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The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)

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Abstract

Introduction

Depression is a common mental disorder and is together with anxiety the global leading cause of all non-fatal burden of disease. Currently supported treatment for depression is antidepressant medication and different psychotherapeutic interventions. Many patients experience, however, adverse effects of antidepressant medication, while at the same time the access to psychotherapeutic interventions are limited. Many patients who suffer from depression turn to complementary and alternative medicine (CAM) and among those modalities often spiritual healing. There is some evidence that consulting a spiritual healer can be beneficial for patients who suffer from depression, and that spiritual healing is associated with low risk. The aim of this protocol is to conduct a pilot RCT (spiritual healing as addition to usual care versus usual care alone) in preparation of a larger trial in adults with moderate depression, to examine feasibility and individuals' experience of spiritual healing.

Methods and analysis

This study is a pilot RCT with two parallel groups. A total of 28 adult patients with moderate depression, diagnosed by the physician and according to the Montgomery and Åsberg Depression Rating Scale (MADRS) criteria will be randomized to spiritual healing in addition to usual care intervention (n=14) or usual care alone (n=14). Ten treatment sessions (each lasting 45-60 minutes) of spiritual healing will be administered as an adjunct to usual care (n=10) and compared to usual care alone (n=10). To investigate participants' experience with spiritual healing, a qualitative study will be included using semi-structured interviews.

Ethics and dissemination

This protocol was approved by regional committees for medical and health research ethics by the identifier (63692) and registered at The Norwegian Centre for Research Data (NSD) (845302) and clinicaltrials.gov (ID: NCT04766242). The results of this protocol will be disseminated through open-access, peer-reviewed publications, in addition to stakeholders´ reporting and presenting at relevant conference.

Strengths and limitations of this study

- Several physicians will recruit patients to the trial providing insight into different methods of usual care
- Because of corona lockdown, only one healer will be implementing the healing sessions as opposed to the two originally planned
- A multi-disciplinary research team consisting of CAM providers, physicians, psychiatrists, and researchers safeguard a whole system research approach
- To enhance patient safety, the research team will record adverse effects of both healing and usual care
- Due to the overload of patients and covid protocols, the implementation of the trial has been negatively affected

Introduction

Depression is a common mental disorder and is together with anxiety the global leading cause of all non-fatal burden of disease (1). The core symptoms of depression are lowered mood, discouragement, loss of sense and meaning in life, lack of interest in other people and ordinary duties, and lack of energy and appetite. In addition, the patients often experience diminished self-esteem, self-reproach and a feeling of guilt. These symptoms may vary in intensity and duration (2, 3). Nevertheless, around half of all people with depression worldwide do not receive appropriate treatment (4). Most mental disorders emerge before the age of 30 (5, 6), and lack of treatment might contribute to disability for many crucial years of an individual's life. In Norway, the 12 month prevalence and lifetime prevalence of depression is 10% and 20% respectively, higher in women than in men (2). Depression has been identified as a strong predictor for use of complementary and alternative medicine (CAM) (7-9). A recent Norwegian study demonstrates that only 10.9% of those with moderate depression and/or anxiety visited psychiatric outpatient services while 17.6 % visited a CAM provider (10). These facts demonstrate that people with depression might be willing to seek help also from less established services, such as CAM providers. Thus, it is possible that different CAM modalities may serve as a substitute or an alternative when access to psychologist/psychiatric services is limited (10-12).

Conventional medicine classifies depression as a mood disorder that manifests itself across a wide range of disease/symptom severity. Depression can be classified as mild, moderate or severe (13). Symptoms must have been persistent for at least two weeks and not be related to other medical or psychiatric diagnoses, or be due to substances (14). The World Health Organization ranks the social costs of depression as the 4th highest of all diseases (15). Furthermore, by 2020 current trends indicate that depression will represent the highest cost to society of any disease (15). Clearly, prevention, early diagnosis and intervention of depression have huge significance.

The most commonly prescribed antidepressant drugs, selective serotonin reuptake inhibitors (SSRIs) have recently been shown to have the best effect on severe depression, and no effect beyond placebo for mild and moderate depression (16, 17). At the same time, SSRIs can be

associated with serious adverse effects (18), and are associated with increased vulnerability to develop a depressive episode later in life (16). Thus, one of the most common treatment options for depression has been documented to be of little or no help beyond placebo for moderate depression while at the same time possibly inducing serious adverse effects.

The Competence Center for Lived Experience and Service Development, investigate the needs for individuals with metal health problems. According to the center, many patients in psychological health care do not want to be treated with medication. These patients must be heard and taken seriously. We cannot force anyone to take medication as long as necessary care and treatment can be provided otherwise (19).

Cognitive behavioural therapy (CBT) or structured psychological therapy (20) should always be offered patients who do not receive, or do not want pharmaceutical antidepressant treatment. However, waiting lists for such treatment are often long due to the lack of competent professionals (psychologists and psychiatrists), especially in rural communities, and at the district psychiatric centers (21). These centers have to prioritize patients with major depression, meaning that patients with moderate depression have less access to CBT.

Spiritual healing for depression

Spiritual healing is one of the most frequently used CAM modalities in Norway (22). It is understood as an energy based therapeutic approach to healing. A spiritual healer uses the hands to balance and harmonise the body and thereby place the client in a position of self-healing (23). The healing treatment focuses on the whole person (physically, psychologically, and emotionally) as well as the environmental factors (support from family, friends, community). Scientific evidence indicates that users typically praise CAM modalities for offering symptoms relief, reducing adverse effects of conventional treatment, enhancing their ability to cope physiologically and emotionally, providing an alternative to pharmaceuticals, and offering a close patient-practitioner relationship during treatment (24).

There is some evidence that spiritual healing can be beneficial for patients who suffer from depression (25, 26) and spiritual healing is associated with low risk (27). In a preliminary study

conducted by this current research group, a mean decrease in depression score of 3.1 points (range 0-4) on a 7 point scale was found (n=9) (28). The symptom was rated on a scale from 0-6 where 0 was "as good as it could be "and 6 was "as bad as it could be" (MYMOP scale (29)). Only one patient reported no change in depression symptoms after healing treatment. None of the patients experienced worsening of depression symptoms during the healing treatment while the majority (n=5) had a reduction of 4 points (28). More research is needed to confirm these findings and to identify modifications needed in the design of a larger RCT.

Objectives

The objectives of this study are to conduct a pilot Randomized Controlled Trial (RCT) (spiritual healing as addition to usual care versus usual care alone) in preparation of a larger trial in adults with moderate depression, and further to examine the feasibility of the study design and the participants´ experience of spiritual healing.

Methods and analysis

This is a multicenter pilot RCT with two parallel arms. Nested within the trial is a qualitative arm.

Design

A total of 28 individuals with moderate depression will be randomized to a spiritual healing intervention as an adjunct to usual care (n=14) or to usual care alone (control) (n=14). We will study the entire spiritual healing package understood as everything a healer does in a consultation (visiting a healer), including the use of hands to balance and harmonize the body and sometimes offering lifestyle advice. Included in the treatment is the interaction between the patient and the therapist. A positive interaction between the patient and the therapist (alliance) is necessary for the patient to feel free to verbally express painful present and past experiences that may be related to the patient's psychological complaints (30, 31) (e.g., pragmatic research approach).

Setting

In Norway, inhabitants receive treatment within the public health care system, while CAM providers, including healers, operate outside this system. Patients themselves generally cover the cost of these visits. Since CAM practices are unregulated, anyone is allowed to use the term healer and treat patients. However, many healers are members of the Norwegian Healing Association that require a professional standard regarding healing skills. To ensure patient safety in cases of interventions related to health issues, members are required to obtain a professional insurance for injury to their patients caused by the treatment.

Study participants

Inclusion criteria

All patients must be 18 years or above, fulfil the criteria for moderate depression diagnosed by a physician, and scores within the range of 20-29 on the MADRS depression rating scale (32). Symptoms must have persisted for two weeks or more. In addition to a MADRS score of 20-29 the physicians who include patients will decide whether the patient is suited for inclusion based on the following observations: a) the patient is too healthy to be referred to District Psychiatric Center (DPS) and b) too ill to remain untreated.

Exclusion criteria

Patients are excluded for the following reasons: Symptoms as direct physiological effects of a substance or a general medical condition; substance abuse; chronic major or bipolar depression or any personality disorder (axis II); endocrine abnormality; medical disorder or treatment that could cause depression; suicidal potential; dementia; depression due to complicated grief; history of psychosis or mania; heart valve disease; poorly controlled hypertension and diabetes mellitus; pregnancy; or inability to complete study forms.

Recruitment

Patients who visit their physician for mood related symptoms and fulfil the inclusion and does not fulfil any of the exclusion criteria,

will be asked by the physician if they want information about the study. If the patients agree, they will receive an information folder and the informed consent. After that, the physician will send an SMS with contact information to the researchers at The National Center for Complementary and Alternative Medicine (NAFKAM). Subsequently, NAFKAM will contact the patients, inform further about the study, and include those who agree to participate. Before randomization, participants must read and sign the informed consent. To collect baseline data, a link to the electronic BDI form will be forwarded to the participants.

Randomization

We will use a randomization system with block sizes that vary from two to six, to eliminate confounders of a personnel or structural nature, thus balancing group allocation throughout the study period. Within each block, an equal number of patients will be randomly allocated to either an intervention group with spiritual healing and usual care, or a control group with usual care alone.

Blinding

Patients will not be blinded regarding treatment allocation, in accordance with a pragmatic research approach. Neither the study physicians nor the study therapist will be blinded. The researchers will be blinded when analysing unidentified patient-reported data.

