PROJECT COLLABRI

The Effects of a Danish model of Collaborative Care for people with Anxiety and Depression in General Practice
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13. APPENDIX 1
1. Introduction and background

1.1 The patient population

Depression and anxiety are common illnesses with a lifetime risk of 17-18% and 14-29 % respectively (1,2). The human costs relating to these illnesses are great, but they also place a significant burden on the economy. It is estimated that the costs related to anxiety and depression are approximately DKK 20 billion per annum and an increasing number of people receive disability pension because of the illnesses (3).

1.2 Current treatment of anxiety and depression in general practice

In Denmark the general practitioner (GP) is the main provider of primary, personal and continuous health care to individuals, families and vulnerable groups in Denmark. Common mental health disorders is a significant element in the general practitioner’s workload, as the vast majority of the population of people with depression and anxiety is diagnosed and treated in primary care. It is agreed that the majority of these patients should continue to be treated here (4), but also that the effort must be optimised as studies show that many patients with anxiety and depression do not get the correct diagnosis and evidence based treatment in general practice (2,4-6).

Some of the obstacles in the current management and organisation of treatment of anxiety, depression and non-psychotic mental health disorders in general are identified below:

- There is a lack of continuity in the management of anxiety, depression other non-psychotic mental health disorders, as there is no organised, coherent treatment regime between general practice and secondary care.
- There is a lack of treatment opportunities. There is currently no obligation for the GP to provide psychotherapy and it is estimated, that only around one third of GPs in Denmark are qualified to provide psychotherapy (7). However, the GP can refer the patient to a psychologist via “Psykologordningen”. All adult patients with depression and patients with anxiety between 18-38 years can receive therapy from a psychologist; however, the patient has to contribute to the cost of the treatment.
• There is a shortage of practice psychiatrists and psychologists trained in Cognitive Behavioral Therapy (CBT) and other evidence based psychological methods. This can delay the specialised treatment of patients who have been referred from the GP.
• The compensation structure does not support the treatment guidelines. As an example, a GP only gets compensation for up to 7 sessions and although the GP has to document supervision he/she does not get compensated for this(8).
• There are no requirements for postgraduate education of GPs which can ensure the continuous professional development.

As mentioned, the vast majority of the population of people with depression is diagnosed and treated in general practice. Under-detection of depression in primary care has been extensively described and could lead to under-treatment (9). Also, over-detection could lead to over-treatment, but is less described in the literature. As referred to in a meta-analysis including 41 studies assessing the accuracy of unassisted diagnoses of depression in primary care, only about 50% of true cases are diagnosed and 15% treated. Conversely, the meta-analysis concludes that about 80% of non-depressed individuals are correctly reassured (9). The findings of the meta-analysis suggest that for every 100 unselected cases seen in primary care, there are more false positives (n=15) than either missed (n=10) or identified cases (n=10) (9). Overall, although diagnosis seems to be modestly improved by the use of scales (screening instruments for depression), a positive effect on overall patient outcomes has not been shown. Only when screening is paired with organised systems of care can outcomes be improved (9). In a Danish observational study investigating high-risk screening with the MDI screening tool (Major Depression Inventory), screening with MDI on clinical indication on depression (called case-finding) and a combination of the two methods, investigators found that screening of patients in high risk groups had a limited effect in addition to the cheaper and less invasive method of case-finding (10). The general practitioners demonstrated a depression diagnostic sensitivity of 87% and a specificity of 67% using a case-finding strategy and the author concludes that a broad case-finding ap-
Approach including a short validation test can help general practitioner when they identify depressed patients. Considering the potential harms of incorrect detection of depression in primary care, there is a need to further investigate the best way to correctly diagnose depression in primary care. Therefore, as part of the Collabri study, a detection study will seek to clarify if a systematic use of the questionnaire MDI (Major Depression Inventory) in patients with suspected depression. This might give the general practitioner better means of detecting depression compared to their usual routine detection. The hypothesis is that systematic use of MDI will increase the probability of finding the patients who actually have a depression amongst patients that the general practitioner evaluate to have a depression (positive predictive value).

1.3 Evidence of Collaborative care

There is national as well as international consensus that optimising anxiety and depression treatment in primary care should be done by introducing shared care interventions such as collaborative care programmes (CC) (1,2). CC stems from the recognition that patients with depression in primary care may require changes in the organisation corresponding to the changes introduced through collaborative care for other chronic diseases (11). Health economy studies indicate that, in spite of there being a need for an investment when introducing CC, the cost tends to be recovered after 3-4 years, and in the long term there are substantial savings to be made because of the reduction in sick leave and people receiving disability pension (12).

CC models can involve different interventions, therefore it is difficult to point out specific “active ingredients”. These ideals have now been transferred to the management of anxiety and depression. A systematic review of the literature from 2009 has shown that CC has an effect on anxiety and depression (evidence level 1a for both diseases) (13). A Cochrane review from 2012 investigating the effects of CC on anxiety and depression concluded that CC is associated with significant improvements in treatment outcomes and for depression for up to 2 years compared with usual care. Thus, the authors conclude that CC represents a useful addition to clinical pathways for adult patients with anxiety and depression. (14).
The literature on collaborative care for depression is therefore fairly robust. However the evidence is primarily based on research conducted in the U.S.\(^1\) and therefore based on an organisational framework not directly applicable to Danish context. Therefore it is not possible to know whether collaborative care for depression and anxiety will have the same effect in Denmark (15). Thus, there is a need to investigate a Danish model for collaborative care for depression and anxiety in Danish context. As the vast majority of the CC studies conducted so far are investigating CC for depression there is a need for further research in CC for anxiety (14).

Collaborative care models are complex interventions, and consist of a number of treatment modalities. The term has evolved since the 90s, as treatment modalities have been continuously updated with the latest knowledge in the field. Four criteria for CC are listed in the Cochrane review (14):

1) A multi-professional approach to treatment
2) Scheduled monitoring and review
3) Enhanced inter-professional communication and
4) A structured treatment plan

A systematic review conducted by Eplov et al. (13) further indicates, that the following elements are essential to the intervention, which have also been integrated into the Danish model (a description of the model follows): Recruitment of staff with psychiatric experience, education of general practitioner and care manager, use of instruments for detection and follow-up, education and treatment of the patient, supervision from a psychiatric specialist and a stepped care approach to treatment where treatment is always commenced on the least invasive and least resource-demanding level.

\(^1\) Of 79 included studies 73 were from U.S, 2 were from Chile, 2 were from the UK, 1 was from Germany and 1 was from India.
2. Collabri – A Danish model for Collaborative Care

Collabri - a Danish model for Collaborative Care takes its point of departure in the four criteria listed in the Cochrane review and the recommendations from the systematic review by Eplov et al. It adapts to the Danish health care system by including coordination with relevant social worker(s) in the municipality and integrating the existing treatment offer by psychologists (Psykologordningen). Similarly, the Collabri model is based on the latest evidence in the field. Below it is described how the four essential elements of collaborative care is addressed in the model.

2.1 A multi-professional approach to treatment

In the Collabri model the following professionals will provide the treatment: Care managers (CM), general practitioners (GP) and psychiatrists/psychologists with psychiatric specialist training. Following recruitment they will all receive a short training. The specific roles and tasks are described in the following.

The Care manager

CM has a medium-long (approx. 3-4 years) health professional qualification e.g. as a nurse or occupational therapist, has experience of working in mental health services and an approved qualification in cognitive therapy. CM has the following responsibilities: Active follow-up (including assessment of disease progression and course), monitoring of adherence and side effects of medical treatment, (CBT), supportive conversations, diagnostic specific treatment, psycho-education, regular contact with social worker(s), conference with GP and both GP and psychiatrist when necessary.

The general practitioner

The GP has the overall treatment responsibility as well as the following roles and functions: diagnostic procedure, initiation of treatment, coordination of treatment intervention with care manager, guidance of care manager, collaboration with care manager on contact with social worker(s), conference with psychiatrist ad hoc and shared consultation with psychiatrist.
GPs who practice in the uptake areas of the Capital Region of Denmark. Requirements of the GPs will be:

- To undergo training in the Collabri model
- To take part in a formalised collaboration with the psychiatrist/psychologist with specialist training in psychiatry
- To carry out assessments and provide treatment cf. the Collabri model
- To participate in the evaluation

The Psychiatrist/psychologist with psychiatric specialist training

The psychiatrists and psychologists with psychiatric specialist training have the following roles and responsibilities: Ensuring adherence to the Collabri model, guiding the CM and GP, supervising the CM and GP and participate in shared consultation with GP.

2.2 Scheduled monitoring and review

Monitoring and reviews are essential in order to achieve the desired results of the treatment of depression or anxiety, including continued symptom relief and reduced risk of side effects or other risks associated with the illness or treatment.

In the Collabri model, the patient is regularly monitored and reviewed at scheduled follow-up sessions. This is central to the model.

Monitoring and review will consist of controls at intervals determined by the degree of illness – as a minimum monthly, and more frequently when needed. It includes:

- Ensuring compliance, pharmacological as well as non-pharmacological
- Assessment of symptom degree by MDI or ASS
- Assessment of suicide risk
- Assessment of side effects
- Evaluation of the need to control other parameters, such as weight, BT and heart rate, blood tests and other tests depending on necessity and comorbidity
- Consider step-up or referral to a psychiatric specialist, especially if deterioration is detected via MDI or ASS, suicidal or psychotic symptoms appear or increase, or other causes for concern
### 2.3 Enhanced inter-professional communication

In the Danish reference programs for anxiety and depression, supervision of GPs has been highlighted (1, 2). Several reports recommend improved systematic collaboration between the primary and secondary system in order to improve the quality of care for patients with anxiety and depression in primary care (5). In the Collabri model care manager and GP will meet minimum weekly and discuss patients. Other communication will happen in the following way:

- Psychiatrist/psychologist with specialist training in psychiatry supervises CM in groups twice monthly
- Psychiatrist/psychologist with specialist training in psychiatry supervises CM individually ad hoc
- Psychiatrist/psychologist with specialist training in psychiatry supervises GPs in groups monthly Psychiatrist/psychologist with specialist training in psychiatry supervises GP individually ad hoc.
- Psychiatrist/psychologist with specialist training in psychiatry, GP and CM have joint consultations ad hoc.

The described communication can happen via video conferences if it is not possible to meet in person, however the weekly communication between CM and GP must be in person.

### 2.4 A structured treatment plan

The treatment of CC for anxiety and depression takes place according to treatment guidelines established on the basis of the Danish Health Board’s Reference program for unipolar depression in adults, the Reference program for anxiety disorders in adults (1, 2), the Danish College of General Practitioners clinical guidelines for unipolar depression and clinical guidelines for anxiety disorders (16, 17), as well as the latest knowledge in the field regarding specific treatment modalities. Overall, a structured treatment plan based on the use of
manuals is developed for each of the four illnesses (generalized anxiety, panic disorder, social phobia and depression) and contains the following elements: detection and diagnosis, general principles of treatment, stepped care and specific treatment modalities.

