minimum, maximum)	30.7 (8.7, 70.9)	33.7 (11.8, 63.0)	33.3 (8.7, 70.9)

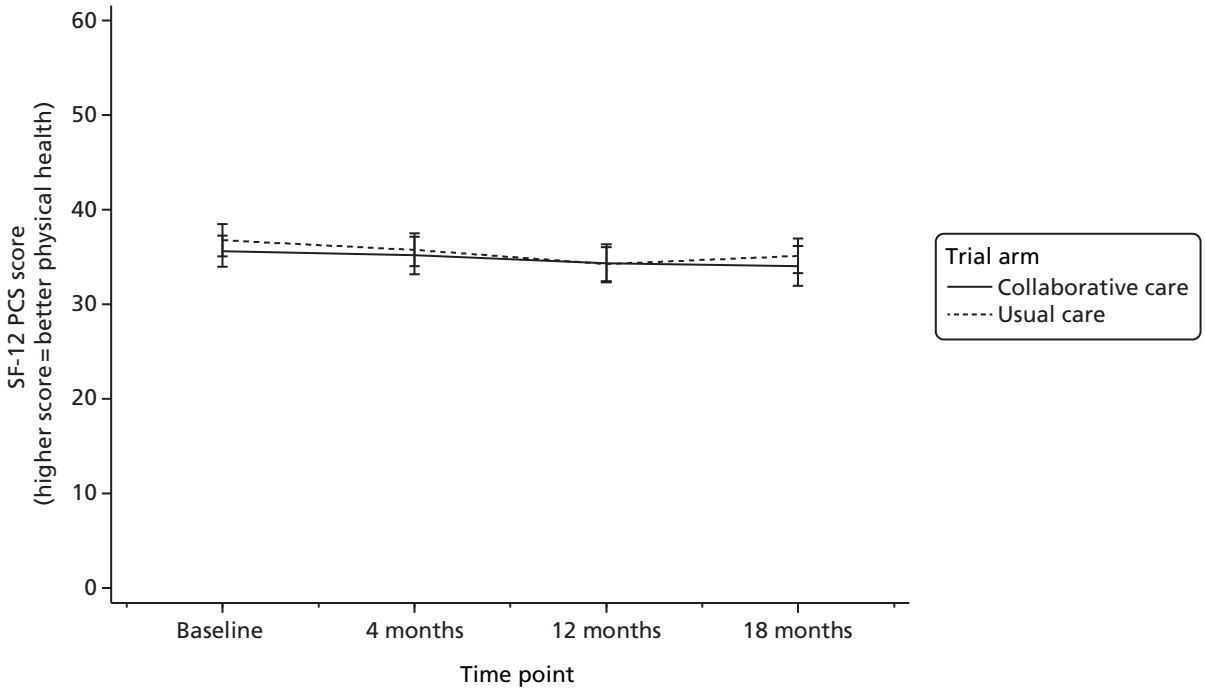

FIGURE 7 Unadjusted mean SF-12 PCS scores (with 95% CIs).

Short Form questionnaire-12 items mental component summary score

The SF-12 MCS scores range from 0 to 100, with higher scores indicating better functioning. Unadjusted means for psychological functioning are presented in *Table 31* and *Figure 8* and the results of the formal statistical analysis by mixed modelling are given in *Table 32*.

The figures indicate that participants' average mental functioning was below the general average for adults (scores of < 50) throughout the trial period, which may be expected in a population with major depressive episodes. At 4 months' follow-up, mental functioning had improved in patients in both arms, but to a greater

TABLE 30 Group difference in mean SF-12 PCS score

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	196	35.5	34.4 to 36.7	211	35.1	34.0 to 36.2	–0.44	–2.00 to 1.23	0.583
12 months	196	34.7	33.6 to 35.9	211	34.5	33.4 to 35.6	–0.24	–1.86 to 1.37	0.769
18 months	196	34.1	33.0 to 35.3	211	34.7	33.5 to 35.8	0.55	–1.09 to 2.18	0.514

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation and baseline SF-12 PCS score.

TABLE 31 Unadjusted SF-12 MCS score descriptive statistics

	Trial arm		
Time	Collaborative care (*N* = 249)	Usual care (*N* = 236)	Total (*N* = 485)
Baseline (*n*)	245	234	479
Mean (SD)	35.4 (9.51)	35.7 (20.53)	35.5 (10.01)
Median (minimum, maximum)	35.8 (10.3, 60.2)	36.2 (2.2, 63.9)	35.9 (2.2, 62.9)
4 months (*n*)	178	188	366
Mean (SD)	41.6 (11.22)	38.6 (10.86)	40.1 (11.12)
Median (minimum, maximum)	41.6 (13.4, 65.5)	37.8 (7.8, 71.3)	39.7 (7.8, 71.3)
12 months (*n*)	166	171	337
Mean (SD)	40.4 (12.12)	38.9 (10.82)	39.7 (11.49)
Median (minimum, maximum)	40.4 (9.6, 67.4)	38.5 (16.0, 68.6)	39.5 (9.6, 68.6)
18 months (*n*)	158	167	325
Mean (SD)	40.1 (11.34)	38.9 (10.84)	39.5 (11.09)
Median (minimum, maximum)	41.3 (14.5, 62.9)	38.4 (1.7, 63.0)	39.0 (1.7, 63.0)

extent in the collaborative care arm, and this difference between arms was statistically significant (mean score difference –3.02, 95% CI –5.04 to –0.99; $p = 0.004$). Participants in both trial arms maintained a score of around 40 at 12 and 18 months' follow-up, and group differences were not statistically significant at these time points.

EuroQol-5 Dimensions, 3 levels

Quality of life using the EQ-5D-3L is measured on five dimensions – mobility, self-care, usual activities, pain/discomfort and anxiety/depression – and participants are given three response options to indicate their level of problems for each dimension. The weighted summary index derived from these dimensions is summarised and formally analysed as part of the CASPER plus health economic evaluation. For the purpose of exploring differences in quality of life between treatment arms, the frequencies of responses for each category in each dimension are presented descriptively in *Table 33* and illustrated in *Figures 9–13*.

The majority of CASPER plus participants indicated no problems or some problems in each of the EQ-5D-3L areas, with few patients having severe difficulties. The most frequent use of the severe category was in the pain/discomfort dimension (around one-quarter of participants). The greatest trial arm differences were seen for usual activities, with the number of patients who had no problems performing usual activities

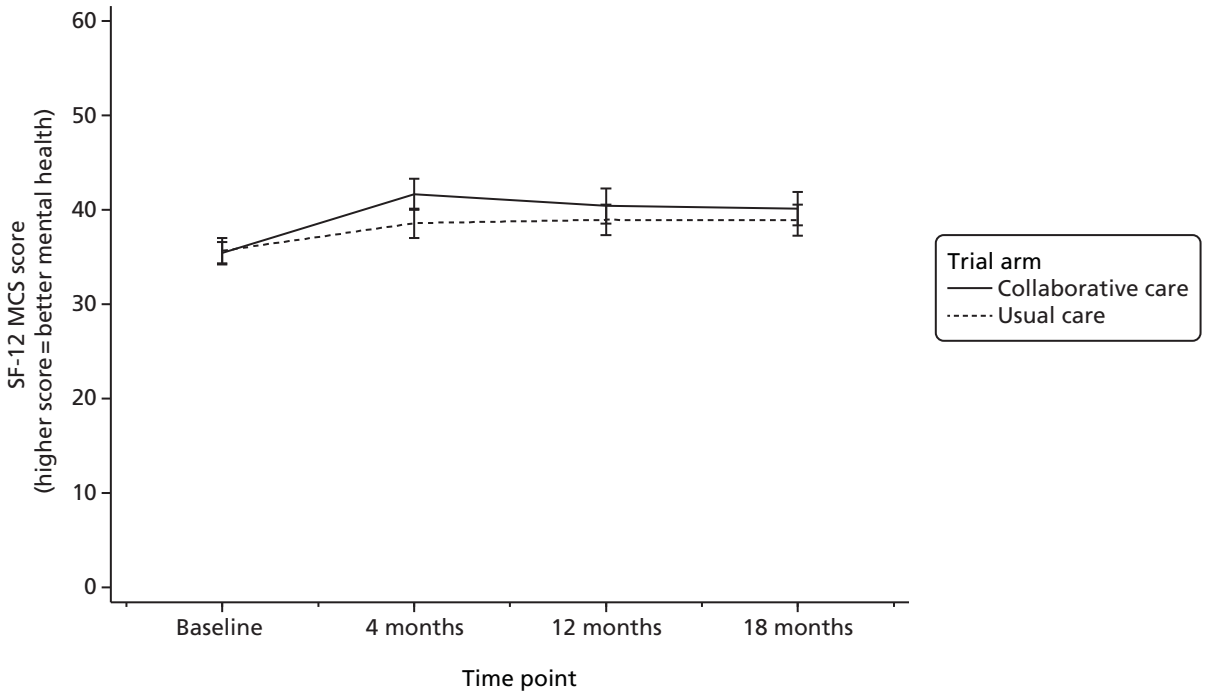

FIGURE 8 Unadjusted mean SF-12 MCS scores (with 95% CIs).

TABLE 32 Group difference in mean SF-12 MCS scores

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*N*	Mean	95% CI	*N*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	196	41.7	40.2 to 43.1	211	38.7	37.3 to 40.1	–3.02	–5.04 to –0.99	0.004
12 months	196	40.5	39.0 to 42.0	211	38.9	37.4 to 40.3	–1.63	–3.73 to 0.46	0.125
18 months	196	40.0	38.5 to 41.5	211	38.8	37.3 to 40.3	–1.18	–3.30 to 0.93	0.273

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score and baseline SF-12 MCS score.

TABLE 33 EQ-5D-3L descriptive statistics

	Trial arm					
	Collaborative care (*N* = 249)			Usual care (*N* = 236)		
Severity[a]	Total *n*	*n*	%	Total *n*	*n*	%
EQ-5D-3L mobility						
Baseline						
Level 1	247	71	29	235	76	32
Level 2	247	176	71	235	157	67
Level 3	247	0	0	235	2	1
4 months						
Level 1	181	56	31	193	36	36
Level 2	181	124	69	193	69	64
Level 3	181	1	1	193	1	1

continued

TABLE 33 EQ-5D-3L descriptive statistics (*continued*)

	Trial arm					
	Collaborative care (*N* = 249)			Usual care (*N* = 236)		
Severity[a]	Total *n*	*n*	%	Total *n*	*n*	%
12 months						
Level 1	168	48	29	175	49	28
Level 2	168	119	71	175	124	71
Level 3	168	1	1	175	2	1
18 months						
Level 1	161	49	30	171	51	30
Level 2	161	111	69	171	120	70
Level 3	161	1	1	171	0	0
EQ-5D-3L self-care						
Baseline						
Level 1	243	163	67	234	175	75
Level 2	243	75	31	234	55	24
Level 3	243	5	2	234	4	2
4 months						
Level 1	179	127	71	192	145	76
Level 2	179	50	28	192	45	23
Level 3	179	2	1	192	2	1
12 months						
Level 1	168	115	68	175	119	68
Level 2	168	48	29	175	55	31
Level 3	168	5	3	175	1	1
18 months						
Level 1	161	110	68	171	121	71
Level 2	161	49	30	171	48	28
Level 3	161	2	1	171	2	1
EQ-5D-3L usual activities						
Baseline						
Level 1	338	136	40	356	124	35
Level 2	338	189	56	356	209	59
Level 3	338	13	4	356	23	6
4 months						
Level 1	253	123	49	314	108	34
Level 2	253	116	46	314	187	60
Level 3	253	14	6	314	19	6
12 months						
Level 1	231	112	48	277	89	48
Level 2	231	108	47	277	165	47
Level 3	231	11	5	277	23	5

TABLE 33 EQ-5D-3L descriptive statistics (*continued*)

	Trial arm					
	Collaborative care (*N* = 249)			Usual care (*N* = 236)		
Severity[a]	Total *n*	*n*	%	Total *n*	*n*	%
18 months						
Level 1	247	64	26	235	66	28
Level 2	247	159	64	235	151	64
Level 3	247	24	10	235	18	8
EQ-5D-3L pain/discomfort						
Baseline						
Level 1	247	34	14	233	27	12
Level 2	247	156	63	233	152	65
Level 3	247	57	23	233	54	23
4 months						
Level 1	180	26	14	192	26	14
Level 2	180	113	63	192	121	63
Level 3	180	41	23	192	45	23
12 months						
Level 1	168	25	15	176	20	11
Level 2	168	102	61	176	114	65
Level 3	168	41	24	176	42	24
18 months						
Level 1	161	23	14	171	23	13
Level 2	161	95	59	171	115	67
Level 3	161	43	27	171	33	19
EQ-5D-3L anxiety/depression						
Baseline						
Level 1	246	26	11	234	25	11
Level 2	246	176	72	234	178	76
Level 3	246	44	18	234	31	13
4 months						
Level 1	178	49	28	192	42	22
Level 2	178	116	65	192	130	68
Level 3	178	13	7	192	20	10
12 months						
Level 1	168	46	27	177	38	21
Level 2	168	104	62	177	123	69
Level 3	168	18	11	177	16	9
18 months						
Level 1	161	36	22	172	34	3
Level 2	161	104	65	172	123	72
Level 3	161	21	13	172	15	1

a Severity: level 1, no problems; level 2, some/moderate problems; and level 3, severe problems.

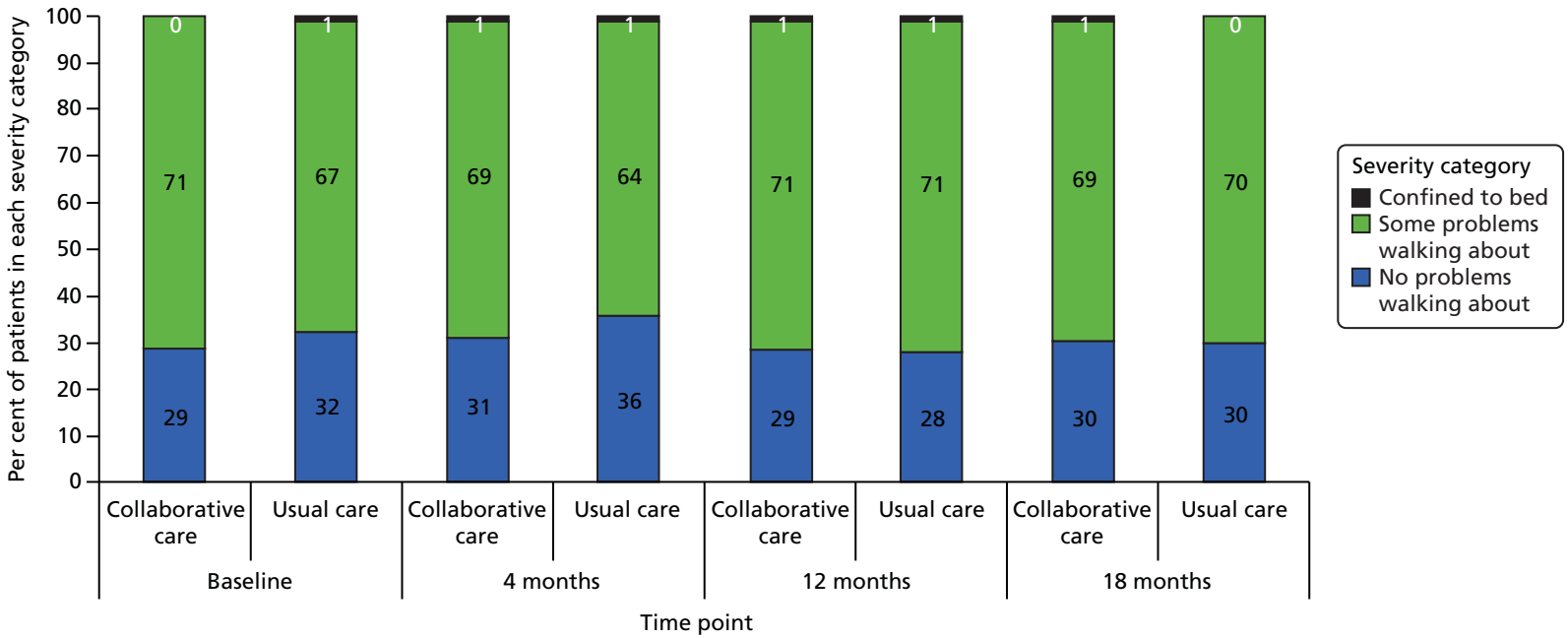

FIGURE 9 The EQ-5D-3L mobility dimension: per cent of patients in each severity category.

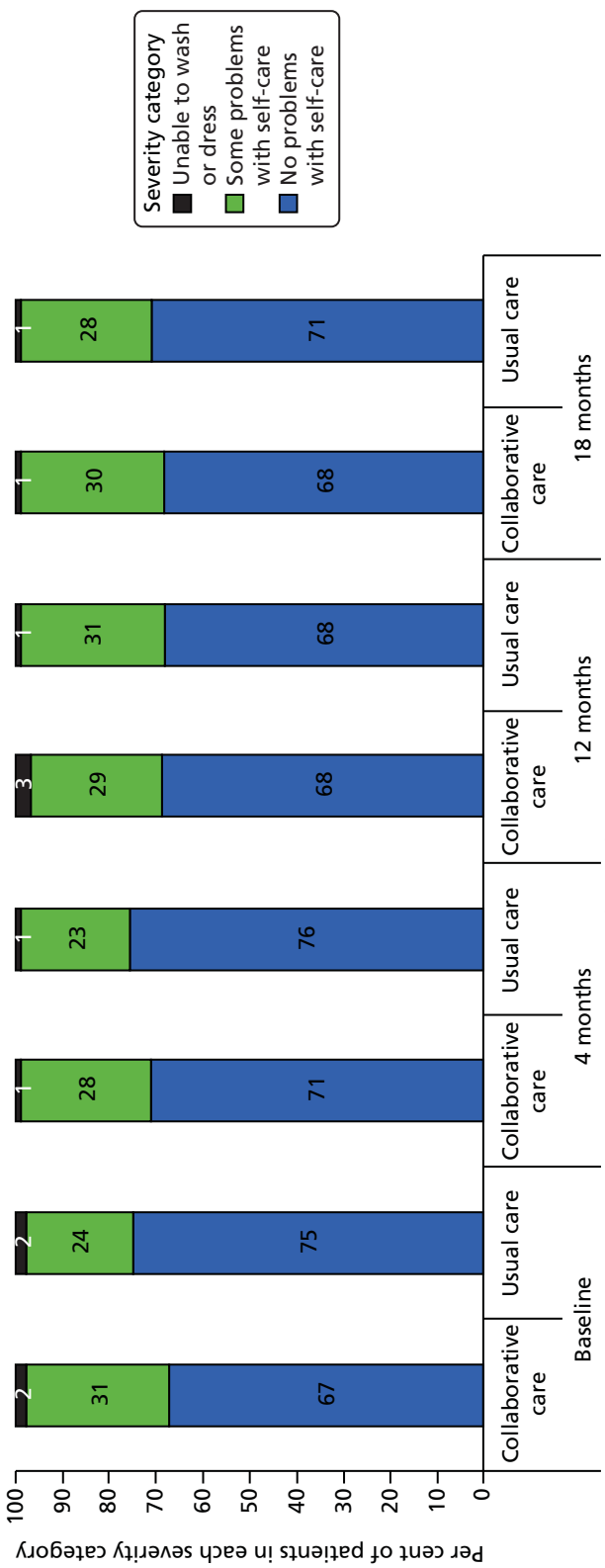

FIGURE 10 The EQ-5D-3L self-care dimension: per cent of patients in each severity category.

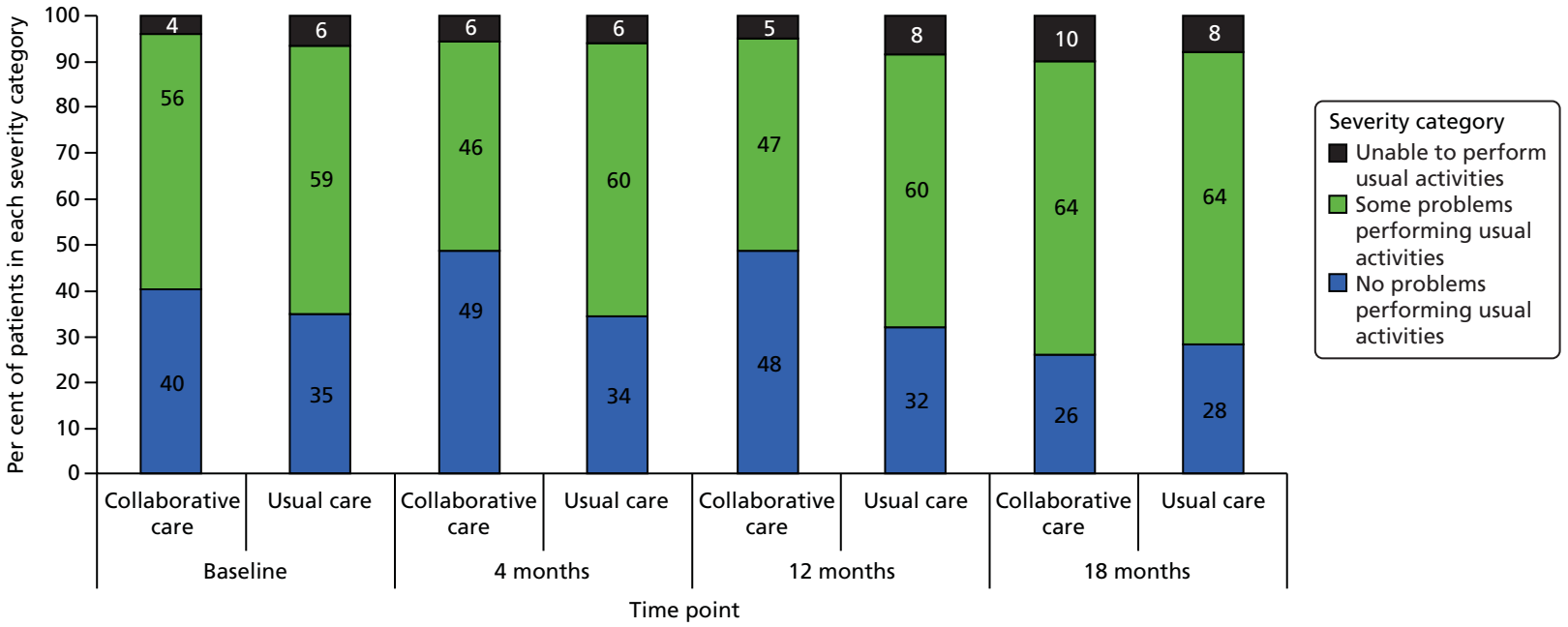

FIGURE 11 The EQ-5D-3L usual activities dimension: per cent of patients in each severity category.

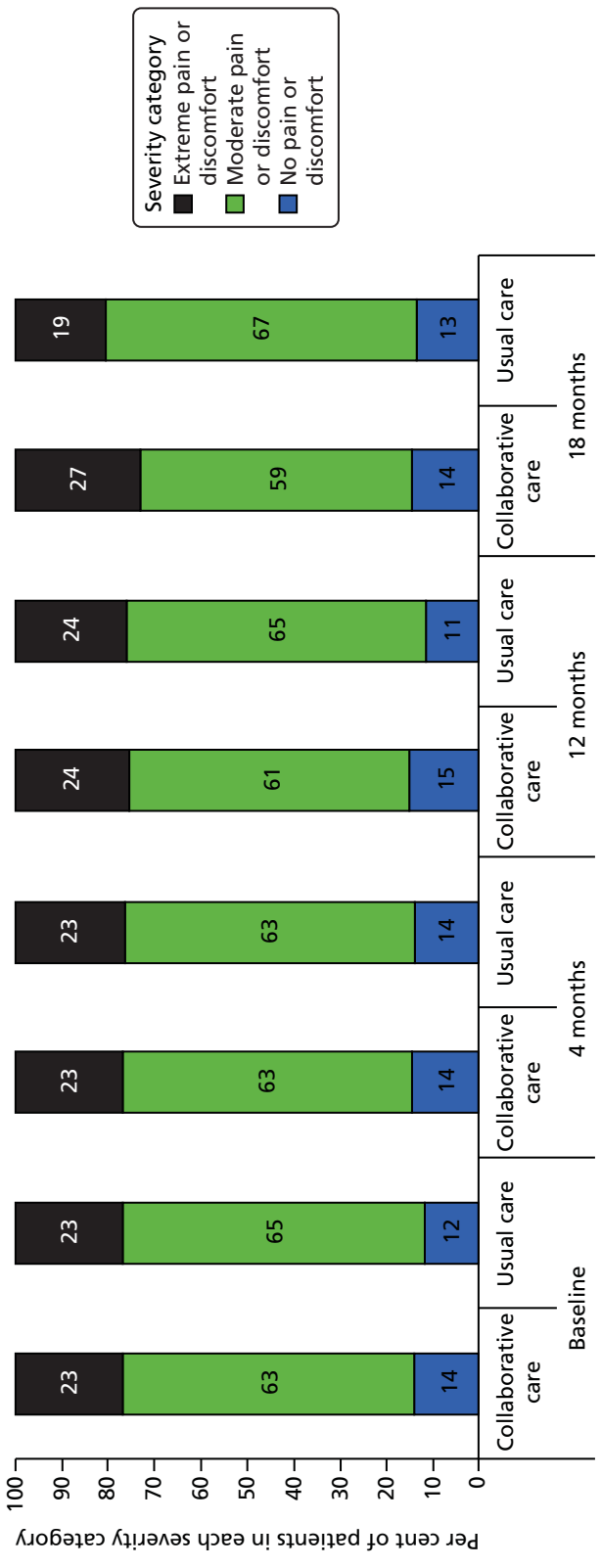

FIGURE 12 The EQ-5D-3L pain/discomfort dimension: per cent of patients in each severity category.

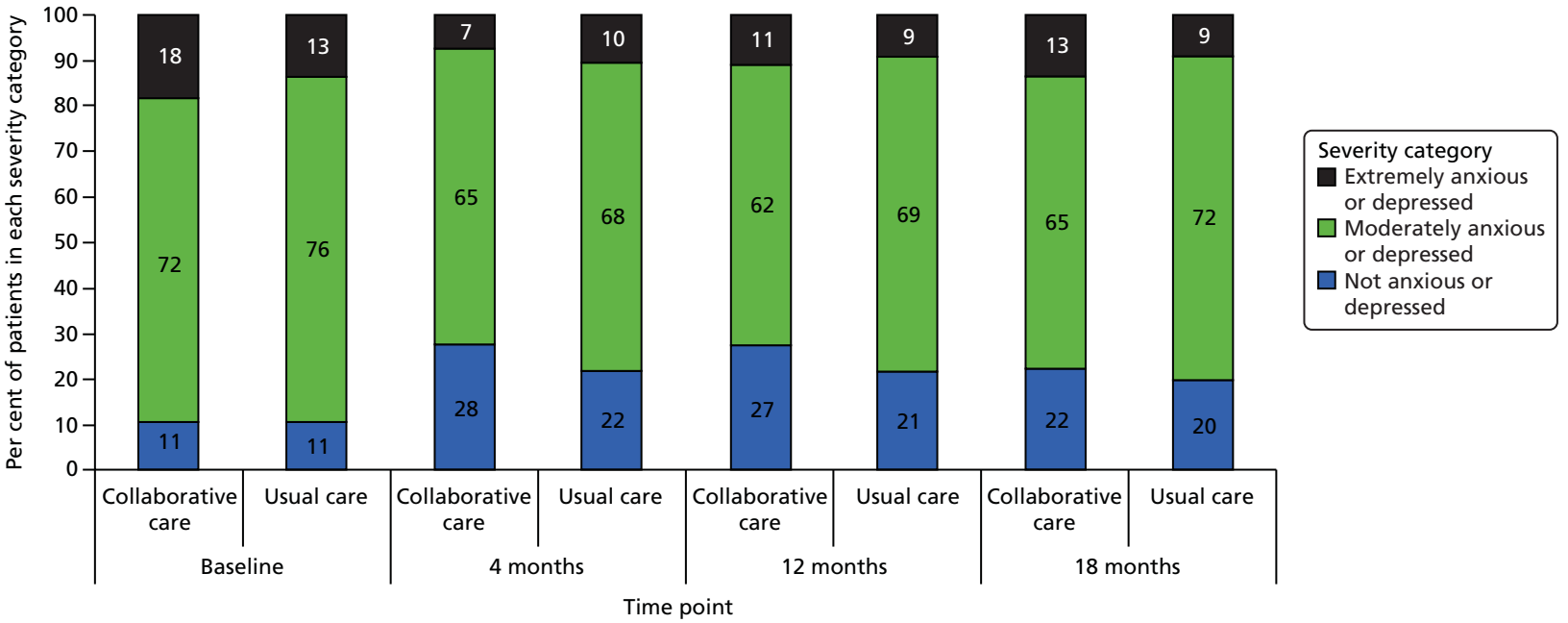

FIGURE 13 The EQ-5D-3L anxiety/depression dimension: per cent of patients in each severity category.

increasing from 40% to 49% at 4 months' follow-up in the collaborative care arm, whereas rates remained stable in the usual-care arm. This difference was maintained at 12 months but not at 18 months. Relatively greater improvements in favour of the intervention arm were also seen for anxiety and depression at 4 and 12 months, the number of people not anxious or depressed being higher in the collaborative care arm, although group differences were of moderate magnitude (around 6%). There were no substantial group differences in the mobility, self-care or pain/discomfort dimensions.

Patient Health Questionnaire-15 items physical health problems

The PHQ-15 is a measure of physical health problems. In this study it had a score range of 0–28 (usual maximum is 30), as a question regarding menstrual problems was removed for the elderly CASPER plus patient population.

Unadjusted means for physical health problems are presented in *Table 34* and *Figure 14*, and the results of the formal statistical analysis by mixed modelling are given in *Table 35*. Physical health problems significantly decreased in the collaborative care arm at 4 months' follow-up; in contrast, in the usual-care group, symptoms remained constant throughout follow-up (mean score difference 1.67, 95% CI 0.98 to 2.36; $p < 0.001$). This difference became smaller but remained statistically significant at 12 months (mean score difference 1.19, 95% CI 0.47 to 1.90; $p = 0.001$), whereas follow-up scores returned to near baseline levels for both groups at 18 months.

Connor–Davidson Resilience Scale-2 items resilience

The two-item CD-RISC2 resilience measure has a score range of 0 to 8, with a higher score indicating greater psychological resilience. Unadjusted means for psychological resilience are presented in *Table 36* and *Figure 15*, and the results of the formal statistical analysis by mixed modelling are given in *Table 37*. Average resilience at baseline was around 5 score points and remained consistent over the 18 months' follow-up for patients in the usual-care group. Among patients in the collaborative care group, average resilience marginally improved but dropped back to baseline levels at 18 months. The group difference was statistically significant at 12 months' follow-up (mean score difference –0.35, 95% CI –0.68 to –0.03; $p = 0.034$).

TABLE 34 Unadjusted PHQ-15 descriptive statistics

	Trial arm		
Time	Collaborative care ($N = 249$)	Usual care ($N = 236$)	Total ($N = 485$)
Baseline *n*	146	234	480
Mean (SD)	12.3 (4.51)	11.9 (4.33)	12.1 (4.42)
Median (minimum, maximum)	12 (2, 26)	11 (2, 24)	12 (2, 26)
4 months *n*	178	187	365
Mean (SD)	9.9 (4.63)	11.5 (4.60)	10.7 (4.68)
Median (minimum, maximum)	10 (2, 22)	11 (1, 22)	10 (1, 22)
12 months *n*	165	178	343
Mean (SD)	10.5 (4.65)	11.7 (4.59)	11.1 (4.64)
Median (minimum, maximum)	10 (3, 23)	11.5 (1, 23)	11 (1, 23)
18 months *n*	161	168	329
Mean (SD)	11.2 (5.22)	11.4 (4.73)	11.3 (4.97)
Median (minimum, maximum)	11 (2, 23)	11 (1, 22)	11 (1, 23)

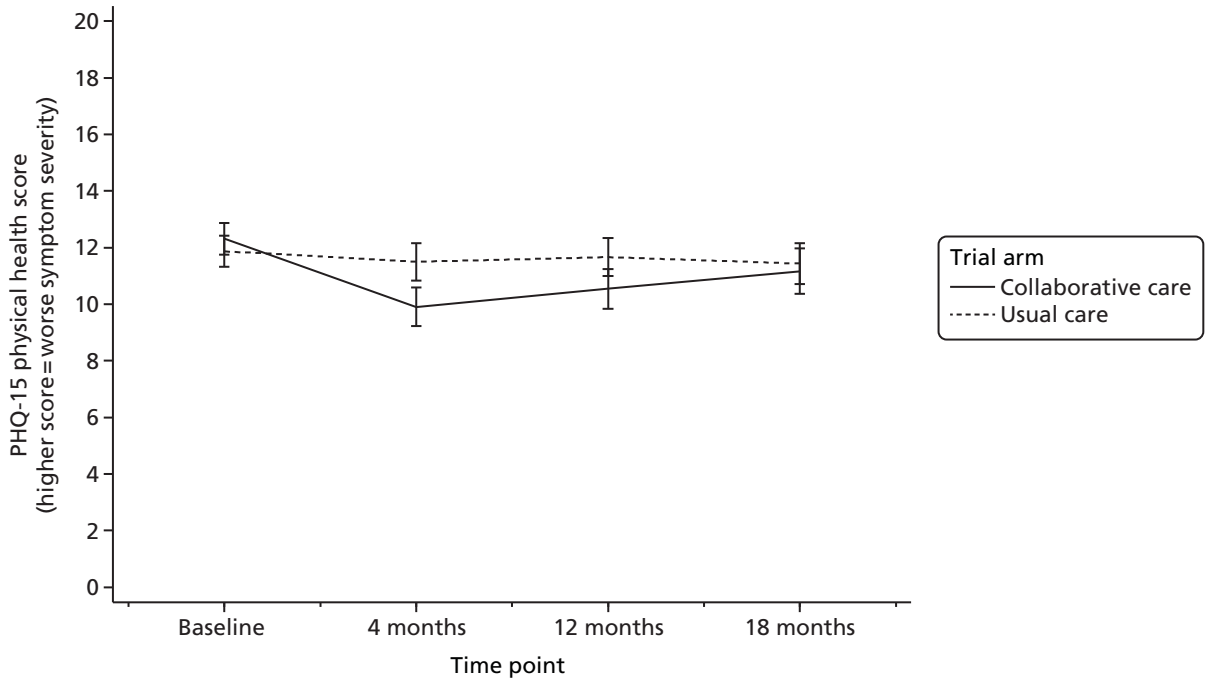

FIGURE 14 Unadjusted mean PHQ-15 scores (with 95% CIs).