Intervention

Primary outcome measures

The study outcome will be recruitment speed, willingness to be randomized, study adherence, and implementation of healing compared to usual care for moderate depression.

Secondary outcome measures

Secondary outcomes will be change in severity of depression measured by Beck Depression Inventory (BDI) (33). This questionnaire will be completed by the study patients at baseline, after 8 and 16 weeks, and 6 and 12 months after inclusion to the study. An adverse effect form will be completed after 8 and 16 weeks. The RELIS adverse effect scale (34) will be used to

measure adverse effects and the questions about adverse effects will be included at the end of the BDI form.

Measurements

The Beck Depression Inventory for Primary Care (BDI-PC) (33) is a screening instrument for depression that minimizes the possibility of yielding spuriously high estimates of depression for patients with medical problems by focusing on symptoms of *sadness, pessimism, past failure, loss of pleasure (anhedonia), self-dislike, self-criticalness*, and *suicidal thoughts* or *wishes*. Each item is rated on a 4-point scale ranging from 0 to 3, and the BDI-PC is scored by summing up all of the highest ratings for each of its seven items. To address the minimum Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV requirement for the duration of moderate depression symptoms, respondents are asked to describe themselves for the "past 2 weeks, including today." We will also collect demographic data such as age, gender, education, household, income, and work. In addition to use of drugs and diary supplements/herbs for depression (questionnaire baseline). In intervention week 10, 16, and 6 and 12 months, adverse effects and change in use of drugs and diary supplements/herbs will be registered.

Qualitative study

To investigate participants' experiences of spiritual healing (n=8) and usual care (n=8) a qualitative study will be included using semi-structured interviews (35) after the intervention period has ended (week 16). The participants (n=16) will be asked about their illness (severity, duration, previous treatment), how they experienced the treatment (advantages and disadvantages) provided during the study, if their expectations were met, and their willingness to be randomized. Furthermore, we will ask about adverse effects from the treatment, and the patient -provider relationship. The control group will be interviewed and asked about their experiences with usual care. Moreover, we will observe and register recruitment speed, study adherence, and implementation of healing compared to usual care.

Treatment plan

Intervention

The spiritual healing will be based on an assessment of the total health situation of the individual patient. Spiritual healing will mainly consist of a treatment where the healers hold their hands for some time at different parts of the patient's body, known as "power points", outside of the patient's clothing. The consultation might also include lifestyle advice. This can necessarily lead to slightly different treatment given to each patient. Each treatment will, however, last for 45-60 minutes.

The healer who will perform the healing is a trained member of the Norwegian Healer Association (Norges Healerforbund). She has been working full time as a spiritual healer for more than 20 years. As a member of the Norwegian healer association, she has liability insurance in cases of harmful effects of the treatment.

Usual care

Throughout the 16-week intervention period, all participants will be advised to follow the treatment plan given by the physician at 5 different clinics in a town south in Norway. *Usual care* may include regular consultations with physicians (every 14th day, duration 30-60 minutes) including counselling about sleep, activity, lifestyle, anti-depressive medication, and sick leave. The participants in the control group will be offered three healing sessions after the 10-week intervention period.

Implementation

The study nurse at NAFKAM will send the link to the questionnaire to the participants at baseline, weeks 8 and 16, and after 6 and 12 months, asking them to complete the questionnaire.

1. When the patient has signed the informed consent the researchers at NAFKAM will formally include the patient according to the randomization system.

2. Included patients will be randomized to spiritual healing plus usual care (intervention group) or usual care alone (control group). Directly after randomization and if assigned

to healingname and phone-number of the patients will be sent by SMS to the spiritual healer. The healer will then contact the patient who will receive the first healing session within 14 days after enrolment. The patient will be offered 10 healing sessions.

3. Patients in the control group will receive usual care as agreed with their physician.

4. Patients in the intervention group and control group are urged to follow the treatment recommendations given by the physician (for example anti-depressant medication).

5. The last follow-up healing treatment session must be completed by the end of week 16 of the study (the day of the first healing session is defined as week 0).

Follow up

1. The study nurse will ask the participants to complete the electronic BDI questionnaire in week 8 and 16. In addition, they will be asked to register information about adverse effects as part of the form.

2. The study nurse will contact the participants after 6 and 12 months and remind them to complete the electronic BDI questionnaire (follow-up data).

3. Interviews will be conducted with participants in both groups at the end of the intervention period (week 16).

Withdrawal and loss to follow-up

If a patient chooses to withdraw before week 16, all data collected will be permanently deleted. If the patient is lost to follow-up, data collected up to the day of drop out will be used for analysis.

Statistical analysis

Differences in BDI score between groups as well as adverse effects will be described descriptively only, due to the pilot nature of the study. The last author (AEK) will perform the statistical analysis. Data analysis will be done utilizing the IBM statistical package SPSS v 28 (http://www.spss.com).

Qualitative analysis

The qualitative data will be analyzed using a descriptive qualitative content analysis (35). Knowledge and understanding of the phenomena under study will be provided through a systematic classification process of coding and identifying themes.

Patient and public involvement

In this study, patients will be interviewed about their study experiences and the main outcomes of this study are recruitment, willingness to randomization and other feasibility measures.

Sample size

No sample size calculation is needed for a pilot RCT. The findings of this pilot study will be used to calculate the sample size in a potential future RCT. A study size of n=16 participants, n=8 in each group is chosen to generate sufficient interviews (saturation on that point is assumed) for the qualitative study (36).

Data handling management

All patient data and the index that links trial numbers with individual participants will be kept under lock, and the key will be in the possession of NAFKAM. Trial number alone will identify all data.

Coding and punching

Data entry will be undertaken at NAFKAM. All data will be read twice to ensure against random bias in the coding and punching process. The first author (TS) will be responsible for obtaining and analyzing the qualitative data.

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment, in here.

MADRS: Montgomery and Åsberg Depression Rating Scale
BDI: Beck Depression Inventory

Ethics and patient safety

The patients will be informed about the study through an information folder and verbally by the study nurse, and, if willing to participate, asked to give a written informed consent. The participants will be informed that they can withdraw from the study at any time without any

consequences. All patients will follow usual care regardless of healing treatment, and adverse effects will be recorded at each treatment session. No systematic studies have been published on adverse effects of spiritual healing for depression. However, previous research has demonstrated that spiritual healing is associated with low risk (27). The study will be conducted in accordance with the Helsinki declaration (37). This protocol was approved by The Regional Committees for Medical and Health Research Ethics (REK) by the identifier (63692) and registered at The Norwegian Centre for Research Data (NSD) (845302) and clinicaltrials.gov (ID: NCT04766242).

Data and safety monitoring

A steering group will be responsible for quality control and meet on a regular basis throughout the study period. The steering group will be convened as an emergency in the event of serious adverse effects associated with the trial to decide on appropriate action to prevent recurrence. Regular meetings will concern any reported adverse effects, protocol violation, the recruitment rate, practical issues concerning local coordination, as well as any issues raised by the participants.

Discussion and conclusion

To the best of our knowledge, this is the first pilot RCT investigating the feasibility of the study design and the participants´ experience of spiritual healing and usual care for patients with moderate depression in Norway. This research team has previously conducted an observational study investigating self-reported effect of healing, with a pre - post design (28). The rationale for the study was that Norwegian patients with chronic diseases and psychological problems reported frequent use of spiritual healing (14-36%) (38). Moreover, 38% of cancer patients in Northern Norway reported to have used spiritual healing (39). Generally, most CAM interventions are under-researched, taking into consideration that they are widely practiced, and limited information is available about their clinical effectiveness and risk profile. Observational studies are well suited to investigate these questions in a real life setting (40).

Therefore, to get more nuanced information, we aimed to map the conditions patients reported when visiting a healer for the first time, and to evaluate the subjective benefits and risks from

the intervention. Results from the above mentioned observational study reported a total of 23% of the participants reported psychological complaints such as anxiety and depression. These complaints were reduced from a pretreatment score of 4.7 to a post treatment score of 2.3, measured by Measure Yourself Medical Outcome Profile (MYMOP) (41). This reduction was achieved after a mean of 4.1 spiritual healing sessions (range 1-17). Forty percent of the participants reported one or more adverse effects after treatment. These were perceived by the participants as minor and transient. However, these results must be interpreted with care since no interference statistical analysis of effect was performed. Due to the lack of a control group, we cannot draw the conclusion that the findings are exclusively due to the spiritual healing treatment.

Based on the findings from this previous observational study, and in preparation for a larger RCT, we want to investigate the recruitment speed, participants' willingness to be randomized, study adherence, and implementation of healing compared to usual care for moderate depression. We will also investigate the change in severity of depression measured by BDI.

Strength and limitations

This protocol must be understood in light of the study limitations. Because of the corona pandemic and lockdown of the society, only one healer will be implementing the healing sessions as opposed to the two originally planned. Due to the overload of patients in clinical practice and implementation of covid protocols (such as vaccination of patients) the implementation of the trial has be negatively affected. The physicians, who will recruit patients to the trial have been occupied with corona patients. However, several physicians working in five different conventional health clinics will recruit patients to the trial providing an insight on different methods of usual care. A multi-disciplinary research team consisting of CAM providers, physicians, psychiatrists, and researchers will safeguard a methodology in line with a whole system research approach. Lastly, to enhance patient safety, the research team will record adverse effects of both healing and usual care.

Figure legends

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment

Declarations

Author contributions

TS and AEK initiated this study, developed the concept and study design. ACI, AHH, OKB and CG contributed with intellectual content. Trine Stub wrote the first draft of the manuscript and all authors reviewed subsequent versions of the manuscript. All authors read and approved the final version of the manuscript.