**General principles of treatment**

In Collabri the treatment is in line with a set of general treatment principles relevant for collaborative care interventions. Besides the four above mentioned criteria for CC, these are:

- **Detection.** Detection of anxiety in the Collabri study will follow the guidelines for general practice recommending the use of the Anxiety Symptom Scale (ASS) in conjunction with ICD-10 criteria. Two methods for detection of depression will be examined in a randomized controlled design; the effect of standard detection vs. case finding with the use of Major Depression Inventory (MDI). Results from this study will create the basis for future detection of depression in the Collabri model.

- **A stepped care approach to treatment as well as active and planned follow up.** The stepped care approach implies offering the most effective and least invasive treatment initially and upgrading and intensifying treatment after review. The English National Institute for Clinical Excellence (NICE) guidelines for anxiety and depression recommend the stepped care approach for the organisation of treatment (18,19), and the Danish reference programs for anxiety and depression identifies the stepped care approach as a good alternative to the current organisation (1,2). Treatment plans include a stepped care plan including the possibility of referral to secondary mental health services. According to illness and severity there will also be planned follow up contacts between the patient and the care manager.

- **Patient involvement in treatment.** In order to ensure informed decision making processes and dialogues about the development and implementation of treatment plans, a high level of information is provided to the patients about the illness, its progression, relapse prevention and treatment options. The care managers will be trained in the shared decision making model and encouraged to use it.
- **Involvement of relatives/carers.** All patients will be informed about the possibility of a relative/carer-consultation and the treatment plan will include involvement of relatives/carers if the patient consents. Relatives/carers will be provided with written information about the illness, its progression etc. and with relevant links and contact details for further information and advice.

- **Guided self-help.** All patients receiving treatment according to the Collabri model can receive psycho-education. Depending on the severity of the illness, patients receive psycho-education integrated within the cognitive behavioral therapy, or they can choose between psycho-education in a group following the Expert Patient Programme (called “Lær at tackle angst og depression” in Denmark) or individual psycho-education carried out by the care manager. “Lær at tackle angst og depression” is developed from “Lær at tackle kronisk sygdom” which is originally developed by researchers at Stanford University. The goal is for the patients to attain tools in order to handle the symptoms of their illness and the difficulties it can present in everyday life, and is thus focused on active self-help. All patients will also receive written information about their illness and the book “Lær at tackle angst og depression”. Relatives/carers will also receive written information about the illness.

**Detection (identification of persons with depression)**

Considering the potential harms of incorrect detection of depression in primary care and the literature concerning different methods of detecting depression in primary care, two methods for detection of depression will be examined in a randomized controlled design; the effect of standard detection vs. case finding coupled with collaborative care intervention. Half of the GPs, selected randomly, perform standard detection and identifies patients with depression as usual. Use of a screening tool is optional in this group. The other half of the GPs perform case-finding detection. GPs in this group have to use the screening tool MDI if they suspect a depression. Results from this study will create the basis for future detection of depression in the Collabri model.
Specific treatment modalities

Medical Treatment
The patient is offered medical treatment in accordance with treatment guidelines in Collabri. These guidelines contain progressing algorithms. The treatment is initiated by the GP and will be monitored by the care manager.

Psychotherapy
The patients in the intervention group is offered cognitive behavioral therapy (CBT) by the care manager in accordance with treatment guidelines in Collabri. If this treatment shows no or limited effect, patients may subsequently be referred to psychotherapeutic treatment by a psychologist based on the existing psychologist scheme (“Psykologordningen”).

Psychoeducation
All patients are offered psycho-education in group in the form of the course “Lær at takle angst and depression” or individual psycho-education carried out by the care manager or as a part of CBT. All patients and relatives/carers are offered written psycho-educational material.

3. The aims of Project Collabri
The aims of Project Collabri are to:

- Develop a Danish model for collaborative care (the Collabri model) for patients with anxiety and depression.
- Study the effect of this model in a cluster randomized design on selected outcomes.
- Describe and analyse the clinical, organisational and managerial challenges and opportunities that apply when the model is introduced, and explain the results from

\[2\] If the GP has specialised training in CBT and normally offer CBT for anxiety and depression the GP can offer CBT on this level.
the randomized controlled study through analysis of the course and effects of the complex intervention.

- Investigate the differences in costs and effects for patients treated under the Collabri model and those receiving treatment as usual (TAU).
- Study the patients perspectives on collaborative care compared with those receiving TAU.

4. Project Collabri – A health Technology Assessment

By conducting four studies Project Collabri seeks to examine collaborative care in accordance with the recommendations of a Health Technology Assessment, thus making sure that the project will be able to generate the knowledge necessary for introducing a new organisation of treatment in primary care. Project Collabri consists of the following four studies:

**Study 1:** A cluster randomized controlled study of the effects of the Collabri model on symptoms of anxiety and depression (see section 5).

**Study 2:** A qualitative study of the conditions, processes and organisational consequences of the implementation of the Collabri model for patients with anxiety and depression (see section 6).

**Study 3:** A health economics evaluation of the Collabri model for patients with anxiety and depression (see section 7).

**Study 4:** A study of the patient perspective of the Collabri model for patients with anxiety and depression (see section 8).
5. **Study 1. A Cluster Randomized Study of the Effect of Collaborative Care on patients with Anxiety and Depression compared to treatment as usual**

5.1 **Aim and hypotheses**

The aim of Study 1 is to investigate the effects of collaborative care (CC) compared to treatment as usual (TAU) in patients with generalized anxiety disorder (GAD), panic disorder (PD), social phobia (SP) or depression consulting their GP in a cluster randomized controlled trial. The study will consist of four sub-studies; three examining the effects of CC on GAD, PD and SP respectively and one examining the effects of CC on depression.

The following hypotheses will be tested in the depression study:

- Patients receiving CC, compared to patients receiving TAU, will show a greater reduction in severity of depression 6 months and 15 months after baseline (primary and secondary examination).
- Patients receiving CC, compared to patients receiving TAU, will show more progress in terms of functional level, quality of life, psychological stress and decreased sick leave (secondary and explorative examinations).
- Case-finding increases the probability of finding the patients who actually have a depression among patients that the general practitioner evaluate to have a depression (positive predictive value) compared to current practice (primary examination).
- There is no difference in the effects of collaborative care given to patients with depression and to patients with depression in combination with somatic illness (explorative examination).
- There is no difference in the effects of CC given to patients with depression and to patients with depression in combination with a personality disorder (explorative examination).

The following hypotheses will be tested in the anxiety studies
Patients with generalized anxiety, social phobia or panic disorder receiving CC, compared to patients receiving TAU, will show greater reduction in severity of anxiety 6 months and 15 months after baseline respectively (primary and secondary examinations).

Patients with generalized anxiety, social phobia or panic disorder receiving CC, compared to patients receiving TAU, will show more progress in terms of functional level, quality of life, psychological stress and decreased sick leave (secondary and explorative examinations).

There is no difference in the effects of CC given to patients with generalized anxiety, social phobia or panic disorder and to patients with generalized anxiety, social phobia or panic disorder in combination with somatic illness (explorative examination).

There is no difference in the effects of CC given to patients with generalized anxiety, social phobia or panic disorder and to patients with generalized anxiety, social phobia or panic disorder in combination with a personality disorder (explorative examination).

5.2 Design and methods

Design
The study is set up as a researcher-blinded cluster randomized controlled trial with participation of an intervention group (treatment according to the Collabri model) and a control group (treatment as usual (TAU)). There will be conducted four RCTs examining the effects of collaborative care according to the Collabri model for patients with generalized anxiety, social phobia, panic disorder or depression. See Figure 1-4 for the flow charts for the depression study and the three anxiety studies respectively. The randomization will be carried out at practice level, where each cluster corresponds to a provider number (ydernummer) consisting of one or more general practitioners. Patients within the clusters (practices) will therefore be allocated to the same group as their GP. To ensure internal and external valid-
ity, the study design takes its point of departure in the CONSORT-statement for cluster randomized studies (20).

Figure 1. Flow-chart for the depression study
Figure 2. Flow-chart for the panic disorder (PD) study
Figure 3: Flow-chart for the social phobia (SP) study

Enrollment

Assessed for eligibility and invited to participate in Collabri (n=no. clusters)
- Excluded (n=no. clusters)
  - Declined to participate (n=no. clusters)
  - Other reasons (n=no. clusters)

Randomization (n=no. clusters)

Allocated to intervention (collaborative care) (n=no. clusters)
- No. clusters did not receive allocated intervention (reason) (n=no. clusters)
- Received allocated intervention (n=no. clusters)
- Practices recruiting patients (n=no. clusters)

Allocated to control intervention (standard treatment) (n=no. clusters)
- No clusters did not receive allocated intervention (reason) (n=no. clusters)
- Received allocated intervention (n=no. clusters)
- Practices recruiting patients (n=no. clusters)

Informed consent is given by patient

Visitation with MINI by research assistant
- No. who meet inclusion criteria and do not meet exclusion criteria (n=no. persons)
- No. who do not meet inclusion criteria (reason) (n=no. persons)

Baseline measurements through self-reporting and interview

Treatment according to the Danish model for CC

Lost to follow-up (n=no. clusters and no. persons)
- Stopped in Collabri (reason) (n=no. clusters and no. persons)
- Lost to follow up (reason) (n=no. clusters and no. persons)

Analysed (n=no. clusters and no. persons)
- Excluded from analysis (reason) (n=no. clusters and no. persons)

Follow-up at 6 and 15 months post baseline

Baseline measurements through self-reporting and interview

Treatment as usual (TAU)

Lost to follow-up (n=no. clusters and no. persons)
- Stopped in Collabri (reason) (n=no. clusters and no. persons)
- Lost to follow up (reason) (n=no. clusters and no. persons)

Analysed (n=no. clusters and no. persons)
- Excluded from analysis (reason) (n=no. clusters and no. persons)
Figure 4: Flow-chart for the generalized anxiety disorder (GAD) study
Description of study participants

Patients will be eligible for the Collaborative Care studies for depression and anxiety if their general practitioner is enrolled in the study and comply with the inclusion and exclusion criteria listed below upon presentation:

Study inclusion criteria for the depression study:

- Age: 18+ years of age
- Danish speaking
- Diagnosis of current depression based on the Mini International Neuropsychiatric Interview (MINI) by researchers that have been trained in using MINI (21). Patients can be referred from the GP on the basis of a panic disorder, generalized anxiety, social phobia or depression diagnoses.
- The patient has given her/his written informed consent to participate in the trial at the described terms.