TABLE 35 Group difference in mean PHQ-15

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	195	10.02	9.52 to 10.52	209	11.69	11.21 to 12.17	1.67	0.98 to 2.36	< 0.001
12 months	195	10.42	9.91 to 10.94	209	11.61	11.12 to 12.10	1.19	0.47 to 1.90	0.001
18 months	195	10.04	10.53 to 11.56	209	11.34	10.84 to 11.84	0.30	–0.43 to 1.02	0.423

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score and baseline PHQ-15 score.

Adverse events

A total of 81 SAEs including deaths were identified in CASPER plus participants over the 18-month follow-up period: 47 events occurred in 41 patients in the collaborative care arm and 34 events occurred in 33 patients in the usual-care arm (*Table 38*). The maximum number of SAEs per person was three, and the average number of SAEs experienced per CASPER plus participant was 0.19 in the collaborative care arm and 0.14 in the usual-care arm.

The majority of SAEs (98%) were assessed as being unrelated to the intervention, and the remaining SAEs were unlikely to be related. A breakdown of these figures by trial arm, as well as by the type and nature of the events, is presented in *Table 39*. The majority of events were unscheduled hospitalisations, with cardiovascular and miscellaneous events being the most likely reason for admissions. Causes of death are further detailed in the *Mortality* section of this report.

TABLE 36 Unadjusted CD-RISC2 descriptive statistics

Time	Trial arm		
	Collaborative care ($N = 249$)	Usual care ($N = 236$)	Total ($N = 485$)
Baseline *n*	247	235	482
Mean (SD)	4.9 (1.81)	4.9 (1.74)	4.9 (1.78)
Median (minimum, maximum)	5 (0, 8)	5 (0, 8)	5 (0, 8)
4 months *n*	176	191	367
Mean (SD)	5.2 (1.78)	5.0 (1.91)	5.1 (1.85)
Median (minimum, maximum)	5 (0, 8)	5 (0, 8)	5 (0, 8)
12 months *n*	168	177	345
Mean (SD)	5.1 (1.84)	4.9 (1.82)	5.0 (1.83)
Median (minimum, maximum)	5 (0, 8)	5 (0, 8)	5 (0, 8)
18 months *n*	161	171	332
Mean (SD)	5.0 (2.03)	4.9 (1.88)	5.0 (1.95)
Median (minimum, maximum)	5 (0, 8)	5 (0, 8)	5 (0, 8)

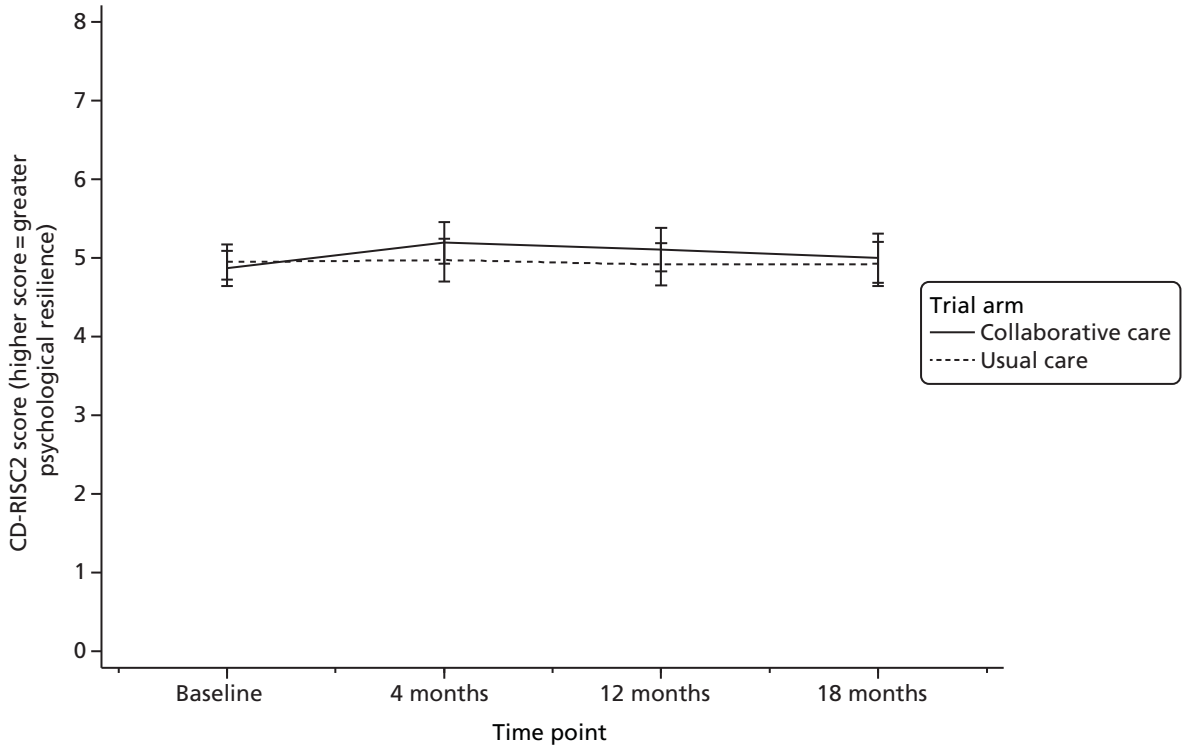

FIGURE 15 Unadjusted mean CD-RISC2 scores (with 95% CIs).

Mortality

A total of 13 participants died during the 18-month follow-up period, six patients in the collaborative care arm (2.4% of randomised patients) and seven patients in the usual-care arm (3.0% of randomised patients). Causes of death are summarised in *Table 40*. A chi-squared test revealed that the difference in mortality rates between treatment arms was statistically significant ($\chi^2_1 = 0.14$; $p = 0.705$).

TABLE 37 Group difference in mean CD-RISC2 score

	Trial arm								
	Collaborative care			Usual care			Group difference		
Estimate at	*n*	Mean	95% CI	*n*	Mean	95% CI	Mean	95% CI	*p*-value
4 months	196	5.19	4.96 to 5.42	211	4.91	4.69 to 5.13	–0.28	–0.59 to 0.04	0.089
12 months	196	5.21	4.97 to 5.44	211	4.86	4.63 to 5.08	–0.35	–0.68 to –0.03	0.034
18 months	196	5.01	4.77 to 5.25	211	4.85	4.62 to 5.08	–0.16	–0.49 to 0.17	0.352

Mixed-effects model adjusted for trial arm, time (4, 12 and 18 months), group × time interaction, PHQ-9 score at randomisation, baseline SF-12 PCS score and baseline CD-RISC2 score.

TABLE 38 Summary of SAEs

	Trial arm		
Adverse event statistic	Collaborative care	Usual care	Total
Total number of adverse events	47	34	81
Number of patients with any adverse event	41	33	74
Per cent of patients with any adverse event	16.5	14.0	15.3
Average number of events per patient			
Mean	0.19	0.14	0.17
Median	0	0	0
Minimum, maximum	0, 3	0, 2	0, 3

All deaths were further recorded as SAEs, and potential relatedness to the trial treatment was assessed as part of the adverse event processing. In total, 92% (12 events) of deaths were categorised as being unrelated to treatment, and 8% (one event) as unlikely to be related to treatment.

Summary of clinical effectiveness analysis

A total of 485 elderly patients in the north of England with a major depressive episode were randomised into the CASPER plus trial: 249 participants were allocated to collaborative care and 236 participants were allocated to usual care. Of those in the collaborative care arm, 83% received at least one treatment session and, on average, participants received a total of six sessions (one face to face and five over the telephone). A total of 83 participants (33%) withdrew from collaborative care treatment before or during treatment, with the most common reasons being not wishing to engage and physical ill health.

Participants were followed up by postal questionnaire at 4 months (80%), 12 months (74%) and 18 months (71%). Trial dropout was greater in the collaborative care arm (22% withdrew) than in the usual-care arm (10%). The primary trial outcome was PHQ-9 depression severity, analysed by a covariance pattern mixed model, adjusting for PHQ-9 depression at randomisation and baseline SF-12 physical functioning. As data from all time points were included in the model, 415 participants (86%) participants were included in the primary analysis. Model estimates at the primary end point of 4 months revealed a statistically significant effect in favour of collaborative care (mean difference 1.92 score points, 95% CI 0.85 to 2.99 score points; $p < 0.001$). However, this difference was not maintained during the long-term follow-up at 12 months ($p = 0.741$) or 18 months ($p = 0.997$).

TABLE 39 Categories of SAEs

	Trial arm					
	Collaborative care (*N* = 47 events)		Usual care (*N* = 34 events)		Total (*N* = 81 events)	
SAE characteristic	*n*	%	*n*	%	*n*	%
Relatedness to the intervention						
Unrelated	46	98.9	33	97.1	79	97.5
Unlikely to be related	1	2.1	1	2.9	2	2.5
Possibly related	–	–	–	–	–	–
Probably related	–	–	–	–	–	–
Definitely related	–	–	–	–	–	–
Type						
Unscheduled hospitalisation	24	51.1	19	55.9	43	53.1
Other medically important condition	17	36.2	8	23.5	25	30.9
Death	6	12.8	7	20.6	13	16.1
Nature of adverse event						
Cancer	3	6.4	3	8.8	6	7.4
Cardiovascular	15	31.9	10	29.4	25	30.9
Infection	5	10.6	5	14.7	10	12.4
Acute infection	4	8.5	1	2.9	5	6.2
Injury from falls	5	10.6	4	11.8	9	11.1
Miscellaneous	14	29.8	11	32.4	25	30.9
Unknown	1	2.1	0	0.0	1	1.2

TABLE 40 Cause of death by trial arm

Trial arm	Cause of death
Collaborative care	11436 – bilateral pneumonia
Collaborative care	12507 – pneumonia
Collaborative care	15355 – ischaemic heart disease and duodenal adenoma
Collaborative care	16870 – congestive cardiac failure
Collaborative care	17898 – chronic obstructive pulmonary disease and breast cancer
Collaborative care	18977 – congestive cardiac failure
Usual care	13133 – cardiac failure
Usual care	15608 – myocardial infarction and bronchial pneumonia
Usual care	18051 – cardiac failure
Usual care	18497 – double pneumonia and kidney failure
Usual care	18913 – lung cancer
Usual care	21395 – ischaemic colitis
Usual care	21800 – small cell carcinoma of the lung

Secondary analyses demonstrated robustness of these results when adjusting for clustering by case managers (20 case managers, ICC < 0.001), additional predictors of depression severit or predictors of non-response and when using multiply imputed data. All mean group differences at 4 months ranged between 1.92 and 1.97 score points. Results were mirrored by the greater reduction of moderately to severely depressed cases (PHQ-9 score of ≥ 10) for collaborative care patients at 4 months' follow-up ($p = 0.001$), which was not maintained long term.

Of the secondary outcomes, collaborative care was associated with decreased anxiety (GAD-7 score) at 4 and 12 months ($p < 0.001$ and $p = 0.024$, respectively), better mental health functioning (SF-12 MCS score) at 4 months ($p = 0.004$) and greater psychological resilience at 12 months ($p = 0.034$). Self-reported prescription of selected antidepressants increased among collaborative care patients at 4 months ($p = 0.025$). Although there were no trial arm differences in physical functioning (SF-12 PCS score), patients in the collaborative care arm had fewer physical health problems (PHQ-15 score) at 4 and 12 months' follow-up than patients in the usual-care arm ($p < 0.001$ and $p = 0.001$, respectively). Group differences were not statistically significant for any of the outcomes at 18 months' follow-up.

A comparable number of SAEs occurred in each trial arm (collaborative care, 47 events; usual care, 31 events). Six participants in the collaborative care arm died during the trial, compared with seven in the usual-care arm ($\chi^2_1 = 0.14$; $p = 0.705$).

Chapter 6 Health economics

The health economic component of the CASPER plus trial was an incremental cost-effectiveness analysis exploring the value for money of the intervention over and above usual care. An analysis of uncertainty is also included to demonstrate the robustness of the results. First, the resource use and costs are estimated, including the costs of providing collaborative care and associated training of health-care professionals, and also the wider costs to the NHS. Second, health outcomes are quantified using QALYs using the SF-6D algorithm.

Resource use and costs

Collaborative care: required resources and associated costs

Case managers were psychological well-being practitioners (PWPs) employed at NHS band 5. Case managers each received training to provide collaborative care as part of the CASPER plus trial. In total, three training events were held covering four regions of the study (York, Leeds, Durham and Newcastle upon Tyne), each consisting of 2 consecutive days of training. The number of attendees per training event varied and efforts were made to provide training in a manner that ensured that the overall costs of travel and accommodation were minimal.

During the training, PWPs were orientated to the case managers' manual, which outlined the overall principles of collaborative care and a 'session-by-session overview' of what case managers aimed to achieve with patients. The training courses for case managers were predominantly provided by two trainers; subsequently, these trainers also supervised case managers during implantation of the collaborative care programme implementation.

The manual stipulated that the programme of treatment should consist of '8–10 mainly telephone contacts with occasional face-to-face contacts over a period of 12 weeks'. In terms of the expectation for each session, it further stated that 'contacts last 45 minutes for session one and 20–30 minutes for each subsequent contact'. The first session was generally held face to face and took place at participants' homes, GP surgeries or other community venues.

Case managers received weekly supervision from a designated supervisor. The schedule of supervision followed a standardised agenda whereby for each patient there was a weekly discussion and case managers would prepare feedback to discuss each case with their supervisor. Supervisors were responsible for providing support to case managers on the process of collaborative care and medication management and on specific psychological interventions. On average, each patient contact was discussed between the case manager and supervisor for approximately 5 minutes.

Case managers provided participant-specific feedback to GPs. In the first instance, case managers worked with and advised participants' GPs on their care. During treatment, case managers would provide a letter to update the GP on participants' progress and, when appropriate, whether or not GPs might consider further treatment. At the end of the programme, case managers also sent a participant-specific summary report to the GP. Supervisors were available to advise case managers on next steps and consultation with GPs. Three letters were prepared and sent over the 12 weeks, requiring approximately 30 minutes of administration per letter. Case managers would also speak to GPs directly if they had any concerns about a participant's medication or overall well-being.

Case managers were also charged with a duty of care to engage outside agencies (such as social services or in response to safeguarding issues) in situations in which they became aware of safety or risk (including abuse). However, the client group had a generally low level of clinical need in this respect, and this additional responsibility was not generally required.

To estimate the personnel costs required to provide collaborative care (as intended within the manual), estimates of NHS unit costs were derived from national reference costs[56] (*Table 41*).

Table 42 summarises the resources required over the 12-week programme of collaborative care and indicates our estimate of the direct cost for base-case analysis. The direct cost of collaborative care (based on the prior estimation within the manual) was calculated to be £494.73. This cost is adopted for the base-case cost as, ex ante, there is insufficient information to anticipate actual levels of required care; however, deviation that did occur will be explored within our sensitivity analyses.

Consequences for health care by trial arm

Patient contacts over the duration of the trial are presented in *Table 43*, which compares the summary statistics for those who accessed collaborative care with the summary statistics for those who accessed usual care. Initial observation suggests that collaborative care in depression results in a small marginal increase in contacts with most services (except GP home visits). However, the mean contact rate with any service is dependent on access to the service and the subsequent level of utilisation.

To test whether or not differences in service use may be attributed to collaborative care, statistical tests must accommodate highly skewed distributions with significant numbers of zero service users and, therefore, specific analytical procedures are required.[60] Applying zero-inflated negative binomial regression[61] allows inference on the effect of collaborative care on two factors: access (using the logistic model) and overall change in the contact rate (using the full model). For full regression outputs see *Appendix 12*.

Having any access to services is indicated by outputs of the logistic models. Across all five resource use categories we may conclude that participants are generally unlikely to access any services. Examining logistic regression outputs related to nurse appointment (see *Appendix 12*, *Table 55*) suggest that collaborative care may increase the likelihood of access (log odd = 14.1944; $p = 0.01$). However, small sample numbers available from this trial mean that inferences regarding the effect of collaborative care should be made with caution.

TABLE 41 Personnel costs required to provide collaborative care

Item	Unit cost (£)	Reference[a]
PWP (band 5)		
Per hour[b]	39	Nurse (mental health)
Patient-related work[b]	52	Nurse (mental health)
Face-to-face contact[b]	74	Nurse (mental health)
PWP (band 6)		
Supervision[b]	49	Nurse team leader
GP		
Appointment	45	'Per patient contact lasting 11.7 minutes'
Home visit	114	'Per out of surgery visit lasting 23.4 minutes'
Telephone consultation	27	'Per telephone consultation lasting 7.1 minutes'
Practice nurse		
Appointment	13.43	'£52 per hour of face-to-face contact, duration of contact 15.5 minutes'
Telephone consultation	6.15	'£52 per hour of face-to-face contact, assumed similar time as GP: 7.1 minutes'

a From Curtis.[56]
b In the absence of specific unit costs for PWPs and supervisors, proxy values of roles at the same NHS band are taken. All price years were 2012/13.

TABLE 42 Summary of the health-care resource required to train and provide collaborative care as an associated base-case cost of the programme

Item	Frequency	Duration	Total quantity	Cost (£)	Description
Training case managers					
Case managers attending	16 case managers	13 hours	208	8112[a]	2 days, 6.5 hours each
Supervision of course	Two trainers, three sessions	13 hours	96 hours	4704[b]	2 days, 6.5 hours each
Manual	One manual/case manager	–	16	80	Printing
Travel and accommodation	For two trainers × two sessions	1 night	4 nights	600	Sessions in Durham and Leeds
Subtotal (total cost of training)				13,496	Cost to train all case mangers
Subtotal (total cost of training per participant)				39.23	249 allocated to the programme
Collaborative care					
Session 1	One per patient	45 minutes	45 minutes	55.50	Assumed by home visit[c]
Sessions 2–10	Median of nine sessions per patient	30 minutes	4.5 hours	234	Assumed by telephone[d]
Supervisions	One per week (12)	5 minutes	1 hour	88	1 hour over 12 weeks[a,b]
GP communication	Three letters	30 minutes	1.5 hours	78	Patient-related work[4]
Engaging outside agencies	0	0	0	0	Not required in CASPER
Subtotal (total cost of intervention per participant)				455.50	
Total cost (training + intervention)				494.73	Cost for base-case analysis

PSSRU, Personal Social Services Research Unit.
a For different tasks performed by the PWP, different costs were associated. For example, for work not requiring any patient contact, a general total staff hourly rate was applied for band 5 (£39 per hour).
b This was also the case for case manager supervision: for work not requiring any patient contact, a general total staff hourly rate was applied for band 6 (£49 per hour).
c For contact in person, the PSSRU unit cost for 'face-to-face time' was applied (£74 per hour).
d For communication occurring over the telephone, the PSSRU unit cost of patient-related work was applied (£52 per hour).

The full model specification accounts for access and subsequent use to test any overall change in the contact rate. Over resource use categories, there is generally no significant difference between groups. However, inference of the effect of collaborative care on nurse telephone consultations suggests an overall increase in the contact rate of 2.25 (95% CI 0.9285 to 5.4403; $p = 0.073$). Again, given the sample size, inferences on the effect of collaborative care should be made with caution.

Cost–consequences and total costs

Unit costs (as presented in *Table 41*) were multiplied by resource utilisation to derive patient-level costs of health care (*Table 44*). Health-care costs of treatment therefore extend beyond the cost of the collaborative care programme (£494.73), increasing wider costs by a mean of £682.27. Overall, the mean total cost in the collaborative care group was £1171.45 (95% CI £1166.99 to £1175.92, $n = 226$), compared with £654.14 (95% CI £650.78 to £657.52, $n = 221$) in the usual-care group.

TABLE 43 Mean use of health-care resources observed in the collaborative care and usual-care groups over 18 months

Categories of health-care resources	Trial arm									
	Intervention					Usual care				
	Mean	SD	Minimum	Maximum	*n*	Mean	SD	Minimum	Maximum	*n*
GP										
Appointment	10.12	7.74	0	41	226	9.63	7.36	0	45	221
Home visit	0.76	2.48	0	21	226	0.80	2.52	0	26	221
Telephone consultation	2.42	3.75	0	27	226	2.20	3.00	0	15	221
Practice nurse										
Appointment	5.40	6.60	0	54	226	5.10	6.11	0	40	221
Nurse										
Telephone consultation	0.37	2.06	0	24	226	0.33	0.89	0	7	221

TABLE 44 Mean costs (£) associated with collaborative care and usual care over 18 months

Categories of cost	Trial arm									
	Intervention					Usual care				
	Mean	SD	Minimum	Maximum	*n*	Mean	SD	Minimum	Maximum	*n*
Collaborative care	489.18	0.00	489.18	489.18	249	0.00	0.00	0.00	0.00	236
GP										
Appointment	455.18	348.12	0.00	1845.00	226	433.51	331.03	0.00	2025.00	221
Home visit	86.76	282.44	0.00	2394.00	226	90.79	286.95	0.00	2964.00	221
Telephone consultation	65.47	101.30	0.00	729.00	226	59.38	81.07	0.00	405.00	221
Practice nurse										
Appointment	72.58	88.62	0.00	725.40	226	68.44	82.02	0.00	537.33	221
Nurse										
Telephone consultation	2.29	12.68	0.00	147.68	226	2.03	5.49	0.00	43.07	221
Total cost	1171.45	523.60	489.18	4273.94	226	654.15	506.38	0.00	3548.87	221

Health benefits

Health-state utility by time point

Utility scores for each participant were estimated from the responses to the SF-6D at baseline and at 4, 12 and 18 months. *Table 45* presents a summary of the unadjusted utility scores by time point and trial arm across all available respondents at each time point.

However, as we can observe, the available sample number by group and across time points declines as the study progresses. For the purpose of illustration, health-state utilities were estimated using a linear-mixed model and estimate group marginal effect for the mean for each time point; *Figure 16* plots the outputs and illustrates trends in estimated utilities by trial arm over the trial period.

Observing differences in baseline utility scores by trial arms suggests that control for baseline utility to estimate cost-effectiveness is important.

TABLE 45 Unadjusted utility scores by trial arm and time

Trial arm	Mean	SD	Median	Minimum	Maximum	*n*
Collaborative care (utility)						
Baseline	0.551	0.105	0.543	0.345	0.863	243
4 months	0.580	0.144	0.580	0.000	0.937	180
12 months	0.565	0.153	0.569	0.000	0.922	171
18 months	0.540	0.154	0.553	0.000	0.895	175
Usual care (utility)						
Baseline	0.559	0.100	0.565	0.345	0.863	233
4 months	0.566	0.139	0.566	0.000	0.922	195
12 months	0.550	0.143	0.580	0.000	0.859	179
18 months	0.535	0.159	0.545	0.000	0.895	165

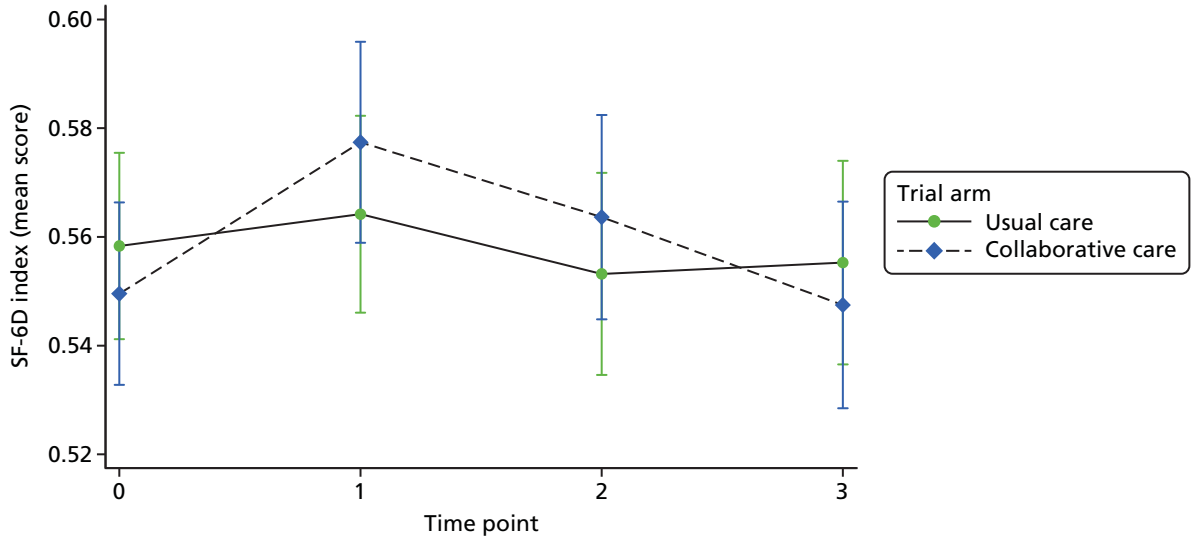

FIGURE 16 Plot of mean (95% CI) of SF-6D indexes over the trial period, by trial arm.

Quality-adjusted life-years

The QALYs were estimated by summing the time-weighted averages of the utility scores between the four time points up to 18 months, for all individuals with information available for complete-case cost-effectiveness analysis. *Table 46* compares the undiscounted QALYs, as well as QALYs discounted at 3% beyond 12 months, by trial arm.

The incremental QALY gained of collaborative care compared with usual care would be 0.011, and this result did not change when QALYs were discounted beyond 12 months. To adjust for baseline utility, we apply ordinary least squares to explain QALYs and controlled for trial arm, age and baseline utility. *Table 47* presents the outputs of the ordinary least squares regression.

Adjusting for baseline utility scores, the collaborative care baseline is associated with an incremental QALY gain of 0.019 (95% CI –0.020 to 0.057; $p = 0.338$). Independent of treatment, baseline utility is significantly predictive of overall QALYs. Given the potential implications of group differences in baseline utility and age, the adjusted incremental QALY gain for collaborative care using the complete-case sample ($n = 362$) informs all subsequent estimates of cost-effectiveness.

TABLE 46 Comparison of QALYs with and without the application of 3% discount rate beyond 12 months

Trial arm	Mean	SD	Median	Minimum	Maximum	*n*
Without a 3% discount beyond 12 months						
Collaborative care	0.900	0.241	0.889	0.036	1.573	175
Usual care	0.889	0.224	0.914	0.044	1.412	187
With a 3% discount beyond 12 months						
Collaborative care	0.893	0.238	0.881	0.036	1.573	175
Usual care	0.882	0.222	0.907	0.044	1.395	187

TABLE 47 Regression analysis controlling for trial arm, age and baseline utility: QALYs

Variables	Coefficient	Standard error	*t*	$p > t$	95% CI
Baseline utility	1.275	0.091	14.070	0.000	1.097 to 1.453
Collaborative care	0.019	0.019	0.960	0.338	–0.020 to 0.057
Age	–0.026	0.016	–1.570	0.118	–0.058 to 0.007
Constant	0.094	0.071	1.320	0.188	–0.046 to 0.233

$n = 362$; $R^2 = 0.3589$.

Cost-effectiveness and uncertainty

Collaborative care for depression resulted in a small but non-significant mean increase in QALYs over the 18-month period, with a higher associated health-care cost. Based on the generic health gains, the mean cost per incremental QALY was £26,016. Examining this ICER, collaborative care for depression falls within the explicit willingness-to-pay range (£20,000–30,000 per QALY)[53] and may represent value for money to the NHS. However, a risk-averse decision-maker may wish to consider the uncertainty in the ICER. Non-parametric bootstrap of the difference in cost and QALYs generates 10,000 replications.

Figure 17 presents results of the bootstrap, depicting the uncertainty surrounding the mean difference in cost and QALYs on the cost-effectiveness plane. The results of the bootstrap indicate the average incremental cost of collaborative care over usual care to be £479.58 (bootstrapped 95% CI £380.55 to £578.61). This demonstrates that a large proportion of the replications fall within the north-east quadrant (82.36%), suggesting that the most likely scenario is that collaborative care in depression increases costs and also creates QALY gains. *Figure 18* illustrates the uncertainty surrounding the ICER and provides 50%, 75% and 95% confidence ellipses. Inference on the 50% confidence ellipse suggests that, based on the current sample size, we cannot absolutely exclude the possibility that collaborative care may reduce health status.

Figure 19 presents the CEAC illustrating the relationship between willingness to pay and the probability that collaborative care would be cost-effective. With reference to the NICE's cost-effectiveness threshold, the likelihood that collaborative care would be cost-effective at £20,000 per QALY is 38.84% and at £30,000 per QALY is 54.94%.

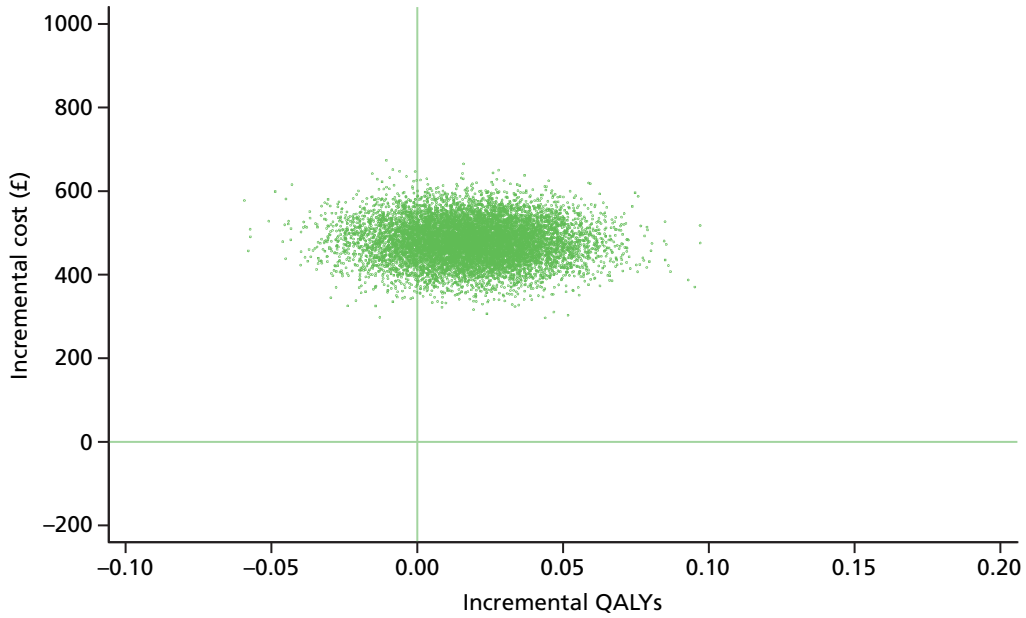

FIGURE 17 Cost-effectiveness plane (controlling for baseline utility). Bootstrap with 10,000 replications.

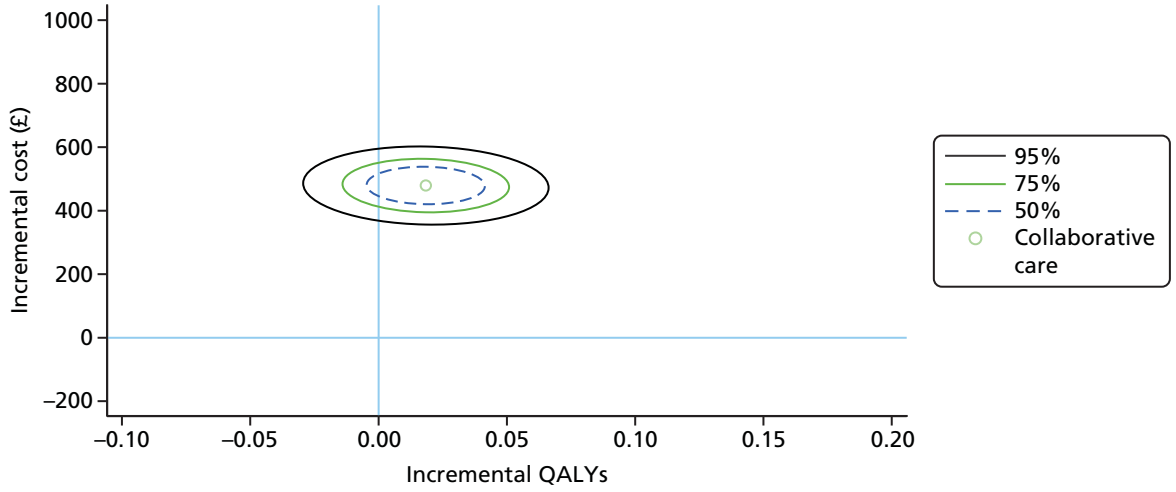

FIGURE 18 Confidence ellipse (controlling for baseline utility).

Sensitivity analysis

Sensitivity analysis: fidelity to intervention sessions and ex post adjustment of the expected direct cost of collaborative care

This analysis seeks to examine documented fidelity of participants to treatment (as observed from data collected using PC-MIS) and to consider how this may adjust our expectation of the cost of implementing collaborative care. *Figure 20* summarises distribution in the number of contacts. The total number of registered sessions shows significant variation, and a bimodal distribution of participant sessions appears evident. This raises the question of whether or not there exists a selection process in early sessions (by consumer, provider or both) that divides patients into two groups. For example, 128 of participants (51%) received five or fewer sessions in the early stage of care and the remaining 49% were most likely to receive 10 sessions.