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Competing interest statement

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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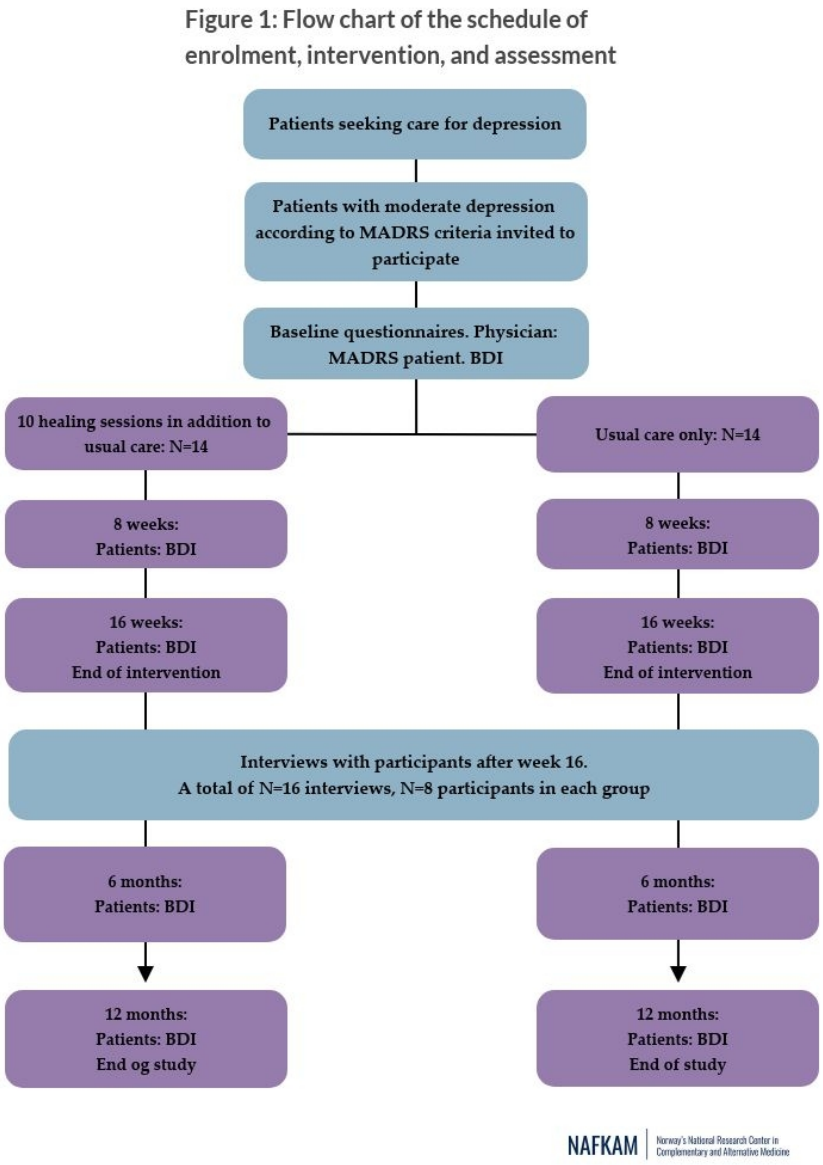

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym. *The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)*
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. *clinicaltrials.gov (ID: NCT04766242)*
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier. *OK*
Funding	4	Sources and types of financial, material, and other support. *Page 16 (funding)*
.Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors. *Page 16 (authors contribution)*
	5b	Name and contact information for the trial sponsor. *Not Applicable (NA)*
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities. *NA*
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee). *NA*
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention. *Page 5-6 (introduction)*
	6b	Explanation for choice of comparators. *Page 5-6 (introduction)*

Objectives	7	Specific objectives or hypotheses. *Page 7 (Objectives)*
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained. *Page 8 (Setting)*
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists). *Page 8 (Inclusion, exclusion criteria)*
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. *Page 10-11 (treatment plan, Intervention)*
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). *Page 14, (Data and safety monitoring)*
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). The *study nurse will contact the participants if not completed the questionnaires.*
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial. *Yes*
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended. *Page 9 (primary and secondary outcome) and page 7 (Design)*
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure). *Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment*

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations. *Page 12 (Statistical analysis)*
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. *Page 8 (Recruitment).*
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions. *Upon signed consent form and completed baseline questionnaire, randomization is performed as described at page 9.*
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned. *Page 9 (Blinding)*
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions? *Page 11 (Implementation).*
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. *Page 9 (Blinding)*
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial. *NA*
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol. *Page 10 (Measurements)*
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols. *Page 15 (Data and safety monitoring) and page 12 (withdrawal and loss to follow-up).*

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. *Page 13 (Data handling management, and coding and punching)*
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. *Page 12 and13.*
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses). *Page 12 and 13.*
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation). *Page 12.*
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed. *NA*
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. *NA*
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct. *Page 10 (Measurements) and page 9 (secondary outcome).*
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor. *NA*
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval. *Page 14-15.*
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators). *Page2 (Abstract)*
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32). *Page 11 (Implementation)*

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable. *NA*
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial. *Page 13.*
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site. *No competing interest*
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators. *Only researchers involved in this project will have access to final trail dataset.*
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation. *NA*
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions. *The result of the trial, will be published in a relevant international journal with authorship following the Vancouver statement.*
	31b	Authorship eligibility guidelines and any intended use of professional writers. *NA*
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code. *NA*
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates. *NA*
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable. *NA*

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)

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The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)

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Abstract

Introduction

Depression is a common mental disorder and the (global) leading cause of all non-fatal burden of disease worldwide. Currently, supported treatment for depression is antidepressant medication and different psychotherapeutic interventions. Many patients experience, however, adverse effects of antidepressant medication, while at the same time the access to psychotherapeutic interventions are limited. Many patients who suffer from depression turn to complementary and alternative medicine (CAM) and among those modalities often spiritual healing. There is some evidence that consulting a spiritual healer can be beneficial for patients who suffer from depression, and that spiritual healing is associated with low risk. The aim of this protocol is to conduct a pilot RCT (spiritual healing as addition to usual care versus usual care alone) in preparation of a larger trial in adults with moderate depression, to examine feasibility and individuals' experience of spiritual healing.

Methods and analysis

This study is a pilot RCT with two parallel groups. A total of 28 adult patients with moderate depression, diagnosed by the physician and according to the Montgomery and Åsberg Depression Rating Scale (MADRS) criteria will be randomized to spiritual healing in addition to usual care (n=14) or usual care alone (n=14). To determine if there is a statistical indication of an effect of healing warranting a full-scale study, the separation test will be used. To investigate participants' experience with spiritual healing, a qualitative study will be included using semi-structured interviews. The data will be analyzed based on a direct content analysis.

Ethics and dissemination

This protocol was approved by regional committees for medical and health research ethics by the identifier (63692) and registered at The Norwegian Center for Research Data (NSD) (845302) and clinicaltrials.gov (ID: NCT04766242). The results will be disseminated through open-access, peer-reviewed publications, in addition to stakeholders´ reporting and presenting at conferences.

Strengths and limitations of this study

- Several physicians will recruit patients to the trial providing insight into different methods of usual care
- Because of COVID-19 lockdown, only one healer will be implementing the healing sessions as opposed to the two originally planned
- A multi-disciplinary research team consisting of CAM providers, physicians, psychiatrists, and researchers safeguard a whole system research approach
- To enhance patient safety, the research team will record adverse effects of both healing and usual care
- Due to the overload of patients and covid protocols, the implementation of the trial has been negatively affected

Introduction

Depression is a common mental disorder and is together with anxiety the (global) leading cause of all non-fatal burden of disease worldwide (1). The core symptoms of depression are lowered mood, discouragement, loss of sense and meaning in life, lack of interest in other people and ordinary duties, and lack of energy and appetite. In addition, the patients often experience diminished self-esteem, self-reproach and a feeling of guilt. These symptoms may vary in intensity and duration (2, 3). Nevertheless, around half of all people with depression worldwide do not receive appropriate treatment (4). Most mental disorders emerge before the age of 30 (5, 6), and lack of treatment might contribute to disability for many crucial years of an individual's life. In Norway, the 12 month prevalence and lifetime prevalence of depression is 10% and 20% respectively, higher in women than in men (2). Depression has been identified as a strong predictor for use of complementary and alternative medicine (CAM) (7-9). A recent Norwegian study demonstrates that only 10.9% of those with moderate depression and/or anxiety visited psychiatric outpatient services while 17.6% visited a CAM provider (10). These facts demonstrate that people with depression might be willing to seek help also from less established services, such as CAM providers. Thus, it is possible that different CAM modalities may serve as a substitute or an alternative when access to psychologist/psychiatric services is limited (10-12).

Conventional medicine classifies depression as a mood disorder that manifests itself across a wide range of disease/symptom severity. Depression can be classified as mild, moderate or severe (13). Symptoms must have been persistent for at least two weeks and not be related to other medical or psychiatric diagnoses, or be due to substances (14). The World Health Organization ranks the social costs of depression as the 4th highest of all diseases (15). Furthermore, by 2020 current trends indicate that depression will represent the highest cost for society of any disease (15). Clearly, prevention, early diagnosis, and intervention of depression have huge significance.

The most commonly prescribed antidepressant drug, selective serotonin reuptake inhibitors (SSRIs), has recently been shown to have the best effect on severe depression, and no effect beyond placebo for mild and moderate depression (16, 17). At the same time, SSRIs can be

associated with serious adverse effects (18), and are associated with increased vulnerability to develop a depressive episode later in life (16). Thus, one of the most common treatment options for depression has been documented to be of little or no help beyond placebo for moderate depression while at the same time possibly inducing serious adverse effects.