Study exclusion criteria:

- High risk of suicide assessed in the Mini International Neuropsychiatric Interview (MINI) and/or by GP
- Psychotic condition detected in the MINI and/or by GP
- Patients with a diagnosis of dementia
- Pregnancy
- Alcohol or substance misuse that hinders the person participating in Collabri treatment as assessed by the practitioner or researcher at inclusion interview

- Patients that are in current psychological or psychiatric treatment due to anxiety or depression
- Patients with a pending disability pension case
- Patients who have been treated for anxiety or depression within the last 6 months
For patients in the intervention group: Patients with depression who want treatment cf. the psychologist scheme (Psykologordningen) and do not want the reference to the psychologist preceded by other treatment, cf. the Collabri model assessed by the GP

- If the patient at the first point of contact with the GP after inclusion by a research assistant is referred to treatment as a part of the secondary psychiatric care system.
- Patients who are assessed by the GP as medically unstable making it impossible for the patient to adhere to treatment
- OCD, PTSD, bipolar affective disorder as assessed in the MINI and/or by the GP

Study inclusion criteria for the three anxiety studies:

- Age: 18+ years
- Danish speaking
- Diagnosis of current anxiety in the form of panic disorder, generalized anxiety or social phobia based on the Mini International Neuropsychiatric Interview (MINI) by researchers that have been trained in using MINI (21). Patients can be referred from the GP on the basis of panic disorder, generalized anxiety, social phobia or depression diagnosis
- The patient has given her/his written informed consent to participate in the trial at the described terms.

Study exclusion criteria:

- High risk of suicide assessed in the Mini International Neuropsychiatric Interview (MINI) and/or by GP
- Psychotic condition assessed in the MINI and/or by GP
- Patients with a diagnosis of dementia
- Pregnancy
- Alcohol or substance misuse that will hinder the person's participation in Collabri treatment assessed by the practitioner or researcher at inclusion interview
- Patients that are in current psychological or psychiatric treatment due to anxiety or depression
- Patients with a pending disability pension case
- Patients who have been treated for anxiety or depression within the last 6 months
- For patients in the intervention group: Patients with anxiety who wants treatment cf. the psychologist scheme (Psykologordningen) and do not want the reference to the psychologist preceded by other treatment, cf. the Collabri model assessed by the GP
- If the patient at the first contact with the GP after inclusion by a research assistant is referred to treatment as a part of the secondary psychiatric care system
- Patients who are assessed medically unstable assessed by the GP in a sense that makes it impossible for the patient to adhere to treatment
- OCD, PTSD, bipolar affective disorder assessed in the MINI and/or by the GP

In the depression study the participants will be included in two different ways, through:
- Standard detection
- Detection with case-finding

For the standard detection group, patients will be eligible for the detection study if they reach the following inclusion criteria:
- Age: 18+ years
- Danish speaking
- The patient has given her/his written informed consent to participate in the trial at the described terms.
- Referred by their GP with a depression diagnosis.

For the detection with case-finding group, patients will be eligible for the detection study if they reach the following inclusion criteria:
- Age: 18+ years
- Danish speaking
- The patient has given her/his written informed consent to participate in the trial at the described terms.
- Referred by their GP with a positive or negative MDI

The exclusion criteria are the same as for the above-mentioned depression study.

**Randomization**

Cluster randomization has been chosen because there is a risk of introducing bias in the form of contamination if the randomization was on an individual level. This risk would be present as the GPs trained in collaborative care would not be able to avoid using their knowledge for both intervention patients and control patients, which would most likely affect the results.

The randomisation process will be centralised and computer-based with hidden randomization sequence and conducted by the Research Centre for Prevention and Health (RCPH). The randomization of the GPs will take place after they have agreed to participate in the study. The randomization will be stratified for three geographical areas: Nordsjælland, Copenhagen area, and Vestegnen.

In both the anxiety studies and the depression study the GPs will be randomized to provide either treatment as usual or collaborative care, according to the Collabri model.

As the aim of the RCT on depression is also to investigate the most effective detection of depression in general practice, a second randomization on the detection method will be made (see the below Figure 5 for illustration of the randomization process). GPs will be randomized to 1) standard detection or 2) case-finding.
Blinding

It is not possible to ensure blinding of the patient and GP, but the blinding of GP allocation will be maintained for researchers in the data collection phase as well as the analysis phase, who only have contact with patients by telephone. Care managers, GPs and psychiatrists/psychologists as well as the patients will be reminded that they cannot reveal to the researchers which group they are allocated to. It will especially be emphasized to the patients, that they cannot talk about the trial or treatment that they are receiving when they are being interviewed by researchers, but they can only answer the questions they are asked regarding effect measures. If the blinding should be broken, the patient is referred to another researcher that will be blinded.
For depression, blinding of the patient diagnosis and possible MDI result will be maintained for the researchers during the MINI interview in order to ensure that the evaluation of diagnosis is not affected by the GPs referral diagnosis. This is especially relevant for the depression detection study. There is no technical solution available that can help ensure the blinding, but the researchers is instructed in not to activate a document with the diagnoses and MDI results until after the MINI diagnostic interview has been conducted.

Consent forms and an identification list with the personal social security number and intervention identification number will be stored in a locked cabinet unavailable for researchers. The intervention groups will be coded and anonymized (e.g. X and Y) so that researchers are blinded in the entire phase of analysis and when writing the conclusion.

**Outcome measures and other registration**

*Primary outcomes for the four collaborative care studies on social phobia, panic disorder, generalized anxiety and depression.*

Social phobia study: Self-reported degree of anxiety measured by the Beck Anxiety Inventory (BAI) (23) at 6 months will be the primary outcome variable.

Panic disorder study: Self-reported degree of anxiety measured by the Beck Anxiety Inventory (BAI) (23) at 6 months will be the primary outcome variable.

Generalized anxiety study: Self-reported degree of anxiety measured by the Beck Anxiety Inventory (BAI) (23) at 6 months will be the primary outcome variable.

Depression study: Self-reported degree of depression measured by the Beck Depression Inventory (BDI) (24) at 6 months will be the primary outcome variable.

*Secondary outcomes for the collaborative care studies on social phobia, panic disorder and generalized anxiety*
• Self-reported degree of anxiety measured by the Beck Anxiety Inventory (BAI) (23) at 15 months.

• Self-reported degree of depression measured by the Beck Depression Inventory (BDI) (24) at 6 months.

• Interviewer reported functional level measured by the Global Assessment of Functioning split (GAF-F) (27,28) scale at 6 months. Obtained through semi-structured interview with research assistant

• Interviewer reported functional level measured by the Global Assessment of Functioning split (GAF-F) (27,28) scale at 15 months. Obtained through semi-structured interview with research assistant

• Self-reported psychological stress measured by the Symptom Checklist (SCL-92) (25) at 6 months.

• Self-reported psychological stress measured by the Symptom Checklist (SCL-92) (25) at 15 months.

Secondary outcomes for the collaborative care study on depression

• Self-reported degree of depression measured by the Beck Depression Inventory (BDI) (24) at 15 months. Self-reported degree of anxiety measured by the Beck Anxiety Inventory (BAI) (23) at 6 months.

• Interviewer reported functional level measured by the Global Assessment of Functioning split (GAF-F) (27,28) scale at 6 months. Obtained through semi-structured interview with research assistant

• Interviewer reported functional level measured by the Global Assessment of Functioning split (GAF-F) (27,28) scale at 15 months. Obtained through semi-structured interview with research assistant

• Self-reported psychological stress measured by the Symptom Checklist (SCL-92) (25) at 6 months.

• Self-reported psychological stress measured by the Symptom Checklist (SCL-92) (25) at 15 months.
- **Explorative outcomes for the four collaborative care studies:** Self-reported quality of life measured by the WHO-5 (26) at 6 and 15 months.
- Personal and Social Performance (PSP) (29) at 6 and 15 months. Obtained through semi-structured interview with research assistant.
- Self-reported side effects measured by PRISE (30) at 6 and 15 months.
- Self-reported health-related quality of life measured by the EQ-5D (EuroQol) (31) at 6 and 15 months.
- Self-reported functional impairment measured using the Sheehan Disability Scale (SDS) (32) at 6 and 15 months.
- Sick leave obtained from the DREAM database at 6 and 15 months. If there is a follow-up at three years; early retirement due to anxiety or depression also obtained from the DREAM database.
- Self-reported self-efficacy measured with the IPQ-R scale (personal control) and two subscales from the Chronic Disease Self-Efficacy Scales (SECD-32); Obtain Help from Community, Family, Friends Scale and Control/Manage Depression Scale at 6 and 15 months.
- Interviewer reported apathy measured by the Apathia scale at 6 and 15 months
- Self-reported degree of depression measured by Beck Depression Inventory (BDI) (24) at 15 months for the three anxiety studies.
- Self-reported degree of anxiety measured by the Beck Anxiety Inventory (BAI) (23) at 15 months for the depression study

**Primary outcome for the depression detection study:**
- Positive predictive value of referral diagnosis in two different detection settings.

**Other registration**

**Safety measurements**

Safety measurements conducted through interviews will be collected at baseline and follow-up at 6 and 15 months. Register data will be collected at 6 and 15 months follow-up.
• Self-reported anxiety and depression symptoms measured by the BAI and BDI (23,24)

6. Suicidal ideation measured by the questions concerning suicidality from the MINI interview (21). Obtained through structured interview with research assistant

• Death (natural, accident, suicide, homicide/violence or unknown). Obtained from the Cause of Death Register
• Life threatening conditions for reasons other than suicide attempts. Obtained from the Green System (GS))
• Number of somatic outpatient services, admissions and inpatient days. Obtained from GS
• Number of psychiatric outpatient services, admissions and inpatient days. Obtained from GS
• Number of sick leave days. Obtained from the DREAM database

**Baseline registration**

At baseline the following will also be registered: Somatic co-morbidity assessed in general practice at enrollment and personality disorder measured by the Standardized Assessment of Personality: Abbreviated Scale (SAPAS) (33).

**6 months follow up**

**Recovery**

Patients will assess whether they felt supported in their recovery by their health care provider at 6 months. The INSPIRE questionnaire will be used in a translated version, that is currently being validated. If a later version is available at the time of project start this will be used.

**Patient satisfaction**

3 Personal communication with Jullie Williams and colleagues from Department for Recovery, Kings College.
Self-reported satisfaction with the treatment will be measured through the CSQ-8 questionnaire together with project specific questions at 6 months.

*Depression detection study*

In the standard detection group: Positive and negative depression results from MDI carried out by the GP and MINI carried out by the research assistant in order to calculate the positive predictive value of diagnosis.

In the case-finding group: Positive and negative depression results from MDI and MINI in order to calculate the positive predictive value of diagnosis and the sensitivity, specificity and negative predictive value of diagnosis.

*Long term follow up*

If founding can be sourced or identified the patients will be contacted up to 10 years after treatment in order to participate in a long term follow-up assessment, or assessments will be made through registers.

*Adherence to the model for Collaborative Care*

To ensure the internal quality of the intervention, an evaluation (fidelity measurement) will be carried out after 6 months with at least once more during the project. The fidelity measurement ensures that the intervention will be carried out according to the description of the Collabri model. On the basis of the assessments, an action plan will be developed, if needed, in order to improve the implementation.