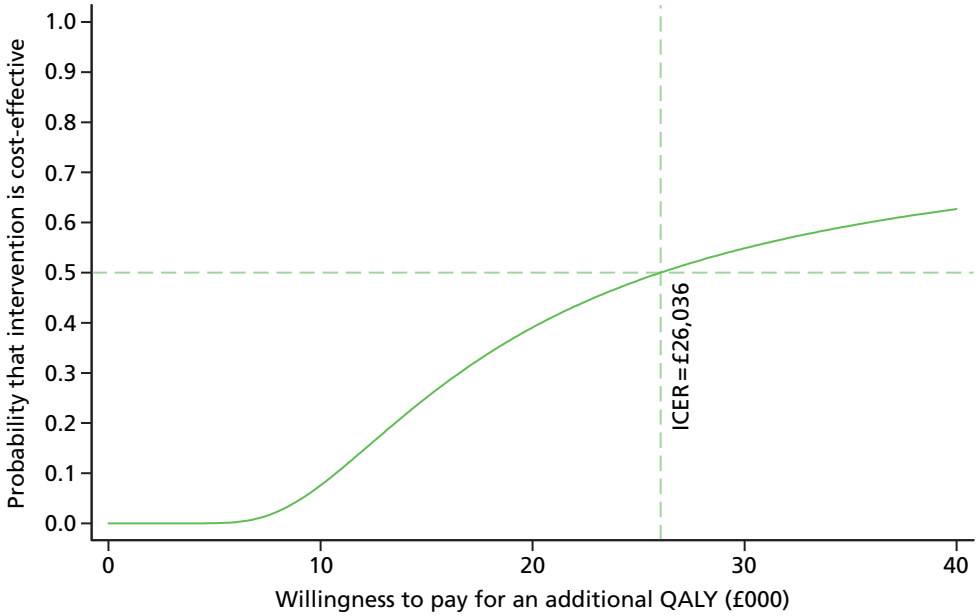

FIGURE 19 Cost-effectiveness acceptability curve (controlling for baseline utility) for the cost per QALY analysis.

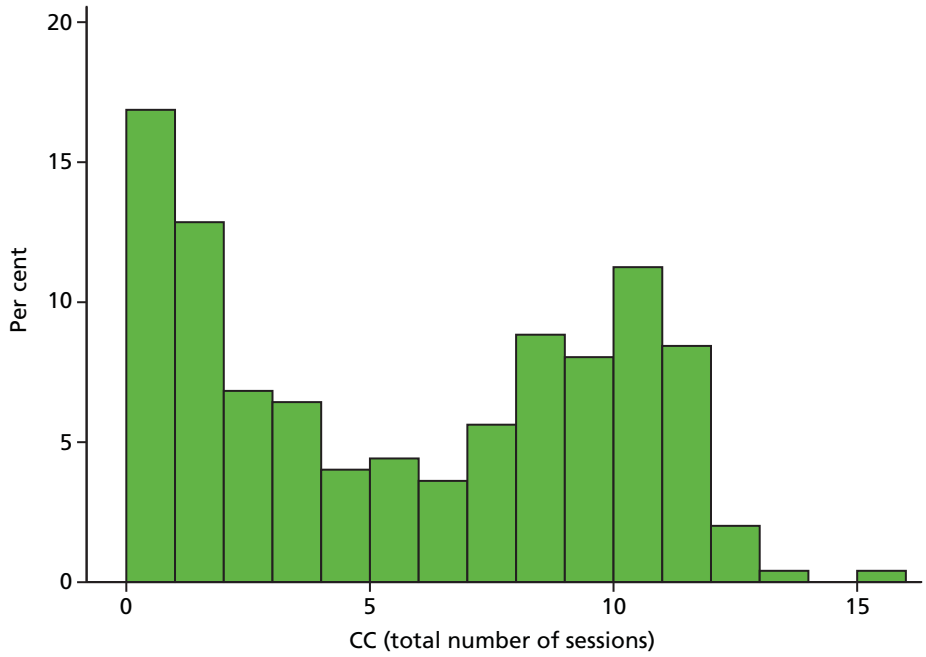

FIGURE 20 Number of sessions of collaborative care. CC, collaborative care.

To examine if health status explains the number of received sessions, *Table 48* presents baseline scores to PHQ-9, GAD-7 and SF-6D contingent on whether or not participants received more or fewer than five sessions. With respect to all three measures, this suggests that the group that received six or more sessions, on average, had poorer health status at baseline. However, reference to 95% CIs would suggest that the between-group difference is not significant.

TABLE 48 Scores at baseline (PHQ-9, GAD-7 and SF-6D index) and subsequent number of sessions

	Baseline scores, mean (95% CI)		
Collaborative care	PHQ-9	GAD-7	SF-6D
Number of sessions			
≤ 5	12.01 (10.26 to 13.76)	9.2 (7.77 to 10.64)	0.553 (0.482 to 0.624)
≥ 6	12.75 (10.96 to 14.55)	9.67 (8.19 to 11.14)	0.548 (0.475 to 0.621)

The next question is, therefore, whether or not the number of sessions is influential on the treatment effect. *Figure 21* illustrates the mean (95% CI) of SF-6D indexes over the trial period comparing usual care with treatment. The trial arms are subdivided into participants who received five or fewer sessions of collaborative care and those who received more than six sessions of care. This provides a clear illustration that a dose–response relation is likely to exist between the number of sessions received and generic health status. Fidelity to, and engagement with, the treatment programme appears to be an important feature in threshold depression.

Table 49 calculates the adjusted direct costs of collaborative care using data from PC-MIS based on session from 174 trial participants. This suggests that, on average, collaborative care received by participants cost £198.25 (95% CI £196.16 to £200.35). Given the available information on health gains, it is difficult to determine how this should be interpreted compared with the expected ex ante cost of £494.73. One interpretation is that, in practice, collaborative care cost £296.48 less than expected.

To examine the value underlying the observed rate of fidelity to treatment, *Figure 22* presents an adjusted CEAC (with ICER) to examine whether, with an intention-to-treat perspective, collaborative care for threshold depression represents value for money or not.

Firstly, given the ratio of average treatment effect to the adjusted cost of collaborative care, an ICER of £10,216 per incremental QALY can be estimated. Costs and QALYs can also be examined by subgroup (i.e. contingent on whether or not participants received more than five sessions of collaborative care).

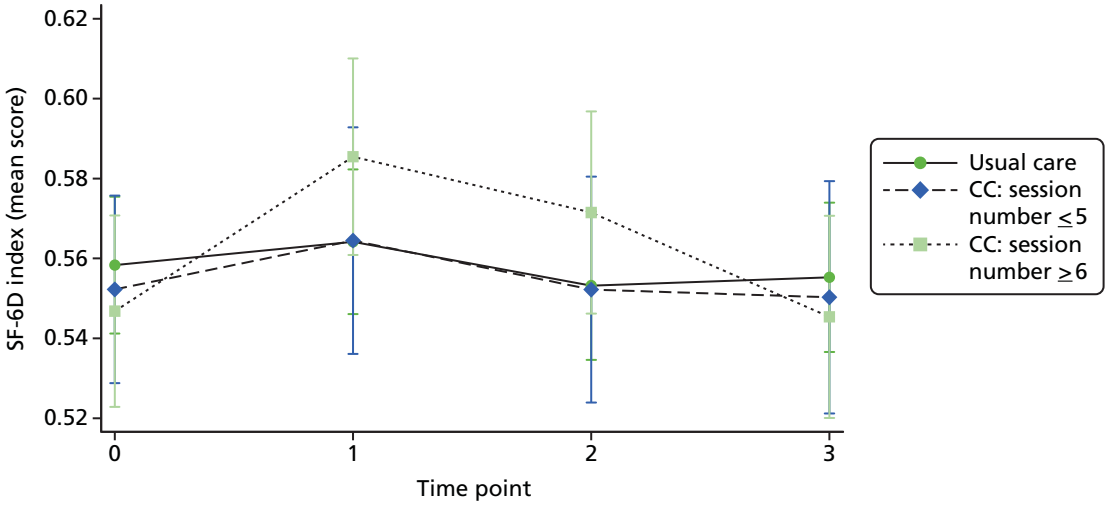

FIGURE 21 Mean (95% CI) of SF-6D indexes over the trial period comparing the usual-care group with trial arms that received either five or fewer sessions of collaborative care or more than six sessions of collaborative care. CC, collaborative care.

TABLE 49 Direct costs of collaborative care (ex post estimation using data from PC-MIS, $n = 174$)

Session	Type of contact (%)			Mean duration (minutes)	Mean cost (£)	Poisson exact (95% CI) (£)
	Face to face	Telephone	E-mail			
1	90.34	9.66	–	60	64.02	62.83 to 65.22
2	5.71	94.29	1.27	31	21.41	20.73 to 22.11
3	6.33	92.41	–	30	19.11	18.47 to 19.77
4	6.34	93.66	–	30	17.95	17.32 to 18.59
5	7.58	92.42	0.83	29	16.68	16.08 to 17.30
6	5.79	93.39	–	29	14.99	14.42 to 15.58
7	6.25	93.75	–	29	14.09	13.53 to 14.66
8	7.14	92.86	1.32	28	11.87	11.37 to 12.40
9	7.89	90.79	–	26	8.30	7.88 to 8.74
10	7.14	92.86	–	27	6.18	5.81 to 6.56
11	7.14	92.86	–	26	2.73	2.49 to 2.99
12	14.29	85.71	–	26	0.43	0.33 to 0.53
13	50	50	–	25	0.21	0.15 to 0.29
14	–	100	–	30	0.15	0.10 to 0.22
15	–	100	–	30	0.15	0.10 to 0.22
Total cost					198.25	196.16 to 200.35

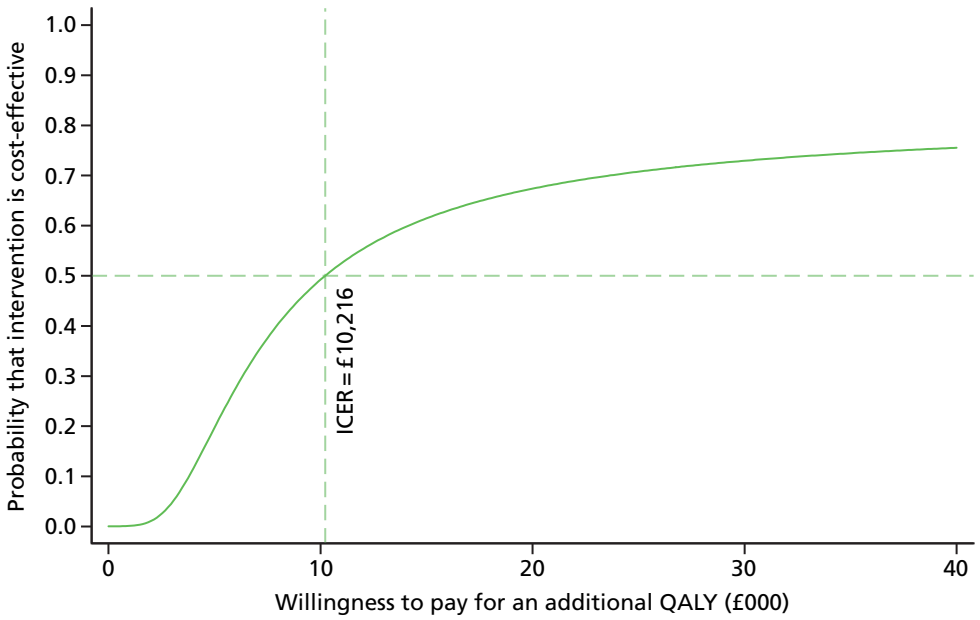

FIGURE 22 Cost-effectiveness acceptability curve (controlling for baseline utility) using ex post estimate of the direct costs of collaborative care.

Table 50 performs a seemingly unrelated regression to inform the cost-effectiveness analysis related to these subgroups.

The results indicate that receiving five or fewer sessions of collaborative care is associated with an average cost of £12 (95% CI –£120 to £143) and results in an average QALY gain of –0.0004 (95% CI –0.0517 to 0.0509); therefore, this strategy is dominated by usual care.

We can also determine that the overall cost of receiving six or more sessions of collaborative care is associated with an average cost of £307 (95% CI £193 to £421.93; $p < 0.001$) and an average QALY gain of 0.0311 (95% CI –0.01375 to 0.0760; $p = 0.174$). Although the statistical significance of the difference in QALY gain is low, despite the reduction in sample size, it remains higher than the average treatment effect presented in *Table 47*. Overall, this suggests that, for individuals who receive six or more sessions of collaborative care, the ICER will be £9876 per QALY.

Figure 23 presents confidence ellipses on the cost-effectiveness plane for each subgroup and clearly illustrates that collaborative care requires a strict minimum number of sessions (i.e. six). Examining the CEAC, we can observe that (for session numbers greater than six) the probability that collaborative care is cost-effective is significantly higher over the explicit reimbursement range (£20,000–30,000 per QALY). These findings suggest that collaborative care may be cost-effective with improved fidelity and that further research to better understand reasons why certain participants do not adhere to the treatment programme (e.g. patient preferences or supply-side competing priorities) is required.

TABLE 50 Seemingly unrelated regression of change in total cost and QALYs explained by sessions of collaborative care controlling for age and baseline utility

Coefficients	Total costs (£) (95% CI)	QALY (95% CI)
Collaborative care: five or fewer sessions	£12 (–£120 to £143)	–0.0004 (–0.0517 to 0.0509)
Collaborative care: six or more session	£307 (£193 to £421.93)****	0.0311 (–0.01375 to 0.0760)*
Age	–£33 (–£117 to £51)	–0.02533 (–0.0582 to 0.0075)*
Baseline utility	–	1.2638 (1.0840 to 1.4436)****
Constant	£560 (£302 to £819)****	0.105 (–0.0365 to 0.2466)*

*$p < 0.2$, **$p < 0.1$, ***$p < 0.01$, ****$p < 0.001$.
Correlation of QALYs and costs = –0.0471; Breusch–Pagan $\chi^2 = 0.790$.

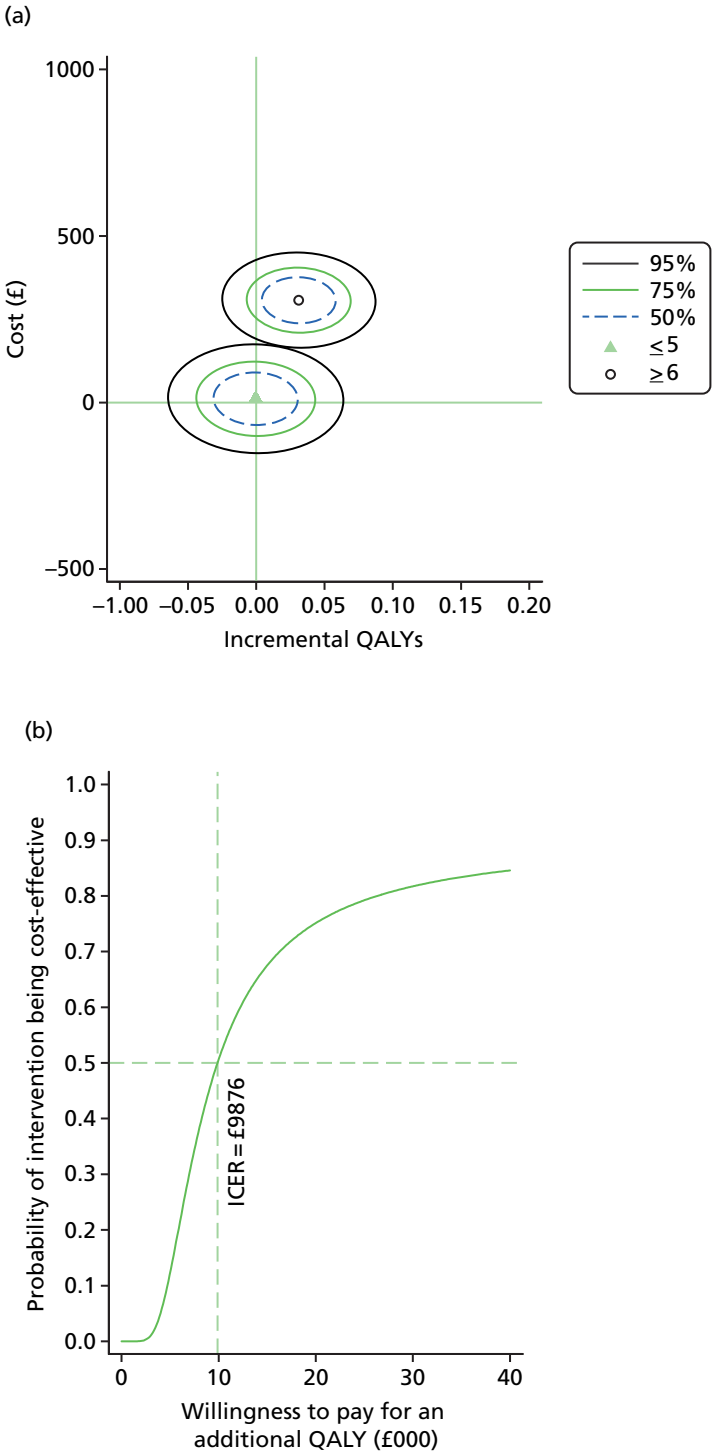

FIGURE 23 (a) Confidence ellipses (comparing collaborative care with more or fewer than six sessions: session number ≤ 5 vs. ≥ 6) and (b) CEAC (for collaborative care with six or more sessions: session number ≥ 6).

Chapter 7 Qualitative findings

Background

Gunn *et al.*[62] reported that GPs perceive patient engagement to be of fundamental importance in dealing with depression. Older people may be reluctant to define their distress as a mental health problem, with implications for treatment acceptance.[13] Simpson *et al.*[63] reported on the experiences of depressed participants receiving collaborative care in the UK, finding that case managers were able to reduce the sense of stigma of being diagnosed with a mental health problem and resolve misconceptions around medication prescribed by the GPs.

Aims

The nested qualitative process evaluation explored the views and experiences of the CASPER plus intervention within the collaborative care framework for the management of depression in older people from the perspectives of participants, case managers and GPs. It considered:

1. Older people's experiences of receiving treatment for depression within a collaborative care framework and the acceptability of the collaborative care intervention. We sought participants' views on depression and their experiences of receiving the intervention from case managers.
2. Case managers' experiences of delivering an intervention for depression within a collaborative care framework.
3. GPs' perspectives of the management of depression and views on the CASPER plus intervention.

The process evaluation explored patient and professional views to determine whether or not service-level integration of care is effective and how it is experienced by participants. It explored whether or not the model of collaborative care intervention fitted within routine practice and was viewed as sustainable. The findings from the CASPER plus RCT (see *Chapter 5*) revealed a statistically significant difference in the primary outcome of depression severity (PHQ-9) between trial arms at 4 months' follow-up in favour of collaborative care, but not at 12 or 18 months' follow-up. Of the secondary outcomes, collaborative care was associated with decreased anxiety (GAD-7 score) at 4 and 12 months, improved mental health functioning (SF-12 MCS score) at 4 months and greater psychological resilience at 12 months. None of the outcomes had a statistically significant difference at 18 months' follow-up.

The qualitative data, presented here, provide insight into:

1. recognising and identifying depression in older people
2. components of the intervention within the collaborative care framework valued by participants
3. how the collaborative care framework fits into current practice.

Methods

Ethics approvals

Ethics approval for the RCT and this qualitative study was gained by Leeds East Research Ethics Committee, Yorkshire & Humber (reference number 10/H1306/61).

Design

We conducted semistructured interviews with trial participants, case managers and GPs to gather in-depth information on their views and experiences of receiving and delivering the intervention and how they perceived the acceptability, engagement and implementation of patient and collaborative care, respectively. Interviews were conducted with trial participants at the end of the intervention period and with case managers delivering the intervention and patient GPs during the intervention.

Sampling

Our aim was to interview a purposive sample of GPs and trial participants, including some participants who declined to take part or who withdrew from the intervention, alongside all the case managers who delivered the intervention. Our approach was to sample participants and GPs from recruiting practices in both urban and rural areas in the north of England and to gather data from areas of differing deprivation indices to achieve a spread in sex, age and socioeconomic status (SES). We aimed to interview all 12 case managers and supervisors and up to 15–20 GPs (or until category saturation was achieved) along with 7–10 participants who did not engage in the intervention and 15 participants who completed the intervention (or until category saturation achieved).

Initially, as numbers were small and recruitment to the trial was slow, we invited all participants who had completed the intervention to take part in a semistructured interview of up to 1 hour. All case managers were invited to be interviewed once they had delivered a course of treatment to at least three participants, and GPs from practices with at least five participants from the collaborative care arm of the trial were invited to be interviewed. Once we had recruited approximately half of our participants this way, we then used a purposive sampling strategy with the aim of gaining a more varied sample of patient and GP participants.

At the start of the CASPER plus qualitative study, following the order of GP practice recruitment, all participants invited to take part were from the central site of York, which included urban and rural practices in the surrounding areas from Harrogate to Hull. Given that most of these areas are of relatively low to moderate deprivation, we used an active selection process to ensure some participants from areas of higher deprivation were invited to be interviewed, such as inner-city Hull.

Participants were sent an invitation pack by post, which comprised a letter, an information leaflet and a consent form with a pre-paid envelope to return to the research team. GPs and case managers were sent an invitation letter, information leaflet and a consent form by e-mail. Before interviews commenced, written informed consent was obtained from all participants (see *Appendices 13–15*).

Data collection

Interviews were carried out by Karen Overend, Katherine Bosanquet and Sarah Nutbrown in a place convenient to the participant and lasted between 20 and 60 minutes. The majority of GPs chose to be interviewed at their practice, although 5 out of 12 asked to be interviewed by telephone. Ten out of the 12 participants requested to be interviewed in their home, with the remaining two choosing to be interviewed by telephone. Nearly all case managers were interviewed in the researcher's office, with three opting for a telephone interview. Interviews were conducted between May 2013 and November 2014. All interviews were digitally recorded (with participants' signed consent), transcribed verbatim and anonymised before data analysis.

A topic guide was developed for each of the three groups (see *Appendices 16–18*). The topic guides were designed with reference to the literature, approved by the research team and developed iteratively as data collection commenced.

Consent

In accordance with ethics guidelines, informed consent was gained by the researcher from each study participant before the interview commenced. An information sheet was sent to the participant in advance, as part of the invitation pack. Before starting the interview, the researcher (interviewer) ensured that this was signed by the participant (interviewee), repeated the main points of the information sheet and aim of the study and gave the participant an opportunity to ask any questions. The researcher assured the participant of

the anonymity and confidentiality of their personal information. GPs and case managers were also given the opportunity to ask questions about the study and were assured anonymity and confidentiality. Consent was obtained from GPs and case managers using the same process as for trial participants.

Data analysis

The interview transcriptions formed the data, through the use of thematic analysis and principles of constant comparison.[64] This was developed iteratively and the topic guides were modified as analysis progressed. The main qualitative researcher on the project (KO) worked closely with the data to identify descriptive coding; this was informed by regular discussion with qualitative supervisor (CC-G) and co-researcher (KB). Analysis was undertaken by individual researchers Karen Overend, Carolyn Chew-Graham and Katherine Bosanquet. Data analysis involved a process of organising the data, descriptive coding, interpretive coding, writing and theorising. Deviant cases were actively sought throughout the analysis and emerging ideas and themes modified in response. Following analysis by individual researchers, themes were agreed during discussion with the full research team.

Findings

In total, 12 GPs, 13 participants (12 who had completed the intervention and one who had withdrawn before commencing therapy) and eight case managers were interviewed (see *Appendix 19*). The main themes identified in the data were 'revealing hidden depression', 'reducing the blind spots', 'an opportunity to talk' and 'moving on' from depression. Our findings are reported in a recent qualitative paper.[65]

Data are presented to support analysis and are labelled by identifier and number.

Revealing hidden depression

For most of the older people we interviewed, being invited to participate in the CASPER plus study seemed to raise their awareness of low mood:

> *It crept up on me really, how I felt. I think it had been coming on for a long time and I didn't realise how bad I'd got until I filled that form in and I just ticked the boxes and posted it.*
>
> *Participant (PT)6*

Several GPs described how taking part in the CASPER plus trial helped to raise awareness of depression in their older population. One GP said:

> *I think it's probably alerted us to one or two of the . . . more needy participants who perhaps were not coming to us for help . . . people have been brought into the system that . . . had sort of dropped out from seeing the GP.*
>
> *GP3*

Some case managers described how some participants admitted they had not spoken to others, including their GPs, about how low they felt:

> *One gentleman that I saw, he said the most useful thing had been the diagnostics, as risk was identified, and so we wrote to the GP about that. And it was . . . the risk was still there when I saw him for the first time so I put that in a letter as well and he said that had kind of opened the door. He would have never gone and spoken to his GP about it.*
>
> *Case manager (CM)2*

> *. . . they [the patient] wouldn't do anything and they wouldn't commit suicide but they feel ashamed I guess of having some thoughts [that they'd be better off dead] . . . and those are the sorts of things they don't always like us to share with the GP because it's back to that stigma, isn't it?*
>
> *CM1*

Although some patient participants did not use labels such as 'depression' or 'low mood', those who did suggested that other older people may fail to recognise or admit their feelings because of the perceived stigma of doing so:

> *. . . people don't talk about it do they, they think it's a weakness don't they? But it is something that you can't help when you are in it, you know as I say you don't realise you are going in it and as much as you try you know sometimes you can't get out it, it gets deeper you know.*
>
> *PT6*

A few patient participants commented on the 'invisibility of depression':

> *. . . you know if I broke an arm I'd get a sling wouldn't I, you know it's fairly obvious, but I suppose with any mental illness you can't see it, you don't know.*
>
> *Withdrawn participant (PTW)1*

Several GPs reported an awareness of the stigma associated with depression, especially in this age group, that may impact on whether or not the patient would raise it within a consultation:

> *It's sort of an age group where they're not as open about depression as maybe younger people are, there's a bit of a stigma attached to it still.*
>
> *GP8*

A few GPs described how they normalised depression in older people; one admitted possibly colluding with the patient in ignoring cues within the primary care:

> *You're sort of aware there are people who have depressive episodes that aren't possibly addressed, they may themselves not really recognise it, and they just think it's part of, you know, getting older.*
>
> *GP3*

> *You'd like to think that primary care is fairly aware of it [depression] anyway. But maybe the temptation is to let sleeping dogs lie, I don't know. So you know, if you diagnose someone with depression you've got to do something about it haven't you?*
>
> *GP6*

Some GPs described a tension between a desire to consider the 'whole' patient and, owing to limited time and treatment options, a tendency to prescribe antidepressants to older people:

> *We often go down a medication route because, well it does help them, and it's very difficult to get other services. And the psychiatry for the elderly tends to be more focused on dementia.*
>
> *GP8*

Several GPs recognised that depression in older people often materialises alongside complex physical conditions or social problems, including loneliness. Some of these GPs disclosed a reluctance to identify the condition, partly because of the absence of a psychological treatment pathway for depression in the over-sixty-fives and a tendency to prioritise physical symptoms over emotional health:

> *I suppose in a busy clinic we probably don't have time to sort of delve into depression along with the sort of 12 and a half minutes of consulting on chronic diseases that's squeezed into 10 minutes, so depression would take another 5 or 6, so . . . we'll probably skip over that unless they bring it to us.*
>
> *GP12*

Being invited to participate in the CASPER plus trial provided an opportunity for some people to talk about depression, enabling them to recognise and seek help for low mood.

Reducing the 'blind spots'

Several case managers and three GPs described how two practitioners working with a patient helped to reduce the 'blind spots', as each professional offered a different perspective:

> *So you've got the benefit of somebody who's looking at a person, never having met them before who can see certain things, versus somebody who has known somebody for some time and can see certain things but, those two people, will have, probably have, blind spots . . . because one person doesn't know that person very well and the other has maybe, over the years, has just sort of formed a fixed idea about somebody. Collaborative working, not only will it progress the patient forward but it will also . . . reduce blind spots, I think, in their care.*
>
> *GP1*

One GP saw the case manager as helping to 'patch up' the gaps in the patient's support network:

> *I think a lot of the difficulty . . . is their support networks have become a bit more fragmented . . . especially those that are bereaved, or have families spread around the country or spread around the world . . . so I can see that maybe we can patch that fragmentation up a little bit . . . it's not the same as having your relatives but having some kind of support, I can see that as a benefit.*
>
> *GP3*

The case managers viewed their role as a facilitator, or 'go-between', who is able to convey information to the GP that the patient may be reluctant to disclose directly:

> *Sometimes, if people can't talk to their GP or don't understand that maybe they had a problem like depression, and don't know how to approach a GP because of stigma and things like that then I've been that facilitator, I've helped them with that process.*
>
> *CM1*

For example, one case manager reported advocating on behalf of a patient who was having problems with pain:

> *. . . she was using cannabis to manage the pain and she felt there was nothing else the doctors could do, so I spoke to her GP and they said she could get a referral to the pain clinic . . . She [the patient] had given up all hope, but she was happy for me to pester them a little bit.*
>
> *CM3*

The GPs and case managers offered different perspectives on participants' health needs, which was seen to reduce 'blind spots' in depression care.

An opportunity to talk

Being offered an opportunity to talk outside the GP consulting room was valued by the majority of participants:

> *The most startling thing about the experience was all my life I've never had anybody to talk to, there're things I wouldn't even discuss with my wife and to have an outsider person that didn't really know me who was impartial . . . that helped me a great deal, just by having someone to discuss things with.*
>
> *PT5*

> *. . . having someone to talk to . . . about things in my life that I would talk to say the family about or friends unless they were extremely close friends, it gave me someone objective to talk to you know, that was removed from my situation.*
>
> *PT2*

Some participants suggested that GPs were not always receptive to discussing problems with mood:

> *You know and the GPs, well they don't, they don't seem to be interested I don't think. Oh, it's depression, take a pill, go away.*
>
> *PT12*

> *I just have a bit of a problem with doctors because I just don't think they do the job that they maybe should be doing, it's a 2-minute interview or whatever, they don't really know your records, they don't know the history, they don't tie things up.*
>
> *PTW1*

In contrast, most participants described the case manager as providing empathic support, being able to offer more time than the GP and knowing how to direct participants to voluntary organisations:

> *. . . she did everything she possibly could . . . I mean she went the extra mile. She spoke to the people at Parkinson's – Parkinson's UK – to see if there was a network somewhere, an advice centre, and things I didn't know she found out for me.*
>
> *PT7*

Patient participants spoke about the benefit of having someone to talk to in confidence, outside the primary care consultation, who was said to listen without judging, allowing them to talk openly about feelings and personal issues:

> *I thought it was very good. And I think the fact that people were bothered, to see how the older people felt . . . I think that was good. You didn't feel like you just got a script thrown at you and you were waiting for God sort of thing . . . it was the fact that someone was interested in how you felt.*
>
> *PT1*

Giving participants an opportunity to talk outside the clinical setting of the primary care consultation room appears to be valued by most of the older people we interviewed and by their GPs.

'Moving on' from depression

Some participants reported how the case manager encouraged them to increase activity and social contact, which the participants felt had improved both their physical health and mood. For example:

> *The telephone conversations for me were helpful. She got me to think about doing things. I'm doing a computer course now and there's a chance I might be able to help them at [voluntary organisation].*
>
> *PT9*

> *It has helped me thinking about things I can do . . . I go in the pool, only in the baby pool but it's good for my legs and my shoulder . . . and you know it makes you feel better once you've done it, not just my legs, but in yourself, you know . . .*
>
> *PT6*

A few participants valued the practical aspects and the techniques learned from the case manager:

> *I've kept a diary all my working life and by going – a daily diary that is – and by going through it we could highlight various things that tip the balance if you like of the scales of happiness and depression and it was highlighted [depression] and between us we figured out a way of coming through it basically.*
>
> *PT5*

> *When we moved onto the technical part of it where they are asking specific questions and giving specific ideas, I find these very useful and in fact I've continued to do those. The ones I am talking about are where you identify things to do . . . and make a list.*
>
> *PT4*

Case management with behavioural activation provides older people with tools to help manage their depressive symptoms and to understand that behaviour and mood are closely linked. Behavioural activation promotes participation in social and physical activity, which may enable older people to 'move on' from depression and to experience improved well-being.

Discussion

To our knowledge this is the first qualitative study to explore the perspectives of older people, case managers and GPs, all of whom were participants in a trial of collaborative care for older people. Our findings support previous studies that suggest that depression in older people may be hidden and that invitation to participate in a trial can serve to uncover depression in participants and to raise awareness in GPs. The findings also illustrate that interaction with the case manager provides older participants with an opportunity to talk outside the primary care consultation, to deal with their low mood and to move forward.

The findings support the literature, which suggests that participation in a trial and active case management can help to reduce stigma and may improve the care for mental health problems, such as depression,[10,66] and that being invited to participate in a trial acted as a catalyst for older people to reflect on their feelings and depression, which may not have been identified outside the trial setting.

Both GPs and participants may normalise depression and view it as an expected consequence of having one or more chronic health conditions.[12,67] GPs may be reluctant to address signs and symptoms of the condition, partly because of the lack of treatment options for older depressed adults and the limited consultation time in which to address the problem. Our results add to the evidence that there is insufficient capacity within existing primary care for psychosocial support of older people with depression[68] and that older people may value a separate space to discuss their problems.