The Competence Center for Lived Experience and Service Development, investigate the needs for individuals with mental health problems. According to the center, many patients in psychological health care do not want to be treated with medication. These patients must be heard and taken seriously. We cannot force anyone to take medication as long as necessary care and treatment can be provided otherwise (19).

Cognitive behavioural therapy (CBT) or structured psychological therapy (20) is a treatment option for patients who do not want pharmaceutical antidepressant treatment. However, waiting lists for such treatment are often long due to the lack of competent professionals (psychologists and psychiatrists), especially in rural communities, and at the district psychiatric centers (21). These centers have to prioritize patients with major depression, meaning that patients with moderate depression have less access to CBT.

Spiritual healing for depression

Spiritual healing is one of the most frequently used CAM modalities in Norway (22). It is understood as an energy based therapeutic approach to healing. A spiritual healer uses the hands to balance and harmonize the body and thereby place the client in a position of self-healing (23). The healing treatment focuses on the whole person (physically, psychologically, and emotionally) as well as the environmental factors (support from family, friends, community). Scientific evidence indicates that users typically praise CAM modalities for offering symptoms relief, reducing adverse effects of conventional treatment, enhancing their ability to cope physiologically and emotionally, providing an alternative to pharmaceuticals, and offering a close patient-practitioner relationship during treatment (24).

There is some evidence that spiritual healing can be beneficial for patients who suffer from depression (25, 26), and spiritual healing is associated with low risk (27). In a preliminary study

conducted by the current research group, a mean decrease in depression score of 3.1 points (range 0-4) on a 7 point scale was found (n=9) (28). The symptom was rated on a scale from 0-6 where 0 was "as good as it could be"and 6 was "as bad as it could be" (MYMOP scale (29)). Only one patient reported no change in depression symptoms after healing treatment. None of the patients experienced worsening of depression symptoms during the healing treatment, while the majority (n=5) had a reduction of 4 points (28). More research is needed to confirm these findings and to identify modifications needed in the design of a larger RCT.

Objectives

The objectives of this study are to conduct a pilot Randomized Controlled Trial (RCT) (spiritual healing as addition to usual care versus usual care alone) in preparation of a larger trial in adults with moderate depression, and further to examine the feasibility of the study design and the participants´ experience of spiritual healing.

Methods and analysis

This is a multicenter pilot RCT with two parallel arms. Nested within the trial is a qualitative arm.

Design

A total of 28 individuals with moderate depression will be randomized to a spiritual healing intervention as an adjunct to usual care (n=14) or to usual care alone (control) (n=14). We will study the entire spiritual healing package understood as everything a healer does in a consultation (visiting a healer), including the use of hands to balance and harmonize the body and sometimes offering lifestyle advice. Included in the treatment is the interaction between the patient and the therapist. A positive interaction between the patient and the therapist (alliance) is necessary for the patient to feel free to verbally express painful present and past experiences that may be related to the patient's psychological complaints (30, 31) (e.g., pragmatic research approach).

Setting

In Norway, inhabitants receive treatment within the public health care system, while CAM providers, including healers, operate outside this system. Patients (themselves) generally cover the cost of these visits themselves. Since CAM practices are unregulated, anyone is allowed to use the term healer and treat patients. However, many healers are members of the Norwegian Healing Association that require a professional standard regarding healing skills. To ensure patient safety in cases of interventions related to health issues, members are required to obtain a professional insurance for injury to their patients caused by the treatment.

Study participants

Inclusion criteria

All patients must be 18 years or above. They have to suffer from depressive difficulties of moderate intensity and fulfil the criteria for depression diagnosed by the physicians included in the study, and score within the range of 20-29 on the MADRS depression rating scale (32, 33). Symptoms must have persisted for two weeks or more. In addition to a MADRS score of 20-29, the physicians who include patients will decide whether the patient is suited for inclusion based on the following observations: a) the patient is too healthy to be referred to District Psychiatric Center (DPS) and b) too ill to remain untreated.

Exclusion criteria

Patients are excluded for the following reasons: Chronic major or bipolar depression or any personality disorder (axis II); endocrine abnormality; suicidal potential; dementia; depression as direct physiological effects of a substance or a medical condition (such as Parkinson disease, epilepsy, and multiple sclerosis); substance abuse; history of psychosis or mania; heart valve disease; poorly controlled hypertension and diabetes mellitus; pregnancy (34); or inability to complete study forms.

Recruitment

Patients who visit their physician for mood related symptoms and fulfil the inclusion and do not fulfil any of the exclusion criteria will be asked by the physician if they want information about

the study. If the patients agree, they will receive an information folder and the informed consent. After that, the physician will send an SMS with contact information to the researchers at The National Center for Complementary and Alternative Medicine (NAFKAM). Subsequently, NAFKAM will contact the patients, inform further about the study, and include those who agree to participate. Before randomization, participants must read and sign the informed consent. To collect baseline data, a link to the electronic BDI form will be forwarded to the participants.

Randomization

We will use a randomization system with block sizes, that vary from two to six, to eliminate confounders of a personnel or structural nature, thus balancing group allocation throughout the study period. Within each block, an equal number of patients will be randomly allocated to either an intervention group with spiritual healing and usual care, or a control group with usual care alone.

Blinding

Patients will not be blinded regarding treatment allocation, in accordance with a pragmatic research approach. Neither the study physicians nor the study therapist will be blinded. The researchers will be blinded when analysing unidentified patient-reported data.

Intervention

Primary outcome measures

The study outcome will be recruitment speed, willingness to be randomized, study adherence, and implementation of healing compared to usual care for moderate depression.

Secondary outcome measures

Secondary outcomes will be change in severity of depression measured by Beck Depression Inventory (BDI) (35). This questionnaire will be completed by the study patients at baseline, after 8 and 16 weeks, and 6 and 12 months after inclusion to the study. The separation test (36) will be used to investigate an indication of an effect of healing in a full-scale study.

An adverse effect form will be completed after 8 and 16 weeks. The RELIS adverse effect scale (37) will be used to measure adverse effects and the questions about adverse effects will be included at the end of the BDI form.

Measurements

The Beck Depression Inventory for Primary Care (BDI-PC) (35) is a screening instrument for depression that minimizes the possibility of yielding spuriously high estimates of depression for patients with medical problems by focusing on symptoms of *sadness*, *pessimism*, *past failure*, *loss of pleasure (anhedonia)*, *self-dislike*, *self-criticalness*, and *suicidal thoughts* or *wishes*. Each item is rated on a 4-point scale ranging from 0 to 3 and summing up all of the highest ratings for each of its seven items scores the BDI-PC. To address the minimum Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV requirement for the duration of moderate depression symptoms, respondents are asked to describe themselves for the "past 2 weeks, including today." We will also collect demographic data such as age, gender, education, household, income, and work, in addition to use of drugs and diary supplements/herbs for depression (questionnaire baseline). In intervention weeks 10, 16, and 6 and 12 months, adverse effects and change in use of drugs and diary supplements/herbs will be registered.

Qualitative study

In a qualitative study, nested within the trial, the investigators will investigate participants' experiences of spiritual healing and usual care. The aim of the study is to collect information about the participants' lived experience of participating in the trial receiving healing and usual care interventions. The study is based on phenomenology as this study design explores what people experienced and focuses on their experience of a phenomenon (38) and will provide the investigators with more nuanced and in-depth data than data obtained only from the questionnaires (24).

The study will draw on data obtained through semi-structured interviews (39) conducted with 16 participants (n=16), eight (n=8) in the intervention group and eight (n=8) in the control group upon completion of the intervention period (week 16).

Based on an interview guide, the participants will be asked about their illness (severity, duration, previous treatment), how they experienced the treatment (advantages and disadvantages) provided during the study, if their expectations were met, and their willingness to be randomized. Furthermore, we will ask about adverse effects from the treatment, and the patient-provider relationship. The control group will be interviewed and asked about their experiences with usual care. Moreover, we will observe and register recruitment speed, study adherence, and implementation of healing compared to usual care.

Treatment plan

The study is planned to start in March 2022 and end of study (data collection) is March 2023.

Intervention

The spiritual healing will be based on an assessment of the total health situation of the individual patient. Spiritual healing will mainly consist of a treatment where the healers hold their hands for some time at different parts of the patient's body, known as "power points", outside the patient's clothing. The consultation might also include lifestyle advice. This can necessarily lead to slightly different treatment given to each patient. Each treatment will, however, last for 45-60 minutes.

The healer who will perform the healing is a trained member of the Norwegian Healer Association (Norges Healerforbund). She has been working full time as a spiritual healer for more than 20 years. As a member of the Norwegian Healer Association, she has liability insurance in cases of harmful effects of the treatment.

Usual care

Throughout the 16-week intervention period, all participants will be advised to follow the treatment plan given by the physician at 5 different clinics in a town south in Norway. *Usual care* may include regular consultations with physicians (every 14th day, duration 30-60 minutes) including counselling about sleep, activity, lifestyle, anti-depressive medication, and sick leave. The participants in the control group will be offered three healing sessions after the 10-week intervention period.

Implementation

The study nurse at NAFKAM will send the link to the questionnaire to the participants at baseline, weeks 8 and 16, and after 6 and 12 months, asking them to complete the questionnaire.

1. When the patient has signed the informed consent, the researchers at NAFKAM will formally include the patient according to the randomization system.

