CASPER PLUS: An RCT sub-study of The CASPER Study

Collaborative Care in Screen-Positive Elders – The CASPER PLUS Trial

Trial Protocol

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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 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. 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 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).

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.

8. References

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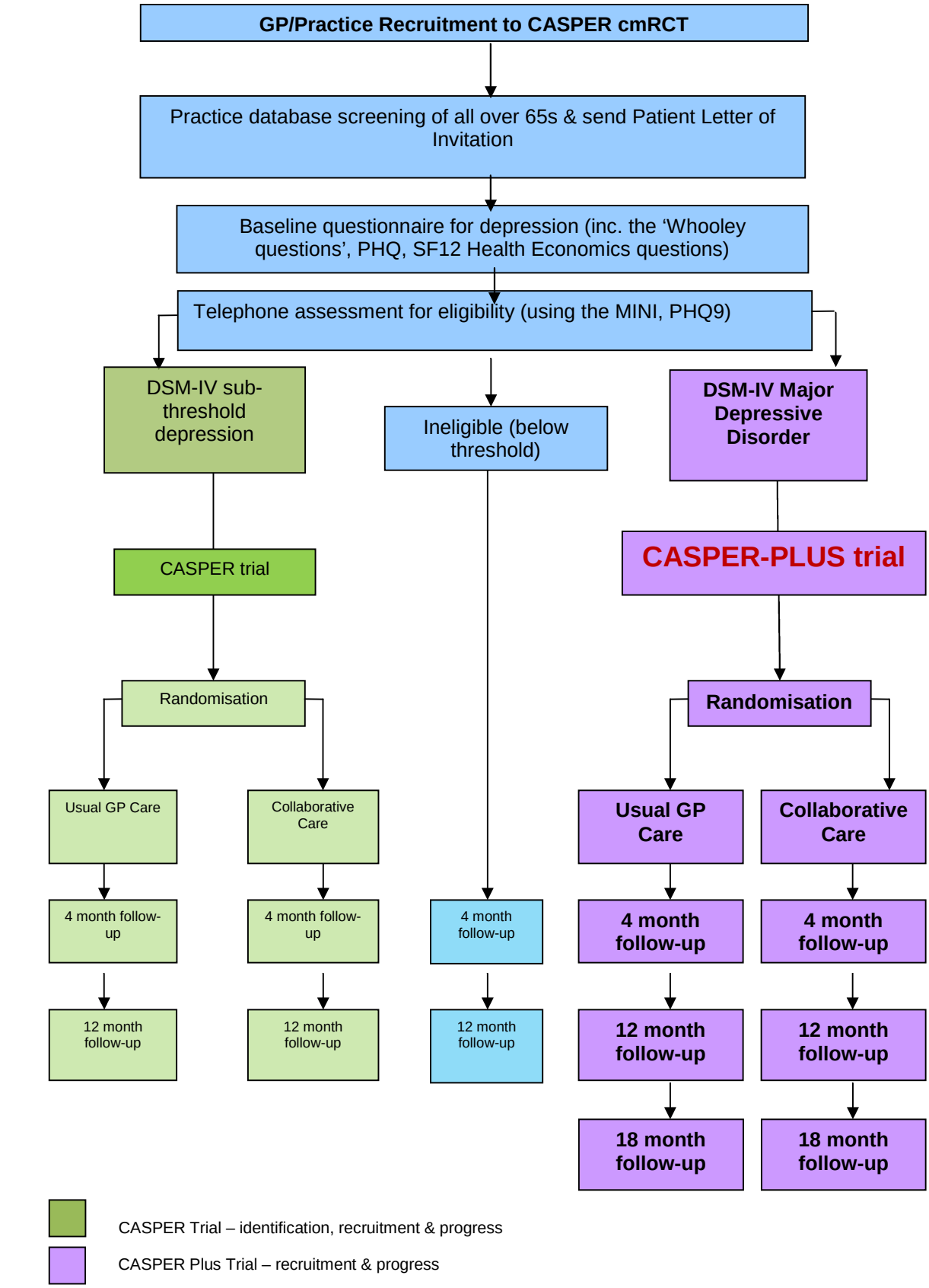
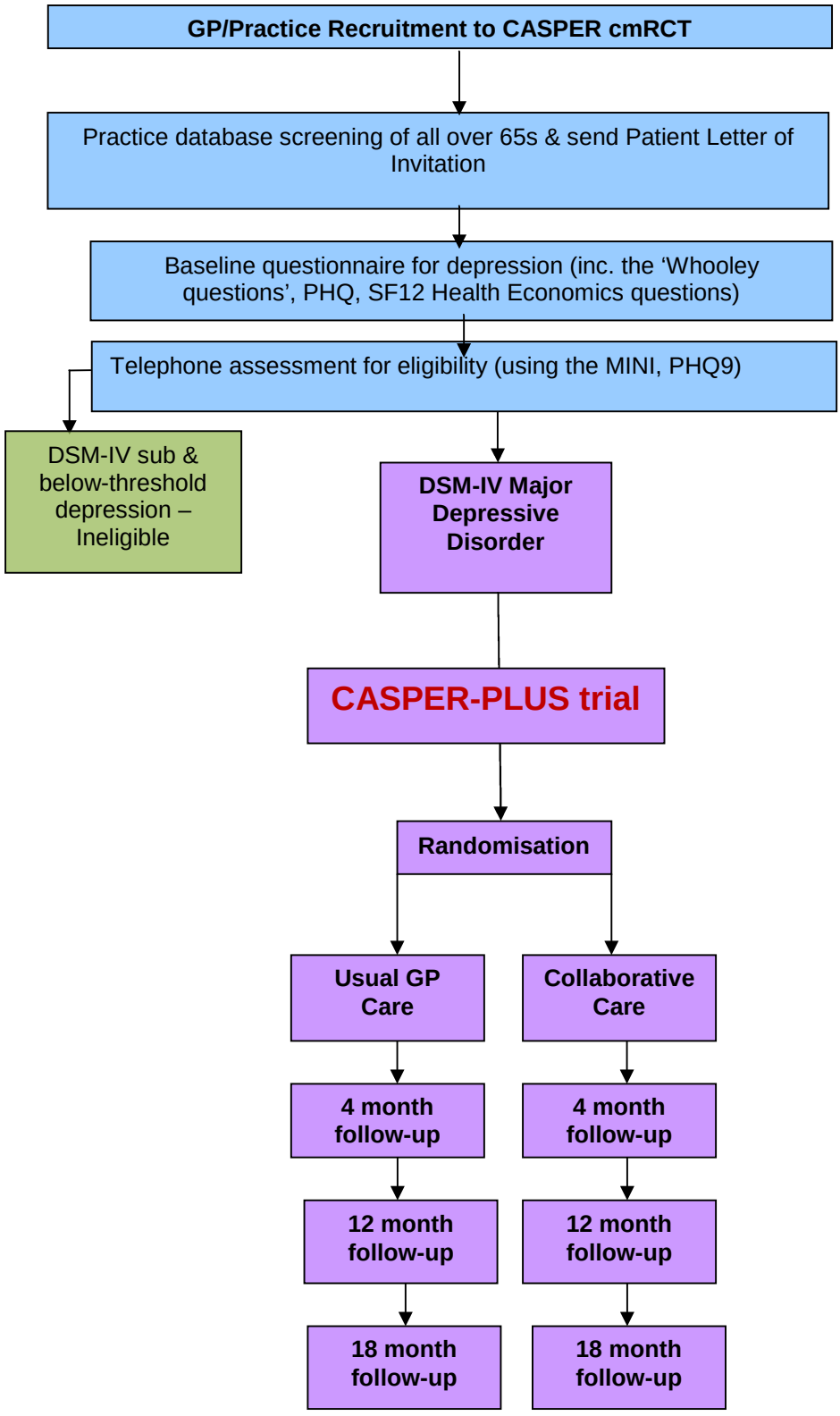
Appendix 1a: The CASPER Study Design during CASPER recruitment



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