*Data Collection*

The data for the four studies will consist of interviewer based data (telephone interview), register data and self-reported data (see table 1 below). Self-assessments will be completed electronically, but it is also possible for patients to get a paper version. If there is one or more items in the questionnaire that have not been answered, the patient is contacted by
the research assistant in order to clarify any doubts the patient may have and to encourage him/her to complete the questionnaire. Data collected through interviews will be conducted by personnel trained in the specific instruments.

Services from the social- and health care system will be collected through the DREAM database and the Green System as well as registers in chosen municipalities. Services in relation to collaborative care will be registered by the care manager and psychiatrists/psychologists with psychiatric training and via the GPs.

Table 1. List of patient specific data to be collected

<table>
<thead>
<tr>
<th>TIMEPOINT</th>
<th>Data collection method</th>
<th>Enroll roll-ment</th>
<th>Post-enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaborative care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment as usual</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1  MDI (screening tool for depression)</td>
<td>GP based</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2  MINI</td>
<td>Interviewer based</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>3  Self-efficacy</td>
<td>Self-reported</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>4  SAPAS</td>
<td>Interviewer based</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>5  GAF</td>
<td>Interviewer based</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>6  PSP</td>
<td>Interviewer based</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>7  SDS</td>
<td>Self-reported</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td></td>
<td>Description</td>
<td>Data Source</td>
<td>X</td>
</tr>
<tr>
<td>---</td>
<td>------------------------------------------------------------------------------</td>
<td>----------------------</td>
<td>---</td>
</tr>
<tr>
<td>8</td>
<td>BDI/BAI</td>
<td>Self-reported</td>
<td>X</td>
</tr>
<tr>
<td>9</td>
<td>WHO-5</td>
<td>Self-reported</td>
<td>X</td>
</tr>
<tr>
<td>10</td>
<td>PRISE</td>
<td>Self-reported</td>
<td>X</td>
</tr>
<tr>
<td>11</td>
<td>EQ-5D-3L</td>
<td>Self-reported</td>
<td>X</td>
</tr>
<tr>
<td>12</td>
<td>SCL-92</td>
<td>Self-reported</td>
<td>X</td>
</tr>
<tr>
<td>13</td>
<td>CSQ-8 (client satisfaction) (34) + project developed questionnaire* and LUP-questions</td>
<td>Self-reported</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Suicidality obtained through the questions from the MINI interview</td>
<td>Interviewer based</td>
<td>X</td>
</tr>
<tr>
<td>15</td>
<td>INSPIRE</td>
<td>Self-reported</td>
<td>X</td>
</tr>
<tr>
<td>16</td>
<td>Death</td>
<td>Register</td>
<td>X</td>
</tr>
<tr>
<td>17</td>
<td>Life-threatening conditions</td>
<td>Register</td>
<td>X</td>
</tr>
<tr>
<td>18</td>
<td>Somatic outpatient services, admissions and inpatient days</td>
<td>Register</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Psychiatric outpatient services, admissions and inpatient days</td>
<td>Register</td>
<td>X</td>
</tr>
</tbody>
</table>

* Is currently under pilot testing.
Furthermore other data in connection with the health economic evaluation will be collected, see Appendix 1.

**Procedure for recruiting patients, giving patient information and collecting informed consent**

The procedure for visitation is described below. This will also describe the procedure for collecting informed consent.

a. The GP enrolled in the study detect the patient according to randomization allocation (see figure 5):
Patients who meet the inclusion- and exclusion criteria and have been detected with depression through standard detection will be offered to participate in the collaborative care study for depression with the embedded detection study.

Patients who meet the inclusion- and exclusion criteria and have been detected with depression through case-finding (GPs assess they have a depression using MDI to guide them, but both patients with MDI positive and MDI negative scores can be referred) will be offered to participate in the collaborative care study for depression with the embedded detection study.

Patients who meet the inclusion- and exclusion criteria and at case-finding have a MDI negative score which the GP rely on (the patient will not be given a depression diagnosis) will be offered to participate in the detection study only. If the MINI is positive, and confirmed by a psychiatrist, the patient will be offered to participate in the collaborative care study for depression. However, the GP must agree on a depression diagnosis in order for the patient to participate.

Patients with anxiety who meet the inclusion- and exclusion criteria will be offered to participate in the collaborative care studies for anxiety.

b. According to the above mentioned characteristics the patients will be asked to participate in a. the depression detection study, b. the collaborative care study with the embedded detection study or c. one of the three collaborative care studies on anxiety.

At the consultation, written information about the study is given to the patient by the GP and oral information about the project is provided on basis of the written material. The material will be specific to intervention and control group participants, and patients who are only offered to participate in the depression detection study will only receive information about this.

The GP makes sure that the information can be given without interruptions and that there is time for the patient to ask questions. The possibility of time for reflection of at least 24 hours will also be stressed to the patient as well as the
possibility of discussing the project with a family member or friend before the patient decides to participate.

- The patient is also provided with a number to call to get additional information about the study. If the patient shows interest in the project (either the depression detection study or any of the collaborative care studies), the GP obtains oral consent from the patient that a research assistant can make contact by telephone in order to conduct a diagnostic interview (MINI interview). A consent form (including a copy to be obtained by the patient) and a stamped addressed envelope is then given to the patient. If possible, patients can scan the consent form and send it by email.

- In the expected few cases where the detection study reveals a depression based on the MINI interview even though the MDI was negative, a psychiatrist in the project will contact the GP in order to discuss the diagnosis. If the there is still discrepancy between diagnoses the patient will be informed and advised to make an appointment with the GP again. At the new consultation the patient will be asked to participate in the collaborative care study on depression if the inclusion- and exclusion criteria are met. If the patient would like an assessor to sit in on the information meeting, a project assistant who has a substantial knowledge about the project can provide information by telephone or in person.

c. The GP initiates relevant treatment.

d. If the patient wishes to participate, the GP completes the relevant referral form and forwards it using either of the following ways: posting it in a stamped addressed envelope, sending it via fax machine, sending it electronically via encrypted e-mail to the research team’s secure e-mail address or via the “e-boks” system (a Danish system for sending digital mail safely). The GP can also telephone the research team and pass on the referral information verbally.

e. The research assistant contacts the possible patient by telephone and schedule a time for conducting a MINI interview. The research assistant makes sure that the interview can proceed without interruptions, and emphasises to the patients that
they cannot tell in which group their GP is allocated to or which diagnosis their GP has given them. If the patient at this stage has decided not to participate in the project, the research assistant cancels the interview. The research assistant makes sure that the patient doesn’t have any questions that can reveal their randomization allocation. If the patient has such questions he/she is referred to a non-blinded Collabri staff member. If the GP allocation is revealed the patient is referred to another research assistant.

f. The research assistant conducts the MINI interview.
   - If the patients participating in the depression detection study meet the inclusion criteria for the detection study and are not excluded by the exclusion criteria they will be asked to send in the written consent form. The participants will be informed that participation is voluntary and not harmful and that they can terminate the study and the interview at any time without consequences for their future treatment.

If the patients offered to participate in the collaborative care studies for depression or anxiety meet the inclusion criteria and are not excluded by the exclusion criteria, the research assistant will continue the interview and assess the interviewer based baseline measures and fill out a self-reported baseline questionnaire. The participants will be informed that participation is voluntary and not harmful, and that they can terminate the study and interviews at any time without consequences for their future treatment. The research assistant informs the patient straight away of the outcome of the MINI interview, and whether the patient is eligible for the referred study or not. If the MINI diagnosis is inconsistent with the GP diagnosis, the research assistant consults a psychiatrist in the Collabri group, who contacts the GP to ensure the diagnosis is correct. The patient will then be informed of the outcome.

The GPs will be informed about the MINI result and the PSP/GAF score by the same method as he/she referred the patient (sent by a non-blinded research assistant).

Participants must give both oral and written consent to participation. The written consent form must be dated and signed. Participants receive a copy, and the original will be locked.
in a cabinet at the research department. If the written consent is not received within a week after MINI interview is conducted, the research assistant will contact the patient and remind them to send in the consent form. If the written consent form is not received after this, the MINI and baseline measurements will be destroyed.

Patients who have been diagnosed with depression by GP: Will be asked to participate in the Collabri study for depression with the embedded detection study and will receive information and a consent form about this.

Patients who have been screened with the MDI tool but have not been diagnosed with depression by GP: Will be asked to participate in the depression detection study and will receive information and a consent form about this.

Patients who have been diagnosed with one of the three anxiety diagnoses by GP: Will be asked to participate in the Collabri study on anxiety and will receive information and a consent form about this.

Patients who have not initially been diagnosed with depression by GP and have only been referred to the depression detection study and are subsequently diagnosed with depression or anxiety through the MINI interview: Will be asked to participate in the Collabri study and will, if the GP agrees to the diagnosis, receive information and a consent form about this.

5.4 Statistical considerations

Sample size calculation

The depression study:

Primary outcome
The primary outcome will be BDI. Clinical relevant treatment response at group level is defined as a difference in degree of depression measured by the Beck Depression Inventory (BDI) of 4 points (35,36). There are no surveys carried out in Denmark, which can contribute to the estimation of the standard deviation (SD) for BDI. However, according to international surveys the SD for BDI can be set at 11 (35, 38-40). There is no knowledge of the size of the inter-class correlation (ICC) in a Danish context, however a review about ICCs in depression in primary care suggests that the ICC can be set at 0.04 (44).

A sample-size calculation based on the above figures shows that 328 participants should be included for depression in order to be able to reject the null-hypothesis that the intervention group and the control group have improved similarly in terms of symptoms with a power of 0.8 and a significance level of 0.05, as we want to compare two groups in order to get results for CC vs. standard treatment for patients with depression.

**Secondary outcomes**

The power for the secondary outcomes for depression has been estimated to be over 0.8 for all figures (45-47).

**The depression detection study:**

On the basis of a study carried out by Michell et al. (9) it is estimated that the positive predictive value with standard detection is 45%. A clinical meaningful and possible (10) increase in the number is estimated to be 60%. On this basis, the material size calculation shows that 480 individuals should be included in order to be able to reject the null-hypothesis that the intervention group and the control group improve similarly in terms of symptoms, with a power of 0.8 and a significance level of 0.05. We want to perform the following comparison: standard identification vs. case-finding. Using case-finding, it is conservatively estimated that only 60% of those who are screened has a depression (10). Thus, up to 400 individuals should be screened in order to include 240 persons (480/2).

**The anxiety studies:**
Primary outcome
The primary outcome will be BAI for each of the three anxiety studies. Clinical relevant treatment response at group level is defined as a difference in degree of anxiety measured by the Beck Anxiety Inventory (BAI) of 4 points (37). There are no surveys carried out in Denmark, which can contribute to the estimation of the standard deviation (SD) for BAI. However, according to international surveys the SD for BAI can be set at 12 (37, 41-43). There is no knowledge of the size of the inter-class correlation (ICC) in a Danish context, however a review about ICCs in anxiety in primary care suggest that the ICC can be set at 0.04 (44).