2. Included patients will be randomized to spiritual healing plus usual care (intervention group) or usual care alone (control group). Directly after randomization and if assigned to healing, name and phone-number of the patients will be sent by SMS to the spiritual healer. The healer will then contact the patient who will receive the first healing session within 14 days after enrolment. The patient will be offered 10 healing sessions.

3. Patients in the control group will receive usual care as agreed with their physician.

4. Patients in the intervention group and control group are urged to follow the treatment recommendations given by the physician (for example anti-depressant medication).

5. The last follow-up healing treatment session must be completed by the end of week 16 of the study (the day of the first healing session is defined as week 0).

Follow up

1. The study nurse will ask the participants to complete the electronic BDI questionnaire in weeks 8 and 16. In addition, they will be asked to register information about adverse effects as part of the form.

2. The study nurse will contact the participants after 6 and 12 months and remind them to complete the electronic BDI questionnaire (follow-up data).

3. Interviews will be conducted with participants in both groups at the end of the intervention period (week 16). See figure 1.

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment

Withdrawal and loss to follow-up

If a patient chooses to withdraw before week 16, all data collected will be permanently deleted. If the patient is lost to follow-up, data collected up to the day of drop out will be used for analysis.

Statistical analysis

Differences in BDI scores between groups as well as adverse effects will be described descriptively only, due to the pilot nature of the study. To investigate whether there is a statistical indication of an effect of healing indicating a later full size-scale trial, we will apply the separation test, a statistical procedure for early-phase research, to decide whether to pursue further research (36). The separation test will be based on calculations regarding the mean reduction in symptoms, and the between-group difference from baseline to weeks 8 and 16, and from baseline to day 6 and 12 months for the intervention group (healing and usual care) versus the control group (usual care).

The last author (AEK) will perform the statistical analysis. Data analysis will be done utilizing the IBM statistical package SPSS v 28 (http://www.spss.com).

Qualitative analysis

The qualitative data will be analyzed based on a directed qualitative content analysis, because the field will benefit from further description (40). Categories and codes will be developed inductively from the data and deductively according to themes of the structured interview guide and the research questions. Included themes will be supported by evidence in form of participants´ statement (quotations).

Patient and public involvement

In this study, patients will be interviewed about their study experiences and the main outcomes of this study are recruitment, willingness to randomization, and other feasibility measures.

Sample size

No sample size calculation is needed for a pilot RCT. The findings of this pilot study will be used to calculate the sample size in a potential future RCT. A study size of n=16 participants, n=8

in each group is chosen to generate sufficient interviews (saturation on that point is assumed) for the qualitative study (41).

Data handling management

All patient data and the index that links trial numbers with individual participants will be kept under lock, and the key will be in the possession of NAFKAM. Trial number alone will identify all data.

Coding and punching

Data entry will be undertaken at NAFKAM. All data will be read twice to ensure against random bias in the coding and punching process. The first author (TS) will be responsible for obtaining and analyzing the qualitative data.

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment, in??? here.

MADRS: Montgomery and Åsberg Depression Rating Scale
BDI: Beck Depression Inventory

Ethics and dissemination

The patients will be informed about the study through an information folder and verbally by the study nurse, and, if willing to participate, asked to give a written informed consent. The participants will be informed that they can withdraw from the study at any time without any consequences. All patients will follow usual care regardless of healing treatment, and adverse effects will be recorded at each treatment session. No systematic studies have been published on adverse effects of spiritual healing for depression. However, previous research has demonstrated that spiritual healing is associated with low risk (27). The study will be conducted in accordance with the Helsinki declaration (42). This protocol was approved by The Regional Committees for Medical and Health Research Ethics (REK) by the identifier (63692) and registered at The Norwegian Center for Research Data (NSD) (845302) and clinicaltrials.gov (ID: NCT04766242).

The results of this protocol will be published in at least two scientific papers in peer-reviewed journals. In addition, results will be presented orally and on posters at national and international

conferences. Following the publication in scientific journals, the project will be communicated through the web portal of (NAFKAM) www.nafkam.no. The Norwegian authorities will also be notified in written communication about the results of the study.

Data and safety monitoring

A steering group will be responsible for quality control and meet on a regular basis throughout the study period. The steering group will be convened as an emergency in the event of serious adverse effects associated with the trial to decide on appropriate action to prevent recurrence. Regular meetings will concern any reported adverse effects, protocol violation, the recruitment rate, practical issues concerning local coordination, as well as any issues raised by the participants.

Discussion

To the best of our knowledge, this is the first pilot RCT investigating the feasibility of the study design and the participants´ experience of spiritual healing and usual care for patients with moderate depression in Norway. This research team has previously conducted an observational study investigating self-reported effect of healing, with a pre - post design (28). The rationale for the study was that Norwegian patients with chronic diseases and psychological problems reported frequent use of spiritual healing (14-36%) (43). Moreover, 38% of cancer patients in Northern Norway reported to have used spiritual healing (44). Generally, most CAM interventions are under-researched, taking into consideration that they are widely practiced, and limited information is available about their clinical effectiveness and risk profile. Observational studies are well suited to investigate these questions in a real life setting (45).

Therefore, to get more nuanced information, we aimed to map the conditions patients reported when visiting a healer for the first time, and to evaluate the subjective benefits and risks from the intervention. Results from the above-mentioned observational study reported that a total of 23% of the participants reported psychological complaints such as anxiety and depression. These complaints were reduced from a pretreatment score of 4.7 to a post treatment score of 2.3, measured by Measure Yourself Medical Outcome Profile (MYMOP) (46). This reduction was achieved after a mean of 4.1 spiritual healing sessions (ranges 1-17). Forty percent of the

participants reported one or more adverse effects after treatment. These were perceived by the participants as minor and transient. However, these results must be interpreted with care since no interference statistical analysis of effect was performed. Due to the lack of a control group, we cannot draw the conclusion that the findings are exclusive due to the spiritual healing treatment.

Based on the findings from the previous observational study, and in preparation for a larger RCT, we want to investigate the recruitment speed, participants' willingness to be randomized, study adherence, and implementation of healing compared to usual care for moderate depression. We will also investigate the change in severity of depression measured by BDI.

Strengths and limitations

This protocol must be understood in light of the study limitations. Because of the COVID-19 pandemic and lockdown of the society, only one healer will be implementing the healing sessions as opposed to the two originally planned. Due to the overload of patients in clinical practice and implementation of pandemic protocols (such as vaccination of patients) the implementation of the trial has been negatively affected. The physicians who will recruit patients to the trial have been occupied with corona patients. However, several physicians working in five different conventional health clinics will recruit patients to the trial providing an insight on different methods of usual care. A multi-disciplinary research team consisting of CAM providers, physicians, psychiatrists, and researchers will safeguard a methodology in line with a whole system research approach. Lastly, to enhance patient safety, the research team will record adverse effects of both healing and usual care.

Figure legends

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment

Declarations

Author contributions

TS and AEK initiated this study, developed the concept and study design. ACI, AHH, OKB and CG contributed with intellectual content. Trine Stub wrote the first draft of the manuscript and

all authors reviewed subsequent versions of the manuscript. All authors read and approved the final version of the manuscript.

Funding

No external funding was received for this study.

Competing interest statement

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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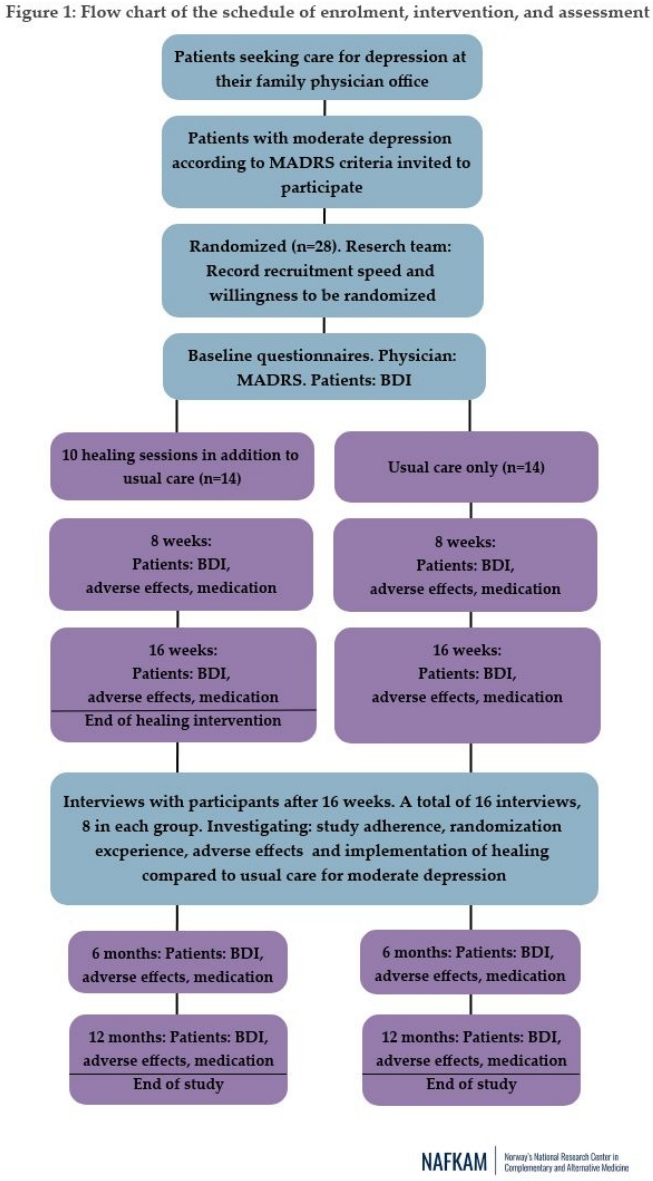