Strengths and weaknesses

This study explored multiple perspectives on the views and experiences of those receiving and delivering a psychosocial intervention for depression within a collaborative care framework. Although we aimed to interview people across a wide demographic range, we found it difficult to recruit GPs and participants from areas of low SES. We believe this may be a reflection of the demographics of trial participation, as people with higher levels of deprivation are less likely to respond to invitation. This means that the group of CASPER plus trial participants we recruited from was disproportionately less deprived than the general population. Similarly, GPs in areas of lower SES were less likely to respond to an invitation to be interviewed. In addition, ethnicity was poorly recorded at GP practices so we were unable to sample on this basis.

Conclusions

Depression is commonly hidden and coexists with physical conditions that are prioritised by both participants and GPs. Being invited to participate in a trial about depression seems to facilitate acceptance of symptoms and may reduce stigma and allow older people to disclose their feelings, name the problem and access care. Older people value an opportunity to talk outside the GP consultation. The findings from this nested qualitative study suggest that a psychosocial intervention delivered by a case manager can provide a valuable resource, which fills a gap in the care of older people with depression. Behavioural activation encourages increased activity and social contact, which may improve physical health symptoms as well as mood. Furthermore, it can enable older people to 'move on' from depression, providing them with the tools to manage their symptoms.

Chapter 8 Discussion

The CASPER plus trial is, to our knowledge, the first large-scale evaluation of the clinical effectiveness and cost-effectiveness of collaborative care in older adults with case-level depression in the UK. The area of research was one that was prioritised by the National Institute for Health Research (NIHR) Health Technology Assessment programme and was identified as a research priority in NICE guidelines on the management of depression.[7] We designed a collaborative care intervention suitable for older people with clinical depression that could feasibly be delivered via expansion of psychological care by the IAPT programme. In the CASPER plus trial outcomes were measured across a broad range of domains including psychological well-being, quality of life, resilience and health-state utility. Important aspects of health service resource use were also recorded. The CASPER plus trial included concurrent qualitative and economic evaluations.

The main findings of the CASPER plus study in relation to (1) trial-based estimates of the clinical effectiveness of collaborative care, (2) trial-based estimates of cost-effectiveness and (3) qualitative examination of acceptability and use of collaborative care will now be discussed in turn.

Trial-based estimate of the clinical effectiveness of collaborative care for subthreshold depression

A group of older adults with *Diagnostic and Statistical Manual of Mental Disorders*-Fourth Edition Major Depressive Disorder were recruited to the CASPER plus study. The mean age of the population was 72 years. There was a high prevalence of coexisting long-term health problems, such as diabetes, arthritis, ischaemic heart disease or chronic respiratory illness.

When offered collaborative care, the majority of participants (83%) engaged with this telephone-based intervention and the mean number of sessions was six.

At 4 months' follow-up there was improvement over time in both groups in terms of depression severity as measured by a commonly used measure of depression severity (the PHQ-9), but a greater level of improvement was recorded in the collaborative care group. There was a statistically significant benefit for collaborative care in terms of the primary outcome of depression severity at 4 months. The magnitude of difference in favour of collaborative care at 4 months was 1.92 PHQ-9 score points (95% CI 0.85 to 2.99 score points; $p < 0.001$). This benefit for collaborative care was not sustained at 12 or 18 months. The score difference at 4 months equates to a standard effect size of 0.34 and is in the range of the effect size that the trial was powered to detect. This finding was robust to a range of sensitivity analyses.

An effect in reducing the prevalence of case-level depression at 4 months was also observed. At 4 months' follow-up, 40% of participants in the collaborative care arm were found to be moderately to severely depressed, compared with 55% in the usual-care group (odds ratio 2.18, 95% CI 1.36 to 3.51). By 12 and 18 months there was no effect for collaborative care.

When a number of secondary outcomes were analysed there was also a benefit for collaborative care. There was a significant and sustained 4- and 12-month improvement in anxiety (as measured by the GAD-7) and somatic complaints (as measured by the PHQ-15). Of note was the fact that common somatic complaints among older people (such as pain, constipation and disrupted sleep patterns) were found to be specifically improved in the collaborative care group compared with the usual-care group.

The population of older adults had important limitations of function consistent with the high levels of physical comorbidity, and this was reflected in low scores on the SF-12 PCS. Physical functioning was below average adult physical health status (scores of < 50) for participants throughout the trial period, as would be

expected in an older population; however, collaborative care had little impact on physical function. Improvements and between-group differences were observed for the MCS of the SF-12 in favour of collaborative care, and in line with changes on other psychological function scales. Improvements were also noted for resilience, as measured by the CD-RISC2 measure at 12 months.

In summary, statistically significant improvements in depression severity were observed in favour of collaborative care in both the short term (4 months) and the medium term (12 months) for secondary outcomes of anxiety and somatisation.

Summary of trial-based estimates of the cost-effectiveness of collaborative care

There was a concurrent cost-effectiveness analysis within the CASPER plus trial, and we were able to derive utility-based estimates of quality of life alongside resource use derived from scrutiny of routinely collected administrative data (GP databases and IAPT databases). Collaborative care was a relatively brief intervention delivered by a low-intensity IAPT therapist. When all costs associated with a fully completed episode of collaborative care were accounted for, the cost to the NHS was £495 per patient. Only around half of the collaborative care participants completed six or more of the eight planned sessions and, when the costs of collaborative care as may be delivered within a typical IAPT service were accounted for, the cost was £198 per patient. There was a non-significant improvement in health-state utilities associated with collaborative care compared with usual care (adjusted QALY gains = 0.019; $p = 0.338$). Resource use was not substantially offset in the collaborative care group, with the total costs reduced by around £51 in the collaborative care group. In the base-case analysis, the incremental cost-effectiveness of collaborative care achieved gains at a cost of £26,010 per QALY. The probability that the incremental cost-effectiveness of collaborative care was less than £20,000 per QALY was 39% and the probability that it fell below the willingness-to-pay threshold of £30,000 per QALY was 55%. When participants who engaged with six or more sessions were included in the analysis, the cost per QALY estimate fell to £9876 per QALY.

Summary of main findings from qualitative examination of acceptability and uptake of collaborative care

The qualitative evaluation explored the perspectives of older people with depression being offered and receiving treatment for depression within a collaborative care framework. It obtained multiple perspectives on the understanding of depression and depression management in older people by investigating both patient and professional views, which provided bottom-up evidence on the acceptability and practicality of the intervention. This type of collaborative care represents an innovative treatment in the NHS, as it involves the delivery of a psychological intervention by a novel mode of delivery (over the telephone).

The qualitative evaluation showed that the intervention was acceptable to a large proportion of participants but that some did not engage with it. Some participants had misgivings about the potential benefits of behaviourally based programmes. Some participants disliked certain aspects of behavioural activation, such as the need to reflect and self-monitor. Others found the activity diaries and 'homework' difficult, requiring too much time and effort. However, case managers learned to adapt treatment and tailor collaborative care to the individual, and this process improved as case managers gained experience.

The qualitative evaluation provided evidence that participants appreciated their personal relationship with the case manager, who was able to facilitate communication with their GP as well as provide them with the opportunity to talk, outside the clinical setting of the primary care consultation room.

Discussion of main findings

The observed standard effect of 0.34 for the primary outcome represents a moderate effect size according to criteria used to classify the magnitude of effect for psychological interventions.[50] The effect size is consistent with findings from systematic reviews of collaborative care, as summarised in a recent Cochrane review,[22] and is also of the same order of magnitude as that seen in UK trials of collaborative care for working-age adults, such as those observed in the recently published CADET[69] and also in the recently completed CASPER trial for older people with lower-severity depression.[29,30] The CASPER plus trial also showed benefits across a range of secondary outcomes, and it was notable that there were improvements in anxiety symptoms, somatoform symptoms and quality of life (mental domain as measured by the SF-12). These benefits were seen in the short term (4 months) and were also sustained at 12 months for secondary outcomes (but not for the outcome of depression severity). At 18 months' follow-up there were no discernible differences between groups.

The proportion of participants with case-level depression at 4 months was reduced among those who received collaborative care. We note that other studies have found longer-term benefits of collaborative care,[70] including studies of collaborative care for older populations,[16] but this finding was not replicated in the CASPER plus trial. When we looked at the prescription of antidepressants in this population, we noted that only a minority of participants were in receipt of any kind of antidepressant. The provision of collaborative care had an impact on the prescription of antidepressants in the short term, with a doubling of antidepressant prescriptions at 4 months' follow-up, but this was not sustained at 12 months. It was in the short term that the greatest benefits were apparent for collaborative care, and this is in line with research which shows a strong relationship between antidepressant prescription rates and the magnitude of benefit from collaborative care.[21] Collaborative care is a complex intervention with multiple components and it is, as yet, unclear how the different components of treatment relate to outcome both in the short and longer term.

We noted from the rates of uptake of the intervention that the majority of participants (83%) engaged well and completed a large number of planned sessions (median six out of eight planned sessions). The qualitative evaluation of collaborative care pointed to aspects of the intervention that participants found helpful. The initial appointment was face to face in order to establish a relationship between the case manager and participant before continuing the sessions as telephone appointments. What was notable was that participants were generally happy to receive collaborative care over the telephone, but that the initial face-to-face meeting was felt to be important. There was some uncertainty whether or not a telephone intervention would be acceptable to older people with depression. It was encouraging to find, from the qualitative study and comments made to case managers, that this was seen by most people to be an acceptable method of delivery. This is important for those who plan services or for therapists who may have misgivings about the telephone-based mode of delivery of a psychosocial intervention. These results are in line with our earlier study of the use of collaborative care for older people with subthreshold depression.

The evidence-supported psychological intervention at the centre of collaborative care in the CASPER plus trial was behavioural activation.[71] The psychological intervention was adapted for use in an older age group at the developmental pilot phase of the CASPER and CASPER plus studies.[49] A reduction in social isolation is an important aspect of the intervention and much of the collaborative care for some participants was focused around this. Although face-to-face contact with the case manager may have provided initial social contact, it would only be in the short term. The case managers sought to reduce social isolation in the long term by ascertaining a participant's needs and preferences regarding social contact. Putting them in touch with organisations, groups and individuals who could help them to increase their social network and opportunities for interaction afforded them long-term benefits.

Case managers worked in a patient-centred way with each participant. There was also a significant use of 'functional equivalence'. If the participant had identified an activity that they had been forced to stop doing in the past, the way they had managed this could be used to illustrate the principle of functional equivalence.

We also found that a small but significant minority of participants did not engage with a psychologically based intervention. Nevertheless, it is notable that the uptake of collaborative care in the context of the CASPER plus trial was broadly in line with (or higher than) a range of primary care-based low-intensity interventions, such as those offered by IAPT services.[72] The results of the CASPER plus trial, therefore, add to an emerging evidence base that behavioural activation is effective for older adults.[73]

The results of the economic evaluation provide robust evidence relating to cost-effectiveness of collaborative care for older people with depression. The CASPER plus trial provides estimates of the overall costs of the intervention, which will be useful for those who may plan services. Within a range of scenarios, collaborative care was found to provide QALY gains within a range of willingness-to-pay thresholds. There are relatively few cost-effectiveness analyses of collaborative care from the perspective of the UK health-care system. The randomised economic research worldwide generally shows that collaborative care is cost-effective.[23] The results of the CASPER plus trial add to emerging evidence of cost-effectiveness of collaborative care in the UK. The economic results of the CASPER trial are broadly in line with the only other UK cost-effectiveness analysis of collaborative care (reporting results of cost per QALY of £14,248 in working-age adults[69]) and also replicate findings from large-scale US studies of collaborative care in older people.[74]

The most recent NICE guidance[7] in relation to the management of depression was unable to recommend collaborative care in this population, and the CASPER plus trial represents a significant advance in the development of randomised knowledge in this area. This research knowledge will be helpful to those who formulate guidelines in the management of depression, including the next iteration of NICE guidelines in the care of depression and the care of psychological problems in the context of long-term physical ill health.[8]

Limitations

The results of the CASPER plus trial need to be considered in the light of limitations that emerged during the study. First, regarding trial design, blinding was not feasible, which means there was potential for contamination at the GP level as well as at an individual level. In addition, many participants would be living geographically close to one another in the same catchment area and in a population of that age it is reasonable to assume that some participants would know each other and share their trial experiences. In either case, we expect that contamination would result in additional benefits to control arm participants, thereby reducing any group differences during follow-up and rendering our result a conservative estimate of the treatment effect. In addition, relating to study design, participants were recruited by means of postal screening of general practice lists, which included patients without a diagnosis of depression; therefore, participants who were identified with depression may not have necessarily presented in usual GP care. Therefore, the results of the CASPER plus trial may not automatically apply to older people who screen-positive for depression in the context of primary care attendance or physical health checks for older people.

Retention and differential attrition between the trial arms was a further limitation. Although follow-up rates were high overall (80% at 4 months), and exceeded the expected trial retention on which the trial was powered, there was a higher rate of attrition in the collaborative care arm compared with the usual-care arm (25% in the collaborative care arm and 14% in the usual-care arm). This was in part accounted for by a number of participants who disengaged from the collaborative care intervention and fully withdrew from the trial at the same time. It remains possible, however, that the patients who withdrew from the trial and did not provide outcome data may have presented a very different outcome profile to those who continued, which may have biased the treatment effect. Based on the very similar baseline characteristics between randomised patients and those available for the primary analysis, as well as our exploration of the impact of missingness, such bias appears less likely. In addition, results of statistical tests relating to the trial's secondary outcomes should be interpreted as exploratory, as no adjustments for multiple testing were made for these analyses.

Another limitation relates to the trial recruitment method whereby participants were invited by their general practices. This resulted in a large number of patients aged ≥ 65 years being invited from each practice, although with relatively low consent rates (mean average 17%), which reduces generalisability. This will have produced a selective sample; however, given that everyone who was invited had equal opportunity to take part and participation was based on patient choice, it was a pragmatic method that would produce similar results if the intervention was rolled out in practice.

Finally, we did not formally assess cognitive impairment. Instead, we asked GPs to screen out any participants with known marked cognitive impairment. For randomised participants, if cognitive impairment was suspected, we informed the GP of this, but we also sought to engage the participant in the intervention for those who were allocated to collaborative care. We do not know the level of cognitive impairment in the current study and the extent to which its presence moderates treatment outcomes.

There were also some important limitations to note on performing the cost-effectiveness analysis. First, although data were collected on secondary care and social care use at each follow-up time point, the data were collected via self-report questionnaires, which were not deemed to be accurate enough data sets to conduct the cost-effective analysis. Therefore, only objective data, obtained from GP administrative systems, informed the cost analysis. Second, it was not possible to provide a reading of participant resource use at baseline, as the study design had approvals to collect health resource use data only from the randomisation date to the study completion date. The baseline was, therefore, outside the period in which participants had consented to provide information.

Chapter 9 Conclusions

There is currently little provision of psychosocial care for older adults with depression. Depression is relatively common among older people and is often associated with long-term health conditions. The CASPER plus trial represents the largest UK trial-based evaluation of a psychosocial intervention for this group. It was found to be effective across a range of depression, psychological and quality-of-life outcomes in the short term. Collaborative care resulted in accelerated improvements in clinical depression at 4 months' follow-up. The effects were less apparent but still present at 12 months' follow-up. The longer-term benefits at 18 months had disappeared when there was no discernible difference between those who received collaborative care and those who received usual care. The intervention was delivered over the telephone by low-intensity psychological therapists, such as those who work in NHS IAPT services. Qualitative research showed this to be an acceptable and valued treatment by the majority of people who were offered collaborative care. A concurrent economic evaluation found that the intervention resulted in gains in QALYs at a cost threshold that is acceptable to the UK health system.

Implications for health care

Collaborative care was acceptable for many of the older adults with depression and could readily be delivered over the telephone, following a first face-to-face meeting. However, although there is, at the policy level, a clearly identified aim to increase uptake of IAPT services in older adults,[75] this has not as yet translated to changes in practice. For example, the most recent annual report on the use of IAPT services[76] indicates that, of over 1,250,000 referrals to IAPT in April 2014 to March 2015, only 79,000 were adults aged $\geq$ 65 years (6.4%). The most recent ONS data (2016)[77] indicate that 17.7% of the UK population is aged $\geq$ 65 years. As a result, it may be worth exploring other methods of delivering the intervention, such as through nurses who conduct comorbidity checks or healthy-living workers. The evaluation of the feasibility and acceptability of delivery by these other professional groups should be a research priority. This may include nurses but should also include any other professional or paraprofessional group that may allow the treatment to be delivered at scale. Certainly, health-care providers will need to ensure that IAPT services have sufficient capacity to enable the provision of collaborative care for older people with depression.

Collaborative care proved clinically effective at improving depression scores and reducing the incidence of case-level depression for older people with depression. The small to moderate effect size of 0.34 may represent limited change at the individual level but it has substantial impact at the population level.[50] Moreover, the robust cost-effectiveness estimates on using collaborative care to treat depression were cost-effective under conventional willingness-to-pay thresholds. This study has shown that collaborative care represents a feasible and effective means of treating depression in primary care. Depression is a relatively common condition, affecting about 5% of older adults. The CASPER plus trial evidence could be used by policy-makers and primary care to improve services and reduce the disease burden of our ageing population.

A final implication for health care relates to the higher drop-out rate from the collaborative care arm and what this would mean for take-up of the intervention in the real world. Some participants found the intervention intrusive and felt that talking and thinking about their symptoms made them feel uncomfortable. This may signal a potential problem if collaborative care were offered in NHS services. As with all psychological services, this type of intervention will not necessarily suit everyone and care should be taken to ascertain the likelihood of this being the case prior to any referral to such a service. Coupled with this is the finding that the greatest level of benefit in relation to costs was found for those who engaged with the intervention for more than five sessions.

Recommendations for research

Analysis of the CASPER plus trial results highlighted a number of future research priorities listed below in order of perceived importance.

- First, a large proportion of the CASPER plus trial had at least one long-term physical health condition, and, although there were some improvements in function and quality of life among participants, there remains little evidence on the clinical effectiveness and cost-effectiveness of collaborative care at treating comorbidities. Evidence from a US trial[78] that tested collaborative care for the treatment of comorbid depression and diabetes mellitus found that it helped improve depression care and outcomes but did not result in improved glycaemic control. Future trials of collaborative care are therefore required to investigate the clinical effectiveness and cost-effectiveness of collaborative care at improving physical and mental health outcomes on older adults with multimorbidities. Given the complexities associated with managing multiple conditions and the increasing number of older adults in our population as it ages, future research in this area is critical. There may also be value in examining the effect of collaborative care in the presence of cognitive impairment.
- Second, many patients in the collaborative care arm discontinued treatment or dropped out of the trial. Further qualitative and quantitative work should explore reasons for this. This should also include maximising the acceptability and effectiveness of collaborative care for this population and identifying the most appropriate target population for the intervention.
- Third, translating the research findings into clinical practice will be challenging and would benefit from further research. This relates both to enabling capacity to deliver the intervention to patients and to be able to target it at those most likely to complete the process and make use of the resource. Future research should also evaluate the feasibility and effectiveness of collaborative care when the case manager is not someone with specific training in mental health. This may include nurses working in primary care but should also include other professionals.
- Fourth, collaborative care is a complex intervention and there is, as yet, little information on how different components relate to outcomes both in the short and longer term. Further work is needed to establish the relationship between treatment components and outcomes.
- Finally, this was a brief intervention and benefit was truncated beyond 12 months. Future research should be conducted to establish how minimal interventions may be offered to ensure that the early gains from treatment are sustained. Trials of 12-month top-up sessions for collaborative care (delivered by telephone) are needed. This would allow the longer term impact of collaborative care and its impact on relapse rates to be investigated. Depression is a recurrent disorder and it would be useful to judge longer term impact on relapse and the prevention of future case-level depression.

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Patient and public involvement in research

The CASPER trial owes great thanks to the users of mental health services and carers who were part of the advisory group, which was established at the end of the pilot phase; their insights and understanding helped improve the relevance and readability of the study documentation.

Contributions of authors

Katharine Bosanquet (Research Fellow, Health Sciences) acted as CASPER study manager since the end of recruitment phase, previously co-ordinated recruitment and the running of the core site, York, managed the collection of objective data from GP practices across all sites and drafted the report.

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All authors approved and/or commented on the final manuscript.

Publications

Papers

Lewis H, Hems D, Bosanquet K, Overend K. Is enough being done to treat depression in the elderly? *Aging Health* 2013;**9**:243–5.

Pasterfield M, Bailey D, Hems DJ, McMillan D, Richards D, Gilbody SM. Adapting manualized Behavioural Activation treatment for older adults with depression. *The Cognitive Behaviour Therapist* 2014;**7**:e5.

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Lewis H, Keding A, Bosanquet K, Bailey D, Gilbody SM, Torgerson D. An randomized controlled trial of Post-it® notes did not increase postal response rates in older depressed participants. *J Eval Clin Pract* 2016;**23**:102–7.

Presentations

Overend K. Collaborative Care for Depression: What is the Magic Ingredient? Systematic Review and Qualitative Meta-Synthesis of Provider and Patient Perspectives. Presented at the Primary Care Mental Health Research Conference, Amsterdam, the Netherlands, 12 May 2016.

Bosanquet K. Geographic Variation in Consent Rates during CASPER plus Randomized Controlled Trial. Presented at the Primary Care Mental Health Research Conference, Durham, UK, 26 March 2015.

Overend K. The CASPER Plus Qualitative Study: Collaborative Care for Older People with Depression. Presented at the Primary Care Mental Health Research Conference, Durham, UK, 26 March 2015.

Chew-Graham C. Case Management for Older People with Depression – A Qualitative Study: 'Reducing the Blind Spots'. Presented at the Society for Academic Primary Care Annual Scientific Meeting Conference, Edinburgh, UK, 20 June 2014.

Overend K, Bosanquet, K. Reducing 'Blind Spots' to Achieve Patient-Centred Care: Early Insights from a Qualitative Study. Presented at the Society for Academic Primary Care North Conference, Kendal, UK, 21–22 November 2013.

Posters

Traviss G, Holmes J, Lewis H, Mitchell N, McMillan D, Hems D, *et al. CASPER – Collaborative cAre for Screen Positive ElderRs*. Presented at British Psychological Society Annual Conference, Harrogate, UK, 2013.

Bosanquet K, Mitchell N, Lewis H, Bailey D, Gabe R, McMillan D, Gilbody S. *Diagnostic Accuracy of Whooley Depression Tool in Older Adults Based in Primary Care in the UK*. Presented at the UK Primary Care Mental Health Research Conference, Manchester, UK, 2013. Won best academic poster award.

Overend K, Lewis H, Bosanquet K, Mann R, Hems D, Bailey D, Chew-Graham C. *The CASPER Plus Nested Qualitative Research Study*. Presented at the UK Primary Care Mental Health Research Conference, Manchester, UK, 2013.

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Bosanquet K. *Objective Data: Measuring Cost-Effectiveness of Healthcare Interventions*. Presented at NIHR CRN Mental Health National Scientific Meeting Conference, York, UK, 2015.

Overend K. *Case Management for Older People with Depression: A Qualitative Study*. Presented at NIHR CRN Mental Health National Scientific Meeting Conference, York, UK, 2015.

Overend K. *The CASPER Plus Qualitative Study: Collaborative Care for Older People with Depression*. Presented at Primary Care Mental Health Research Conference, Durham, UK, 2015.

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- British Broadcasting Corporation (BBC1). *Inside Out North East & Cumbria* [interview with Gilbody S, Foster DJ and Bailey D]. London, 15 October 2012.
- British Broadcasting Corporation (BBC Radio York). *BBC Radio York* [interview with Gilbody S]. York, 15 October 2012.
- British Broadcasting Corporation (BBC1). *Look North* [interview with a GP whose practice participated in the CASPER study]. London, 15 October 2012.

Data sharing statement

Reasonable requests for patient-level data should be made to the corresponding author and will be considered by the CASPER plus trial management group. Consent for data sharing was not obtained but the presented data are anonymised and risk of identification is low.

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Appendix 1 Regulatory approvals

TABLE 51 Regulatory approvals

Trust	Research and development approval granted
NHS East Riding of Yorkshire	18 November 2010
NHS Hull	6 January 2011
NHS North Yorkshire and York	18 November 2010
NHS Leeds	29 September 2011
NHS County Durham	21 October 2011
NHS Darlington	21 October 2011
NHS Middlesbrough	21 October 2011
NHS Stockton-on-Tees	21 October 2011
NHS Hartlepool	21 October 2011
NHS Redcar and Cleveland	21 October 2011
Northumberland Tyne and Wear NHS Foundation Trust	15 February 2013
NHS North of Tyne	5 March 2013

Appendix 2 CollAborative care for Screen-Positive ElderRs plus participant invite letter

GP practice letter head

<Patient name>
<Patient address1>
<Patient address2>
<Patient address3>
<Patient postcode>

Our ref: <admin code>

<Date>

Dear <Patient name>

Invitation to help us with CASPER research project

Would you like to help us? Our Practice is supporting research being carried out by the University of York. They have asked us to send details of their study to all patients aged 65 and over who are registered with our Practice. Are you willing to take part?

This research is looking at the physical and mental health of people who are 65 and over. It wants to find out if there is a better way of providing care for people who are feeling down in the dumps, or just fed up with life. In other words, people who are depressed. Is this new way going to be better than the way GPs care for their patients now? We don't know yet, so we hope the results of this research will help us decide the best way to help you – help us help you! We hope that the study results will improve care for people who are finding life difficult.

We are sending you an information leaflet with this letter. It explains York University's research in detail. It tells you about CASPER – what it is and what it does. There are 2 forms: one yellow and one blue. Fill in the yellow consent form if you want to take part. Send it to the research team in the addressed envelope we have sent you. You don't need a stamp. Fill in the blue form and send it back if you don't want to take part. You don't have to – it's up to you. The care you get from your GP won't be affected in any way if you can't help.

If you have any queries, please contact [local study co-ordinator name and institution] on [local phone number]. If there is no answer, leave a message on the answerphone and someone will call you back.

Thank you for reading this letter.

Yours sincerely

[Lead GP signature and name]

Appendix 3 CollAborative care for Screen-Positive ElderRs plus participant consent form

CASPER

Admin Code:

<Patient name> **< Admin code>**
<Address1> <NHS number>
<Address2>
<Address3>
<Postcode>

<Date of birth> <GP code> <GP practice code>

PARTICIPANT CONSENT FORM

If you wish to take part in the ***CASPER*** study, **please place your initials in each of the boxes below, sign and date this form, and complete the questions overleaf. Please return these forms in the pre-paid envelope provided.** If you (or a relative or friend) would like to ask more questions about this study before deciding whether to take part, please do not hesitate to contact [local researcher], the local study co-ordinator on [telephone number].
All the information on this form will be kept confidential and won't be released to anyone outside the research team

Please initial each box

1. I confirm that I have read and understand the information sheet version 2.10 dated 4th April 2014 for the above study and have had the opportunity to ask questions by phoning the contact number provided. **I agree to take part in the *CASPER* study.** INITIALS
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, and without my medical care or legal rights being affected. INITIALS
3. I understand that sections of my health care records may be looked at by researchers from the University of York, and that information held by the NHS Information Centre and the NHS Central Register may be used to keep in touch with me and follow up my health status for the duration of the study. INITIALS
4. I understand that information, including my date of birth and postcode, to be shared with the NHS Information Centre, specifically for service auditing purposes. I give permission for these individuals to have access to my records. INITIALS
5. I agree to my GP being informed of my participation in the study and of any health concerns the CASPER study team may become aware of during my participation. INITIALS

Name of patient

Today's Date / /

Signature

Your telephone number

Your mobile number

Your email address

Other research studies
Researchers from the *CASPER* team would like to contact men and women who agree to take part in the main *CASPER* study to see if they would be interested in helping with other related studies – these are entirely optional. Please indicate if you would like to be sent information about related studies.

□ **Yes, please send me information about related studies** □ **No, thank you**

Appendix 4 CollAborative care for Screen-Positive ElderRs plus decline form

Admin code:

DECLINE FORM

We would find it really helpful to have a wide range of men and women over the age of 65 joining this study.

However, we quite understand if you do not wish to take part. If this is the case, we would be grateful if you could tell us the reason(s) why by placing a tick in as many boxes as apply to you from the list below:-

I am not interested in taking part in this study ☐

I would not want to speak / see a case manager ☐

I feel too unwell to take part in this study ☐

The information sheet did not tell me enough about the study ☐

Other reason ☐

Please give more details here if you would like to:-

_____

_____

_____

It would be very helpful if you would be willing to give us some brief details about yourself. **We will not be able to identify you from this form, and we will not contact you again.** We will use the anonymous information that you provide to help us see if there are any differences between those who agree to take part and those who decline. **If you wish, please complete the background information questions overleaf, and return these forms in the pre-paid envelope provided. Thank you very much.**

Appendix 5 CollAborative care for Screen-Positive EldeRs plus participant information sheet

Your invitation to take part in a research study

Can you help?

We would like to invite you to take part in our research study. It is important for you to understand why the study is being done and what taking part involves, before you decide. Please read this information sheet carefully and discuss it with your family or friends if you want to. There may be something which needs to be made clearer, or perhaps you would like help to complete the forms. If so, please call us – our contact details are given at the end of this leaflet.

What is the purpose of the study?

This study is trying to find out more about the physical and mental health of people aged 65 and over. It is important to see if a new and different way of providing care is a better way of helping you than the care GPs usually give you. The study results may help us make choices about how to provide care to people who are feeling depressed or not feeling their best.

The way that people feel can affect many other parts of their life. Feeling low is often linked to other things like sleeping badly, not wanting to see people, having no motivation to do anything and not seeing a future – to name a few. As people get older they often have to deal with physical health problems and long-term conditions. Many have to cope with the loss of loved ones or loss of their job or role in society. Not being able to move about so freely anymore can lead to loss of independence and feelings of being isolated and lonely. Any of these different things can affect how people feel, and one thing on top of another can in some cases lead people to feelings of hopelessness and despair.

We are trying to learn more about the health and wellbeing of older adults to try to improve services and treat people as a whole person.

Why have you been approached?

A number of local GP practices are supporting this study. They are writing to patients who are 65 and over registered with their practice. Your practice has identified you as someone who may be suitable to take part.

Do you have to take part?

No, it is up to you to choose whether to take part or not. This information sheet explains all the different parts of the study. Please feel free to contact us if you would like more information, our details are at the end of this leaflet. You will be asked to sign a consent form if you decide to take part. We will send you a copy for you to keep. Please keep this

information sheet as well. Even if you consent to take part you are still free to stop at any time without giving a reason. The standard of care you get from your GP won't change if you decide not to take part, or if you decide to stop once you've started.

Expenses and payments

We will pay for all postage but we are not able to offer any expenses or payments to those who take part in the study.

What will be involved if you agree to take part in the study?

You will be asked to complete a questionnaire about yourself. You will send it back to us in the stamped addressed envelope provided. You may also receive a telephone call from one of our research team to ask you a few more questions over the telephone. You will then be sent a questionnaire: after 4 months, 12 months and 18 months – to be filled in and sent back in addressed envelopes. No stamps required. You may be asked if you would like to take part in an interview to discuss your views about mental wellbeing and the new way of giving care. We will only invite a very small number of people to do this and taking part is voluntary. When the study has finished the results will then published, a summary of which will be made available to you.

What taking part in the trial involves

We don't yet know if the new type of care is any better than the care already offered by your GP to treat depression and improve the feelings of people who are finding life difficult. We need to compare the two methods of giving care to see if there is a difference. Comparing these two different types of care is called a 'trial'. It means half the people in the trial will get the new care and half will get usual GP care.

Once you have sent back your questionnaire to us, we will look through your replies to see if you fit with our needs for the trial. If you do, one of our team will call you to ask you some more questions. We will then place you in one of the three groups – either collaborative care, usual GP care or self-help workbook group. This is done by a computer purely by chance.

At the end of your time in the study, we will ask your GP about any medicines you were prescribed and the number of visits you made to the practice whilst taking part in the study.

What will happen if you are allocated to the collaborative care group?

It means you will get a new type of care called collaborative care. This is when health workers work together as a team with patients and GPs. In your case, you will have a health worker called a case manager to work with you on a one to one basis. He or she will set out to help you. Together you will plan changes that could make your mental health, your wellbeing, and your life – better.

If you are chosen to receive collaborative care, your case manager will contact you to arrange a convenient time to meet you. The first meeting may take place at your home, at your GP practice or over the telephone. After this, you will speak with your case manager each week for up to 10 weeks. This is normally done over the telephone but if you prefer it can be face to face. During your weekly sessions your case manager will discuss a range of issues with you, *e.g.* how you have been feeling since you last spoke, and how to deal with any bad feelings you have had since then. Each time you speak it will last up to 1 hour and at the end, you and your case manager may plan some things for you to do before your next speak.

Taking part in this study does not require you to travel. A case manager will come and visit you at your home or over the telephone if that is what you prefer. Any other discussions can be done over the telephone with the research team, so you do not need to travel anywhere.

What will happen if you are randomly allocated to the usual care group?

Your GP care will continue as normal if you are allocated to the usual care group. We will still ask you to fill in and send back the questionnaires mentioned above. By being in this group you still play a vital part in this study. The information you provide enables us to see whether collaborative care gives better results than usual GP care. We need to compare the two different groups.

What will happen if you are randomly allocated to the self-help booklet group?

It means that you will get a new method of delivering care in the form of a self-help workbook. You will be sent a self-help workbook through the post to read and work through in your own time at a pace that suits you. You will receive up to three telephone calls from a research assistant to offer assistance with the workbook and answer any questions that you may have.

What will happen if you are not eligible to take part in the trial?

If you are found not to be eligible for the trial, this means your symptoms of low mood or depression are not at the level we need for this study. You will not be allocated to the collaborative care, usual care or self-help workbook groups. Your involvement in the trial will finish at this point**.** The care you normally receive from your GP will continue as usual.

What are the possible benefits of taking part in this study?

We cannot promise that taking part in this study will help you. Taking part could help improve the treatment offered to people suffering depression in the future. Collaborative care has been recommended by the government for use in the NHS, but it is not widely available. By taking part in this study you may receive treatment that isn't normally offered to people.