Based on the above figures for anxiety (SD and ICC), the sample-size-calculations shows that 364 individuals should be included in each of the three anxiety studies, 1092 individuals in total, to be able to reject the null-hypothesis that the intervention group and the control group have improved similarly in terms of anxiety symptoms with a power of 0.8 and a significance level of 0.05.

Secondary outcomes
The power for the secondary outcomes for anxiety has been estimated to be over 0.8 for all figures (43,46,48).

As we are not sure we will be able to recruit or maintain 48 GPs it might be necessary to reduce the number to 44. This affects the three sample size calculations and thereby the number of patients we need to include in the studies. In the table below the figures are listed if we have to reduce to 44 GPs.

<table>
<thead>
<tr>
<th>Participants required in the depression detection study</th>
<th>Participants required in the collaborative care depression study</th>
<th>Participants required in the collaborative care anxiety studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>484</td>
<td>336</td>
<td>1122</td>
</tr>
</tbody>
</table>

In total 1572 participants will be included in the randomized controlled study investigating the effects of collaborative care on anxiety and depression. 1092 of these will be participants with symptoms of GAD, panic disorder or social phobia and 480 will be participants.
with depression. With a conservative caseload of 100 patients per care manager it would be possible to include up to 2000 patients in the study during 12 months, as we have 8 care managers. By including 48 GPs, each GP has to include 10-11 persons with depression and 23-26 persons with anxiety (8-9 patients with GAD, panic disorders and social phobia respectively) over a 12 months period. This is possible as 12 months prevalence rates indicates that a GP with 1600 registered patients on average will see 140 patients with a depression, 32 patients with social phobia, 37 patients with panic disorder and 24 patients with generalized anxiety per year (2, 49).

**Statistical methods**

The Collaborative care studies will be conducted according to the statistical principle “intention-to-treat”, which means that once a person is included in the project, he/she stays in the study population to be followed, regardless of whether the person later meets the exclusion criteria.

In the depression detection study the positive predictive value will be calculated for both groups and compared.

Linear mixed effects regression models will be used to compensate for the cluster randomization as well as potential confounders. To account for repeated measures, multilevel regression models with random effects will be used. This makes it possible to take “missing at follow-up” into account under the assumption of “missing at random” by including covariates, that are associated with missing values at follow-up. This method introduces less bias than the method where the last observation is used instead of the missing values as well as the method where only cases with complete follow-up information is eligible in the analysis.

7. **Study 2. Qualitative study of conditions, processes and organisational consequences of the implementation of collaborative care for anxiety and depression**
6.1 Aim
The primary aim of this study is to describe and analyse the clinical, organisational and managerial challenges and opportunities involved in the attempt to introduce collaborative care in the treatment of patients with anxiety and depression. Central to this is the question of how the assumptions, tools and activities of the Collabri-intervention relate to existing perceptions, technologies, roles, work routines and regulative conditions in general practice.

6.2 Design, methods and participants
The study is a qualitative study primarily employing observations and interviews. The data collection will focus on the three central elements of the Collabri-intervention: A) The education of GPs and CMs, B) The introduction of CMs into general practice, C) The supervision of – and shared consultation with – GPs and CMs by a specialist in psychiatry.
During the intervention, 6-8 general practices will be followed via observations and interviews. The observations will focus on the attempt to incorporate the care managers into the workflow in general practice comprising e.g. the shared consultations with a psychiatrist, the conferences between the GP and care manager, and possibly the patient consultations given by care managers and/or GPs. The clinics will be strategically selected to obtain variations in type of practice and geographic location. Interviews will be made with the observed practices and their associated CMs and psychiatrists as well as with approximately 10 other practices (depending on the level of saturation).

6.3 Analysis
The analysis of the qualitative data material will be based on initial inductive thematic analysis focusing on the overall aims of the study followed by a theoretical analysis focusing on the dimensions and concepts suggested by Normalization Process Theory. The analysis will be performed by at least two researchers in order to facilitate quality assurance via analytical triangulation. Furthermore, the material will be analysed through perspectives from organisational research, anthropology and medicine.
Study 2 is described in more detail in Appendix 2.
8. **Study 3. Health Economic Evaluation of A Shared Care Intervention for Patients with Anxiety and Depression**

**7.1 Aim**

The aim of this study is to investigate the cost-effectiveness of the Collabri-intervention. Cost effectiveness is measured by the differences in costs and effects between patients receiving the intervention and patients in a control group.

**7.2 Analysis**

The health economic study is carried out as a data-based analysis of costs associated with the treatment of anxiety and depression by traditional /existing therapies (standard treatment) compared to 'collaborative care'.

Health economic study:

1. Assessment of the average cost associated with the treatment of anxiety and depression by traditional / existing therapies?
2. Assessment of the average cost associated with the treatment of anxiety and depression using 'collaborative care'?
3. Assessment of the cost effects of 'collaborative care'?
4. Assessment of how 'collaborative care' affect:
   - Sick leave
   - Functional level
   - The need for home care and home help
   - Need for social interventions
   - The need for labor market interventions
   - The need for treatment resulting from earlier identification and earlier intervention
   - The need for treatment due to increased recovery and self-care
   - Other relevant factors
The focus is on cost effects in relation to the treatment needs sick leave and labor market attachment, as the information is available from the national registers, and since it is particularly in these areas that 'collaborative care' is expected to have an effect.

The health economic study is divided into the following subtasks:

1. Calculation of cost of the intervention ('collaborative care'). The average incremental cost per patient is calculated as the total cost divided by the number of patients in the intervention group. The calculation is based on information collected by questionnaire, supplemented by telephone interviews.

2. The average cost per patient associated with the treatment of anxiety and depression, respectively 'collaborative care' and standard treatment is calculated and compared in order to estimate the average incremental cost (or savings) per patient. The analysis is performed from society perspective. Comparability of intervention and control group at baseline will be examined by the use of relevant registry data. The calculation includes the cost of treatment in the primary and secondary sectors, and costs of prescription drugs found in the national registries. Additional costs of 'collaborative care' compared with standard therapy will be included.

The time that patients and caregivers use in the treatment are excluded. The time period is defined to 9 months after inclusion in the study. There will be conducted sub-analyses of the costs for the first 3 months after inclusion in the study and for the next 6 months in order to examine differences in need for treatment resulting from earlier identification and earlier intervention/enhanced recovery and self-care.

In order to make the estimate, KORA need the information on CPR number of participants in the intervention and control groups as well as the date of their inclusion in the study. The calculation is also based on register data from the LPR and LPR PSYCH, health insurance register and drug database. Furthermore, there will be collected data from the Civil Registration System in order to take into account the deaths and migrations in the period.
3. Calculation of any average gain per patient in relation to sick leave and labor market association (decrease in productivity).

There will be conducted regression analysis in order to examine whether there are significant differences between the intervention and control groups in terms of sick leave and labor market association (production losses) when controlling for other relevant factors. If there are significant differences between regions, average gain per patient (reduction in output) by receiving 'collaborative care' compared with standard therapy will be estimated. The time period is defined to 9 months after inclusion in the study. It is assumed that the analysis can draw on the data collected under sections 2, including information on CPR number of participants in the intervention and control groups and date of inclusion in the study. In addition, the calculation is based on the inventory register data from DREAM and relevant data from other registries.

4. Reporting in an overall report.

As part of the health economic study there will be collected background information on the patients in the intervention and control groups from the national registers, including:

- Gender
- Age
- Medical History
- Business
- Level of education
- Marital status

Study 3 is described in more detail in Appendix 3.

9. Study 4. Patients’ perspectives on collaborative care

8.1 Aim
The objective of this study is to analyze patients' perspective on the Collabri-intervention:

1. How do citizens/patients with anxiety or depression experience the organization and effects of traditional/existing therapies?

2. How do citizens/patients with anxiety and depression experience the organization and effects of 'collaborative care'?

How experienced 'collaborative care' influence:

- The effect of assessment and treatment
- Dialogue with the relevant occupational professional
- Support from the relevant occupational professional - in relation to the treatment and the level of support and care in general
- Information about diagnosis and treatment pathways

### 8.2 Design and methods

The examination of the patient perspectives is based on two parts. First, a questionnaire on patients' experience of the treatment, and second, three focus group interviews with patients. Both the questionnaire and focus group interviews will be conducted in relation to both the control and intervention group, which makes it possible to compare the two groups with each other: if the groups' experiences with the treatment differ, what factors in the treatment are conferred the greatest value in the two groups and whether the control and intervention groups differ in terms of experience of having received appropriate and adequate treatment, etc.

Ad 1) The questionnaire on satisfaction with treatment includes questions around the following themes:

- Data on the course of treatment
- The experience of the patient-therapist relationship and experience of mutual respect (inspired by the CSQ-18 and SSS 10)
- Satisfaction with the treatment (Danish translation of the CSQ-8 and questions from LUP'en)
Background data on the patient (may need to be included in the patient chart but is drawn from the clinical forms if they detect something similar).

The questionnaire on patient satisfaction should be completed as soon as possible after the end of treatment. In the Capital Region it will be included in the joint questionnaire collected at six-month follow-up. This is considered as the absolute maximum time period after the end of treatment, that the form meaningfully can be completed. To the extent that there can be obtained email addresses of informants this will be a considerable advantage, as it will give the opportunity to move participants to answer and thus ensure a high response.

Analysis of the survey will also include subgroup analysis and thus address the question of patients with different background characteristics (gender, age, diagnosis, disease course) experience different degrees of satisfaction with Collaborative Care treatment and other treatment. If possible, there will also be some involvement of the clinical endpoints in the analysis of the questionnaires, so that it is investigated whether patients who are most satisfied with the treatment are also those who have experienced the greatest effect on clinical endpoints.

Ad 2) The focus groups are organized similarly after treatment is completed. The focus groups will partly deal with the same themes and will also take advantage of the qualitative method in part on get information of the other themes that patients believe to be relevant for the treatment and, more generally, management of the disease in relation to their everyday lives; secondly, what conceptual framework that patients submit to their experience of illness and treatment. There will be an open, investigative approach.

In the Capital Region, there will be conducted three focus group interviews with six to eight patients in each group, with participants from both the control and intervention group. Bringing together participants across the two groups will provide an opportunity for patients to discuss the different experiences in relation to each other. Thereby it becomes possible to focus on the discovered differences between 'collaborative care' and general treatment by general practitioner.
The analysis of the qualitative data will be based on a content analysis, and will uncover the following conditions:

- Satisfaction with the perceived treatment: How satisfied are patients with the treatment compared to the treatment that has been given so far in general practice?
- To what extent do patients perceive that the treatment has been effective?

**Patient selection and rejection of treatment**

Patients have increasingly become consumers, can choose among, for example, treatment by general practitioner in private practice, psychologists or psychiatrists, offer of therapy given at the local job center or by alternative practitioners. In this perspective, it becomes crucial to examine how the field of treatment looks from a patient perspective, what services they feel that they have access to, and how patients make choices to join an offer of treatment, and which position 'collaborative care' get in the this field.

Study 4 is described in more detail in appendix 3.