Figure 1: Flow chart of the schedule of enrollment, intervention, and assessment

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym. *The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)*
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. *clinicaltrials.gov (ID: NCT04766242)*
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier. *OK*
Funding	4	Sources and types of financial, material, and other support. *Page 16 (funding)*
.Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors. *Page 16 (authors contribution)*
	5b	Name and contact information for the trial sponsor. *Not Applicable (NA)*
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities. *NA*
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee). *NA*
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention. *Page 5-6 (introduction)*
	6b	Explanation for choice of comparators. *Page 5-6 (introduction)*

Objectives	7	Specific objectives or hypotheses. *Page 7 (Objectives)*
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained. *Page 8 (Setting)*
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists). *Page 8 (Inclusion, exclusion criteria)*
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. *Page 10-11 (treatment plan, Intervention)*
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). *Page 14, (Data and safety monitoring)*
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). The *study nurse will contact the participants if not completed the questionnaires.*
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial. *Yes*
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended. *Page 9 (primary and secondary outcome) and page 7 (Design)*
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure). *Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment*

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations. *Page 12 (Statistical analysis)*
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. *Page 8 (Recruitment).*
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions. *Upon signed consent form and completed baseline questionnaire, randomization is performed as described at page 9.*
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned. *Page 9 (Blinding)*
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions? *Page 11 (Implementation).*
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. *Page 9 (Blinding)*
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial. *NA*
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol. *Page 10 (Measurements)*
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols. *Page 15 (Data and safety monitoring) and page 12 (withdrawal and loss to follow-up).*

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. *Page 13 (Data handling management, and coding and punching)*
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. *Page 12 and13.*
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses). *Page 12 and 13.*
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation). *Page 12.*
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed. *NA*
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. *NA*
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct. *Page 10 (Measurements) and page 9 (secondary outcome).*
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor. *NA*
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval. *Page 14-15.*
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators). *Page2 (Abstract)*
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32). *Page 11 (Implementation)*

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable. *NA*
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial. *Page 13.*
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site. *No competing interest*
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators. *Only researchers involved in this project will have access to final trail dataset.*
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation. *NA*
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions. *The result of the trial, will be published in a relevant international journal with authorship following the Vancouver statement.*
	31b	Authorship eligibility guidelines and any intended use of professional writers. *NA*
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code. *NA*
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates. *NA*
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable. *NA*

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

BMJ Open

The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)

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The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)

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Abstract

Introduction

Depression is a common mental disorder and the (global) leading cause of all non-fatal burden of disease worldwide. Currently, supported treatment for depression is antidepressant medication and different psychotherapeutic interventions. Many patients experience, however, adverse effects of antidepressant medication, while at the same time the access to psychotherapeutic interventions are limited. Many patients who suffer from depression turn to complementary and alternative medicine (CAM) and among those modalities often spiritual healing. There is some evidence that consulting a spiritual healer can be beneficial for patients who suffer from depression, and that spiritual healing is associated with low risk. The aim of this protocol is to conduct a pilot RCT (spiritual healing as addition to usual care versus usual care alone) in preparation of a larger trial in adults with moderate depression, to examine feasibility and individuals' experience of spiritual healing.

Methods and analysis

This study is a pilot RCT with two parallel groups. A total of 28 adult patients with moderate depression, diagnosed by the physician and according to the Montgomery and Åsberg Depression Rating Scale (MADRS) criteria will be randomized to spiritual healing in addition to usual care (n=14) or usual care alone (n=14). To determine if there is a statistical indication of an effect of healing warranting a full-scale study, the separation test will be used. To investigate participants' experience with spiritual healing, a qualitative study will be included using semi-structured interviews. The data will be analyzed based on a direct content analysis.

Ethics and dissemination

This protocol was approved by regional committees for medical and health research ethics by the identifier (63692) and registered at The Norwegian Center for Research Data (NSD) (845302) and clinicaltrials.gov (ID: NCT04766242). The results will be disseminated through open-access, peer-reviewed publications, in addition to stakeholders´ reporting and presenting at conferences.

Strengths and limitations of this study

- Several physicians will recruit patients to the trial providing insight into different methods of usual care
- Because of COVID-19 lockdown, only one healer will be implementing the healing sessions as opposed to the two originally planned
- A multi-disciplinary research team consisting of CAM providers, physicians, psychiatrists, and researchers safeguard a whole system research approach
- To enhance patient safety, the research team will record adverse effects of both healing and usual care
- Due to the overload of patients and COVID-19 protocols, the implementation of the trial has been negatively affected

Introduction

Depression is a common mental disorder and is together with anxiety the (global) leading cause of all non-fatal burden of disease worldwide (1). The core symptoms of depression are lowered mood, discouragement, loss of sense and meaning in life, lack of interest in other people and ordinary duties, and lack of energy and appetite. In addition, the patients often experience diminished self-esteem, self-reproach and a feeling of guilt. These symptoms may vary in intensity and duration (2, 3). Nevertheless, around half of all people with depression worldwide do not receive appropriate treatment (4). Most mental disorders emerge before the age of 30 (5, 6), and lack of treatment might contribute to disability for many crucial years of an individual's life. In Norway, the 12 month prevalence and lifetime prevalence of depression is 10% and 20% respectively, higher in women than in men (2). Depression has been identified as a strong predictor for use of complementary and alternative medicine (CAM) (7-9). A recent Norwegian study demonstrates that only 10.9% of those with moderate depression and/or anxiety visited psychiatric outpatient services while 17.6% visited a CAM provider (10). These facts demonstrate that people with depression might be willing to seek help also from less established services, such as CAM providers. Thus, it is possible that different CAM modalities may serve as a substitute or an alternative when access to psychologist/psychiatric services is limited (10-12).

Conventional medicine classifies depression as a mood disorder that manifests itself across a wide range of disease/symptom severity. Depression can be classified as mild, moderate or severe (13). Symptoms must have been persistent for at least two weeks and not be related to other medical or psychiatric diagnoses, or be due to substances (14). The World Health Organization ranks the social costs of depression as the 4th highest of all diseases (15). Furthermore, by 2020 current trends indicate that depression will represent the highest cost for society of any disease (15). Clearly, prevention, early diagnosis, and intervention of depression have huge significance.

The most commonly prescribed antidepressant drug, selective serotonin reuptake inhibitors (SSRIs), has recently been shown to have the best effect on severe depression, and no effect beyond placebo for mild and moderate depression (16, 17). At the same time, SSRIs can be

associated with serious adverse effects (18), and are associated with increased vulnerability to develop a depressive episode later in life (16). Thus, one of the most common treatment options for depression has been documented to be of little or no help beyond placebo for moderate depression while at the same time possibly inducing serious adverse effects.

The Competence Center for Lived Experience and Service Development, investigate the needs for individuals with mental health problems. According to the center, many patients in psychological health care do not want to be treated with medication. These patients must be heard and taken seriously. We cannot force anyone to take medication as long as necessary care and treatment can be provided otherwise (19).

Cognitive behavioural therapy (CBT) or structured psychological therapy (20) is a treatment option for patients who do not want pharmaceutical antidepressant treatment. However, waiting lists for such treatment are often long due to the lack of competent professionals (psychologists and psychiatrists), especially in rural communities, and at the district psychiatric centers (21). These centers have to prioritize patients with major depression, meaning that patients with moderate depression have less access to CBT.

Spiritual healing for depression

Spiritual healing is one of the most frequently used CAM modalities in Norway (22). It is understood as an energy based therapeutic approach to healing. A spiritual healer uses the hands to balance and harmonize the body and thereby place the client in a position of self-healing (23). The healing treatment focuses on the whole person (physically, psychologically, and emotionally) as well as the environmental factors (support from family, friends, community). Scientific evidence indicates that users typically praise CAM modalities for offering symptoms relief, reducing adverse effects of conventional treatment, enhancing their ability to cope physiologically and emotionally, providing an alternative to pharmaceuticals, and offering a close patient-practitioner relationship during treatment (24).

There is some evidence that spiritual healing can be beneficial for patients who suffer from depression (25, 26), and spiritual healing is associated with low risk (27). In a preliminary study

conducted by the current research group, a mean decrease in depression score of 3.1 points (range 0-4) on a 7 point scale was found (n=9) (28). The symptom was rated on a scale from 0-6 where 0 was "as good as it could be"and 6 was "as bad as it could be" (MYMOP scale (29)). Only one patient reported no change in depression symptoms after healing treatment. None of the patients experienced worsening of depression symptoms during the healing treatment, while the majority (n=5) had a reduction of 4 points (28). More research is needed to confirm these findings and to identify modifications needed in the design of a larger RCT.

Objectives

The objectives of this study are to conduct a pilot Randomized Controlled Trial (RCT) (spiritual healing as addition to usual care versus usual care alone) in preparation of a larger trial in adults with moderate depression, and further to examine the feasibility of the study design and the participants´ experience of spiritual healing.

Methods and analysis

This is a multicenter pilot RCT with two parallel arms. Nested within the trial is a qualitative arm.

Design

A total of 28 individuals with moderate depression will be randomized to a spiritual healing intervention as an adjunct to usual care (n=14) or to usual care alone (control) (n=14). We will study the entire spiritual healing package understood as everything a healer does in a consultation (visiting a healer), including the use of hands to balance and harmonize the body and sometimes offering lifestyle advice. Included in the treatment is the interaction between the patient and the therapist. A positive interaction between the patient and the therapist (alliance) is necessary for the patient to feel free to verbally express painful present and past experiences that may be related to the patient's psychological complaints (30, 31) (e.g., pragmatic research approach).