What are the possible disadvantages?

It takes up some of your time. It takes time to complete questionnaires. It takes a bit more time for those who receive collaborative care – up to 1 hour per week for 8-10 weeks. There will also be some short bits of homework to do that you agree with your case manager. For those in the self-help workbook group, some time will be spent reading the booklet and working through the activities.

Will the information in the study be confidential?

We will treat any information you provide us with in confidence. We will store all your information safely. We will not mention your name in any publications about the study and we will make sure that no individuals can be identified in the study results.

Will you be approached about taking part in any other studies?

If you agree to take part in this research, you may be invited to join other research studies on mental wellbeing being carried out by the CASPER team. You do not have to agree to take part in any other similar studies. If you do agree, we will send you more information about these to help you decide.

Will your GP be involved?

We will tell your GP if you agree to take part in this research. We will also get in touch with your GP if we have any concerns about your health while you are helping us with the study. If you are in the collaborative care group, your case manager will liaise with your GP about your care at regular intervals during the time you spend with them.

What if there is a problem?

Get in touch with us if you have any concerns or if there is anything you'd like to ask about the study – our contact details are at the end of this leaflet. If you would prefer to speak to the local principal investigator ([PI name and contact telephone]) or the chief investigator, Professor Simon Gilbody (telephone number: 01904 321370, email: sg519@york.ac.uk) you can contact them directly.

We don't expect the study to cause any harm or upset: but we want to make it clear that we cannot compensate you. If you are harmed due to someone's negligence, then you have grounds for legal action. Please be aware that you may have to pay for it. If you want to complain about anything to do with this study the normal National Health Service complaints service is still there for you.

If you would like to take part in the study, what do you need to do now?

Please fill in and sign the yellow form and its background information sheet. Then return them both in the addressed envelope provided. You do not need a stamp. We are happy to help you complete the forms. Please phone us, our contact details are at the end of this leaflet. If you decide to take part in the study we will write to you in a few weeks' time to let

you know that you are registered on the study. We will ask you to fill in a simple questionnaire. We will also let your GP know that you are involved in the study.

If you're not sure – where can you get more information about the study?

We are happy to answer any questions. Please get in touch with [name] the study co-ordinator, on [local co-ordinator's phone number].

If you don't want to take part in the study, what do you need to do now?

Please complete the blue form and its background information sheet. Return them both in the addressed envelope provided. You do not need a stamp. **We will not be able to know who you are from these forms, and we will not get in touch with you again.** We will use the information you send back to find out if there are any differences between those who agree to take part and those who decide not to.

Is there anyone else you can talk to about the study?

Please contact INVOLVE (**Tel:** 02380 651088) for general information about research. Please contact Mind (**Tel:** 0845 766 0163) for more general information about mental wellbeing.

How can you find out about the results of the study?

We will send a summary of the results to everyone who has taken part in the study when it has finished and the results have been published. You can contact your GP practice or us directly if you decide not to take part in the study, but would still like to receive a copy of the results.

Who is involved in organising and funding this study?

The Department of Health's National Institute of Health Research Health Technology Assessment programme has funded this research study. It is organised by the University of York who is working with teams at different sites in areas around Leeds, Durham and Newcastle. All research funded by the Department of Health is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This research was looked at and approved by Leeds East Research Ethics Committee.

What will happen to all your documentation from the study?

We will store any documentation you send us safely for a minimum of 5 years after the study ends. It will then be professionally destroyed. Paper records will be handled by researchers and statisticians and kept in locked cabinets. Electronic records will be locked onto a computer server at York Trials Unit. Only a few people will be able to use it.

Thank you for reading this information sheet

If you need any further information please get in touch with us. A friend or relative may speak to us on your behalf if you wish. There is an answering machine available 24 hours a day, so please leave a message and one of the research team will contact you as soon as possible. The CASPER study also has a website at www.casper.org.uk

Contact details:-
Study co-ordinator: [local name]
Tel: [local phone number]
Address: [local study centre address]

Appendix 6 CollAborative care for Screen-Positive ElderRs plus background information sheet

Admin code:

Please answer the following questions:

BACKGROUND INFORMATION

1. What is your date of birth? ☐☐ / ☐☐ / 1 9 ☐☐ (day / month / year)

2. Are you? Male ☐ Female ☐

3 a) Over the past month have you been bothered by feeling down, depressed or hopeless? Yes ☐ No ☐

b) Over the past month have you been bothered by having little or no interest or pleasure in doing things? Yes ☐ No ☐

4 Have you fallen in the last 12 months? Yes ☐ No ☐ Can't recall ☐

5. Are you a carer? Yes ☐ No ☐ Don't know ☐

6. Are you a smoker? Yes ☐ No ☐ Don't know ☐

7. On average, do you drink 3 or more units of alcohol each day? (1½ pints of beer *or* 3 glasses of wine *or* 3 short measures of spirits) Yes ☐ No ☐ Don't know ☐

8. Do you experience any of the following health problems? (tick all that apply)

Diabetes	☐	Osteoporosis	☐	High blood pressure	☐	Rheumatoid arthritis	☐	Osteoarthritis	☐
Stroke	☐	Cancer	☐	Respiratory conditions (e.g. COPD, asthma, bronchitis)	☐	Eye condition (e.g.cataract, glaucoma macular degeneration)	☐	Heart disease (e.g.heart attack, heart failure, angina)	☐
Other	☐	Please state: _____							

9. Did your education continue after the minimum school leaving age? Yes ☐ No ☐

10. Do you have a degree or equivalent professional qualification? Yes ☐ No ☐

11. To which of these ethnic groups do you consider you belong? (Please tick one box)

White ☐ Asian or Asian British ☐ Black or Black British ☐

Other ethnic group ☐ Please describe: _____

Appendix 7 CollAborative care for Screen-Positive ElderRs plus baseline questionnaire

CONFIDENTIAL

CASPER

Baseline Questionnaire

Participant's trial ID number: ☐☐ - ☐☐☐☐☐

Date questionnaire sent: ☐☐ / ☐☐ / 2 0 ☐☐

Day *Month* *Year*

Funded by:

NIHR HTA code 08/19/04
ISRCTN 02202951
CASPER baseline qr v2.5 4Jan13

Organised by:

North East Hub Mental Health Research Network
The University of York
National Institute for Health Research
University of Leeds
Northumberland, Tyne and Wear NHS Foundation Trust
Tees, Esk and Wear Valleys NHS Foundation Trust

1836551920

PLEASE READ ALL THE INSTRUCTIONS BEFORE COMPLETING THE QUESTIONNAIRE

Thank you for agreeing to take part in this study. The responses you give in this questionnaire will help us find out which is the best way to improve mental well-being amongst those over the age of 65.

Please answer ALL the questions. Although some of the questions may not seem relevant to yourself or may appear similar, they do give us valuable information.

If you find it difficult to answer the question, please give the best answer you can.

Please follow the instructions for each section carefully.

For each section, if you are asked to put a cross in the box, please use a cross rather than a tick, as if you were filling out a ballot paper.

For example in the following question, if your answer to the question is yes, you should place a cross firmly in the box next to yes.

Do you drive a car?

Yes ☒

No ☐

If you are asked to write your answer, please do so by entering your answer in the box provided, for example:

How old are you? | 7 | 5 | years

Please use a black or blue pen for all the questions.

Please do not use a pencil or any other coloured pen.

If you have any queries or problems completing this questionnaire please contact your local study centre:

[redacted]

2108551923

Please enter the date you are completing this questionnaire:

		/			/	2	0		
Day			*Month*			*Year*			

SECTION 1

This section is about how you have been feeling over the **last 2 weeks**.
Answer each question by placing a cross in the box that best describes your answer.

1. Little interest or pleasure in doing things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Feeling down, depressed, or hopeless

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Trouble falling or staying asleep, or sleeping too much

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Feeling tired or having little energy

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Poor appetite or overeating

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Feeling bad about yourself - that you are a failure or have let yourself or your family down

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Trouble concentrating on things, such as reading the newspaper or watching television

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

8. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

9. Thoughts that you would be better off dead, or of hurting yourself in some way

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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Over the **last 2 weeks**, how often have you been bothered by any of the following problems?

1. Feeling nervous, anxious or on edge

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Not being able to stop or control worrying

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Worrying too much about different things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Trouble relaxing

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Being too restless that it is hard to sit still

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Becoming easily annoyed or irritable

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Feeling afraid as if something awful might happen

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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SECTION 2

This section is about any physical health problems you may be experiencing.
Please cross one box for each health problem.

During the **past 4 weeks**, how much have you been bothered by any of the following problems?

1. Stomach pains

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

2. Back pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

3. Pain in your arms, legs, or joints (e.g. knees, hips)

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

4. Headaches

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

5. Chest pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

6. Dizziness

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

7. Fainting spells

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

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8. Feeling your heart pound or race

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

9. Shortness of breath

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

10. Pain or problems during sexual intercourse

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

11. Constipation, loose bowels, or diarrhoea

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

12. Nausea, gas, or indigestion

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

13. Feeling tired or having low energy

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

14. Trouble sleeping

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

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SECTION 3

This section asks you about how you've been feeling.

Answer each question by placing a cross in the box that best describes your answer.

1a. Over the **past month** have you been bothered by feeling down, depressed or hopeless?

Yes ☐ No ☐

1b. Over the **past month** have you been bothered by having little or no interest or pleasure in doing things?

Yes ☐ No ☐

2a. I tend to bounce back after illness or hardship

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

2b. I am able to adapt to change

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

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SECTION 4

This section asks for your views about your health. This information will help us keep track of how you feel and how well you are able to do your usual activities.

Answer each question by placing a cross in the box that best describes your answer.

1. In general, would you say your health is:
(please cross one box only)

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

2. During a typical day does **your health** limit you in **moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

3. During a typical day does **your health** limit you in climbing **several** flights of stairs? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

4. During the **past 4 weeks**, how much of the time have you accomplished less than you would like in regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

5. During the **past 4 weeks**, how much of the time have you been limited in performing any kind of work or other regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

6. During the **past 4 weeks**, how much of the time have you accomplished less than you would have liked in your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

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7. During the **past 4 weeks**, how much of the time have you done work or other activities less carefully than usual **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (both outside the home and housework)?
(please cross one box only)

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

9. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt calm and peaceful ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

10. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** did you have a lot of energy ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

11. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt downhearted and depressed?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

12. During the **past 4 weeks** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives etc.)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

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SECTION 5

This section also asks about your health in general.

By placing a cross in one box in each group below, please indicate which statements best describes your own **health state today**.

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

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SECTION 6

This section is about any medication you have been prescribed to improve your mental well-being.

Are you **currently** prescribed any of the medicines listed below?

Yes ☐ No ☐ Don't know ☐

If 'Yes', please cross all that apply.

Dosulepin ☐	Sertraline ☐	Venlafaxine ☐
Lofepramine ☐	Fluoxetine ☐	Duloxetine ☐
Citalopram ☐	Paroxetine ☐	Trazodone ☐
Mirtazapine ☐	Other ☐ *please list any other medications below*	

1.	2.
3.	4.
5.	6.
7.	8.
9.	10.

If you **are** prescribed one of these medicines but have stopped taking it for any reason please place a cross in this box. ☐

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SECTION 7

This section asks about any health care you have received as a patient **for any reason** (please do not include any visits to your GP practice).

Answer each question by placing a cross in the box that best describes your answer.

Attending hospital

1a. During the **last 6 months** have you stayed overnight in hospital?

Yes ☐ No ☐ (go to 2a) Don't know ☐

1b. If 'Yes', On how many separate occasions did you stay overnight in hospital? ☐☐

Please provide some details for each occasion you stayed in hospital (e.g. hip replacement, fall).

(if you have stayed more than 2 occasions, we will contact you for further details)

1c. **First hospital visit**

1d. After your hospital visit were you:

- Transferred to community hospital (e.g. for rehabilitation) ☐
- Discharged back to your home ☐
- Other (please state) ☐

1e. **Second hospital visit**

1f. After your hospital visit were you:

- Transferred to community hospital (e.g. for rehabilitation) ☐
- Discharged back to your home ☐
- Other (please state) ☐

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Other visits to hospital

2a. Have you attended Accident and Emergency in the **last 6 months**?

Yes ☐ No ☐ (go to 3a) Don't know ☐

2b. If 'Yes', how many times have you attended Accident and Emergency in the **last 6 months**? ☐☐

3a. Have you attended Hospital Outpatients in the **last 6 months**?

Yes ☐ No ☐ (go to 4a) Don't know ☐

3b. If 'Yes', how many times have you attended Hospital Outpatients in the **last 6 months**? ☐☐

4a. Have you attended hospital as a day case/procedure patient in the **last 6 months**?

Yes ☐ No ☐ (go to 5a) Don't know ☐

4b. If 'Yes', how many times have you attended hospital as a day case/procedure in the **last 6 months?** ☐☐

NHS transport services

5a. Have you used a '999' emergency ambulance in the **last 6 months**?

Yes ☐ No ☐ (go to 6a) Don't know ☐

5b. If 'Yes', how many times have you used a '999' emergency ambulance in the **last 6 months**? ☐☐

6a. Have you used the Patient Transport Service in the **last 6 months**?

Yes ☐ No ☐ (go to 7a) Don't know ☐

6b. If 'Yes', how many times have you used the Patient Transport Service in the **last 6 months**? ☐☐

Other NHS services

7a. Have you gone to an NHS Walk-in Centre in the **last 6 months**?

Yes ☐ No ☐ (go to 8a) Don't know ☐

7b. If 'Yes', how many times have you been to an NHS Walk-in Centre in the **last 6 months**? ☐☐

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8a. Have you called NHS Direct (the NHS telephone helpline) in the **last 6 months**?

Yes ☐ No ☐ (go to 9a) Don't know ☐

8b. If 'Yes', how many times have you called NHS Direct (the NHS telephone helpline) in the **last 6 months**? ☐☐

Support services

9a. Do you receive any home help?

Yes ☐ No ☐ (go to 10a) Don't know ☐

9b. Thinking about the **last 6 months**, of these how many months did you have home help? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐

9c. Thinking about the **last 6 months**, typically, how many times a week did home help visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

10a. Does a care worker visit you at home?

Yes ☐ No ☐ (go to 11a) Don't know ☐

10b. Thinking about the **last 6 months**, of these how many months did a care worker visit you at home? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐

10c. Thinking about the **last 6 months**, typically, how many times a week did a care worker visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

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11a. Do you use meals on wheels?

Yes ☐ No ☐ (go to 12a) Don't know ☐

11b. Thinking about the **last 6 months**, of these how many months did you use meals on wheels? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐

11c. Thinking about the **last 6 months**, typically, how many times a week did you use meals on wheels?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

12a. Do you go to any community centres?

Yes ☐ No ☐ Don't know ☐

12b. Thinking about the **last 6 months**, typically, how many times a week do you go to a community centre?

0 ☐ 1-2 ☐ 2-3 ☐ 3-4 ☐ 4+ ☐

12c. Which community centres do you attend?

☐

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SECTION 8

This section is about your views on how well you understood the different aspects of the CASPER Study before you signed the consent form.

Each of the 10 questions below relates to a different aspect. Answer each question by circling the number that best describes your answer

For example:
If you didn't understand them at all, please circle 1.
If you understood it very well, please circle 5.
If you understand it somewhat, please circle a number between 1 and 5.

		I didn't understand this at all				I understood this very well
1.	What the researchers are trying to find out in the study	1	2	3	4	5
2.	How long you will be in the study	1	2	3	4	5
3.	The treatments and procedures you will undergo	1	2	3	4	5
4.	The possible risks and discomforts of participating in the study	1	2	3	4	5
5.	The possible benefits to you of participating in the study	1	2	3	4	5
6.	How your participation in this study may benefit future patients	1	2	3	4	5
7.	The effects of the study on the confidentiality of your medical records	1	2	3	4	5
8.	Whom you should contact if you have questions or concerns about the study	1	2	3	4	5
9.	The fact that participation in the study is voluntary	1	2	3	4	5
10.	Overall, how well did you understand the study when you signed the consent form?	1	2	3	4	5

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SECTION 9

This final section is a list of important life events. For each life event please circle 'Yes' if you have experienced that life event **over the last year** and 'No' if you have not. For those that you have experienced, please also indicate the date that the event occurred with as much accuracy as you can.

Life event	Y / N	Timing Month / Year
You yourself suffered a serious illness, injury or an assault	Yes No	☐☐ / ☐☐
A serious illness, injury or assault happened to a close relative	Yes No	☐☐ / ☐☐
Your child, spouse or parent died	Yes No	☐☐ / ☐☐
A close family friend or another relative (niece, cousin, grandchild) died	Yes No	☐☐ / ☐☐
You had a separation due to marital difficulties	Yes No	☐☐ / ☐☐
You broke off a steady relationship	Yes No	☐☐ / ☐☐
You had a serious problem with a close friend, neighbour or relative	Yes No	☐☐ / ☐☐
You became unemployed or you were seeking work unsuccessfully for more than one month	Yes No	☐☐ / ☐☐
You were sacked from your job	Yes No	☐☐ / ☐☐
You had a major financial crisis	Yes No	☐☐ / ☐☐
You had problems with the police and a court appearance	Yes No	☐☐ / ☐☐
Something you valued was lost or stolen	Yes No	☐☐ / ☐☐

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If you have any general comments about the study, or this questionnaire, please write them below.

Thank you for completing this questionnaire.
Please return it in the pre-paid envelope provided.

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Appendix 8 Exploring risk in research interviews assessment form

Exploring Risk in Research Interviews

Participant ID code: _____ **PHQ-9 Score:** _____

PHQ-9 probing question: "Can you tell me more about why you answered (several days* / more than half the days* / nearly every day*delete) to 'Thoughts that you would be better off dead, or of hurting yourself in some way'?"
Details of disclosed thoughts (please record verbatim as far as possible)

Plans	
1. Do you know how you would kill yourself? If **Yes** – details	Yes / No
2. Have you made any actual plans to end your life? If **Yes** – details	Yes / No
Actions	
3. Have you made any actual preparations to kill yourself? If **Yes** – details	Yes / No
4. Have you ever attempted suicide in the past? If **Yes** – details	Yes / No
Prevention	
5. Is there anything stopping you killing or harming yourself at the moment? If **Yes** – details	Yes / No
6. Do you feel that there is any immediate danger that you will harm or kill yourself? If **Yes** – details	Yes / No

Researcher name:
Researcher signature: **Date:**

CASPER

Participant Suicide Intention Form

The participant below has expressed thoughts of suicidal intent / self-harm on the PHQ-9 of a questionnaire or during their diagnostic interview.

Participant ID code: ☐

Risk of Suicide / Self-harm identified from

Question 9 of PHQ-9 on a questionnaire	3 (*nearly every day)*	☐
	2 (*more than half the days*)	☐
	1 *(several days)*	☐
Question 9 of PHQ-9 during diagnostic interview	3 (*nearly every day)*	☐
	2 (*more than half the days*)	☐
	1 *(several days)*	☐
Question 3g of MINI during diagnostic interview	*'Yes'* to past two weeks (not to past episode)	☐

Summary of how procedure was enacted

(Which clinician gave advice, what advice was given, was risk judged as passive or active? If advised to contact GP – name of practice, name of GP spoken to, date etc.)

Researcher name:
Researcher signature: **Date:**

Local clinical lead name:
Local clinical lead signature: **Date:**

Appendix 9 CollAborative care for Screen-Positive EldeRs plus 4-month follow-up questionnaire

CONFIDENTIAL

CASPER

Four Month Follow-up Questionnaire

Participant's trial ID number: ☐☐ - ☐☐☐☐☐

Date questionnaire sent: ☐☐ / ☐☐ / 2 0 ☐☐

Day *Month* *Year*

Funded by:
NIHR HTA code 08/19/04
ISRCTN 02202951
CASPER 4mth qr v2.3 8Feb12

Organised by:
The University of York
University of Leeds
Durham University

5383130485

PLEASE READ ALL THE INSTRUCTIONS BEFORE COMPLETING THE QUESTIONNAIRE

Thank you for agreeing to take part in this study. The responses you give in this questionnaire will help us find out which is the best way to improve mental well-being amongst those over the age of 65.

Please answer ALL the questions. Although some of the questions may not seem relevant to yourself or may appear similar, they do give us valuable information.

If you find it difficult to answer the question, please give the best answer you can.

Please follow the instructions for each section carefully.

For each section, if you are asked to put a cross in the box, please use a cross rather than a tick, as if you were filling out a ballot paper.

For example in the following question, if your answer to the question is yes, you should place a cross firmly in the box next to yes.

Do you drive a car?

Yes ☒

No ☐

If you are asked to write your answer, please do so by entering your answer in the box provided, for example:

How old are you? | 7 | 5 | years

Please use a black or blue pen for all the questions.

Please do not use a pencil or any other coloured pen.

If you have any queries or problems completing this questionnaire please contact your local study centre:

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Please enter the date you are completing this questionnaire:

		/			/	2	0		
Day			*Month*			*Year*			

SECTION 1

This section is about how you have been feeling over the **last 2 weeks**.
Answer each question by placing a cross in the box that best describes your answer.

1. Little interest or pleasure in doing things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Feeling down, depressed, or hopeless

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Trouble falling or staying asleep, or sleeping too much

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Feeling tired or having little energy

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Poor appetite or overeating

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Feeling bad about yourself - that you are a failure or have let yourself or your family down

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Trouble concentrating on things, such as reading the newspaper or watching television

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

8. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

9. Thoughts that you would be better off dead, or of hurting yourself in some way

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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Over the **last 2 weeks**, how often have you been bothered by any of the following problems?

1. Feeling nervous, anxious or on edge

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Not being able to stop or control worrying

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Worrying too much about different things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Trouble relaxing

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Being too restless that it is hard to sit still

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Becoming easily annoyed or irritable

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Feeling afraid as if something awful might happen

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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SECTION 2

This section is about any physical health problems you may be experiencing.
Please cross one box for each health problem.

During the **past 4 weeks**, how much have you been bothered by any of the following problems?

1. Stomach pains

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

2. Back pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

3. Pain in your arms, legs, or joints (e.g. knees, hips)

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

4. Headaches

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

5. Chest pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

6. Dizziness

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

7. Fainting spells

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

8. Feeling your heart pound or race

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

9. Shortness of breath

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

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10. Pain or problems during sexual intercourse

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

11. Constipation, loose bowels, or diarrhoea

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

12. Nausea, gas, or indigestion

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

13. Feeling tired or having low energy

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

14. Trouble sleeping

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

SECTION 3

This section asks you about how you've been feeling.

Answer each question by placing a cross in the box that best describes your answer.

1a. I tend to bounce back after illness or hardship

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

1b. I am able to adapt to change

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

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SECTION 4

This section asks for your views about your health. This information will help us keep track of how you feel and how well you are able to do your usual activities.

Answer each question by placing a cross in the box that best describes your answer.

1. In general, would you say your health is:
(please cross one box only)

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

2. During a typical day does **your health** limit you in **moderate actvities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

3. During a typical day does **your health** limit you in climbing **several** flights of stairs? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

4. During the **past 4 weeks**, how much of the time have you accomplished less than you would like in regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

5. During the **past 4 weeks**, how much of the time have you been limited in performing any kind of work or other regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

6. During the **past 4 weeks**, how much of the time have you accomplished less than you would have liked in your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

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7. During the **past 4 weeks**, how much of the time have you done work or other activities less carefully than usual **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (both outside the home and housework)?
(please cross one box only)

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

9. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt calm and peaceful ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

10. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** did you have a lot of energy ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

11. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt downhearted and depressed?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

12. During the **past 4 weeks** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives etc.)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

1417130489

SECTION 5

This section also asks about your health in general.

By placing a cross in one box in each group below, please indicate which statements best describes your own **health state today**.

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

9366130480

SECTION 6

This section is about any medication you have been prescribed to improve your mental well-being.

Are you **currently** prescribed any of the medicines listed below?

Yes ☐ No ☐ Don't know ☐

If 'Yes', please cross all that apply.

Dosulepin ☐	Sertraline ☐	Venlafaxine ☐
Lofepramine ☐	Fluoxetine ☐	Duloxetine ☐
Citalopram ☐	Paroxetine ☐	Trazodone ☐
Mirtazapine ☐	Other ☐ *please list any other medications below*	

1. _____ 2. _____

3. _____ 4. _____

5. _____ 6. _____

7. _____ 8. _____

9. _____ 10. _____

If you **are** prescribed one of these medicines but have stopped taking it for any reason please place a cross in this box. ☐

2774130486

SECTION 7

This final section is about any health care you have received as a patient **for any reason** (please do not include any visits to your GP practice).

Answer each question by placing a cross in the box that best describes your answer.

Attending hospital

1a. During the **last 4 months** have you stayed overnight in hospital?

Yes ☐ No ☐ (go to 2a) Don't know ☐

1b. On how many separate occasions did you stay overnight in hospital? ☐☐

Please provide some details for each occasion you stayed in hospital (e.g. hip replacement, fall).

(If you have stayed more than 2 occasions, we will contact you for further details)

1c. **First hospital visit**

1d. After your hospital visit were you:

Transferred to community hospital (e.g. for rehabilitation) ☐

Discharged back to your home ☐

Other (please state) ☐

1e. **Second hospital visit**

1f. After your hospital visit were you:

Transferred to community hospital (e.g. for rehabilitation) ☐

Discharged back to your home ☐

Other (please state) ☐

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Other visits to hospital

2a. Have you attended Accident and Emergency in the **last 4 months**?

Yes ☐ No ☐ (go to 3a) Don't know ☐

2b. If 'Yes', how many times have you attended Accident and Emergency in the **last 4 months**? ☐☐

3a. Have you attended Hospital Outpatients in the **last 4 months**?

Yes ☐ No ☐ (go to 4a) Don't know ☐

3b. If 'Yes', how many times have you attended Hospital Outpatients in the **last 4 months**? ☐☐

4a. Have you attended hospital as a day case/procedure patient in the **last 4 months**?

Yes ☐ No ☐ (go to 5a) Don't know ☐

4b. If 'Yes', how many times have you attended hospital as a day case/procedure in the **last 4 months?** ☐☐

NHS transport services

5a. Have you used a '999' emergency ambulance in the **last 4 months**?

Yes ☐ No ☐ (go to 6a) Don't know ☐

5b. If 'Yes', how many times have you used a '999' emergency ambulance in the **last 4 months**? ☐☐

6a. Have you used the Patient Transport Service in the **last 4 months**?

Yes ☐ No ☐ (go to 7a) Don't know ☐

6b. If 'Yes', how many times have you used the Patient Transport Service in the **last 4 months**? ☐☐

Other NHS services

7a. Have you gone to an NHS Walk-in Centre in the **last 4 months**?

Yes ☐ No ☐ (go to 8a) Don't know ☐

7b. If 'Yes', how many times have you been to an NHS Walk-in Centre in the **last 4 months**? ☐☐

1234130486

8a. Have you called NHS Direct (the NHS telephone helpline) in the **last 4 months**?

Yes ☐ No ☐ (go to 9a) Don't know ☐

8b. If 'Yes', how many times have you called NHS Direct (the NHS telephone helpline) in the **last 4 months**? ☐☐

Support services

9a. Do you receive any home help?

Yes ☐ No ☐ (go to 10a) Don't know ☐

9b. Thinking about the **last 4 months**, of these how many months did you have home help? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐

9c. Thinking about the **last 4 months**, typically, how many times a week did home help visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

10a. Does a care worker visit you at home?

Yes ☐ No ☐ (go to 11a) Don't know ☐

10b. Thinking about the **last 4 months**, of these how many months did a care worker visit you at home? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐

10c. Thinking about the **last 4 months**, typically, how many times a week did a care worker visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

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11a. Do you use meals on wheels?

Yes ☐ No ☐ (go to 12a) Don't know ☐

11b. Thinking about the **last 4 months**, of these how many months did you use meals on wheels? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐

11c. Thinking about the **last 4 months**, typically, how many times a week did you use meals on wheels?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

12a. Do you go to any community centres?

Yes ☐ No ☐ Don't know ☐

12b. Thinking about the **last 4 months**, typically, how many times a week do you go to a community centre?

0 ☐ 1-2 ☐ 2-3 ☐ 3-4 ☐ 4+ ☐

12c. Which community centres do you attend?

3872130486

If you have any general comments about the study, or this questionnaire, please write them below.

Thank you for completing this questionnaire.
Please return it in the pre-paid envelope provided.

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Appendix 10 CollAborative care for Screen-Positive ElderRs plus 12-month follow-up questionnaire

CONFIDENTIAL

CASPER

Twelve Month Follow-up Questionnaire

Participant's trial ID number: [ ][ ] - [ ][ ][ ][ ][ ]

Date questionnaire sent: [ ][ ] / [ ][ ] / [2][0][ ][ ]
Day *Month* *Year*

Funded by:
NIHR HTA code 08/19/04
ISRCTN 02202951
CASPER 12mth qr v2.3 8Feb12

Organised by:
The University of York
University of Leeds
Durham University

0225581328

PLEASE READ ALL THE INSTRUCTIONS BEFORE COMPLETING THE QUESTIONNAIRE

Thank you for agreeing to take part in this study. The responses you give in this questionnaire will help us find out which is the best way to improve mental well-being amongst those over the age of 65.

Please answer ALL the questions. Although some of the questions may not seem relevant to yourself or may appear similar, they do give us valuable information.

If you find it difficult to answer the question, please give the best answer you can.

Please follow the instructions for each section carefully.

For each section, if you are asked to put a cross in the box, please use a cross rather than a tick, as if you were filling out a ballot paper.

For example in the following question, if your answer to the question is yes, you should place a cross firmly in the box next to yes.

Do you drive a car?

Yes ☒

No ☐

If you are asked to write your answer, please do so by entering your answer in the box provided, for example:

How old are you? | 7 | 5 | years

Please use a black or blue pen for all the questions.

Please do not use a pencil or any other coloured pen.

If you have any queries or problems completing this questionnaire please contact your local study centre:

[redacted]

6847581324

Please enter the date you are completing this questionnaire:

		/			/	2	0		
Day			*Month*			*Year*			

SECTION 1

This section is about how you have been feeling over the **last 2 weeks**.
Answer each question by placing a cross in the box that best describes your answer.

1. Little interest or pleasure in doing things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Feeling down, depressed, or hopeless

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Trouble falling or staying asleep, or sleeping too much

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Feeling tired or having little energy

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Poor appetite or overeating

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Feeling bad about yourself - that you are a failure or have let yourself or your family down

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Trouble concentrating on things, such as reading the newspaper or watching television

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

8. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

9. Thoughts that you would be better off dead, or of hurting yourself in some way

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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Over the **last 2 weeks**, how often have you been bothered by any of the following problems?

1. Feeling nervous, anxious or on edge

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Not being able to stop or control worrying

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Worrying too much about different things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Trouble relaxing

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Being too restless that it is hard to sit still

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Becoming easily annoyed or irritable

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Feeling afraid as if something awful might happen

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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SECTION 2

This section is about any physical health problems you may be experiencing.
Please cross one box for each health problem.

During the **past 4 weeks**, how much have you been bothered by any of the following problems?

1. Stomach pains

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

2. Back pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

3. Pain in your arms, legs, or joints (e.g. knees, hips)

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

4. Headaches

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

5. Chest pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

6. Dizziness

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

7. Fainting spells

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

8. Feeling your heart pound or race

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

9. Shortness of breath

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

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10. Pain or problems during sexual intercourse

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

11. Constipation, loose bowels, or diarrhoea

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

12. Nausea, gas, or indigestion

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

13. Feeling tired or having low energy

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

14. Trouble sleeping

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

SECTION 3

This section asks you about how you've been feeling.

Answer each question by placing a cross in the box that best describes your answer.

1a. I tend to bounce back after illness or hardship

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

1b. I am able to adapt to change

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

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SECTION 4

This section asks for your views about your health. This information will help us keep track of how you feel and how well you are able to do your usual activities.

Answer each question by placing a cross in the box that best describes your answer.

1. In general, would you say your health is:
(please cross one box only)

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

2. During a typical day does **your health** limit you in **moderate actvities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

3. During a typical day does **your health** limit you in climbing **several** flights of stairs? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

4. During the **past 4 weeks**, how much of the time have you accomplished less than you would like in regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

5. During the **past 4 weeks**, how much of the time have you been limited in performing any kind of work or other regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

6. During the **past 4 weeks**, how much of the time have you accomplished less than you would have liked in your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

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7. During the **past 4 weeks**, how much of the time have you done work or other activities less carefully than usual **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (both outside the home and housework)?
(please cross one box only)

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

9. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt calm and peaceful ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

10. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** did you have a lot of energy ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

11. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt downhearted and depressed?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

12. During the **past 4 weeks** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives etc.)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

3106581329

SECTION 5

This section also asks about your health in general.

By placing a cross in one box in each group below, please indicate which statements best describes your own **health state today**.

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

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SECTION 6

This section is about any medication you have been prescribed to improve your mental well-being.

Are you **currently** prescribed any of the medicines listed below?

Yes ☐ No ☐ Don't know ☐

If 'Yes', please cross all that apply.

Dosulepin ☐	Sertraline ☐	Venlafaxine ☐
Lofepramine ☐	Fluoxetine ☐	Duloxetine ☐
Citalopram ☐	Paroxetine ☐	Trazodone ☐
Mirtazapine ☐	Other ☐ *please list any other medications below*	

1.	2.
3.	4.
5.	6.
7.	8.
9.	10.

If you **are** prescribed one of these medicines but have stopped taking it for any reason please place a cross in this box. ☐

3827581329

SECTION 7

This final section is about any health care you have received as a patient **for any reason** (please do not include any visits to your GP practice).

Answer each question by placing a cross in the box that best describes your answer.

Attending hospital

1a. During the **last 8 months** have you stayed overnight in hospital?