**10. Organisation in Project Collabri**

**Treatment**

The patient treatment will preferably be carried out in general practitioner clinics or in local community settings such as local authority health centers. The care manager will be working in the clinic or in the local community but employed and managed by the secondary care system. In the Capital Region of Denmark 8 care managers will be employed as well as 1 1/2 psychiatrists or psychologists specialized in psychiatry. The psychiatrists/psychologists and care managers will be based at the Psychiatric Centers in Frederiksberg, Copenhagen and Nordsjælland and will work jointly with the GPs allocated to the intervention group. Center Copenhagen and Psychiatric Center Nordsjælland.
**Research**

Study 1 contains two Ph.D.-studies (medical doctor Ursula Ødum Brinck-Claussen, Msc in Public Health Science Nadja Kehler Curth).

Senior researchers and supervisors are: Professor Merete Nordentoft, Mental Health Copenhagen; Senior consultant, Ph.D. Lene Falgaard Eplov, Mental Health Centre Copenhagen; Annette Sofie Davidsen, Associate Professor, superintendent, D.Sci., The Research Unit for General Practice in Copenhagen; Senior researcher, Ph.D. Kaj Sparle Christensen, The Research Unit for General Practice in Århus; Head of Clinic John Hagel Mikkelsen, Mental Health Centre Frederiksberg; General Practitioner Merete Lundsteen; Senior Consultant, Ph.D. Claudio Csillag, Mental Health Nordsjælland; Senior Consultant, D.Sci. Marianne Lau, Psychotherapy Centre Stolpegård; Lene Falgaard Eplov is Principal Investigator.

The data collection is carried out by the two Ph.D.-students together with up to three research assistants\(^5\) at Mental Health Centre Copenhagen.

Study 2 will be carried out lead by the Research Unit for General Practice in Copenhagen.

The following will take part in the research: Marius Brostrøm Kousgaard, Senior Researcher, PhD, MSc Political Science, Annette Sofie Davidsen, Associate Professor, Specialist in Family Medicine, Marianne Lau, Consultant Psychiatrist, Dr Med Sci. and Susanne Reventlow, Research Director, Adjunct Professor, Specialist in Family Medicine, Anthropologist, DrMedSci. Study 2 also contains one PhD student (Gritt Overbeck, PhD-student, MA Psychology of Language).

Study 3 and 4 will be carried out by the The Danish Institute for Local and Regional Government Research (KORA), lead by Senior Project Manager Marie Jakobsen and Senior Researcher Katrine Johansen\(^6\) respectively.

**Management**

The organisation of the project is presented in Danish in Figure 6 below. The project is led by a steering group. The aim of the steering group is to ensure the progress of the research

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\(^5\) Or three Ph.D.-students and two research assistants.

\(^6\) Katrine Johansen is no longer employed by KORA but another project manager will take over.
project as a whole and in the respective organisations. In the Capital Region of Denmark a lead project manager (Lone Tonsgaard) will ensure the general management of the project together with a project manager in charge of implementation of the intervention (Per Sørensen) and a project manager in charge of the research project (Lene Falgaard Eplov). To ensure the administration of the project, two full-time staff members support the project managers (Rikke Vinding and Tine Bjerregaard Kryger/Lisa Poulsen (both half time on the project)).

Figure 6. Project Management Organisation

Studies 2-4 are conducted in four regions, Region Nordjylland, Region Midtjylland, Region Sjælland and Region Hovedstaden.
11. Ethical considerations

The trial will be conducted in compliance with this protocol, the Helsinki Declaration in its latest version, good clinical practice guidelines and follow the rules for informed consent. No substantial deviation from the protocol will be implemented without the prior review and approval of the regulatory authorities. Personally identifiable information collected in the study will be treated according to the Danish law “Lov om behandling af personoplysninger”. Other collected data (in the form of recorded interviews, transcriptions, observation notes, and video recordings) will be stored as confidential in a secure cupboard. Data is stored electronically, will be in coded filed. The project will also be carried out in accordance with the applicable guidelines for social science research ethics. When communicating the results, the participating persons and clinics will be made anonymous.

Prior to commencement the project will be evaluated by the scientific ethics committee in the Capital Region of Denmark, and it has been reported to the regional joint application for Health Science Research (ID number: 2007-58-0015.) in order to apply for approval at the Danish Data Protection Agency. The project will be registered on the web site Clinical-Trials.gov.

For every patient there will be a case record form (CRF) marked with an identification number. Data about the patient will be kept here, such as effect measures, side effects, etc. An identification list with the civil registration number (cpr.) and case record numbers will be stored in a sealed cupboard and in an entry restricted folder on an internal electronic drive (the v-drive), separated from the other patient material.

The participants’ consent has to be voluntary and informed, and given both verbally and written. Written declarations of consent must be dated and signed, the participants will receive a copy and the original will be stored in the CRF. On the consent form, there is no option for the patient to choose to be informed if any significant information about the patient’s health condition is revealed. This is not considered relevant, as the research assistants will only retrieve self-reported information at baseline and follow up, which will be
known to both patient and GP. The participants will be informed of their rights to exit the study at any point if they wish and without consequences for their future treatment.

Previous international experience does not indicate that the intervention provided by the Collabri model is associated with side effects for the patients. In order to minimize the possible risks of discomfort, the research interviews will be conducted in a flexible manner and interspersed with breaks if necessary. The extent of the interviews will be a maximum of two hours and questionnaires will take a maximum of an hour to complete. It will be possible to fill out questionnaires in stages. If the participants experience the interview as stressful or uncomfortable, the interview can be conducted in stages or they can without further ado step out of the trial, without it affecting their ability to receive current or future treatment.

The care managers in Collabri all have experience of working in mental health services. The GPs that informs the patients about the trial will be given sufficient information to enable them to inform patients adequately. This is provided via a training program before commencement of the project and distribution of written information material.

If the Collabri model shows to be more effective than treatment as usual in general practice, these results can contribute to improving the care and treatment for patients with anxiety and depression in primary care.

**Participant discontinuation and withdrawal**

If participants wish to exit the trial, there are three options:

- They no longer want to receive treatment according to the Collabri model (only patients in the intervention group), but would like to participate in the study and the follow-up after 6 and 15 months. Information from the initial and follow-up interviews and questionnaires will be included in the analysis
- They do not want to participate in the follow-up after 6 and 15 months. Information from the initial interview and questionnaires will be included in the analysis
• They do not want to receive treatment according to the Collabri model (only patients in the intervention group), and no longer wish to take part in the study. Any information relating to their participation is deleted and will not be included in the analysis.

If the participants wish to withdraw from the depression detection study, any information relating to their participation will be deleted and will not be included in the analysis.

There is currently no known circumstances that can lead to exclusion from further participation in the study once a participant is included. If such circumstances that conditions exclusion comes to our knowledge, the participant will be notified. It should be noted that referral to the secondary care system (i.e. because of a deterioration of depression, increased risk of suicide or psychotic condition) is a part of the model that is being tested, which means that participants who are being referred are still included in the study and followed up unless they choose to exit the project.

**Detection considerations**

Considering the potential harms of incorrect detection of depression in primary care, a quality randomized controlled trial investigating the effect of a potentially better detection of depression is important. In the study, we try to minimize the risk and potential harm of a false positive result by using a diagnostic test (MINI) after a positive MDI screening result. Also, if the GP suspects depression although the screening with MDI is negative, the GP can still refer the patient to the study.

**12. Financial support**

Project Collabri is financed by a grant from the Danish Ministry of Health “Pulje til styrket samarbejde mellem behandlingspsykiatrien og almen praksis (shared care)”. The amount granted for the Capital Region of Denmark is 30.046.409 Dkr. If further financial support is
received the Scientific Committee will be notified and the participant information will be updated.

13. Plan for publication

In study 1 a protocol for the three RCTs on anxiety and one for depression will be published on Trialsjournal.com. Results from 6 month follow-up and 15 month follow-up will be published in international journals as well as in 2-3 Ph.D- theses. Positive, negative and inconclusive results will be published. In study 2 a Ph.D thesis and one or more papers in an international journal will be published. In study 3 a minimum of one paper on the health economic analysis will be published in a relevant scientific health economics journal. In study 4 three papers are expected to be published. Furthermore, it is expected that a synthesis of the analysis will be published in another relevant journal, possibly in Danish. Furthermore, a short summary of the results will be drafted and written in layman’s language for decision-makers.
List of References

47. Kivi M, Eriksson MC, Hange D, Petersson EL, Vernmark K, Johansson B, Björkelund C. Internet-Based Therapy for Mild to Moderate Depression in Swedish Primary Care: Short Term Results from the PRIM-NET Randomized Controlled Trial. Cogn Behav Ther. 2014 Jun 9:1-10.
14. Appendix

Appendix 1. Other variables in the health economics analysis

<table>
<thead>
<tr>
<th>Variables that can be collected internally in Collabri</th>
<th>Calculated in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hour-/day calculation in connection with education from GPs and CM</td>
<td>Hours/days specified with the GP and CMs name and attendance</td>
</tr>
<tr>
<td>Expenses in connection with the provider of the education to GP/CM /psychiatrist/psychologist</td>
<td>Kroner/øre with date</td>
</tr>
<tr>
<td>Transport in connection with the education (only GPs)</td>
<td>Hours</td>
</tr>
<tr>
<td>Expenses for facilities (GP)</td>
<td>Kroner/øre</td>
</tr>
</tbody>
</table>

**Variable collected from registers**

- Use of psychologist (both control and intervention)
- LPR/expenses database
- GPs services (both control and intervention)

Collabri

Study 2
Qualitative study of conditions, processes and organisational consequences of the implementation of collaborative care for anxiety and depression

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Annette Sofie Davidsen, Associate Professor, Specialist in Family Medicine, PhD
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Marianne Lau, Consultant Psychiatrist, DrMedSci
Susanne Reventlow, Research Director, Adjunct Professor, Specialist in Family Medicine, Anthropologist, DrMedSci

The Research Unit for General Practice in Copenhagen

September 2013
Introduction

This study focuses on the conditions, activities and challenges related to the implementation of collaborative care for anxiety and depression. The collaborative care intervention (COLLABRI) consists in reorganising the cooperation between general practice and hospital based psychiatry in order to facilitate knowledge transfer, optimise resource use and improve the quality of treatment for patients with anxiety and depression. However, changing health care practices according to evidence-based recommendations has proved notoriously difficult in the past (Grimshaw et al. 2001, Oxman et al. 1995, Timmermans & Berg 2003) and implementing new knowledge and technologies usually requires a considerable – and often underestimated – amount of work (Nicolini 2006, Vikkelsø & Vinge 2004). This is particularly the case for complex interventions, like collaborative care, which involves several active components, several kinds of actors, and requires a high level of knowledge and skills from the actors supposed to implement and use the intervention (Craig et al. 2008). Thus, complex interventions are not always in alignment with existing logics, routines and infrastructures, and new interventions have several explicit and implicit implications which are not equally acceptable for all the parties involved. The implementation challenge is often increased in cross-sector and cross-professional interventions, where actors with different institutional positions can have differing interests and scopes of action (Antoft 2005, Kousgaard 2008, Seeman 1996, Seeman & Antoft 2002). Due to the complexity involved in implementing and evaluating modern health interventions, researchers and research institutions have increasingly emphasised the importance of carrying out process evaluations to better describe and understand the reception, progress and results of new health interventions (Medical Research Council 2008) – often using qualitative methods (Lewin, Glenton, Oxman 2009; O’Cathain 2009).