Setting

In Norway, inhabitants receive treatment within the public health care system, while CAM providers, including healers, operate outside this system. Patients (themselves) generally cover the cost of these visits themselves. Since CAM practices are unregulated, anyone is allowed to use the term healer and treat patients. However, many healers are members of the Norwegian Healing Association that require a professional standard regarding healing skills. To ensure patient safety in cases of interventions related to health issues, members are required to obtain a professional insurance for injury to their patients caused by the treatment.

Study participants

Inclusion criteria

All patients must be 18 years or above. They have to suffer from depressive difficulties of moderate intensity and fulfil the criteria for depression diagnosed by the physicians included in the study, and score within the range of 20-29 on the MADRS depression rating scale (32, 33). Symptoms must have persisted for two weeks or more. In addition to a MADRS score of 20-29, the physicians who include patients will decide whether the patient is suited for inclusion based on the following observations: a) the patient is too healthy to be referred to District Psychiatric Center (DPS) and b) too ill to remain untreated.

Exclusion criteria

Patients are excluded for the following reasons: Chronic major or bipolar depression or any personality disorder (axis II); endocrine abnormality; suicidal potential; dementia; depression as direct physiological effects of a substance or a medical condition (such as Parkinson disease, epilepsy, and multiple sclerosis); substance abuse; history of psychosis or mania; heart valve disease; poorly controlled hypertension and diabetes mellitus; pregnancy (34); or inability to complete study forms.

Recruitment

Patients who visit their physician for mood related symptoms and fulfil the inclusion and do not fulfil any of the exclusion criteria will be asked by the physician if they want information about

the study. If the patients agree, they will receive an information folder and the informed consent. After that, the physician will send an SMS with contact information to the researchers at The National Center for Complementary and Alternative Medicine (NAFKAM). Subsequently, NAFKAM will contact the patients, inform further about the study, and include those who agree to participate. Before randomization, participants must read and sign the informed consent. To collect baseline data, a link to the electronic BDI form will be forwarded to the participants.

Randomization

We will use a randomization system with block sizes, that vary from two to six, to eliminate confounders of a personnel or structural nature, thus balancing group allocation throughout the study period. Within each block, an equal number of patients will be randomly allocated to either an intervention group with spiritual healing and usual care, or a control group with usual care alone.

Blinding

Patients will not be blinded regarding treatment allocation, in accordance with a pragmatic research approach. Neither the study physicians nor the study therapist will be blinded. The researchers will be blinded when analysing unidentified patient-reported data.

Intervention

Primary outcome measures

The study outcome will be recruitment speed, willingness to be randomized, study adherence, and implementation of healing compared to usual care for moderate depression.

Secondary outcome measures

Secondary outcomes will be change in severity of depression measured by Beck Depression Inventory (BDI) (35). This questionnaire will be completed by the study patients at baseline, after 8 and 16 weeks, and 6 and 12 months after inclusion to the study. The separation test (36) will be used to investigate an indication of an effect of healing in a full-scale study.

An adverse effect form will be completed after 8 and 16 weeks. The RELIS adverse effect scale (37) will be used to measure adverse effects and the questions about adverse effects will be included at the end of the BDI form.

Measurements

The Beck Depression Inventory for Primary Care (BDI-PC) (35) is a screening instrument for depression that minimizes the possibility of yielding spuriously high estimates of depression for patients with medical problems by focusing on symptoms of *sadness*, *pessimism*, *past failure*, *loss of pleasure (anhedonia)*, *self-dislike*, *self-criticalness*, and *suicidal thoughts* or *wishes*. Each item is rated on a 4-point scale ranging from 0 to 3 and summing up all of the highest ratings for each of its seven items scores the BDI-PC. To address the minimum Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV requirement for the duration of moderate depression symptoms, respondents are asked to describe themselves for the "past 2 weeks, including today." We will also collect demographic data such as age, gender, education, household, income, and work, in addition to use of drugs and diary supplements/herbs for depression (questionnaire baseline). In intervention weeks 10, 16, and 6 and 12 months, adverse effects and change in use of drugs and diary supplements/herbs will be registered.

Qualitative study

In a qualitative study, nested within the trial, the investigators will investigate participants' experiences of spiritual healing and usual care. The aim of the study is to collect information about the participants' lived experience of participating in the trial receiving healing and usual care interventions. The study is based on phenomenology as this study design explores what people experienced and focuses on their experience of a phenomenon (38) and will provide the investigators with more nuanced and in-depth data than data obtained only from the questionnaires (24).

The study will draw on data obtained through semi-structured interviews (39) conducted with 16 participants (n=16), eight (n=8) in the intervention group and eight (n=8) in the control group upon completion of the intervention period (week 16).

Based on an interview guide, the participants will be asked about their illness (severity, duration, previous treatment), how they experienced the treatment (advantages and disadvantages) provided during the study, if their expectations were met, and their willingness to be randomized. Furthermore, we will ask about adverse effects from the treatment, and the patient-provider relationship. The control group will be interviewed and asked about their experiences with usual care. Moreover, we will observe and register recruitment speed, study adherence, and implementation of healing compared to usual care.

Treatment plan

The study is planned to start in March 2022 and end of study (data collection) is March 2023.

Intervention

The spiritual healing will be based on an assessment of the total health situation of the individual patient. Spiritual healing will mainly consist of a treatment where the healers hold their hands for some time at different parts of the patient's body, known as "power points", outside the patient's clothing. The consultation might also include lifestyle advice. This can necessarily lead to slightly different treatment given to each patient. Each treatment will, however, last for 45-60 minutes.

The healer who will perform the healing is a trained member of the Norwegian Healer Association (Norges Healerforbund). She has been working full time as a spiritual healer for more than 20 years. As a member of the Norwegian Healer Association, she has liability insurance in cases of harmful effects of the treatment.

Usual care

Throughout the 16-week intervention period, all participants will be advised to follow the treatment plan given by the physician at 5 different clinics in a town south in Norway. *Usual care* may include regular consultations with physicians (every 14th day, duration 30-60 minutes) including counselling about sleep, activity, lifestyle, anti-depressive medication, and sick leave. The participants in the control group will be offered three healing sessions after the 10-week intervention period.

Implementation

The study nurse at NAFKAM will send the link to the questionnaire to the participants at baseline, weeks 8 and 16, and after 6 and 12 months, asking them to complete the questionnaire.

1. When the patient has signed the informed consent, the researchers at NAFKAM will formally include the patient according to the randomization system.

2. Included patients will be randomized to spiritual healing plus usual care (intervention group) or usual care alone (control group). Directly after randomization and if assigned to healing, name and phone-number of the patients will be sent by SMS to the spiritual healer. The healer will then contact the patient who will receive the first healing session within 14 days after enrolment. The patient will be offered 10 healing sessions.

3. Patients in the control group will receive usual care as agreed with their physician.

4. Patients in the intervention group and control group are urged to follow the treatment recommendations given by the physician (for example anti-depressant medication).

5. The last follow-up healing treatment session must be completed by the end of week 16 of the study (the day of the first healing session is defined as week 0).

Follow up

1. The study nurse will ask the participants to complete the electronic BDI questionnaire in weeks 8 and 16. In addition, they will be asked to register information about adverse effects as part of the form.

2. The study nurse will contact the participants after 6 and 12 months and remind them to complete the electronic BDI questionnaire (follow-up data).

3. Interviews will be conducted with participants in both groups at the end of the intervention period (week 16). See figure 1.

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment

Withdrawal and loss to follow-up

If a patient chooses to withdraw before week 16, all data collected will be permanently deleted. If the patient is lost to follow-up, data collected up to the day of drop out will be used for analysis.

Statistical analysis

Differences in BDI scores between groups as well as adverse effects will be described descriptively only, due to the pilot nature of the study. To investigate whether there is a statistical indication of an effect of healing indicating a later full size-scale trial, we will apply the separation test, a statistical procedure for early-phase research, to decide whether to pursue further research (36). The separation test will be based on calculations regarding the mean reduction in symptoms, and the between-group difference from baseline to weeks 8 and 16, and from baseline to day 6 and 12 months for the intervention group (healing and usual care) versus the control group (usual care).

The last author (AEK) will perform the statistical analysis. Data analysis will be done utilizing the IBM statistical package SPSS v 28 (http://www.spss.com).

Qualitative analysis

The qualitative data will be analyzed based on a directed qualitative content analysis, because the field will benefit from further description (40). Categories and codes will be developed inductively from the data and deductively according to themes of the structured interview guide and the research questions. Included themes will be supported by evidence in form of participants´ statement (quotations).

Patient and public involvement

In this study, patients will be interviewed about their study experiences and the main outcomes of this study are recruitment, willingness to randomization, and other feasibility measures.

Sample size

No sample size calculation is needed for a pilot RCT. The findings of this pilot study will be used to calculate the sample size in a potential future RCT. A study size of n=16 participants, n=8

in each group is chosen to generate sufficient interviews (saturation on that point is assumed) for the qualitative study (41).

Data handling management

All patient data and the index that links trial numbers with individual participants will be kept under lock, and the key will be in the possession of NAFKAM. Trial number alone will identify all data.

Coding and punching

Data entry will be undertaken at NAFKAM. All data will be read twice to ensure against random bias in the coding and punching process. The first author (TS) will be responsible for obtaining and analyzing the qualitative data.

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment, in??? here.