Yes ☐ No ☐ (go to 2a) Don't know ☐

1b. On how many separate occasions did you stay overnight in hospital? ☐☐

Please provide some details for each occasion you stayed in hospital (e.g. hip replacement, fall).

(If you have stayed more than 2 occasions, we will contact you for further details)

1c. **First hospital visit**

1d. After your hospital visit were you:

- Transferred to community hospital (e.g. for rehabilitation) ☐
- Discharged back to your home ☐
- Other (please state) ☐

1e. **Second hospital visit**

1f. After your hospital visit were you:

- Transferred to community hospital (e.g. for rehabilitation) ☐
- Discharged back to your home ☐
- Other (please state) ☐

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Other visits to hospital

2a. Have you attended Accident and Emergency in the **last8 months**?

Yes ☐ No ☐ (go to 3a) Don't know ☐

2b. If 'Yes', how many times have you attended Accident and Emergency in the **last 8 months**? ☐☐

3a. Have you attended Hospital Outpatients in the **last 8 months**?

Yes ☐ No ☐ (go to 4a) Don't know ☐

3b. If 'Yes', how many times have you attended Hospital Outpatients in the **last 8 months**? ☐☐

4a. Have you attended hospital as a day case/procedure patient in the **last 8 months**?

Yes ☐ No ☐ (go to 5a) Don't know ☐

4b. If 'Yes', how many times have you attended hospital as a day case/procedure in the **last 4 months?** ☐☐

NHS transport services

5a. Have you used a '999' emergency ambulance in the **last 8 months**?

Yes ☐ No ☐ (go to 6a) Don't know ☐

5b. If 'Yes', how many times have you used a '999' emergency ambulance in the **last 8 months**? ☐☐

6a. Have you used the Patient Transport Service in the **last 8 months**?

Yes ☐ No ☐ (go to 7a) Don't know ☐

6b. If 'Yes', how many times have you used the Patient Transport Service in the **last8 months**? ☐☐

Other NHS services

7a. Have you gone to an NHS Walk-in Centre in the **last 8 months**?

Yes ☐ No ☐ (go to 8a) Don't know ☐

7b. If 'Yes', how many times have you been to an NHS Walk-in Centre in the **last 8 months**? ☐☐

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8a. Have you called NHS Direct (the NHS telephone helpline) in the **last 8 months**?

Yes ☐ No ☐ (go to 9a) Don't know ☐

8b. If 'Yes', how many times have you called NHS Direct (the NHS telephone helpline) in the **last 8 months**? ☐☐

Support services

9a. Do you receive any home help?

Yes ☐ No ☐ (go to 10a) Don't know ☐

9b. Thinking about the **last 8 months**, of these how many months did you have home help? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐ 7 months ☐ 8 months ☐

9c. Thinking about the **last 8 months**, typically, how many times a week did home help visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

10a. Does a care worker visit you at home?

Yes ☐ No ☐ (go to 11a) Don't know ☐

10b. Thinking about the **last 8 months**, of these how many months did a care worker visit you at home? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐ 7 months ☐ 8 months ☐

10c. Thinking about the **last 8 months**, typically, how many times a week did a care worker visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

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11a. Do you use meals on wheels?

Yes ☐ No ☐ (go to 12a) Don't know ☐

11b. Thinking about the **last 8 months**, of these how many months did you use meals on wheels? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐ 7 months ☐ 8 months ☐

11c. Thinking about the **last 8 months**, typically, how many times a week did you use meals on wheels?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

12a. Do you go to any community centres?

Yes ☐ No ☐ Don't know ☐

12b. Thinking about the **last 8 months**, typically, how many times a week do you go to a community centre?

0 ☐ 1-2 ☐ 2-3 ☐ 3-4 ☐ 4+ ☐

12c. Which community centres do you attend?

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If you have any general comments about the study, or this questionnaire, please write them below.

Thank you for completing this questionnaire.
Please return it in the pre-paid envelope provided.

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Appendix 11 CollAborative care for Screen-Positive ElderRs plus 18-month follow-up questionnaire

CONFIDENTIAL

CASPER

Eighteen Month Follow-up Questionnaire

Participant's trial ID number: ☐☐ - ☐☐☐☐☐

Date questionnaire sent: ☐☐ / ☐☐ / 2 0 ☐☐
Day *Month* *Year*

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CASPER 18mth qr v2.1 28May13

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North East Hub Mental Health Research Network
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Northumberland, Tyne and Wear NHS NHS Foundation Trust
The University of York
University of Leeds
Tees, Esk and Wear Valleys NHS NHS Foundation Trust

0084030094

PLEASE READ ALL THE INSTRUCTIONS BEFORE COMPLETING THE QUESTIONNAIRE

Thank you for agreeing to take part in this study. The responses you give in this questionnaire will help us find out which is the best way to improve mental well-being amongst those over the age of 65.

Please answer ALL the questions. Although some of the questions may not seem relevant to yourself or may appear similar, they do give us valuable information.

If you find it difficult to answer the question, please give the best answer you can.

Please follow the instructions for each section carefully.

For each section, if you are asked to put a cross in the box, please use a cross rather than a tick, as if you were filling out a ballot paper.

For example in the following question, if your answer to the question is yes, you should place a cross firmly in the box next to yes.

Do you drive a car?

Yes ☒

No ☐

If you are asked to write your answer, please do so by entering your answer in the box provided, for example:

How old are you? | 7 | 5 | years

Please use a black or blue pen for all the questions.

Please do not use a pencil or any other coloured pen.

If you have any queries or problems completing this questionnaire please contact your local study centre:

[redacted]

9837030099

Please enter the date you are completing this questionnaire:

		/			/	2	0		
Day			*Month*			*Year*			

SECTION 1

This section is about how you have been feeling over the **last 2 weeks**.
Answer each question by placing a cross in the box that best describes your answer.

1. Little interest or pleasure in doing things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Feeling down, depressed, or hopeless

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Trouble falling or staying asleep, or sleeping too much

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Feeling tired or having little energy

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Poor appetite or overeating

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Feeling bad about yourself - that you are a failure or have let yourself or your family down

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Trouble concentrating on things, such as reading the newspaper or watching television

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

8. Moving or speaking so slowly that other people could have noticed. Or the opposite - being so fidgety or restless that you have been moving around a lot more than usual

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

9. Thoughts that you would be better off dead, or of hurting yourself in some way

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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Over the **last 2 weeks**, how often have you been bothered by any of the following problems?

1. Feeling nervous, anxious or on edge

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

2. Not being able to stop or control worrying

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

3. Worrying too much about different things

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

4. Trouble relaxing

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

5. Being too restless that it is hard to sit still

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

6. Becoming easily annoyed or irritable

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

7. Feeling afraid as if something awful might happen

Not at all	Several days	More than half the days	Nearly every day
☐	☐	☐	☐

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SECTION 2

This section is about any physical health problems you may be experiencing.
Please cross one box for each health problem.

During the **past 4 weeks**, how much have you been bothered by any of the following problems?

1. Stomach pains

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

2. Back pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

3. Pain in your arms, legs, or joints (e.g. knees, hips)

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

4. Headaches

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

5. Chest pain

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

6. Dizziness

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

7. Fainting spells

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

8. Feeling your heart pound or race

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

9. Shortness of breath

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

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10. Pain or problems during sexual intercourse

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

11. Constipation, loose bowels, or diarrhoea

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

12. Nausea, gas, or indigestion

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

13. Feeling tired or having low energy

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

14. Trouble sleeping

Not bothered at all	Bothered a little	Bothered a lot
☐	☐	☐

SECTION 3

This section asks you about how you've been feeling.

Answer each question by placing a cross in the box that best describes your answer.

1a. I tend to bounce back after illness or hardship

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

1b. I am able to adapt to change

Not true at all	Rarely true	Sometimes true	Often true	True nearly all of the time
☐	☐	☐	☐	☐

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SECTION 4

This section asks for your views about your health. This information will help us keep track of how you feel and how well you are able to do your usual activities.

Answer each question by placing a cross in the box that best describes your answer.

1. In general, would you say your health is:
(please cross one box only)

Excellent	Very Good	Good	Fair	Poor
☐	☐	☐	☐	☐

2. During a typical day does **your health** limit you in **moderate activitie**s, such as moving a table, pushing a vacuum cleaner, bowling or playing golf? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

3. During a typical day does **your health** limit you in climbing **several** flights of stairs? If so, how much?
(please cross one box only)

Yes, limited a lot	Yes, limited a little	No, not limited at all
☐	☐	☐

4. During the **past 4 weeks**, how much of the time have you accomplished less than you would like in regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

5. During the **past 4 weeks**, how much of the time have you been limited in performing any kind of work or other regular daily activities **as a result of your physical health**?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

6. During the **past 4 weeks**, how much of the time have you accomplished less than you would have liked in your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

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7. During the **past 4 weeks**, how much of the time have you done work or other activities less carefully than usual **as a result of any emotional problems** (such as feeling depressed or anxious)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (both outside the home and housework)?
(please cross one box only)

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐	☐	☐	☐	☐

9. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt calm and peaceful ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

10. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** did you have a lot of energy ?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

11. This question is about how you feel and how things have been with you during the **past 4 weeks**. Please give the one answer that comes closest to the way you have been feeling. How much during the **past 4 weeks** have you felt downhearted and depressed?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

12. During the **past 4 weeks** how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives etc.)?
(please cross one box only)

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

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SECTION 5

This section also asks about your health in general.

By placing a cross in one box in each group below, please indicate which statements best describes your own **health state today**.

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

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SECTION 6

This section is about any medication you have been prescribed to improve your mental well-being.

Are you **currently** prescribed any of the medicines listed below?

Yes ☐ No ☐ Don't know ☐

If 'Yes', please cross all that apply.

Dosulepin ☐	Sertraline ☐	Venlafaxine ☐
Lofepramine ☐	Fluoxetine ☐	Duloxetine ☐
Citalopram ☐	Paroxetine ☐	Trazodone ☐
Mirtazapine ☐	Other ☐ *please list any other medications below*	

1. _____ 2. _____

3. _____ 4. _____

5. _____ 6. _____

7. _____ 8. _____

9. _____ 10. _____

If you **are** prescribed one of these medicines but have stopped taking it for any reason please place a cross in this box. ☐

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SECTION 7

This final section is about any health care you have received as a patient **for any reason** (please do not include any visits to your GP practice).

Answer each question by placing a cross in the box that best describes your answer.

Attending hospital

1a. During the **last 6 months** have you stayed overnight in hospital?

Yes ☐ No ☐ (go to 2a) Don't know ☐

1b. On how many separate occasions did you stay overnight in hospital? ☐☐

Please provide some details for each occasion you stayed in hospital (e.g. hip replacement, fall).

(If you have stayed more than 2 occasions, we will contact you for further details)

1c. **First hospital visit**

1d. After your hospital visit were you:

Transferred to community hospital (e.g. for rehabilitation) ☐

Discharged back to your home ☐

Other (please state) ☐

1e. **Second hospital visit**

1f. After your hospital visit were you:

Transferred to community hospital (e.g. for rehabilitation) ☐

Discharged back to your home ☐

Other (please state) ☐

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Other visits to hospital

2a. Have you attended Accident and Emergency in the **last 6 months**?

Yes ☐ No ☐ (go to 3a) Don't know ☐

2b. If 'Yes', how many times have you attended Accident and Emergency in the **last 6 months**? ☐☐

3a. Have you attended Hospital Outpatients in the **last 6 months**?

Yes ☐ No ☐ (go to 4a) Don't know ☐

3b. If 'Yes', how many times have you attended Hospital Outpatients in the **last 6 months**? ☐☐

4a. Have you attended hospital as a day case/procedure patient in the **last 6 months**?

Yes ☐ No ☐ (go to 5a) Don't know ☐

4b. If 'Yes', how many times have you attended hospital as a day case/procedure in the **last 6 months?** ☐☐

NHS transport services

5a. Have you used a '999' emergency ambulance in the **last 6 months**?

Yes ☐ No ☐ (go to 6a) Don't know ☐

5b. If 'Yes', how many times have you used a '999' emergency ambulance in the **last 6 months**? ☐☐

6a. Have you used the Patient Transport Service in the **last 6 months**?

Yes ☐ No ☐ (go to 7a) Don't know ☐

6b. If 'Yes', how many times have you used the Patient Transport Service in the **last 6 months**? ☐☐

Other NHS services

7a. Have you gone to an NHS Walk-in Centre in the **last 6 months**?

Yes ☐ No ☐ (go to 8a) Don't know ☐

7b. If 'Yes', how many times have you been to an NHS Walk-in Centre in the **last 6 months**? ☐☐

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8a. Have you called NHS Direct (the NHS telephone helpline) in the **last 6 months**?

Yes ☐ No ☐ (go to 9a) Don't know ☐

8b. If 'Yes', how many times have you called NHS Direct (the NHS telephone helpline) in the **last 6 months**? ☐☐

Support services

9a. Do you receive any home help?

Yes ☐ No ☐ (go to 10a) Don't know ☐

9b. Thinking about the **last 6 months**, of these how many months did you have home help? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐ 7 months ☐ 8 months ☐

9c. Thinking about the **last 6 months**, typically, how many times a week did home help visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

10a. Does a care worker visit you at home?

Yes ☐ No ☐ (go to 11a) Don't know ☐

10b. Thinking about the **last 6 months**, of these how many months did a care worker visit you at home? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐ 7 months ☐ 8 months ☐

10c. Thinking about the **last 6 months**, typically, how many times a week did a care worker visit?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

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11a. Do you use meals on wheels?

Yes ☐ No ☐ (go to 12a) Don't know ☐

11b. Thinking about the **last 6 months**, of these how many months did you use meals on wheels? (please count any month where you have had a visit)

0 months ☐ 1 month ☐ 2 months ☐ 3 months ☐ 4 months ☐ 5 months ☐ 6 months ☐ 7 months ☐ 8 months ☐

11c. Thinking about the **last 6 months**, typically, how many times a week did you use meals on wheels?

0 days ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days ☐ 5 days ☐ 6 days ☐ 7 days ☐

12a. Do you go to any community centres?

Yes ☐ No ☐ Don't know ☐

12b. Thinking about the **last 6 months**, typically, how many times a week do you go to a community centre?

0 ☐ 1-2 ☐ 2-3 ☐ 3-4 ☐ 4+ ☐

12c. Which community centres do you attend?

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If you have any general comments about the study, or this questionnaire, please write them below.

Thank you for completing this questionnaire.
Please return it in the pre-paid envelope provided.

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Appendix 12 Zero-inflated negative binomial regression

TABLE 52 Zero-inflated negative binomial regression explaining the effect of collaborative care vs. usual care on the incidence rate ratio of GP appointments

GP appointments	IRR	Standard error	*z*	*p* > *z*	95% CI
Full model					
Collaborative care	0.9726	0.0733	–0.3700	0.713	0.8391 to 1.1274
Constant	10.3623	0.5436	44.5700	0.000	9.3498 to 11.4845
Logistic model					
Collaborative care	0.5384	0.9378	0.5700	0.566	–1.2996 to 2.3764
Constant	–3.9940	0.7827	–5.1000	0.000	–5.5281 to –2.4599

IRR, incidence rate ratio.
N (total) = 357; *n* (GP appointment > 0) = 343; *n* (GP appointment = 0) = 14.

TABLE 53 Zero-inflated negative binomial regression explaining the effect of collaborative care vs. usual care on the incidence rate ratio of GP home visits

GP home visits	IRR	Standard error	*z*	*p* > *z*	95% CI
Collaborative care	1.2358	0.5291	0.4900	0.621	0.5340 to 2.8599
Constant	0.6066	0.1356	–2.2400	0.025	0.3914 to 0.9401
Logistic model					
Collaborative care	17.3135	15682.5500	0.0000	0.999	–30720 to 30755
Constant	–19.0563	15682.5500	0.0000	0.999	–30756 to 30718

IRR, incidence rate ratio.
N (total) = 357; *n* (GP home visits > 0) = 71; *n* (GP home visits = 0) = 286.

TABLE 54 Zero-inflated negative binomial regression explaining the effect of collaborative care vs. usual care on the incidence rate ratio of GP telephone consultations

GP telephone consultation	IRR	Standard error	z	*p* > z	95% CI
Collaborative care	1.3146	0.2366	1.5200	0.129	0.9238 to 1.8707
Constant	2.1911	0.3857	4.4600	0.000	1.5517 to 3.0939
Logistic model					
Collaborative care	1.4852	2.2885	0.6500	0.516	–3.0003 to 5.9706
Constant	–2.8972	2.7483	–1.0500	0.292	–8.2838 to 2.4894

IRR, incidence rate ratio.
N (total) = 357; *n* (GP telephone consultation > 0) = 206; *n* (GP telephone consultation = 0) = 151.

TABLE 55 Zero-inflated negative binomial regression explaining the effect of collaborative care vs. usual care on the incidence rate ratio of nurse appointments

Nurse appointment	IRR	Standard error	z	$p > z$	95% CI
Collaborative care	0.9935	0.1244	–0.0500	0.959	0.7774 to 1.2698
Constant	5.3825	0.4368	20.7400	0.000	4.5911 to 6.3104
Logistic model					
Collaborative care	14.1944	2213.3500	0.0100	0.995	–4324 to 4352
Constant	–18.0387	2213.3490	–0.0100	0.993	–4356 to 4320

IRR, incidence rate ratio.
N (total) = 357; *n* (nurse appointment > 0) = 299; *n* (nurse appointment = 0) = 58.

TABLE 56 Zero-inflated negative binomial regression explaining the effect of collaborative care vs. usual care on the incidence rate ratio of nurse telephone consultations

Nurse telephone consultation	IRR	Standard error	z	$p > z$	95% CI
Collaborative care	2.2476	1.0137	1.8000	0.073	0.9285 to 5.4403
Constant	0.3607	0.0757	–4.8600	0.000	0.2390 to 0.5441
Logistic model					
Collaborative care	16.5231	3127.0730	0.0100	0.996	–6112 to 6145
Constant	–16.7359	3127.0740	–0.0100	0.996	–6146 to 6112

IRR, incidence rate ratio.
N (total) = 357; *n* (nurse telephone consultation > 0) = 61; *n* (nurse telephone consultation = 0) = 296.

Appendix 13 CollAborative care for Screen-Positive ElderRs plus participant interview consent form

CASPER Plus Participant Interview Consent Form

Contact Name:
Contact Details: [redacted]

		Please initial each box
1.	I confirm that I have read and understand the information sheet [v2.1 10Oct12] for this study and have had the opportunity to ask questions.	☐
2.	I understand that my participation in a short interview for this study is voluntary and I am free to withdraw at any time without giving any reason.	☐
3.	I understand that the interview will be recorded on a digital voice recorder and the sound file will be stored on a secure computer at the University of York.	☐
4.	I understand that the interview will be strictly confidential and I will be anonymous in any written reports from the research.	☐
5.	I understand that anonymous written quotations from the interview(s) and observations may be used in presentations and in teaching.	☐
6.	I understand that my details (e.g. name, practice, address) will be strictly confidential, stored securely at the University of York and will not be passed on to any individual within or outside the University.	☐
7.	I agree to take part in the above study by taking part in the interview.	☐

_____ _____
_____

Name of Participant (print) Date Signature

Appendix 14 CollAborative care for Screen-Positive EldeRs plus case manager/supervisor interview consent form

CASPER Plus Case Manager/Supervisor Interview Consent Form

Contact Name: [Name of researcher]
Department of Health Sciences, University of York, YO10 5DD

Contact Details: Tel: [phone number of researcher] Email: [email address of researcher]

	Please initial each box
1. I confirm I have read and understand the information sheet [v2.1 10Oct12]for this study and have had the opportunity to ask questions.	☐
2. I understand that my participation in an interview for this study is voluntary and I am free to withdraw at any time without giving any reason.	☐
3. I understand that the interview will be recorded on a digital voice recorder and the sound file stored on a secure computer at the University of York.	☐
4. I understand that the interview will be strictly confidential and that I will be anonymous in any written reports from the research.	☐
5. I understand that anonymous written quotations from the interview may be used in presentations and in teaching.	☐
6. I understand that my details (e.g. name, address) will be strictly confidential, stored securely at the University of York and will not be passed on to any individual within or outside the University.	☐
7. I agree to take part in the above study by taking part in the interview.	☐

Name of Case Manager (print) Date Signature

_____

Appendix 15 CollAborative care for Screen-Positive EldeRs plus general practitioner interview consent form

CASPER Plus GP Interview Consent Form

Contact Name: [redacted]

Contact Details:

		Please initial each box
1.	I confirm I have read and understand the information sheet for this study [v2.1 10Oct12] and have had the opportunity to ask questions.	☐
2.	I understand that my participation in an interview for this study is voluntary and I am free to withdraw at any time without giving any reason.	☐
3.	I understand that the interview will be recorded on a digital voice recorder and the sound file stored on a secure computer at the University of York.	☐
4.	I understand that the interview will be strictly confidential and that I will be anonymous in any written reports from the research.	☐
5.	I understand that anonymous written quotations from the interview may be used in presentations and in teaching.	☐
6.	I understand that my details (e.g. name, address) will be strictly confidential, stored securely at the University of York and will not be passed on to any individual within or outside the University.	☐
7.	I agree to take part in the above study by taking part in the interview.	☐

_____ _____ _____

Name of General Practitioner (print) Date Signature

Appendix 16 Qualitative case manager topic guide

Interviews with patients as part of the CASPER Plus Study

Interview key questions for 'Collaborative Care' participants

This guide summarises the main areas to be explored in each interview about views and experiences relating to CC. The questions are intended as a starting point to ensure primary issues are covered, whilst allowing flexibility for new issues to emerge.

Thank participant for agreeing to be interviewed. Remind them they have consented to the interview being digitally recorded, the recording will be stored securely and the transcript will be anonymised, but they are welcome to stop the interview at any point if they wish.

Understanding and thoughts on BA/Collaborative Care:

- Could you start by telling me why you decided to take part in the study?
- What were your expectations, what did you expect to happen during the study?

Experiences

- What did you think of the experience?
- How do you refer to/label the problems you've been having, what do you call it?
- How did you feel about being allocated a CM? How did you get on with them? How flexible would you say they were?
- What did you feel about the support you received from their CM?
- Was there anything about the process you didn't like? (prompt) for example, some people have felt the pack was repetitive.
- Did you feel the care was centred on them? Did you feel in control of process?
- Apart from time, what do you think you got from your CM?
- Did you see the sessions with the CM as fitting into a wider CC process?
- Overall, did you find the process acceptable, valuable and effective?

Other experiences

- Did participating in CC make a difference to your appointments with their GP?
- Do you usually see the same GP at the surgery? If not, why not?
- If you went to GPs about how you were feeling who would you see, and why?
- If emotional problems are ***not*** something they speak to GP about, why is that?
  Prompts: Is it a time issue? Do you think GP wouldn't be interested in non-medical concern? What would cause you to seek help from GP about mood?

- What do you think of the idea that people over 75 should have a named GP?
- Would you value seeing the same GP each time, or not?
- What do you think are differences between telephone and face-to-face interviews?
- What are your views on the self-help guide and completing the questionnaire?
- How did you feel about coming to the end of your sessions?

Has CC made a difference?

- Has it affected the way you manage low mood?
- Are you doing anything different now, such as being more active?

Links between how they feel physically and emotionally

- Do you see physical and emotional conditions as separate?
- Do you think there's a link between these two? For example, if you are feeling pain do you think that affects your mood? Do they think your physical condition changes when your mood improves?

Previous experiences of counselling

- Have you had any counselling previously… or BA? How did this differ from what you have received through CASPER?

Thoughts on seeking out a group

- Have you looked at joining any possible groups? If not, what sort of group would you be interested in? Prompt: e.g one for your peer group/creative activities/for a specific condition or specially for carers for example?
- If it became available in future, would you be interested in refresher sessions with the CMs as part of a group?

Medication matters

- Were you on medication for your mood when receiving CC? If so, did you talk to CM about this?
- Do you see the CM as someone you could talk to about medication? Or do you think this is something to talk only to GP about?
- Do you think the CM and GP might speak to each other about your medication?
- If yes, how would you feel about this?

General questions

- What would your thoughts be, if CC were introduced at your GP practice?
- What do you think would be the benefits of this for you? And for others?
- If it did happen, what barriers would you see to it working?
- Is it something you believe might work? If so, how might it work best?

Any other thoughts or questions?

- Any other points or questions?
- Thank you

Appendix 17 Qualitative case manager topic guide

[CASPERPlusQualitative study case manager – interview topic guide]

Interviews with case managers as part of the CASPERPlus study

Key Interview Questions for case managers

This topic guide summarises the main areas to be explored in each interview about the CM's relationships and liaison with Practice Nurses and GPs, their views about the effectiveness of collaborative care and their experiences of delivering the intervention.
As with any qualitative interviews, these headings are intended as a starting point to ensure the primary issues are covered, whilst allowing flexibility for new issues to emerge. All consenting Case Managers working with CASPER Plus participants will be interviewed. CMs will be interviewed once during the study, after completing the intervention with at least three patient participants.

Introduction and background

Thoughts and views

- What are your views on CC?
- What do you think are the benefits or value of the BA intervention?
- How do you see BA fitting within CC process - do you view BA and CC framework as two separate processes?
- What are your views on the effectiveness of overall CC process?
- What are our thoughts on participants' understanding and acceptability of CC?
- What, apart from time, do you think you give to participants?
- How do you see your role?

- **Views on Medication Management**
- Thoughts on the use of psychological interventions with antidepressants
- Views on medication management (MM)

- **Other views**
- Views on use of manuals/questionnaires/diary
- Views on supervision (from both CM and supervisor perspective)
- How do they manage final sessions/ helping participant to continue?

Experiences

- Broadly, what has been your experience of being involved in the study?
- Apart from GP and themselves, who do they see in the CC process? e.g. participants with LTCs, do you have any communication with specialists, or with the GP about participant's condition?
- Have you had any involvement with carers or family members of participants? If so, what benefits or problems have you experienced when involving carers?
- Do you think there is a role for carers and family members during BA?

- How is what you do (CC) different from other types of GP collaboration?
- How do you manage complex patients?
- Can you tell me about your experiences or views on links between a patient's emotional and physical condition. (prompt) If one gets better, does the other?
- How do you manage final sessions with participant? How do you think participants view with session?
- What do you think are the differences between telephone and face-to-face interviews?
- What are your views about the value of the trial?

Operational Questions

Contact with GP

- How do you see the GPs' awareness of the CC process within their practice?
- Letters sent at four stages - has the GP responded to any letters?
- Which method of communication did GPs prefer, e.g. by telephone/written reports on individual patients?
- How often did GPs like to be contacted?
- Under what circumstances/at what point in the CC process did GPs prefer to be contacted? e.g. urgent cases or risk?
- How easy has it been to contact GP?

Experiences of medication management

- How, if at all, do you engage with GP around MM?
- What have been your experiences so far of MM? Have you had contact with GP around patient's medication?
- Are you from an IAPT background or other? Has your training influenced your approach to MM?
- Any further thoughts on MM? How do you see MM fitting within primary care and IAPT services?

Speculative questions

- If CC were implemented into the GP practice, what would your thoughts be?
- If it happened, what barriers do you see, in terms of collaborative working with the GPs?
- Is it something you could see working? If so, how do you suggest it might be possible?
- Any other thoughts on making the CC model a sustainable process?
- Any thoughts on barriers to the participant? e.g. difficulty reading/deafness.

Any other issues?

- Are there any other issues you would like to raise?
- Thank you

Appendix 18 Qualitative general practitioner topic guide

[CASPERPlus Qualitative study – GP Key Questions

Interviews with GPs as part of the CASPERPlus study
Key Questions

Key Questions for GPs

Thoughts and views

GP's views on BA and Collaborative Care (CC)

- Why did your practice take part and why did you agree to be interviewed? (e.g. interest in mental health or research?)
- What do you know about the intervention, BA?
- How do you see BA fitting within CC framework?
- What is your understanding of CC for mental health? Do you see it as *different* to shared care? What sort of collaboration do you do currently, i.e. co-located, face to face? What is your role in delivering this?
- What are your views on the potential, value and effectiveness of CC?
- Do you think your patients understand what CC is? Why do you think they get involved in research?
- What do you think of the plan that people over 75 should have a named GP?
- How do they see your own role in managing depression for older people?
- What do you do as a GP for this group?
- What is your usual treatment pathway for patients with moderate to severe depression?
- If medication, how do you see the CM's involvement (if at all) in this area of patient care?
- How do you see the role of the CM? CM has been described as the glue that keeps CC together, would you agree?
- Are you aware of any contact by the CMs with patients' carers or families?
- Has your awareness of CC affected your attitude to identifying or addressing depression in older people?

Experiences:

- Since we've started recruiting from your practice, what has been your experience in general?
- What is the practice procedure for dealing with mental health? (prompt) e.g. is there a GP to whom patients automatically gravitate?
- Your experiences of delivering CC for older people with depression?

Experiences of Medication Management:

- Have any CMs contacted you about any patient medication issues?
- How do you think medication management might fit in with collaborative care delivered through primary care?

Operational Questions

Preferred method of communication.

- How, and how often would you *prefer* to be contacted?
- At what point in the process?
- Do you view letters from CMs? (sent at four stages)
    1. at consent stage
    2. with patient's GDS-15 score and management plan
    3. after four or five sessions
    4. on completion
- What is the usual process in the practice when receiving these letters?
- Do you remember seeing any of these letters? Did you respond to them?
- Have you spoken to the CMs personally?

Speculative questions

- If CC were implemented into practice, what would your thoughts be?
- Is this something you could see working?
- What barriers do you see?
- How do you think it might be possible?
- What do you see as your role in Collaborative Care?

Views on CM's role?

- What do you see as the CM's role, e.g. medication management?
- How would you like this role to work?
- What are your thoughts on CMs working within the practice?

Perceived differences between telephone and face-to-face contact

- What do you see as the differences between telephone and face-to-face contact between CMs and their patients?
- Any other thoughts on making the CC model a sustainable process?

Any other issues?

- Any other issue you would like to raise
- Thank you

Appendix 19 Qualitative demographics tables

All eight case managers who agreed to be interviewed were female and aged between 27 and 50 years. All case managers had been trained as NHS PWPs as part of the IAPT initiative. They each had several years experience of delivering low-intensity psychological interventions. In addition, two of the case managers were involved in training case managers for the CASPER plus trial and in their supervision.

TABLE 57 Demographics of patient participants

Identification number	Sex	Age range (years)	Index of Multiple Deprivation number (decile)	Face to face or telephone?	Urban/rural general practice
PT1	Female	75–80	1	Face to face	Urban
PT2	Male	75–80	9	Face to face	Urban
PT3	Male	65–70	5	Face to face	Rural
PT4	Male	81–85	8	Face to face	Rural
PT5	Male	65–70	2	Face to face	Urban
PT6	Female	65–70	10	Face to face	Rural
PT7	Female	65–70	10	Face to face	Rural
PT8	Female	65–70	10	Face to face	Urban
PT9	Male	65–70	2	Face to face	Urban
PT10	Female	65–70	8	Telephone	Urban
PT11	Female	75–80	9	Face to face	Urban
PT12	Female	65–70	9	Telephone	Urban
PT1(withdrawn)	Male	65–70	6	Face to face	Rural

TABLE 58 Demographics of case managers interviewed

Identification number	Sex	Years of experience[a]	Interview type
CASE MANAGER1	Female	8	Face to face
CASE MANAGER2	Female	9	Face to face
CASE MANAGER3	Female	4	Face to face
CASE MANAGER4	Female	4	Face to face
CASE MANAGER5	Female	4	Telephone
CASE MANAGER6	Female	3	Telephone
CASE MANAGER7	Female	3	Telephone
CASE MANAGER8	Female	5	Face to face

a Experience in years of delivering a low-intensity psychological intervention.

TABLE 59 Demographics of GPs interviewed

Identification number	Sex	Practice size	Index of Multiple Deprivation number[a]	Urban/rural general practice
GP1	Male	14,886	5	Urban
GP2	Male	10,150	6	Urban
GP3	Male	19,879	10	Rural
GP4	Female	18,083	8	Rural
GP5	Male	24,353	5	Urban
GP6	Male	15,915	4	Urban
GP7	Male	6961	6	Urban
GP8	Female	13,000	3	Urban
GP9	Female	18,083	8	Rural
GP10	Female	11,893	6	Rural
GP11	Male	7183	10	Rural
GP12	Male	15,432	5	Rural

a Lower numbers indicate a lower SES.

Appendix 20 CollAborative care for Screen-Positive EldeRs plus protocol version 2.1 (original)

CASPER PLUS: An RCT sub-study of The CASPER Study

Collaborative Care in Screen-Positive Elders – The CASPER PLUS Trial

CASPER PLUS

Trial Protocol

The CASPER Study is funded by:

NIHR Health Technology Assessment programme funded project

CASPER PLUS Trial Protocol v2.1 30Mar12

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Overview

As a sub-study of The CASPER Study, CASPER PLUS is a trial of a primary care-based intervention for older people with depression. Depression in older people is common and associated with poor quality of life, increased morbidity and mortality and increased health and social care use. It is under-recognised and sometimes inadequately treated in primary care. Current management is mostly limited to the prescription of anti-depressants; where there may be poor concordance.

Psychological treatments may not be offered or available in practice; and the evidence for psychological interventions uses models of care which are of a higher intensity such that they could not feasibly be delivered in primary care in sufficient volume to meet the needs of older people. An intervention known as **collaborative care** involves a brief patient-centred psycho-social package of care delivered by by a case manager working to a defined protocol; medication management and with supervision of the case manager by a specialist, which facilitates liaison across the primary /secondary interface. Collaborative Care has shown promising trial results in the United States. However the transferability of this model of service to the UK NHS cannot be assumed. NICE has identified this as an important intervention that should be subject to further trials.