Based on the above, the primary aim of this study is to describe and analyse the clinical, organisational and managerial challenges and opportunities involved in the attempt to introduce collaborative care in the treatment of patients with anxiety and depression. Central to this is the question of how the assumptions, tools and activities of the COLLABRI-
intervention relate to existing perceptions, technologies, roles, work routines and regulative conditions in general practice.

**Theoretical perspective: Normalization Process Theory (NPT)**

Theoretically, the study is inspired by Normalization Process Theory (NPT). NPT is a middle range theory for investigating how new ideas and technologies are implemented and embedded in organizational settings (Bamford et al. 2012; May 2009; May & Finch 2009). NPT is a theoretical expansion of the Normalization Process Model (NPM), which was specifically developed for studying complex interventions in health care (Gask et al. 2010; May 2006; May et al. 2007). The starting point for NPT is that new ideas and technologies become imbedded in social contexts because of people working to implement them. Therefore NPT points attention to the work actors do to define, initiate and implement new ideas and technologies. According to NPT, there are four generative mechanisms/domains that affect the dynamics and outcomes of implementation processes: Coherence, Cognitive participation, Collective action and Reflexive monitoring.

**1. Coherence.**

How well a new intervention gets embedded in an organisational setting depends on whether the relevant actors apprehend the intervention as meaningful and have a clear understanding of their role in implementation process. Coherence is about the ways that an intervention is framed and defined by its proponents and about the way that the intervention is perceived by the actors supposed to implement the intervention. A high degree of coherence is obtained when actors share a common understanding of the intervention and its specific components and when the actors attach positive expectations to the benefits of the intervention. Since such sense-making work is an ongoing process, the actors may change their perceptions and understandings of the intervention during implementation.

**2. Cognitive participation.**

Cognitive participation is about the engagement of actors in a new intervention. This domain concerns the initial work of preparing the ground for the intervention (e.g. by making
agreements with key actors about their participation) as well as the subsequent and ongoing work of getting the actors to accept the specific tasks that they are supposed to undertake as part of the intervention. This means that the actors must find their contribution to be appropriate and worthwhile. The degree of cognitive participation can be traced in the chains of interaction that altogether make up an implementation process. The analytic focus is on factors that promote or inhibit actors’ participation in the intervention.

This dimension involves four factors that promote or inhibit the actors’ practical implementation of an intervention:

- **Interactional workability** is about what happens when the actors attempt to operationalise the intervention in daily practice (e.g. the clinical encounter). How does the work required by the intervention fit with current work practices and how does the intervention affect these practices?

- **Relational integration** concerns the relationships of knowledge and confidence that are affected by – and affect – the implementation of the intervention. How does the intervention relate to existing knowledge among the actors and how do the actors regard the expertise of other actors in relation to the intervention?

- **Skill-set workability** concerns the dynamics between the intervention and the existing distribution of work and skills in the implementing organisation(s). How are tasks allocated among professionals (and patients) in response to the intervention? Are the necessary skills available for performing the intervention as planned?

- **Contextual integration** is about the relationship between the intervention and its political and organisational context. This involves questions of resource allocation and the extent of management/political support from actors outside the immediate implementation setting. Since a complex intervention will be affected by the context, the primary focus here is on structural factors that support or inhibit the actors in enacting the intervention.
4. Reflexive monitoring.
While working to implement an intervention, the actors will continuously appraise (informally and/or formally) the activities related to the intervention and the consequences of these activities. Such assessments may change how the intervention is understood and valued by the actors (coherence); how the actors devote their time and energy to the intervention (cognitive participation); and how the intervention is structured and delivered (collective action).

Research Questions
Inspired by the theoretical framework of NPT, the following research questions are raised concerning the implementation of collaborative care as a complex intervention:

**Coherence:**
How do GPs, care managers and psychiatric supervisors initially make sense of the CC-intervention? Do they find it comprehensible and meaningful and how congruent are the understandings of the different actors?

**Cognitive participation:**
How and why do (or don’t) GPs, care managers and psychiatric supervisors initially take an interest in – and – engage with the CC-intervention?

**Collective action:**
What challenges do GPs, care managers and psychiatric supervisors face when trying to implement collaborative care?
How does the implementation of collaborative care affect work processes and task allocation in general practice?
How do the GPs assess the expertise and performance of the care managers?
How do the institutional conditions of general practice (such as remuneration terms and organisation structures) influence the implementation of the intervention?

**Reflexive monitoring:**
How do GPs, their personnel, care managers, psychiatrists experience and assess collaborative care in terms of its value for themselves and their patients? And how do these assessments affect their participation in the intervention?

**Methods and materials**

**Data Collection**
The study is a qualitative study primarily employing observations and interviews. The data collection will focus on the three central elements of the CC-intervention: A) The education of GPs and care managers, B) The introduction of care managers into general practice, C) The supervision of – and shared consultation with – GPs and care managers by a specialist in psychiatry.

During the intervention, 6-8 general practices will be followed via observations and interviews, in order to open up the ‘black box’ of the implementation processes (Grol 2001). The clinics will be strategically selected (Patton 2002) to obtain variations in type of practice and geographic location. The data collection will consist of the following three activities:

1. **Observations of introductory teaching activities and supervision for care managers and GPs.**

The observations are carried out in order to identify the expectations and demands made by the intervention on general practice and in order to observe the participants’ immediate attitudes and responses to these demands (which will provide information related to coherence and cognitive participation).

2. **Observations in general practice**
Each of the selected practices will be observed 3-4 days during the intervention. The observations will focus on the attempt to incorporate the care managers into the workflow in general practice comprising e.g. the shared consultations with a psychiatrist, the conferences between the GP and care manager, and possibly the patient consultations given by care managers and/or GPs. The observations will be done to produce detailed information on how the intervention elements are being translated in the clinic (with an eye for any variations), and to obtain a reference point for interviews with the professionals. If feasible, we will in some cases use video observations rather than direct observation.

3. Semi-structured interviews
During the intervention, semi-structured interviews (Kvale 1996) will be conducted with the participants from general practice and psychiatry. The interviews will focus on the professionals’ experiences and assessments regarding the implementation, usability and consequences of the intervention. Interviews will be made with the observed practices and their associated care managers and psychiatrists as well as with approximately 10 other practices (depending on the level of saturation).

Data Analysis
The analysis of the qualitative data material will be based on initial inductive thematic analysis (Taylor & Bogdan 1984, Gibbs 2007) focusing on the overall aims of the study followed by a theoretical analysis focusing on the dimensions and concepts suggested by Normalization Process Theory (cf. Macfarlane & O’Reilly-de Brún 2012, Bamford et al. 2012). The analysis will be performed by at least two researchers in order to facilitate quality assurance via analytical triangulation (Patton 1999). Furthermore, the composition of the project group makes it possible to analyse the material through perspectives from organisational research, anthropology and medicine.
Ethics
The project will be performed in accordance with the applicable guidelines for social science research ethics. The data collected (in the form of recorded interviews, transcriptions, observation notes, and video recordings) will be stored as confidential material. When reporting the results, the individual informants and clinics will be made anonymous.

Perspectives and dissemination
The findings from the qualitative study will a) contribute to an understanding of the results from the randomised controlled trial of the COLLABRI project and b) serve as input in the general assessment – and potential further development – of the collaborative care intervention and similar initiatives.
We plan to publish three articles from the study in relevant scientific journals (e.g. BMC Health Services Research, BMC Family Practice, and Implementation Science) as well as an article in Danish, which summarises the results of the study. The results will also be presented at scientific conferences and in relevant professional and political-administrative forums.

Project Management and organisation
The study is managed and carried out by researchers from the Research Unit for General Practice in Copenhagen. Associate Professor, Specialist in Family Medicine, PhD, Annette Sofie Davidsen (ASD) is the project manager. ASD is also a member of the project group for Study 1 and will be responsible for the contact to the other research groups in the COLLABRI project. Besides solid qualitative research competencies, ASD has a thorough knowledge of general practice and the psychiatric sector. ASD will work closely together with senior researcher, MSc political science, PhD, Marius Brostrøm Kousgaard (MBK) who has several years of experience with qualitative research on implementation processes in health care. In addition, PhD-student, Gritt Overbeck, has been attached to the project, under the supervi-

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sion of ASD and MBK. The project team will meet regularly in order to ascertain the status of the project and to ensure progress. Finally, Research Director, Adjunct Professor, Specialist in Family Medicine, Anthropologist, DrMedSci, Susanne Reventlow (SR) and Consultant Psychiatrist, DrMedSci, Marianne Lau will contribute with professional collaboration during the different phases of the project. As Head of Research at the Research Unit for General Practice in Copenhagen, SR has the overall responsibility for Study 2. SR is also a member of the steering group for Study 1.

Time schedule

Year 1: Literature studies, design specification, appointments with respondents, data collection.
Year 2: Data collection, transcription, data analysis.
Year 3: Data collection, data analysis, publishing activities
(Year 4: Continuation of publishing activities).

References


Appendix 3. Descriptions of Study 3 and 4

15. Opgaveløsning og analysedesign

KORA bidrager til den nationale evaluering med en sundhedsøkonomisk undersøgelse og en undersøgelse af patienternes perspektiver på behandlingen.

Undersøgelsesspørgsmål

Regionerne har indgået aftale om følgende undersøgelsesspørgsmål/evalueringsparametre for den sundhedsøkonomiske undersøgelse og undersøgelsen af patienternes oplevelse af behandlingen.

Sundhedsøkonomisk undersøgelse:

1. Hvad er de gennemsnitlige omkostninger forbundet med behandling af angst og depression ved traditionelle/hidtidige behandlingsformer?
2. Hvad er de gennemsnitlige omkostninger forbundet med behandling af angst og depression ved anvendelse af ’collaborative care’?
3. Hvad er de omkostningsmæssige effekter ved anvendelse af ’collaborative care’?
   o Hvordan påvirker ’collaborative care’:
     ▪ Sygefravær
     ▪ Funktionsniveau
     ▪ Behov for hjemmepleje og hjemmehjælp mv.
     ▪ Behov for sociale indsatser
     ▪ Behov for arbejdsmarkedsindsatser
     ▪ Behandlingsbehovet som følge af tidligere opsporing og tidligere Intervention
     ▪ Behandlingsbehovet som følge af øget recovery og egenomsorg
     ▪ Andre relevante forhold

Det er efterfølgende aftalt, at der fokuseres på omkostningsmæssige effekter i forhold til behandlingsbehov, sygefravær og tilknytning til arbejdsmarkedet, da oplysninger herom er tilgængelige fra de nationale registre, og da det især er på disse områder, at ’collaborative care’ forventes at have en effekt.