MADRS: Montgomery and Åsberg Depression Rating Scale
BDI: Beck Depression Inventory

Ethics and dissemination

The patients will be informed about the study through an information folder and verbally by the study nurse, and, if willing to participate, asked to give a written informed consent. The participants will be informed that they can withdraw from the study at any time without any consequences. All patients will follow usual care regardless of healing treatment, and adverse effects will be recorded at each treatment session. No systematic studies have been published on adverse effects of spiritual healing for depression. However, previous research has demonstrated that spiritual healing is associated with low risk (27). The study will be conducted in accordance with the Helsinki declaration (42). This protocol was approved by The Regional Committees for Medical and Health Research Ethics (REK) by the identifier (63692) and registered at The Norwegian Center for Research Data (NSD) (845302) and clinicaltrials.gov (ID: NCT04766242).

The results of this protocol will be published in at least two scientific papers in peer-reviewed journals. In addition, results will be presented orally and on posters at national and international

conferences. Following the publication in scientific journals, the project will be communicated through the web portal of (NAFKAM) www.nafkam.no. The Norwegian authorities will also be notified in written communication about the results of the study.

Data and safety monitoring

A steering group will be responsible for quality control and meet on a regular basis throughout the study period. The steering group will be convened as an emergency in the event of serious adverse effects associated with the trial to decide on appropriate action to prevent recurrence. Regular meetings will concern any reported adverse effects, protocol violation, the recruitment rate, practical issues concerning local coordination, as well as any issues raised by the participants.

Discussion

To the best of our knowledge, this is the first pilot RCT investigating the feasibility of the study design and the participants´ experience of spiritual healing and usual care for patients with moderate depression in Norway. This research team has previously conducted an observational study investigating self-reported effect of healing, with a pre - post design (28). The rationale for the study was that Norwegian patients with chronic diseases and psychological problems reported frequent use of spiritual healing (14-36%) (43). Moreover, 38% of cancer patients in Northern Norway reported to have used spiritual healing (44). Generally, most CAM interventions are under-researched, taking into consideration that they are widely practiced, and limited information is available about their clinical effectiveness and risk profile. Observational studies are well suited to investigate these questions in a real life setting (45).

Therefore, to get more nuanced information, we aimed to map the conditions patients reported when visiting a healer for the first time, and to evaluate the subjective benefits and risks from the intervention. Results from the above-mentioned observational study reported that a total of 23% of the participants reported psychological complaints such as anxiety and depression. These complaints were reduced from a pretreatment score of 4.7 to a post treatment score of 2.3, measured by Measure Yourself Medical Outcome Profile (MYMOP) (46). This reduction was achieved after a mean of 4.1 spiritual healing sessions (ranges 1-17). Forty percent of the

participants reported one or more adverse effects after treatment. These were perceived by the participants as minor and transient. However, these results must be interpreted with care since no interference statistical analysis of effect was performed. Due to the lack of a control group, we cannot draw the conclusion that the findings are exclusive due to the spiritual healing treatment.

Based on the findings from the previous observational study, and in preparation for a larger RCT, we want to investigate the recruitment speed, participants' willingness to be randomized, study adherence, and implementation of healing compared to usual care for moderate depression. We will also investigate the change in severity of depression measured by BDI.

Strengths and limitations

This protocol must be understood in light of the study limitations. Because of the COVID-19 pandemic and lockdown of the society, only one healer will be implementing the healing sessions as opposed to the two originally planned. Due to the overload of patients in clinical practice and implementation of pandemic protocols (such as vaccination of patients) the implementation of the trial has been negatively affected. The physicians who will recruit patients to the trial have been occupied with COVID-19 patients. However, several physicians working in five different conventional health clinics will recruit patients to the trial providing an insight on different methods of usual care. A multi-disciplinary research team consisting of CAM providers, physicians, psychiatrists, and researchers will safeguard a methodology in line with a whole system research approach. Lastly, to enhance patient safety, the research team will record adverse effects of both healing and usual care.

Figure legends

Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment

Declarations

Author contributions

TS and AEK initiated this study, developed the concept and study design. ACI, AHH, OKB and CG contributed with intellectual content. Trine Stub wrote the first draft of the manuscript and

all authors reviewed subsequent versions of the manuscript. All authors read and approved the final version of the manuscript.

Funding

No external funding was received for this study.

Competing interest statement

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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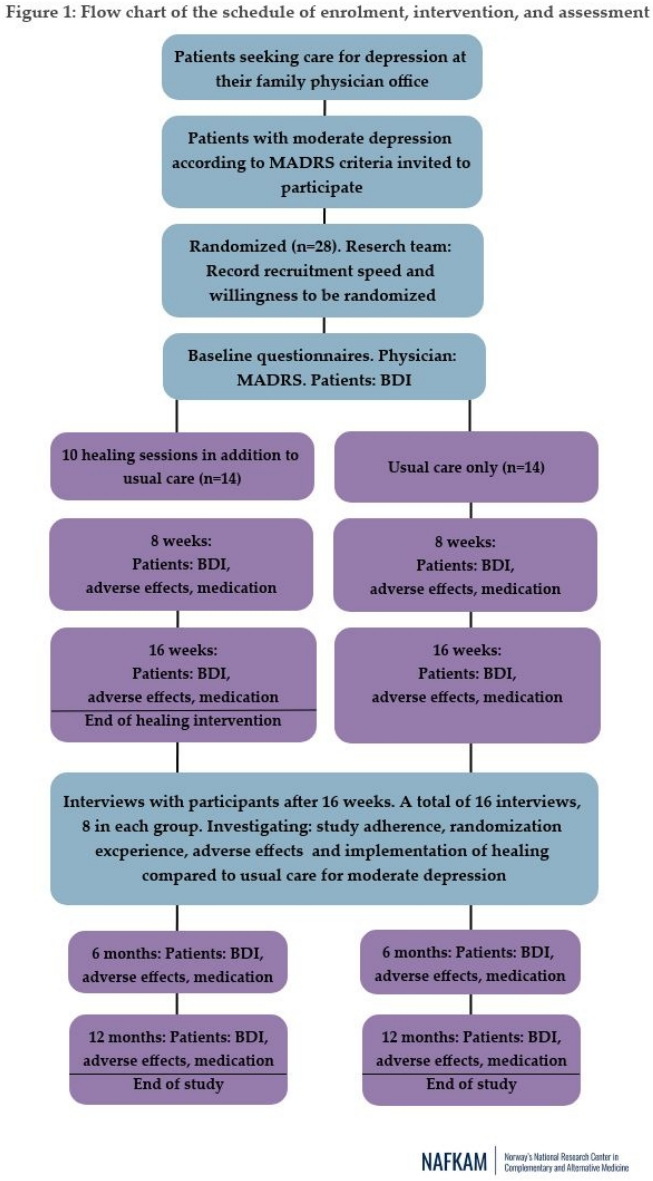

Figure 1: Flow chart of the schedule of enrollment, intervention, and assessment

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description
Administrative information		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym. *The impact of spiritual healing on moderate depression in adults: A study protocol of a pilot randomized controlled trial (RCT)*
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry. *clinicaltrials.gov (ID: NCT04766242)*
	2b	All items from the World Health Organization Trial Registration Data Set
Protocol version	3	Date and version identifier. *OK*
Funding	4	Sources and types of financial, material, and other support. *Page 16 (funding)*
.Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors. *Page 16 (authors contribution)*
	5b	Name and contact information for the trial sponsor. *Not Applicable (NA)*
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities. *NA*
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee). *NA*
Introduction		
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention. *Page 5-6 (introduction)*
	6b	Explanation for choice of comparators. *Page 5-6 (introduction)*

Objectives	7	Specific objectives or hypotheses. *Page 7 (Objectives)*
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)
Methods: Participants, interventions, and outcomes		
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained. *Page 8 (Setting)*
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists). *Page 8 (Inclusion, exclusion criteria)*
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered. *Page 10-11 (treatment plan, Intervention)*
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease). *Page 14, (Data and safety monitoring)*
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests). The *study nurse will contact the participants if not completed the questionnaires.*
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial. *Yes*
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended. *Page 9 (primary and secondary outcome) and page 7 (Design)*
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure). *Figure 1: Flow chart of the schedule of enrolment, intervention, and assessment*

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations. *Page 12 (Statistical analysis)*
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size. *Page 8 (Recruitment).*
Methods: Assignment of interventions (for controlled trials)		
Allocation:		
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions. *Upon signed consent form and completed baseline questionnaire, randomization is performed as described at page 9.*
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned. *Page 9 (Blinding)*
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions? *Page 11 (Implementation).*
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how. *Page 9 (Blinding)*
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial. *NA*
Methods: Data collection, management, and analysis		
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol. *Page 10 (Measurements)*
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols. *Page 15 (Data and safety monitoring) and page 12 (withdrawal and loss to follow-up).*

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol. *Page 13 (Data handling management, and coding and punching)*
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol. *Page 12 and13.*
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses). *Page 12 and 13.*
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation). *Page 12.*
Methods: Monitoring		
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed. *NA*
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. *NA*
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct. *Page 10 (Measurements) and page 9 (secondary outcome).*
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor. *NA*
Ethics and dissemination		
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval. *Page 14-15.*
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators). *Page2 (Abstract)*
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32). *Page 11 (Implementation)*

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable. *NA*
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial. *Page 13.*
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site. *No competing interest*
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators. *Only researchers involved in this project will have access to final trail dataset.*
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation. *NA*
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions. *The result of the trial, will be published in a relevant international journal with authorship following the Vancouver statement.*
	31b	Authorship eligibility guidelines and any intended use of professional writers. *NA*
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code. *NA*
Appendices		
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates. *NA*
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable. *NA*

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.