CASPER PLUS will run seamlessly as part of the recruitment procedures of a cohort of older people with depression with whom we will conduct trials to inform practice and policy (the CASPER older persons' cohort multiple RCT - cmRCT). Using this same cohort, we seek to conduct the definitive trial of collaborative care in older people with above threshold, major depressive disorder. Since we already identify people with 'sub threshold' depression in the existing cohort, we can conduct this important trial relatively quickly and at lower cost. The conduct of this trial will significantly enhance the randomised evidence base in the care of older people with depression, and will inform future service provision; satisfying a research priority identified by NICE.

1. Background

Depression accounts for the greatest burden of disease among all mental health problems, and is expected to become the second-highest among all general health problems by 2020.[1] By the age of 75, 1 in 7 older people meet formal diagnostic criteria for depression. Projected demographic changes mean that population strategies to tackle depression will increasingly have to address the specific needs of older people.[2] Amongst older people, depressive syndromes often affect people with chronic medical illnesses, cognitive impairment, social isolation or disability.

Older people with a long-term condition are five times more likely to suffer depression. 50% of people with Parkinson's disease will suffer depression, 25% following stroke, 20% with coronary heart disease, 24% neurological disease and 42% chronic lung disease.[3] Beyond personal suffering and family disruption, depression worsens the outcomes of many medical disorders and promotes disability. The impairments in quality of life associated with depression are comparable to those of major physical illness. Amongst older people, a clinical diagnosis of major depression is the strongest predictor for impaired quality of life (QoL).[4]

Current UK policies under the Quality and Outcomes Framework (QOF) advocate case-finding for depression amongst those with chronic physical health problems such as heart disease and diabetes. [5] Once detected, evidence supported guidelines advocate the prescription of anti-depressant drugs and appropriate provision of psychological care.[6,7] However, an enduring critique has been that depression is not well managed even when this is revealed through case-finding.[2] Management in primary care usually involves the prescription of antidepressant medication, with poor concordance and suboptimal dosages. The provision of psychological or social interventions addressing issues of poor adaptation, loss, depressive thinking or social withdrawal is woefully inadequate. For example, there has been

minimal provision of psychological treatment for older people under the Improving Access to Psychological Therapies (IAPT) programme.

Despite being encouraged to case-find for depression in older people there is little evidence that this has translated into better management for this disorder. The current proposal introduces a feasible intervention for this group of patients which is known as 'Collaborative care'.

The role of collaborative care

The vast majority of depression in older people can (quite appropriately) be managed entirely in primary care, without recourse to specialist mental health services.[2,6,8] A range of individual treatments have been shown to be effective in the management of depression in older people, including anti-depressants and psychosocial interventions.[6] However, a repeated observation amongst all people with depression has been the failure to integrate these effective elements of care into routine primary care services.[9] Similarly the volume of people with depression necessitates that low intensity interventions are the only feasible strategy that can be used in managing depression within the population.

Despite recent investment under the Improving Access to Psychological Therapies (IAPT) initiative, the capacity for specialist mental health services to provide this care is constrained and demand would quite quickly outstrip supply. Hence any feasible strategy will be both low intensity and offered within primary care.[10]

The ubiquity of depression in primary care settings and the poor integration/co-ordination of care have led to strategies to re-engineer the delivery of care. This form of care borrows much from chronic disease management and facilitates the delivery of effective forms of treatment (such as pharmacotherapy and/or brief psychological therapy). This model of care is often referred to as **collaborative care** or **case management**.[11] According to a recent BMJ editorial on the management of depression in older people *'Innovations in the management of depression have been evaluated. The best*

results come from models that use multifaceted interventions and principles of collaborative care.' [2] We would concur with this observation and the CASPER research group has contributed much to the evidence base of collaborative care and in the evaluation/implementation of this model of care to the UK. We have for example, conducted the definitive reviews of this intervention, [13,14] and have completed the first trial of collaborative care in the UK.[14] We have recently completed an MRC-funded evaluation of clinical and cost effectiveness of Collaborative Care in depressed working age adults (PI Richards). Within the new Improving Access to Psychological Therapies (IAPT) programme, we have implemented this model of care for over 7000 working age adults with depression in demonstration sites.[15] We have also developed computer-based case management systems to facilitate symptom management and supervision of case managers (the PC-MIS system).

Our own reviews in this area have shown collaborative care to be a potentially effective and efficient means of delivering care for depression. Based upon analyses of 36 trials (12,000 participants), we have shown that collaborative care is effective in the short and medium term in alleviating depressive symptoms and improving quality of life. [12] Moreover collaborative care is known to be cost effective in reducing healthcare utilisation and in improving overall quality of life. [16] *See CASPER protocol for details of the United States IMPACT study of collaborative care in older adults (aged over 60).*

1.2 The wider CASPER Study

The CASPER study (see Appendix 1) - a cohort study and randomised controlled trial looking at the effectiveness of collaborative care in older patients with sub-threshold depression [14] - uses a database screening approach in recruiting patients. A randomised controlled trial would be the best approach to evaluate its effects.

1.3 Research Objectives

The research objectives of the CASPER PLUS sub-study are:

1. To establish the clinical effectiveness of a collaborative care intervention for older people with screen-positive above-threshold

('major depressive episode') depression within a definitive RCT.
2. To examine the cost effectiveness of a collaborative care intervention for older people with screen-positive above-threshold ('major depressive episode') depression within a definitive RCT.

2. Method

2.1 Design

As a sub-study of the CASPER trial, CASPER PLUS will follow the same design and recruit from the same wider cohort, using a pragmatic multi-centred randomised controlled trial. Patients will be randomly allocated to one of two interventions:

1. Collaborative care with behavioural activation and active surveillance
2. Usual primary care management of above-threshold depression (major depressive episode) offered by the patient's GP, in line with NICE depression guidance and local service provision

2.2 Inclusion / exclusion criteria

For the CASPER PLUS sub-study all patients at participating CASPER GP practices who have been identified as eligible to receive an invitation mailing will be included. Those patients identified at the screening phase as having above-threshold, case level depression will be eligible to enter the CASPER PLUS sub study.

Inclusion criteria

CASPER participants will be identified by comprehensive screening strategies in primary care (replicating that which is incentivised in QOF-compliant case finding for those with CHD and diabetes). Our target population will be older people (aged 65 and above) who screen-positive for depression on the recommended QOF 2 question brief depression screen (sometimes referred to as the 'Whooley' questions after their initial validation study [21]), but who on further assessment have DSM-IV Major Depressive Disorder (MDD).[22] The Whooley questions are detailed in Box 1. [21,23]

Box 1: QOF-compliant (DEP1) brief screening questions

1. 'Over the past month have you been bothered by feeling down, depressed or hopeless?'
2. 'Over the past month, have you been bothered by having little interest or pleasure in doing things? A positive answer to one or both of these questions raises the possibility of depression and necessitates a full assessment for the presence or absence of clinically significant depressive syndrome.

The **exclusion criteria** are:

- Known alcohol dependency (as recorded on GP records)
- Any known co-morbidity that would in the GP's opinion make entry to the trial inadvisable (e.g. recent evidence of self harm, known current thoughts of self harm, significant cognitive impairment)
- Other factors that would make an invitation to participate in the trial inappropriate (e.g. recent bereavement; terminal malignancy)
- Known to be experiencing psychotic symptoms (as recorded on GP records)

2.3 Recruitment and Randomisation

2.4 Intervention

Collaborative Care with behavioural activation and active surveillance

Patients who meet our pragmatic inclusion criteria will be individually randomised into one of two intervention groups: (1) Collaborative Care (including Behavioural Activation) intervention with medication monitoring and management, or (2) usual care. This is a pragmatic trial [20] and we will impose few restrictions on routine practice and will have no direct influence on the prescription of medication (which will remain entirely in the control of GPs). The actual delivery of this service within the pilot trial will be studied using a concurrent process evaluation – utilising a mixed methods research design.

Eligible participants who have consented to be in the trial will be randomised to a treatment group using the computer-based York Trials Unit telephone randomisation service.

Our experimental intervention will be a bespoke collaborative care designed and delivered specifically for those aged 65 or over with above threshold, case-level depression over 6-8 weekly sessions. The intervention manual has been adapted from the existing CASPER manual used in the pilot study. Collaborative care will be delivered by a case manager (a primary care mental health worker) within a 'stepped care framework', such that those whose depression deteriorates are 'stepped up' from low intensity care to a more intensive form of management including medication monitoring.

The five core components of the intervention are described below:

1. **PATIENT-CENTRED ASSESSMENT AND ENGAGEMENT:** patients are first assessed in their own residential setting. The severity of depression and associated behavioural and social deficits are assessed. The presence of depressive symptoms and behavioural deficits are described and patient information materials are given.

2. **SYMPTOM MEASUREMENT AND MONITORING:** a standardised assessment of symptom severity is made. Symptom tracking (to judge response, failure to respond or deterioration) is then made at all subsequent patient contacts.

3. **MEDICATION MANAGEMENT:** the prescription of anti-depressant medication is entirely at the discretion of the General Practitioner. We will encourage GPs to consider NICE guidance in their prescribing decisions. The concordant use of medication by patients will be encouraged by the case manager if a prescription has been initiated by the GP. Patient concerns (such as addiction) and non-compliance will be addressed during sessions. There will be active liaison with GPs to

encourage follow up patient appointments with the GP if poor concordance is noted.

4. **ACTIVE FOLLOW-UP:** all patients are followed up by the CM for eight weeks using face to face meetings or telephone contacts. Our own experience is that telephone contacts are acceptable and that patients can be engaged using this means of communication.[18] We have adapted this means of delivery in the light of the specific needs of those over 75.

5. **DELIVERY OF BEHAVIOURAL ACTIVATION (BA):** patients are offered the option of behavioural activation delivered over eight sessions by their case manager. BA consists of a structured programme of reducing the frequency of negatively reinforced avoidant behaviours in parallel with increasing the frequency of positively reinforcing behaviours to improve functioning and raise mood. During this time patients will remain under the medical care of their General Practitioner. We have demonstrated that BA is potentially effective in older adults.[17] and have recently demonstrated the effectiveness of this approach in working age adults.[19]

Higher intensity treatments for depression will be facilitated by the GP and by conventional mental health services for older people, and will not be directly influenced by this trial. The additional elements of collaborative care include: telephone support; symptom monitoring and active surveillance (facilitated by computerised case management systems – PC-MIS); medication monitoring; low intensity psychosocial intervention (behavioural activation). The work of case managers is supervised by an older persons' mental health specialist (old age psychiatrist or psychologist).

Control intervention

Participants allocated to the control condition will receive usual primary care management of case level depression offered by their GP, in line with NICE depression guidance and local service provision.

Recruitment method

Screening of all over 65s from GP practice lists: in our existing portfolio of trials at the York Trials Unit, we have pioneered the use of postal screening questionnaires sent to all over 75s based upon practice registers. This has resulted in above-target recruitment to our trials in falls and osteoporosis by this method. We would follow up all participants who return screening questionnaires and express an interest in finding out about the trial. The pilot study of CASPER has been successful in recruiting 100 participants and met criteria for retention during the first year of the study.

2.5 Outcome measures

Primary outcome: We will measure depression severity at four months by self report using the Patient Health Questionnaire 9 – PHQ9. We will also measure outcome at 12 and 18 months using the PHQ9 to examine any sustained impact of the intervention.

Our secondary outcome is binary and is the presence/absence of depression diagnosis as ascertained by interview. For this secondary measure we will use a criterion-based assessment of depression according to the American Psychiatric Association DSM-IV (established by the validated interviewer-administered diagnostic schedule MINI). We will also measure DSM-IV depression status at 4, 12 months and 18 months (using the PHQ9); health related quality of life (SF-12); health-state utility (EQ5D) at 4 months, 12 months and 18 months.

2.6 Qualitative study

In addition to the quantitative data collected in the nested trial, we will collect qualitative data obtained from focus groups.

3. Statistical considerations

3.1 Sample size

Our overall sample size for our definitive trial will be 450 (225 per arm). The sample size of our definitive trial is inexorably linked to (1) the specified minimally important difference; (2) ICC and (3) caseload size. A conservative assumption of an **ability to detect an effect size of 0.35,** based upon ICC=0.02 and caseload size 20 will require 180 participants in the intervention arm. This effect size is in line with the IMPACT US trial [25] and the point estimate from our UK pilot trial.

TABLE: SAMPLE SIZE CALCULATION INCORPORATING ICC VALUES, CASELOAD SIZES AND LOSS TO FOLLOW UP

Effect size* (based upon US trial and UK pilot trial.	Conventional sample size (assumes no clustering)	Caseload size	Plausible ICC within therapists' caseloads	Design Effect/Inflation factor	Effective sample size (adjusted for clustering)	Inflation for 20% loss to follow up (final sample size)
D=0.35	260	20	0.02	1.38	360	450

3.2 Analysis

Statistical analysis of clinical data

We will analyse the data on an intention to treat basis. The primary outcome of depression severity (a continuous outcome as measured by a score on the PHQ9 depression severity measure) will be used in a linear regression model to compare collaborative care with usual care. The analysis will be adjusted for baseline depression severity (as measured by the PHQ9) and physical/functional limitations (as measured by the SF36 physical functioning scale).[24] Standardised effect sizes and the corresponding 95% confidence intervals will be presented for the primary outcome of depression severity. Two-sided 95% confidence intervals will be calculated.

For each outcome measure the number of non-responders will be calculated for each treatment group and response rates compared. We will undertake sensitivity analyses to explore the impact of missing data using multiple imputations by chained equations which will be performed using the ICE package in Stata. All secondary analyses will be conducted using linear or

logistic regression, depending on the outcome measure, adjusting for the same covariates as the primary analysis. All analyses will adjust for within-therapist clustering using multi-level modelling with the Huber-White sandwich estimator.

3.3 Analysis of economic data

The economic evaluation will take the form of within-trial cost-utility analysis that will determine the incremental cost per quality adjusted life year for treatment with collaborative care against usual care in individuals with depression. The primary analyses will be conducted from the UK NHS and personal and social services (PSS) perspective following NICE evaluation guidance.

Primary and secondary healthcare and societal costs will include intervention-related costs, health service use costs and personal social services costs, in line with the recommendations by NICE. The cost data will be collected to fully reflect the management of depression and its cost in both collaborative care and usual care group, and these will be analysed within a societal perspective. Intervention (and control) group costs will be based on the delivery costs within the trial and include supervision and appropriate capital and overhead amounts. Patient questionnaires and case record review will be used to collect data on the use of health services and personal social services. Unit costs for these items will be drawn from the NHS reference costs and the personal social services resource use databases.

The effectiveness of the intervention will be evaluated using the standard quality of life measures which have been shown to be sensitive to change in relation to depression, and also physical healthcare problems common amongst older adults. These will be collected at regular intervals using patient questionnaires. These will then be evaluated over the 18 months trial period to estimate the total quality-adjusted life years for both intervention and control groups.

Economic analyses will compare the costs and effectiveness at the final 18-month follow-up of collaborative versus usual care to capture the economic impact of events such as relapse, although we will conduct an initial preliminary analysis at six months to coincide with the primary clinical analyses. Although the distribution of costs is commonly skewed in populations of this kind, analyses will compare mean costs using standard parametric t-tests with covariates for pre-specified baseline stratification factors plus baseline costs. The robustness of the parametric tests will be confirmed using bias-corrected, non-parametric bootstrapping.

We will explore the joint distribution of costs and effects in a cost-effectiveness analysis (CEA) using an incremental approach to determine the incremental cost-effectiveness ratio with uncertainty estimates around it. The cost-effectiveness acceptability curve (CEAC) will be used to represent the probability that collaborative care is cost-effective compared to usual care for a range of maximum monetary values (ceiling ratios) that a UK decision maker may be willing to pay for an increase in one unit of quality-adjusted life years. This is the recommended decision-making approach to dealing with the uncertainty that exists around the estimates of expected costs and expected effects associated with the interventions under investigation and uncertainty regarding the maximum cost-effectiveness ratio that a decision-maker would consider acceptable.

Furthermore, a net benefit analysis will be undertaken to evaluate the net monetary gain that can be achieved with implementation of collaborative care. The net benefit approach will estimate the monetary gain by weighting the incremental quality-adjusted life years by ceiling ratios and taking away the incremental cost of the intervention. This in turn will allow the decision makers to determine the value of the intervention in terms of monetary gains.

3.4 Qualitative analysis

Our qualitative analysis aims, as outlined in The CASPER Trial protocol are:

1. To inform the efficient conduct of the main trial phase (recruitment, randomisation and follow up).
2. To refine the content and delivery of the collaborative care intervention based on early experience from the pilot phase of the trial.
3. To understand the barriers and facilitators to the delivery, uptake and implementation of collaborative care for older people.

4. Ethical issues

NRES approval has been received to conduct the CASPER study, using the recruitment method described above. We are aware that older people with above-threshold depression (experiencing a major depressive episode) represent a vulnerable group. However, we do not anticipate any major ethical issues since we will only offer interventions recommended in recent guidance issued by NICE. Where participation in the trial is felt to be detrimental to health and wellbeing, we will not make an approach to participate. Participants will not be denied any form of care that is currently available in the NHS by participating in the trial, since participants allocated to usual care will still have full access to NICE recommended treatments, subject to local provision of services.

4.1 Anticipated risks and benefits

The trial does not involve new medicinal products or any invasive/potentially harmful procedures and is therefore considered low risk for participants.

All participants will receive usual GP care, and therefore no treatment will be withheld by participating in this trial. This trial may in fact benefit individual participants, since collaborative care is not routinely offered to our target group (screen-positive sub-threshold and above-threshold depression). By participating in this trial, participants will also receive a more intensive level of monitoring than that normally received in primary care. Participants who become more depressed or become suicidal will be more readily identified and directed to appropriate care.

4.2 Informing participants of anticipated risks and benefits

The Patient Information Sheet will provide potential participants with information about the possible benefits and anticipated risks of taking part in the study either as a participant in the epidemiological cohort or additionally in the trial. Participants will be given the opportunity to discuss this issue with their GP or trial co-ordinator prior to consenting to participate. The trial co-ordinator will inform the participant if new information comes to light that may affect the participant's willingness to participate in the trial.

4.3 Obtaining consent

Potential participants will receive an information pack about the trial. The pack will contain an invitation letter, Patient Information Sheet, a consent and a decline form and demographic questionnaire. The Patient Information Sheet will be produced using the current guidelines for researchers on writing information sheets and consent forms, posted on the NRES website.

4.4 Retention of study documentation

All data will be stored for a minimum of 5 years after the end of final analysis of the study and will be accessed by the Trial Statistician. All paper records will be stored in secure storage facilities. Personal identifiable paper records will be stored separately from anonymised paper records. All electronic records will be stored on a password protected server within York Trials Unit.

5. Project Timetable

November 2011	HTA approval of the CASPER PLUS RCT gained
February 2012	CASPER PLUS collaborative care manual produced for use in trial.
Mar-Apr 2012	Submission of application for substantial amendment to REC, CLRN and local R&D

April-May 2012	Approval letters gained from Ethics committee, all local PCTs and R&Ds. Amendment approved.
June 2012	Recruitment to CASPER PLUS RCT begins in Leeds and York. Primary care mental health workers begin work, and patients studied in concurrent process evaluation to refine intervention.
July 2013	Recruitment to the sub-study trial ends
Dec 2014	Follow up period of sub-study trial ends

6. PPI strategy

To enhance our service user and public involvement strategy, we are collaborating with a new initiative, funded by NIHR HTA Programme, the CASPER PPI strategy will be led by Dr June Wainwright, the Service User Representative for the NIHR Mental Health Research Network. Our PPI strategy has two key components: (i) involving service user representatives in the CASPER-PLUS research programme; and (ii) disseminating our research in a format appropriate for service users. With regard to (i), we will establish a trial management group (TMG); which will meet monthly to oversee the progress of the trial and include service user representation. Service users will also: check our understanding of key concepts; advise on our approach; inform the interpretation of results and comment on reports and academic papers. The TMG for the project will consist of a service user with lived experience of depression (our service user and carer collaborator JW has lived experience of depression). We will also invite a service user/carer to sit on the Trial Steering Committee (TSC). JW will facilitate the recruitment of the service user/carer to the TSC through her extensive and long-standing links with networks of users and carers in the mental health area and her experience of involvement in research. JW currently runs a training programme (based in the southern section of the regional MHRN which includes York) to support users and carers who wish to contribute to research. We are therefore confident we will be able to recruit an additional service user

to Trial Steering Committee, and that they will receive support from JW to be an active participant. JW will be able to provide continued service user input to the research team beyond the TMG and will be an active member of the project team. We now include a cost item for PPI/service user involvement, so that this activity can be supported and users' contribution can be reimbursed in line with recommendations from INVOLVE.

7. Monitoring Adverse Events

All serious adverse events that are treatment related will be recorded and immediately reported to the Data Monitoring and Ethics Committee (DMEC), MHRA trial sponsor and ethics committee except those that the CASPER protocol identifies as not requiring immediate reporting. The immediate report will be followed up by a detailed, written report and further information if requested. Inherent in the nature of the population under scrutiny is the risk of suicide and deliberate self-harm. We will follow good clinical practice in monitoring for suicide risk during all patient encounters with trial participants. Where any risk to patients due to expressed thoughts of self-harm is encountered, we will report these directly to the GP (with the patients' expressed permission) or will seek advice from the general practitioner if there are any concerns about immediate risk. Serious adverse events that are fatal or life-threatening will be recorded and reported to the TSC and ethics committee within 7 days of knowledge of such cases. All other suspected serious unexpected adverse events will be reported to the DMEC, MHRA, trial sponsor and ethics committee within 15 days of first knowledge. All serious adverse events that are treatment related will be recorded and immediately reported to the Data Monitoring and Ethics Committee (DMEC), MHRA trial sponsor and ethics committee except those that the protocol or investigator's brochure identifies as not requiring immediate reporting. The immediate report will be followed up by a detailed, written report and further information if requested. Inherent in the nature of the population under scrutiny is the risk of suicide and deliberate self-harm. We will follow good clinical practice in monitoring for suicide risk during all patient encounters with trial participants. Where any risk to patients due to expressed thoughts of self-harm is

encountered, we will report these directly to the GP (with the patients' expressed permission) or will seek advice from the general practitioner if there are any concerns about immediate risk. Serious adverse events that are fatal or life-threatening will be recorded and reported to the TSC and ethics committee within 7 days of knowledge of such cases. All other suspected serious unexpected adverse events will be reported to the DMEC, MHRA, trial sponsor and ethics committee within 15 days of first knowledge.

We will follow the same suicide protocol as CASPER. For details, see Appendix 4 of the CASPER Trial protocol.

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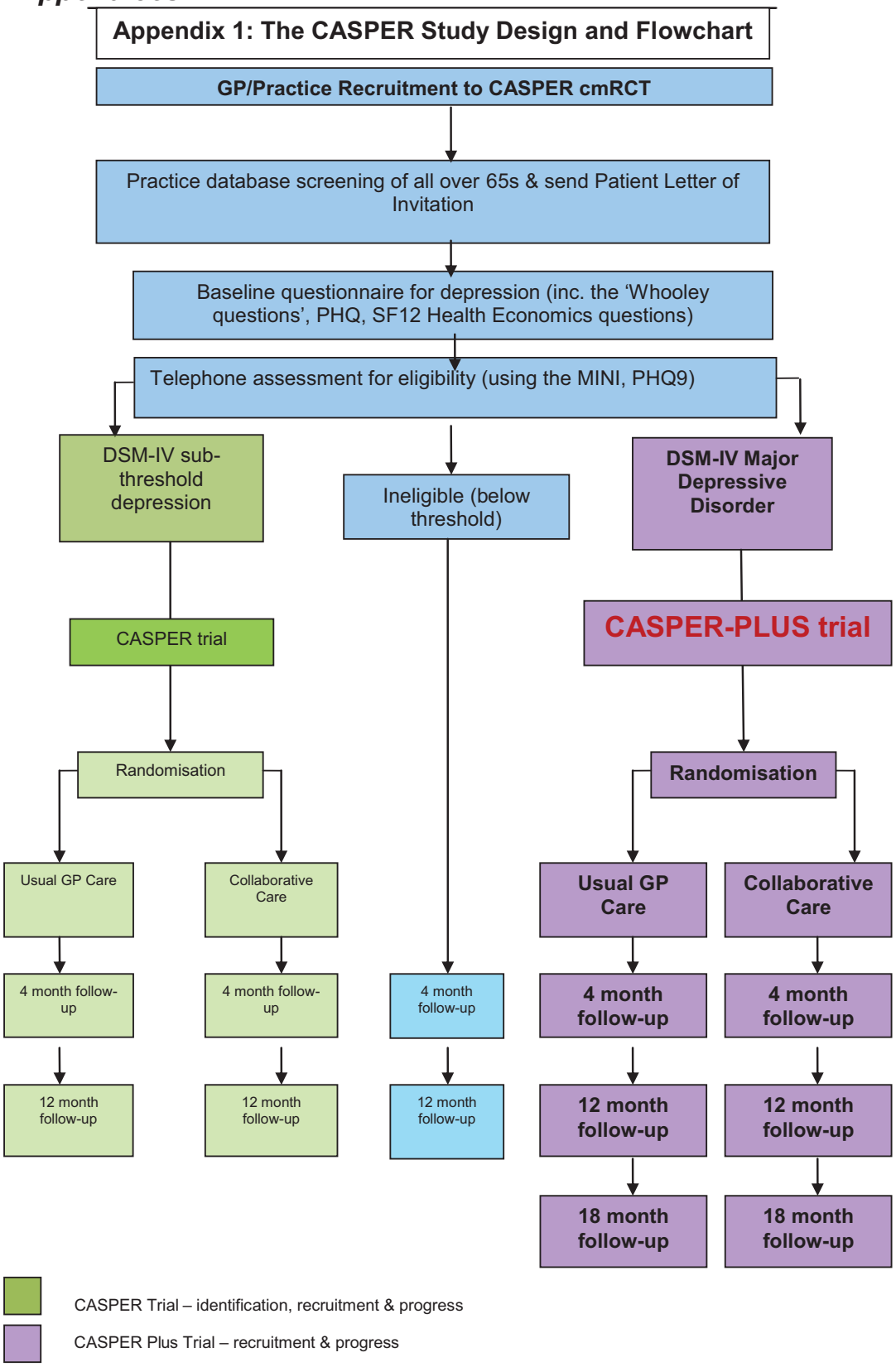
9. Appendices



Appendix 2: Data Collection Schedule

	Invitation	Baseline	Depression assessment	4 mth follow up	12 mth follow up	18mth follow up
Consent/Decline form	•					
Demographic questionnaire	•					
Whooley questionnaire	•	•				
Physical health problems	•					
Falls questions	•					
PHQ-9		•	•	•	•	•
SF-12		•		•	•	•
EQ-5D		•		•	•	•
GAD-7		•		•	•	•
PHQ-15		•		•	•	•
CD-RISC2		•		•	•	•
Medication questionnaire		•		•	•	•
Diagnostic interview (MINI)			•			
Economic evaluation		•		•	•	•
Objective medication data		•		•	•	•

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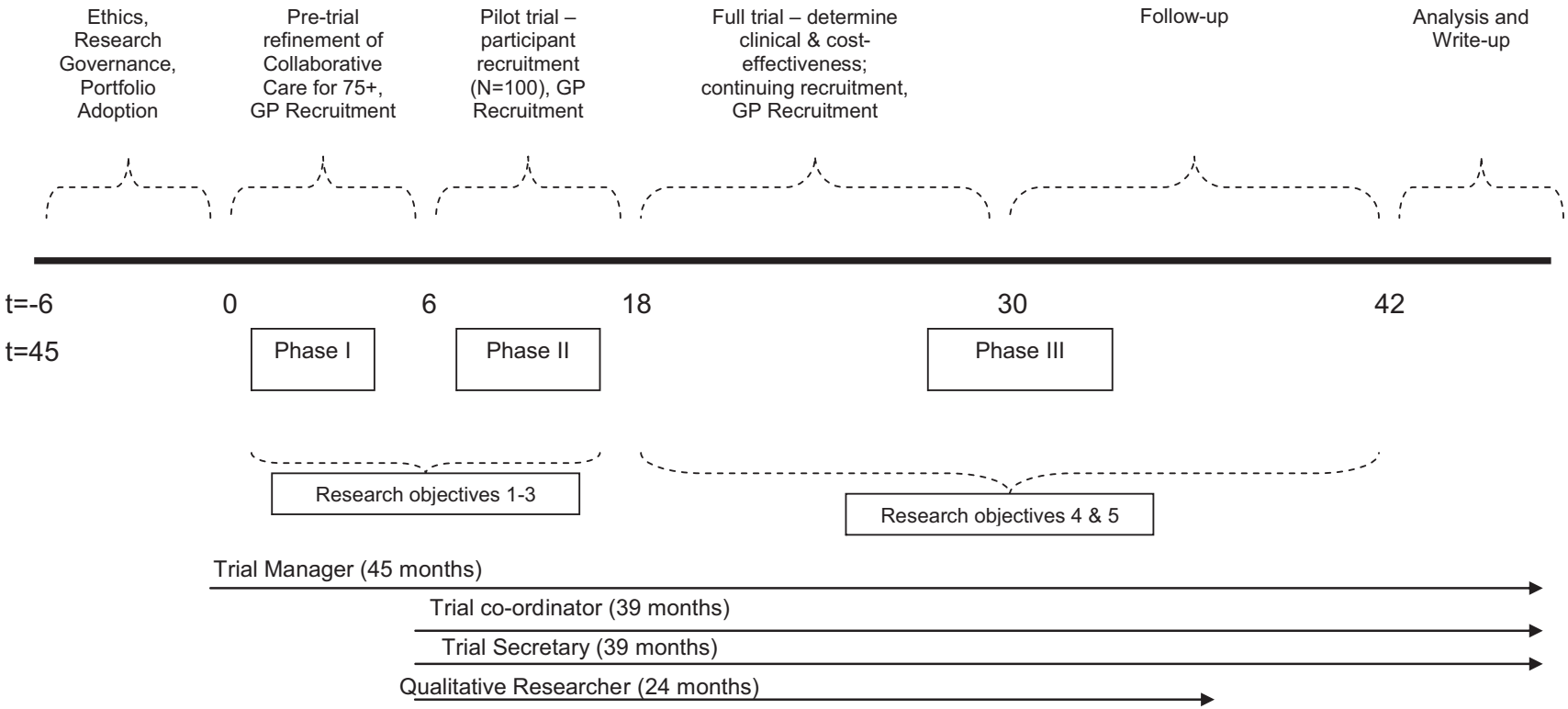
Appendix 3: CASPER Study – overview of phased approach and timeline



Appendix 21 CollAborative care for Screen-Positive EldeRs plus protocol version 2.6 (final version)

CASPER PLUS: An RCT sub-study of The CASPER Study

Collaborative Care in Screen-Positive Elders – The CASPER PLUS Trial

CASPER PLUS

Trial Protocol

The CASPER Study is funded by:

NHS National Institute for Health Research

The CASPER Research Collaborative

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Overview

As a sub-study of The CASPER Study, CASPER PLUS is a trial of a primary care-based intervention for older people with depression. Depression in older people is common and associated with poor quality of life, increased morbidity and mortality and increased health and social care use. It is under-recognised and sometimes inadequately treated in primary care. Current management is mostly limited to the prescription of anti-depressants; where there may be poor concordance.

Psychological treatments may not be offered or available in practice; and the evidence for psychological interventions uses models of care which are of a higher intensity such that they could not feasibly be delivered in primary care in sufficient volume to meet the needs of older people. An intervention known as **collaborative care** involves a brief patient-centred psycho-social package of care delivered by a case manager working to a defined protocol; medication management and with supervision of the case manager by a specialist, which facilitates liaison across the primary /secondary interface. Collaborative Care has shown promising trial results in the United States. However the transferability of this model of service to the UK NHS cannot be assumed. NICE has identified this as an important intervention that should be subject to further trials.

CASPER PLUS will run seamlessly as part of the recruitment procedures of a cohort of older people with depression with whom we will conduct trials to inform practice and policy (the CASPER older persons' cohort multiple RCT - cmRCT). Using this same cohort, we seek to conduct the definitive trial of collaborative care in older people with above threshold, major depressive disorder. Since we already identify people with 'sub threshold' depression in the existing cohort, we can conduct this important trial relatively quickly and at lower cost. The conduct of this trial will significantly enhance the randomised evidence base in the care of older people with depression, and will inform future service provision; satisfying a research priority identified by NICE.

1. Background

Depression accounts for the greatest burden of disease among all mental health problems, and is expected to become the second-highest among all general health problems by 2020.[1] By the age of 75, 1 in 7 older people meet formal diagnostic criteria for depression. Projected demographic changes mean that population strategies to tackle depression will increasingly have to address the specific needs of older people.[2] Amongst older people, depressive syndromes often affect people with chronic medical illnesses, cognitive impairment, social isolation or disability.

Older people with a long-term condition are five times more likely to suffer depression. 50% of people with Parkinson's disease will suffer depression, 25% following stroke, 20% with coronary heart disease, 24% neurological disease and 42% chronic lung disease.[3] Beyond personal suffering and family disruption, depression worsens the outcomes of many medical disorders and promotes disability. The impairments in quality of life associated with depression are comparable to those of major physical illness. Amongst older people, a clinical diagnosis of major depression is the strongest predictor for impaired quality of life (QoL).[4]

Current UK policies under the Quality and Outcomes Framework (QOF) advocate case-finding for depression amongst those with chronic physical health problems such as heart disease and diabetes. [5] Once detected, evidence supported guidelines advocate the prescription of anti-depressant drugs and appropriate provision of psychological care.[6,7] However, an enduring critique has been that depression is not well managed even when this is revealed through case-finding.[2] Management in primary care usually involves the prescription of antidepressant medication, with poor concordance and suboptimal dosages. The provision of psychological or social interventions addressing issues of poor adaptation, loss, depressive thinking or social withdrawal is woefully inadequate. For example, there has been

minimal provision of psychological treatment for older people under the Improving Access to Psychological Therapies (IAPT) programme.