Undersøgelse af patienternes perspektiver på behandlingen:
1. Hvordan oplever borgere/patienter med angst eller depression tilrettelæggelse og effekter af traditionelle/hidtidige behandlingsformer?
2. Hvordan oplever borgere/patienter med angst og depression tilrettelæggelse og effekter af ’collaborative care’?
   - Hvordan opleves ’collaborative care’ at påvirke:
     - Effekten af udredning og behandling
     - Dialogen med de relevante fagprofessionelle
     - Støtten fra de relevante fagprofessionelle – i relation til behandling og i relation til støtte og omsorg i øvrigt
     - Information om udrednings- og behandlingsforløb

16. Hovedopgaver og anvendte metoder i opgaveløsningen

**Hovedopgave 1: Sundhedsøkonomisk undersøgelse**

Den sundhedsøkonomiske undersøgelse gennemføres som en registerbaseret analyse af omkostninger forbundet med behandling af angst og depression ved traditionelle/hidtidige behandlingsformer (standardbehandling) sammenlignet med ’collaborative care’ i hver af region.


Oversigten nedenfor viser, hvordan undersøgelsesspørgsmålene ovenfor besvares, herunder operationalisering af evalueringsparametre og datagrundlag.

<table>
<thead>
<tr>
<th>Undersøgelsesspørgsmål/evalueringsparametre</th>
<th>Operationalisering</th>
<th>Datagrundlag</th>
</tr>
</thead>
<tbody>
<tr>
<td>2) Hvad er de gennemsnitlige omkost-</td>
<td>Som punkt 1 for interventionsgruppen</td>
<td>Data, som regionerne skal leveres: (1) Oplysninger om CPR-nr. på personer i interventionsgruppen samt dato for inklusion i studiet. (2) Oplysninger om indhold og organisering af ’collaborative care’.</td>
</tr>
</tbody>
</table>
Hvad er de omkostningsmæssige effekter ved anvendelse af ’collaborative care’?

3) Hvad er de omkostningsmæssige effekter ved anvendelse af ’collaborative care’?

Gennemsnitlige meromkostninger (eller besparelser) pr. patient i interventionsgruppen sammenlignet med kontrolgruppen.

Som punkt 1 og 2 ovenfor samt punkterne a-d nedenfor.

a) Sygefravær

Antal uger, hvor patienten har modtaget sygedagpenge (langvarigt sygefravær).

DREAM-registeret. Ellers som under punkt 1 og 2 ovenfor.

b) Tilknytning til arbejdsmarkedet

Antal uger, hvor patienten har modtaget dagpenge, kontaktjælpe, revalidering og andre relevante overførselsindkomster.

DREAM-registeret. Ellers som under punkt 1 og 2 ovenfor.

c) Behandlingsbehovet som følge af tidligere opsporing og tidligere intervention

Delanalyse af omkostninger i de første 3 måneder efter inklusion i studiet.

Som punkt 1 og 2 ovenfor.

d) Behandlingsbehovet som følge af øget recovery og egenomsorg

Delanalyse af omkostningerne i de efterfølgende 6 måneder (måned 4-9) efter inklusion i studiet.

Som punkt 1 og 2 ovenfor.

Den sundhedsøkonomiske undersøgelse opdeles i følgende delopgaver:

1. Opgørelse af omkostninger ved interventionen (’collaborative care’) i hver region.
2. Opgørelse og sammenligning af de gennemsnitlige omkostninger pr. patient forbundet med behandling af angst og depression ved henholdsvis ’collaborative care’ og standardbehandling i hver region.
3. Opgørelse af evt. gennemsnitlig gevinst pr. patient i forhold til sygefravær og tilknytning til arbejdsmarkedet (reduktion af produktionstab).
4. Afrapportering.

De enkelte delopgaver er nærmere beskrevet nedenfor.

Ad 1) Meromkostningerne ved interventionen (’collaborative care’) set i forhold til standardbehandling opgøres for hver region. De gennemsnitlige meromkostninger pr. patient opgøres som de samlede omkostninger divideret med antallet af patienter i interventionsgruppen. For at kunne lave opgørelsen skal KORA bruge oplysninger om indhold og organisering af ’collaborative care’ projekterne i de enkelte regioner, antal patienter i interventionsgruppen og oplysninger om meromkostninger, fx lønudgifter til ’care managers’ og speciallæger i psykiatri/psykologer. Opgørelsen baseres på oplysninger indsamlet fra regionerne ved spørgeskema suppleret med telefoninterview.

Ad 2) De gennemsnitlige omkostningerne pr. patient forbundet med behandling af angst og depression ved henholdsvis ’collaborative care’ og standardbehandling opgøres og sammen-

**Ad 3)** Der gennemføres regressionsanalyse for at undersøge, om der er signifikante forskelle mellem interventions- og kontrolgruppen med hensyn til sygefravær og tilknytning til arbejdsmarkedet (produktionstab), når der kontrolleres for andre relevante forhold. Dette undersøges for alle regioner under ét og for hver region for sig. Hvis der er signifikante forskelle, estimeres den gennemsnitlige gevinst pr. patient (reduktion af productionstab) ved at modtage ’collaborative care’ sammenlignet med standardbehandling. Tidsperioden afgrænses til 9 måneder efter inclusion i studiet. Det forudsættes, at analysen kan trække på de data, som er indsamlet under punkt 2, herunder oplysninger om CPR-nr. på deltagere i interventions- og kontrolgruppen i de enkelte regioner og dato for inclusion i studiet. Herudover baseres opgørelsen på registerdata fra DREAM og relevante data fra andre registre. 

**Ad 4)** Aftrapporteringen omfatter en samlet rapport. Struktur for rapporten aftales med Region Hovedstadens Psykiatri. 

Som led i den sundhedsøkonomiske undersøgelse indsamles baggrundsplysninger om patienterne i interventions- og kontrolgruppen fra de nationale registre, herunder:

- Køn
Hovedopgave 2: Undersøgelse af patienternes perspektiver på behandlingen

Undersøgelsen af patientperspektiver baserer sig på to dele. For det første et spørgeskema om patienternes oplevelse af behandlingen, og for det andet 12 fokusgruppeinterview med patienterne. Både spørgeskemaet og fokusgruppeinterviewene vil blive gennemført i forhold til både kontrol- og interventionsgruppe, hvilket giver mulighed for at sammenligne de to grupper med hinanden: om gruppernes oplevelser og erfaringer med behandlingen adskiller sig, hvilke forhold i behandlingen der tillægges størst værdi i de to grupper og hvorvidt kontrol- og interventionsgruppe adskiller sig hvad angår oplevelse af at have modtaget relevant og dækkende behandling m.m.

Ad 1) Spørgeskemaet om tilfredshed med behandlingen indeholder spørgsmål omkring følgende temaer:

- Data om behandlingsforløbet
- Oplevelse af patient-behandler-relationen og oplevelse af gensidig respekt (inspireret af CSQ-18 og SSS-10)
- Tilfredshed med behandlingen (danske oversættelse af CSQ-8 og spørgsmål fra LUP’en)
- Baggrundssdata om patienten (skal måske indgå i patienttilfredshedsskemaet men bliver trukket fra de kliniske skemaer, hvis de registrerer noget tilsvarende)

Spørgeskemaet om patienttilfredshed skal udfyldes så hurtigt som muligt efter behandlingens afslutning. I Region Hovedstaden vil det indgå i det fælles spørgeskema, der indsamles ved seks måneders opfølgningen. Dette vurderes som absolut maksimum tidsperiode efter behandlingens afslutning, at skemaet meningsfuldt kan udfyldes. Til patienterne i Region Midtjylland, Region Nordjylland og Region Sjælland laves spørgeskemaet som et elektronisk skema i survey xacts og der vil blive udsendt et link til de patienter, der indgår i kontrol og interventionsgruppe. I det omfang, der kan fremskaffes e-mail adresser på informanterne vil dette være en betydelig fordel, da det vil give mulighed for at rykke deltagerne for besvarelse og dermed sikre en høj besvarelse.
Analyse af spørgeskemaundersøgelsen vil også omfatte subgruppeanalyser og dermed belyse spørgsmålet om patienter med forskellig baggrundskarakteristika (køn, alder, diagnose, sygdomsforløb) oplever forskellige grader af tilfredshed med hhv. Collaborative Care behandling og anden behandling. Hvis det er muligt, vil der også ske en vis inddragelse af de kliniske effektmål i analysen af spørgeskemaerne, således at det bl.a. undersøges om patienter, der er mest tilfredse med behandlingen også er dem, der har oplevet den største effekt på de kliniske effektmål.

Ad 2) Fokusgrupperne afholdes tilsvarende efter behandlingen er afsluttet. Fokusgrupperne vil dels behandle de samme temaer og vil derudover også udnytte den kvalitative metode til dels af få belyst, hvilke andre temaer, som patienterne vurderer som relevante for behandling og mere generelt håndtering af sygdommen i forhold til deres hverdagsliv; dels hvilken forståelsesmæssig ramme, som patienterne lægger over deres oplevelse af sygdom og behandling. Der vil blive tale om en åben, undersøgende tilgang.

Der gennemføres i alt 12 fokusgruppeinterview med seks til otte patienter i hver gruppe. Der gennemføres 3 fokusgruppeinterviews i hver region, med deltagere fra både kontrol og interventionsgruppen. At samle deltagerne på tværs af de to grupper vil give mulighed for, at patienterne diskuterer de forskellige oplevelser i forhold til hinanden, og at det derfor bliver muligt at stille skarpt på de erfaredes forskelle mellem ’collaborative care’ og almindelig behandling hos praktiserende læge.

Analysen af de kvalitative data vil tage udgangspunkt i en indholdsanalyse, og vil bl.a. afdække følgende forhold:

* **Tilfredshed med den oplevede behandling:** Hvor tilfredse er patienterne med behandlingen sammenholdt med den behandling, der er blevet givet hidtil i almen praksis? I hvilken grad oplever patienterne, at behandlingen har haft effekt?

* **Patienters til- og fravalg af behandling:** Patienter er i stigende grad blevet forbrugere, som kan vælge blandt f.eks. behandling hos egen læge, privatpraktiserende psykologer eller psykiatere, tilbud om terapi givet på det lokale jobcenter og alternative behandlere. I det perspektiv bliver det centralt at undersøge, hvordan behandlingsfeltet ser ud fra et patientperspektiv, hvilke ydelser de oplever at have adgang til, og hvordan patienterne træffer valg om
at tilslutte sig et behandlingstilbud, samt hvilken position ’collaborative care’ får i dette behandlingsfelt.

*Behandlingen i patientens liv:* Hvilken rolle spiller behandlingen i forhold til de ting, der er på spil i patientens hverdagsliv, herunder risici for stigmatisering og selvstigmatisering.