Despite being encouraged to case-find for depression in older people there is little evidence that this has translated into better management for this disorder. The current proposal introduces a feasible intervention for this group of patients which is known as 'Collaborative care'.

The role of collaborative care

The vast majority of depression in older people can (quite appropriately) be managed entirely in primary care, without recourse to specialist mental health services.[2,6,8] A range of individual treatments have been shown to be effective in the management of depression in older people, including anti-depressants and psychosocial interventions.[6] However, a repeated observation amongst all people with depression has been the failure to integrate these effective elements of care into routine primary care services.[9] Similarly the volume of people with depression necessitates that low intensity interventions are the only feasible strategy that can be used in managing depression within the population.

Despite recent investment under the Improving Access to Psychological Therapies (IAPT) initiative, the capacity for specialist mental health services to provide this care is constrained and demand would quite quickly outstrip supply. Hence any feasible strategy will be both low intensity and offered within primary care.[10]

The ubiquity of depression in primary care settings and the poor integration/co-ordination of care have led to strategies to re-engineer the delivery of care. This form of care borrows much from chronic disease management and facilitates the delivery of effective forms of treatment (such as pharmacotherapy and/or brief psychological therapy). This model of care is often referred to as **collaborative care** or **case management**.[11] According to a recent BMJ editorial on the management of depression in older people *'Innovations in the management of depression have been evaluated. The best*

results come from models that use multifaceted interventions and principles of collaborative care.' [2] We would concur with this observation and the CASPER research group has contributed much to the evidence base of collaborative care and in the evaluation/implementation of this model of care to the UK. We have for example, conducted the definitive reviews of this intervention, [13,14] and have completed the first trial of collaborative care in the UK.[14] We have recently completed an MRC-funded evaluation of clinical and cost effectiveness of Collaborative Care in depressed working age adults (PI Richards). Within the new Improving Access to Psychological Therapies (IAPT) programme, we have implemented this model of care for over 7000 working age adults with depression in demonstration sites.[15] We have also developed computer-based case management systems to facilitate symptom management and supervision of case managers (the PC-MIS system).

Our own reviews in this area have shown collaborative care to be a potentially effective and efficient means of delivering care for depression. Based upon analyses of 36 trials (12,000 participants), we have shown that collaborative care is effective in the short and medium term in alleviating depressive symptoms and improving quality of life. [12] Moreover collaborative care is known to be cost effective in reducing healthcare utilisation and in improving overall quality of life. [16] *See CASPER protocol for details of the United States IMPACT study of collaborative care in older adults (aged over 60).*

1.2 The wider CASPER Study

The CASPER study (see Appendix 1) - a cohort study and randomised controlled trial looking at the effectiveness of collaborative care in older patients with sub-threshold depression [14] - uses a database screening approach in recruiting patients. A randomised controlled trial would be the best approach to evaluate its effects.

1.3 Research Objectives

The research objectives of the CASPER PLUS sub-study are:

1. To establish the clinical effectiveness of a collaborative care intervention for older people with screen-positive above-threshold

('major depressive episode') depression within a definitive RCT.
2. To examine the cost effectiveness of a collaborative care intervention for older people with screen-positive above-threshold ('major depressive episode') depression within a definitive RCT.

2. Method

2.1 Design

As a sub-study of the CASPER trial, CASPER PLUS will follow the same design and recruit from the same wider cohort, using a pragmatic multi-centred randomised controlled trial until completion of the CASPER trial recruitment phase. Following this, CASPER Plus will adopt a more focused approach to recruitment in General Practice, concentrating on searches for patients with known depression or known to be at greater risk of depression.

Patients will be randomly allocated to one of two interventions:

1. Collaborative care with behavioural activation and active surveillance
2. Usual primary care management of above-threshold depression (major depressive episode) offered by the patient's GP, in line with NICE depression guidance and local service provision

2.2 Inclusion / exclusion criteria

For the CASPER PLUS sub-study all patients at participating CASPER GP practices who have been identified as eligible to receive an invitation mailing will be included. Those patients identified at the screening phase as having above-threshold, case level depression will be eligible to enter the CASPER PLUS sub study.

Inclusion criteria

CASPER participants will be identified by comprehensive screening strategies in primary care (replicating that which is incentivised in QOF-compliant case finding for those with CHD and diabetes). Our target population will be older people (aged 65 and above) who screen-positive for depression on the

recommended QOF 2 question brief depression screen (sometimes referred to as the 'Whooley' questions after their initial validation study [21]), but who on further assessment have DSM-IV Major Depressive Disorder (MDD).[22] The Whooley questions are detailed in Box 1. [21,23]

Box 1: QOF-compliant (DEP1) brief screening questions

1. 'Over the past month have you been bothered by feeling down, depressed or hopeless?'
2. 'Over the past month, have you been bothered by having little interest or pleasure in doing things? A positive answer to one or both of these questions raises the possibility of depression and necessitates a full assessment for the presence or absence of clinically significant depressive syndrome.

The **exclusion criteria** are:

- Known alcohol dependency (as recorded on GP records)
- Any known co-morbidity that would in the GP's opinion make entry to the trial inadvisable (e.g. recent evidence of self harm, known current thoughts of self harm, significant cognitive impairment)
- Other factors that would make an invitation to participate in the trial inappropriate (e.g. recent bereavement; terminal malignancy)
- Known to be experiencing psychotic symptoms (as recorded on GP records)
- Actively engaged in a psychological intervention or therapy at the time of randomisation (screened at diagnostic interview).

2.3 Recruitment and Randomisation

2.4 Intervention

Collaborative Care with behavioural activation and active surveillance

Patients who meet our pragmatic inclusion criteria will be individually randomised into one of two intervention groups: (1) Collaborative Care (including Behavioural Activation) intervention with medication monitoring and management, or (2) usual care. This is a pragmatic trial [20] and we will

impose few restrictions on routine practice and will have no direct influence on the prescription of medication (which will remain entirely in the control of GPs). The actual delivery of this service within the pilot trial will be studied using a concurrent process evaluation – utilising a mixed methods research design.

Eligible participants who have consented to be in the trial will be randomised to a treatment group using the computer-based York Trials Unit telephone randomisation service.

Our experimental intervention will be a bespoke collaborative care designed and delivered specifically for those aged 65 or over with above threshold, case-level depression over 6-8 weekly sessions. The intervention manual has been adapted from the existing CASPER manual used in the pilot study. Collaborative care will be delivered by a case manager (a primary care mental health worker) within a 'stepped care framework', such that those whose depression deteriorates are 'stepped up' from low intensity care to a more intensive form of management including medication monitoring.

The five core components of the intervention are described below:

1. **PATIENT-CENTRED ASSESSMENT AND ENGAGEMENT:** patients are first assessed in their own residential setting, GP practice or by telephone. The severity of depression and associated behavioural and social deficits are assessed. The presence of depressive symptoms and behavioural deficits are described and patient information materials are given or sent in advance to the participant.

2. **SYMPTOM MEASUREMENT AND MONITORING:** a standardised assessment of symptom severity is made. Symptom tracking (to judge response, failure to respond or deterioration) is then made at all subsequent patient contacts.

3. **MEDICATION MANAGEMENT:** the prescription of anti-depressant medication is entirely at the discretion of the General Practitioner. We will encourage GPs to consider NICE guidance in their prescribing decisions. The concordant use of medication by patients will be encouraged by the case manager if a prescription has been initiated by the GP. Patient concerns (such as addiction) and non-compliance will be addressed during sessions. There will be active liaison with GPs to encourage follow up patient appointments with the GP if poor concordance is noted.

4. **ACTIVE FOLLOW-UP:** all patients are followed up by the CM for eight weeks using face to face meetings or telephone contacts. Our own experience is that telephone contacts are acceptable and that patients can be engaged using this means of communication.[18] We have adapted this means of delivery in the light of the specific needs of those over 65.

5. **DELIVERY OF BEHAVIOURAL ACTIVATION (BA):** patients are offered the option of behavioural activation delivered over eight sessions by their case manager. BA consists of a structured programme of reducing the frequency of negatively reinforced avoidant behaviours in parallel with increasing the frequency of positively reinforcing behaviours to improve functioning and raise mood. During this time patients will remain under the medical care of their General Practitioner. We have demonstrated that BA is potentially effective in older adults.[17] and have recently demonstrated the effectiveness of this approach in working age adults.[19]

Higher intensity treatments for depression will be facilitated by the GP and by conventional mental health services for older people, and will not be directly influenced by this trial. The additional elements of collaborative care include: telephone support; symptom monitoring and active surveillance (facilitated by computerised case management systems – PC-MIS); medication monitoring;

low intensity psychosocial intervention (behavioural activation). The work of case managers is supervised by an older persons' mental health specialist (old age psychiatrist or psychologist).

For the purpose of quality evaluation and to ensure fidelity to the Collaborative Care model, we propose to record a sub-sample of patient consultations with around 6 - 8 Case Managers who deliver the intervention to 3 – 4 participants each (24 – 32 participants in total). As a secondary aim, we wish to use the recordings to refine the content or delivery of the intervention.

To gain an overview of how the treatment progresses, we would aim to record a maximum of 4 sessions of the 8-10 consultations that Case Managers have with participants. We would purposively sample Case Managers with different backgrounds, including those with long-term experience of working with psychosocial interventions for older people as well as others with less experience.

Control intervention

Participants allocated to the control condition will receive usual primary care management of case level depression offered by their GP, in line with NICE depression guidance and local service provision.

Recruitment method

Screening of all over 65s from GP practice lists: in our existing portfolio of trials at the York Trials Unit, we have pioneered the use of postal screening questionnaires sent to all over 75s based upon practice registers. This has resulted in above-target recruitment to our trials in falls and osteoporosis by this method. We will follow those participants who sign the consent form, return screening questionnaires and meet the inclusion criteria for the CASPER Plus trial. Following the completion of the recruitment phase of the CASPER trial, all ineligible participants will be thanked for their interest in the study but not followed up. The pilot study of CASPER has been successful in

recruiting 100 participants and met criteria for retention during the first year of the study. In addition to sending postal screening questionnaires, participants may be recruited directly by GPs.

2.5 Outcome measures

Primary outcome: We will measure depression severity at four months by self report using the Patient Health Questionnaire 9 – PHQ9. We will also measure outcome at 12 and 18 months using the PHQ9 to examine any sustained impact of the intervention.

Our secondary outcome is binary and is the presence/absence of depression diagnosis as ascertained by interview. For this secondary measure we will use a criterion-based assessment of depression according to the American Psychiatric Association DSM-IV (established by the validated interviewer-administered diagnostic schedule MINI). We will also measure DSM-IV depression status at 4, 12 months and 18 months (using the PHQ9); health related quality of life (SF-12); health-state utility (EQ5D) at 4 months, 12 months and 18 months.

2.6 Qualitative study

In addition to the quantitative data collected in the nested trial, we will collect qualitative data obtained from focus groups and/or face to face interviews.

3. Statistical considerations

3.1 Sample size

Our overall sample size for our definitive trial will be 450 (225 per arm). The sample size of our definitive trial is inexorably linked to (1) the specified minimally important difference; (2) ICC and (3) caseload size. A conservative assumption of an **ability to detect an effect size of 0.35,** based upon ICC=0.02 and caseload size 20 will require 180 participants in the intervention arm. This effect size is in line with the IMPACT US trial [25] and the point estimate from our UK pilot trial.

TABLE: SAMPLE SIZE CALCULATION INCORPORATING ICC VALUES, CASELOAD SIZES AND LOSS TO FOLLOW UP

Effect size* (based upon US trial and UK pilot trial.	Conventional sample size (assumes no clustering)	Caseload size	Plausible ICC within therapists' caseloads	Design Effect/Inflation factor	Effective sample size (adjusted for clustering)	Inflation for 20% loss to follow up (final sample size)
D=0.35	260	20	0.02	1.38	360	450

3.2 Analysis

Statistical analysis of clinical data

We will analyse the data on an intention to treat basis. The primary outcome of depression severity (a continuous outcome as measured by a score on the PHQ9 depression severity measure) will be used in a linear regression model to compare collaborative care with usual care. The analysis will be adjusted for baseline depression severity (as measured by the PHQ9) and physical/functional limitations (as measured by the SF36 physical functioning scale).[24] Standardised effect sizes and the corresponding 95% confidence intervals will be presented for the primary outcome of depression severity. Two-sided 95% confidence intervals will be calculated.

For each outcome measure the number of non-responders will be calculated for each treatment group and response rates compared. We will undertake sensitivity analyses to explore the impact of missing data using multiple imputations by chained equations which will be performed using the ICE package in Stata. All secondary analyses will be conducted using linear or logistic regression, depending on the outcome measure, adjusting for the same covariates as the primary analysis. All analyses will adjust for within-therapist clustering using multi-level modelling with the Huber-White sandwich estimator.

3.3 Analysis of economic data

The economic evaluation will take the form of within-trial cost-utility analysis that will determine the incremental cost per quality adjusted life year for treatment with collaborative care against usual care in individuals with depression. The primary analyses will be conducted from the UK NHS and personal and social services (PSS) perspective following NICE evaluation guidance.

Primary and secondary healthcare and societal costs will include intervention-related costs, health service use costs and personal social services costs, in line with the recommendations by NICE. The cost data will be collected to fully reflect the management of depression and its cost in both collaborative care and usual care group, and these will be analysed within a societal perspective. Intervention (and control) group costs will be based on the delivery costs within the trial and include supervision and appropriate capital and overhead amounts. Patient questionnaires and case record review will be used to collect data on the use of health services and personal social services. Unit costs for these items will be drawn from the NHS reference costs and the personal social services resource use databases.

The effectiveness of the intervention will be evaluated using the standard quality of life measures which have been shown to be sensitive to change in relation to depression, and also physical healthcare problems common amongst older adults. These will be collected at regular intervals using patient questionnaires. These will then be evaluated over the 18 months trial period to estimate the total quality-adjusted life years for both intervention and control groups.

Economic analyses will compare the costs and effectiveness at the final 18-month follow-up of collaborative versus usual care to capture the economic impact of events such as relapse, although we will conduct an initial preliminary analysis at six months to coincide with the primary clinical analyses. Although the distribution of costs is commonly skewed in populations of this kind, analyses will compare mean costs using standard parametric t-tests with covariates for pre-specified baseline stratification factors plus baseline costs. The robustness of the parametric tests will be confirmed using bias-corrected, non-parametric bootstrapping.

We will explore the joint distribution of costs and effects in a cost-effectiveness analysis (CEA) using an incremental approach to determine the incremental cost-effectiveness ratio with uncertainty estimates around it. The

cost-effectiveness acceptability curve (CEAC) will be used to represent the probability that collaborative care is cost-effective compared to usual care for a range of maximum monetary values (ceiling ratios) that a UK decision maker may be willing to pay for an increase in one unit of quality-adjusted life years. This is the recommended decision-making approach to dealing with the uncertainty that exists around the estimates of expected costs and expected effects associated with the interventions under investigation and uncertainty regarding the maximum cost-effectiveness ratio that a decision-maker would consider acceptable.

Furthermore, a net benefit analysis will be undertaken to evaluate the net monetary gain that can be achieved with implementation of collaborative care. The net benefit approach will estimate the monetary gain by weighting the incremental quality-adjusted life years by ceiling ratios and taking away the incremental cost of the intervention. This in turn will allow the decision makers to determine the value of the intervention in terms of monetary gains.

3.4 Qualitative analysis

Our qualitative analysis aims, as outlined in The CASPER Trial protocol are:

1. To inform the efficient conduct of the main trial phase (recruitment, randomisation and follow up).
2. To refine the content and delivery of the collaborative care intervention based on early experience from the pilot phase of the trial.
3. To understand the barriers and facilitators to the delivery, uptake and implementation of collaborative care for older people.

4. Ethical issues

NRES approval has been received to conduct the CASPER study, using the recruitment method described above. We are aware that older people with above-threshold depression (experiencing a major depressive episode) represent a vulnerable group. However, we do not anticipate any major ethical

issues since we will only offer interventions recommended in recent guidance issued by NICE. Where participation in the trial is felt to be detrimental to health and wellbeing, we will not make an approach to participate. Participants will not be denied any form of care that is currently available in the NHS by participating in the trial, since participants allocated to usual care will still have full access to NICE recommended treatments, subject to local provision of services.

4.1 Anticipated risks and benefits

The trial does not involve new medicinal products or any invasive/potentially harmful procedures and is therefore considered low risk for participants.

All participants will receive usual GP care, and therefore no treatment will be withheld by participating in this trial. This trial may in fact benefit individual participants, since collaborative care is not routinely offered to our target group (screen-positive sub-threshold and above-threshold depression). By participating in this trial, participants will also receive a more intensive level of monitoring than that normally received in primary care. Participants who become more depressed or become suicidal will be more readily identified and directed to appropriate care.

4.2 Informing participants of anticipated risks and benefits

The Patient Information Sheet will provide potential participants with information about the possible benefits and anticipated risks of taking part in the study either as a participant in the epidemiological cohort or additionally in the trial. Participants will be given the opportunity to discuss this issue with their GP or trial co-ordinator prior to consenting to participate. The trial co-ordinator will inform the participant if new information comes to light that may affect the participant's willingness to participate in the trial.

4.3 Obtaining consent

Potential participants will receive an information pack about the trial. The pack will contain an invitation letter, Patient Information Sheet, a consent and a decline form and demographic questionnaire. The Patient Information Sheet will be produced using the current guidelines for researchers on writing information sheets and consent forms, posted on the NRES website.

4.4 Retention of study documentation

All data will be stored for a minimum of 5 years after the end of final analysis of the study and will be accessed by the Trial Statistician. All paper records will be stored in secure storage facilities. Personal identifiable paper records will be stored separately from anonymised paper records. All electronic records will be stored on a password protected server within York Trials Unit.

5. Project Timetable

November 2011	HTA approval of the CASPER PLUS RCT gained
February 2012	CASPER PLUS collaborative care manual produced for use in trial.
Mar-Apr 2012	Submission of application for substantial amendment to REC, CLRN and local R&D
April-May 2012	Approval letters gained from Ethics committee, all local PCTs and R&Ds. Amendment approved.
June 2012	Recruitment to CASPER PLUS RCT begins in Leeds and York. Primary care mental health workers begin work, and patients studied in concurrent process evaluation to refine intervention.
July 2013	Recruitment to the sub-study trial ends
Dec 2014	Follow up period of sub-study trial ends

6. PPI strategy

To enhance our service user and public involvement strategy, we are collaborating with a new initiative, funded by NIHR HTA Programme, the CASPER PPI strategy will be led by Dr June Wainwright, the Service User Representative for the NIHR Mental Health Research Network. Our PPI strategy has two key components: (i) involving service user representatives in the CASPER-PLUS research programme; and (ii) disseminating our research in a format appropriate for service users. With regard to (i), we will establish a trial management group (TMG); which will meet monthly to oversee the progress of the trial and include service user representation. Service users will also: check our understanding of key concepts; advise on our approach; inform the interpretation of results and comment on reports and academic papers. The TMG for the project will consist of a service user with lived experience of depression (our service user and carer collaborator JW has lived experience of depression). We will also invite a service user/carer to sit on the Trial Steering Committee (TSC). JW will facilitate the recruitment of the service user/carer to the TSC through her extensive and long-standing links with networks of users and carers in the mental health area and her experience of involvement in research. JW currently runs a training programme (based in the southern section of the regional MHRN which includes York) to support users and carers who wish to contribute to research. We are therefore confident we will be able to recruit an additional service user to Trial Steering Committee, and that they will receive support from JW to be an active participant. JW will be able to provide continued service user input to the research team beyond the TMG and will be an active member of the project team. We now include a cost item for PPI/service user involvement, so that this activity can be supported and users' contribution can be reimbursed in line with recommendations from INVOLVE.

7. Monitoring Adverse Events

All serious adverse events that are treatment related will be recorded and immediately reported to the Data Monitoring and Ethics Committee (DMEC), MHRA trial sponsor and ethics committee except those that the CASPER

protocol identifies as not requiring immediate reporting. The immediate report will be followed up by a detailed, written report and further information if requested. Inherent in the nature of the population under scrutiny is the risk of suicide and deliberate self-harm. We will follow good clinical practice in monitoring for suicide risk during all patient encounters with trial participants. Where any risk to patients due to expressed thoughts of self-harm is encountered, we will report these directly to the GP (with the patients' expressed permission) or will seek advice from the general practitioner if there are any concerns about immediate risk. Serious adverse events that are fatal or life-threatening will be recorded and reported to the TSC and ethics committee within 7 days of knowledge of such cases. All other suspected serious unexpected adverse events will be reported to the DMEC, MHRA, trial sponsor and ethics committee within 15 days of first knowledge. All serious adverse events that are treatment related will be recorded and immediately reported to the Data Monitoring and Ethics Committee (DMEC), MHRA trial sponsor and ethics committee except those that the protocol or investigator's brochure identifies as not requiring immediate reporting. The immediate report will be followed up by a detailed, written report and further information if requested. Inherent in the nature of the population under scrutiny is the risk of suicide and deliberate self-harm. We will follow good clinical practice in monitoring for suicide risk during all patient encounters with trial participants. Where any risk to patients due to expressed thoughts of self-harm is encountered, we will report these directly to the GP (with the patients' expressed permission) or will seek advice from the general practitioner if there are any concerns about immediate risk. Serious adverse events that are fatal or life-threatening will be recorded and reported to the TSC and ethics committee within 7 days of knowledge of such cases. All other suspected serious unexpected adverse events will be reported to the DMEC, MHRA, trial sponsor and ethics committee within 15 days of first knowledge.

We will follow the same suicide protocol as CASPER. For details, see Appendix 4 of the CASPER Trial protocol.

CASPER PLUS Trial Protocol v2.6 4Apr14

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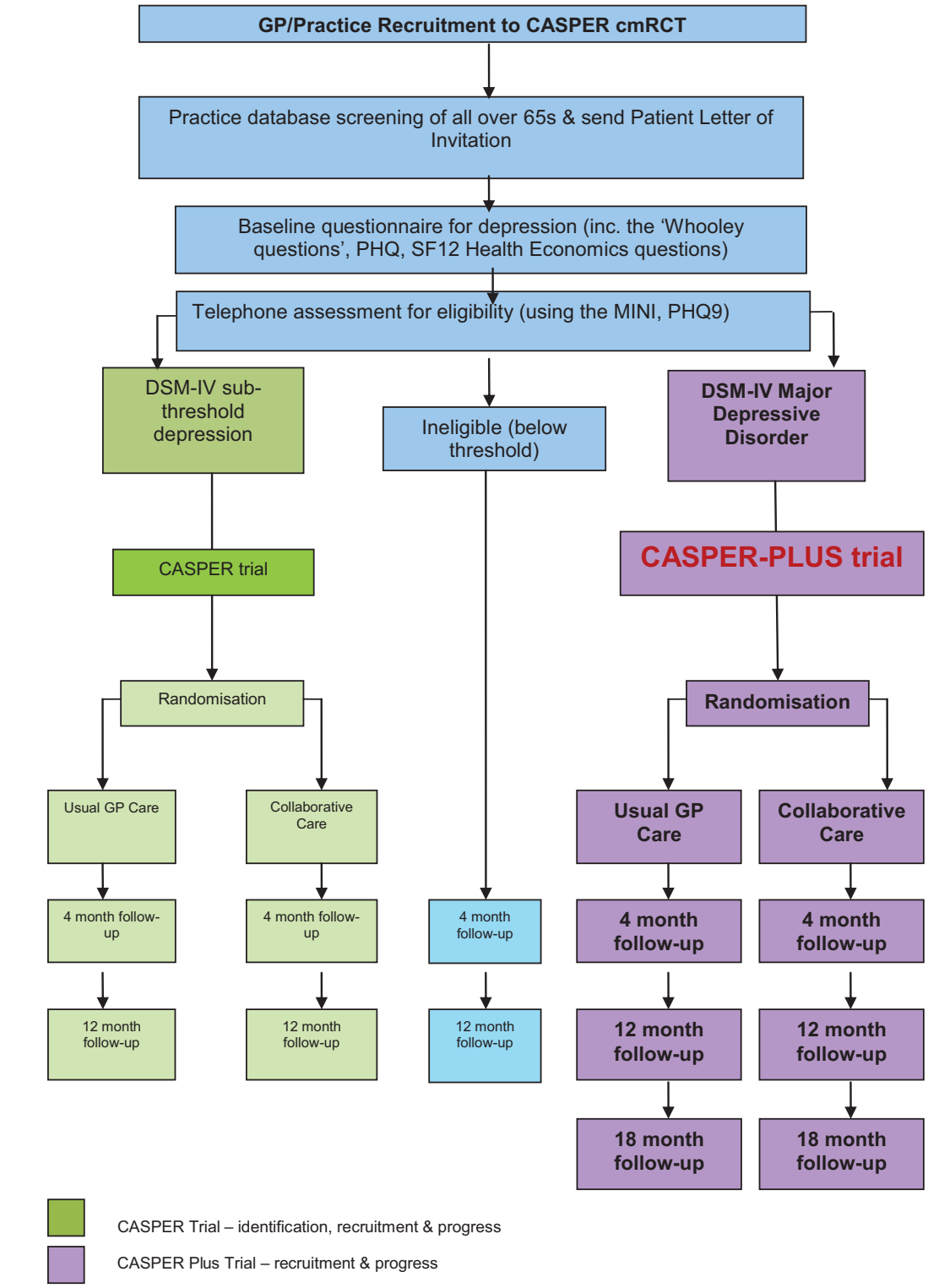
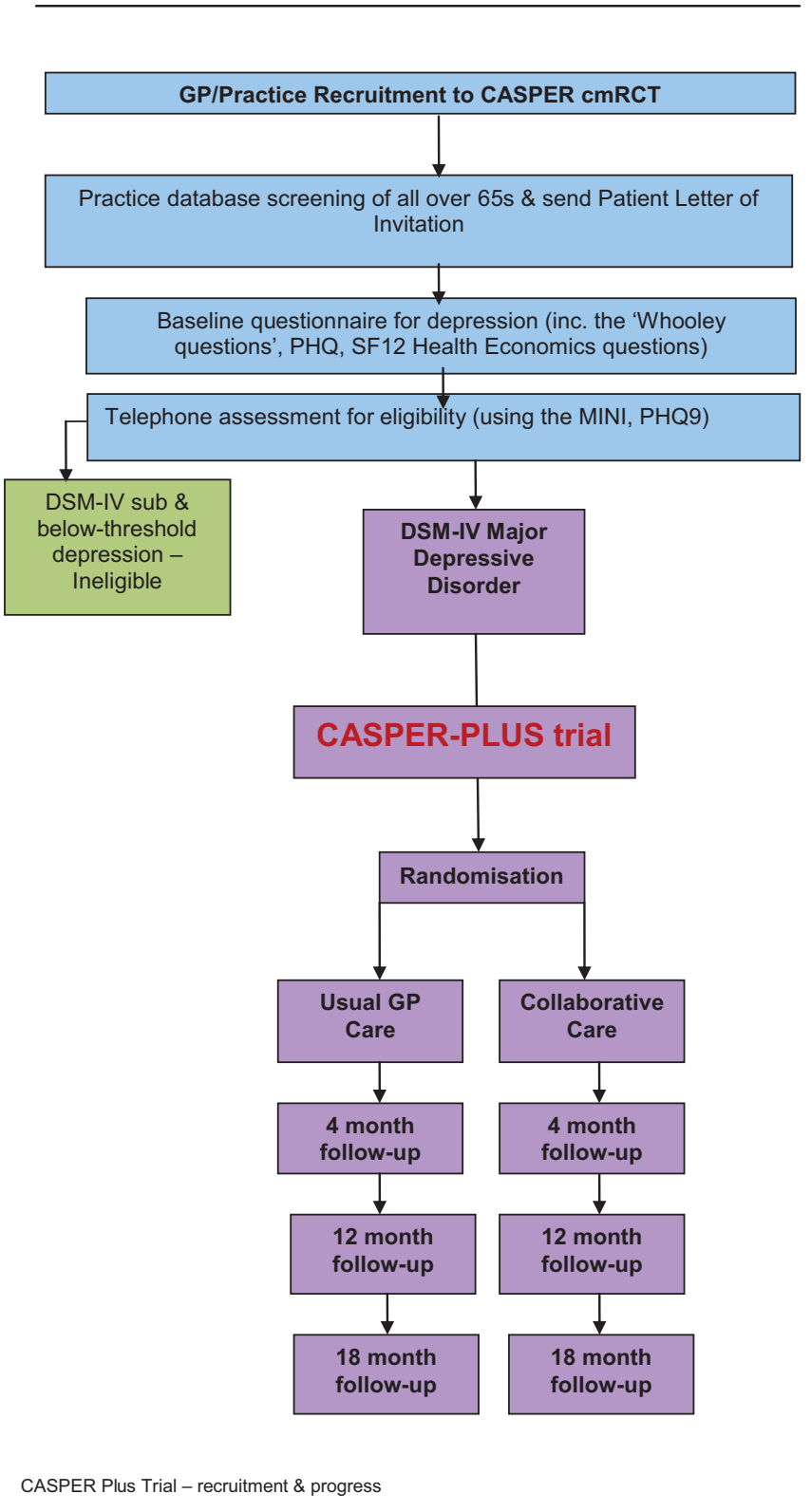
Appendix 1a: The CASPER Study Design during CASPER recruitment



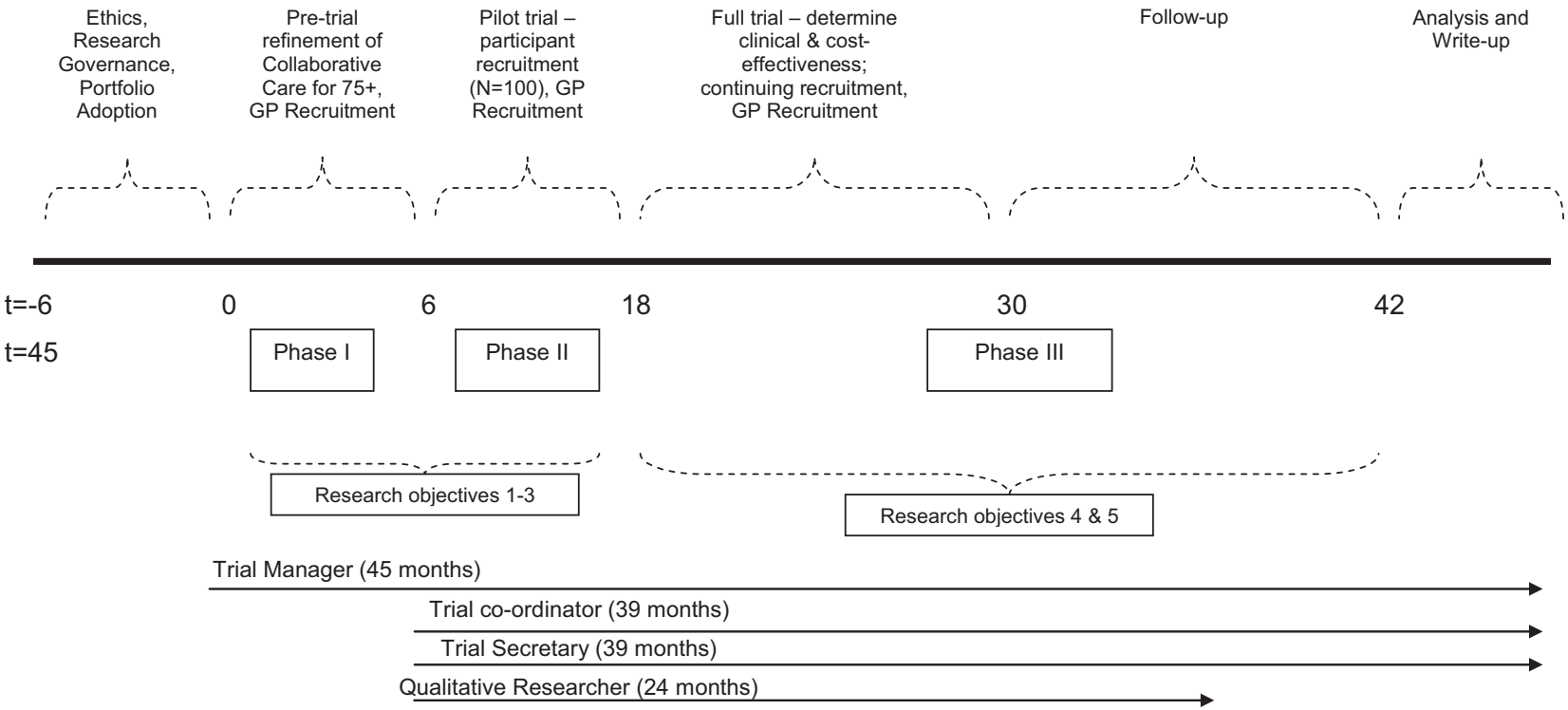
Appendix 1b: The CASPER Study Design post CASPER recruitment



Appendix 2: Data Collection Schedule

	Invitation	Baseline	Depression assessment	3 mth follow up	12 mth follow up	18mth follow up
Consent/Decline form	•					
Demographic questionnaire	•					
Whooley questionnaire	•	•				
Physical health problems	•					
Falls questions	•					
PHQ-9		•	•	•	•	•
SF-12		•		•	•	•
EQ-5D		•		•	•	•
GAD-7		•		•	•	•
PHQ-15		•		•	•	•
CD-RISC2		•		•	•	•
Medication questionnaire		•		•	•	•
Diagnostic interview (MINI)			•			
Economic evaluation		•		•	•	•
Objective medication data		•		•	•	•

Appendix 3: CASPER Study – overview of phased approach and timeline



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