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Morita Therapy for depression and anxiety (Morita Trial): a pilot randomised controlled trial

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Keywords

Morita Therapy; Depression; Major Depressive Disorder; Feasibility study; Pilot randomised controlled trial

Abstract

Objective. To address uncertainties prior to the design and conduct of a fully-powered randomised controlled trial of Morita Therapy plus treatment as usual (TAU) versus TAU alone, or to determine that such a trial is not appropriate and/or feasible.

Design. Pilot parallel group randomised controlled feasibility trial.

Setting and participants. Participants aged ≥18 with DSM Major Depressive Disorder, with or without DSM anxiety disorder(s), recruited from General Practice record searches in Devon, UK.

Interventions. We randomised participants on a 1:1 basis stratified by symptom severity, concealing allocation using a secure independent web-based system, to receive TAU (Control) or eight to twelve sessions of Morita Therapy, a Japanese psychological therapy, plus TAU (Intervention).

Outcomes. Rates of recruitment, retention and treatment adherence; variance and estimated between-group differences in follow-up scores (on the PHQ-9 (depressive symptoms); GAD-7 (anxiety symptoms); SF-36/ WSAS (quality of life); MASA (attitudes)) and their correlation with baseline scores.

Results. We recruited 68 participants, 5.1% (95% CI 3.4% to 6.6%) of those invited (34 Control; 34 Intervention); 64/68 (94%; 95% CI 88.3% to 99.7%) provided follow-up data. Participants had a mean age of 49 and mean PHQ-9 score of 16.8; 61% were female. 24/34 (70.6%) adhered to the minimum treatment dose. The follow-up PHQ-9 pooled SD was 6.4 (95% CI 5.5 to 7.8); the magnitude of correlation between baseline and follow-up PHQ-9 scores was 0.42 (95% CI 0.19 to 0.61). 66.7% and 30.0% of participants recovered in the intervention and control groups respectively; 66.7% and 13.3% responded to treatment in the intervention and control groups respectively.

Conclusions. A large-scale trial of Morita Therapy would require 133 participants per group and is feasible with minor modifications to the pilot trial protocol. Morita Therapy shows promise in the treatment of depression and may provide patients with a distinct alternative to current treatments.

Trial registration. Current Controlled Trials ISRCTN17544090.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first randomised controlled trial of Morita Therapy for depression in English-speaking countries.
- Our pilot trial used mixed methods to address the procedural, methodological and clinical uncertainties associated with a large-scale trial.
- Criteria for success were specified a priori.
- The patients, clinicians and researchers were not blinded to group allocation, although self-report measures were used to reduce detection bias.

INTRODUCTION AND OBJECTIVES

Depression and generalised anxiety disorder (GAD) are the two most common mental health disorders: lifetime prevalence has been estimated at 16.2% and 5.7% for depression and GAD respectively, and one in six people in the UK experience such a disorder each year[1-3]. Globally, depression is the leading cause of disability, affecting 350 million people worldwide[4]. For individuals, depression is often chronic and recurrent, and rates of comorbidity and risk for suicide are high[2, 5-7]. Furthermore, the comorbidity between anxiety and depression makes a strong contribution to the total disability attributed to mental disorders[8-10]. Overall, the cost of depression and anxiety in the UK is significant at an annual rate of £17bn in lost output and direct health care costs, and a £9bn impact on the Exchequer through benefit payments and lost tax receipts[11].

Medication and Cognitive Behavioural Therapy (CBT) have the strongest evidence-base for treating these conditions, with each recommended by the National Institute for Health and Care Excellence (NICE)[12, 13]. However, many people are resistant to such interventions[14]. Indeed, current treatments appear to have had little impact on the prevalence of common mental disorders in the UK, and both depression and anxiety remain chronic disorders despite the available interventions[8, 15]. Recovery (defined as Patient Health Questionnaire 9 (PHQ-9)[16] score <10) is reached by fewer than 50% of patients who complete a NICE recommended psychological therapy within the 'Improving Access to Psychological Therapies' (IAPT) service, thereby increasing patients' risk of future relapses and the maintenance of chronic and recurring problems[17-19]. Similarly, studies suggest that between one third and half of depressed patients treated with psychotherapy or antidepressant medication do not respond to treatment (typically defined as a 50% reduction in symptoms)[20-26]. Thus, there is scope to develop and test new potentially effective treatments for depression and anxiety.

Morita Therapy is a Japanese psychotherapy developed by Dr Shōma Morita in 1919, and informed by Zen Buddhist principles[27, 28]. It is a holistic approach aiming to improve everyday functioning rather than targeting specific symptoms[29]. Through conceptualising unpleasant emotions as part of the natural ecology of human experience, Morita Therapy seeks to re-orientate patients in the natural world and potentiate their natural healing capacity. Morita therapists thus

help patients to move away from symptom preoccupation and combat, which are considered to exacerbate symptoms and interfere with this natural recovery process[30]. By helping patients to accept symptoms as natural phenomena which ebb and flow as a matter of course, Morita Therapy is in sharp contrast to the focus of established Western approaches on symptom reduction and control[31]. In Morita Therapy, patients are taught to live with, rather than be without, their symptoms.

Whilst other psychological therapies (such as Acceptance and Commitment Therapy[32]) also foster patients' acceptance of symptoms, through Morita's four experiential stages of rest and increasing action-taking, acceptance has a uniquely active, spontaneous and paradoxical quality: it cannot be brought about by deliberate cognitive reappraisal or meditative exercises (as per other approaches), only through everyday behavioural experience[29, 33, 34]. Indeed, according to Morita's unique method of shifting patients' attention away from self-reflection and immersing them in their environments, any efforts to consciously accept symptoms are considered counter-productive: maintaining focus on and therefore exacerbating symptoms[29, 34]. Thus, Morita Therapy is a unique psychotherapy with the potential to provide patients in the UK with a distinct and meaningful alternative to current treatment options.

Originally developed as an inpatient treatment for psychological problems similar to GAD, Morita Therapy is now applied to a wider range of conditions, including depression[29]. The approach is practiced in Japan and applied to a limited degree in countries including Australia, China, North America, Russia and Rwanda[29]. With few randomised controlled trials (RCTs) of Morita Therapy having been conducted worldwide, initial evidence for the efficacy of the approach is largely based on case studies, predominantly conducted in Japan[35] (Minami, M. 2011). However, Morita Therapy is untested within the UK, and to date no RCTs of Morita Therapy for depression have been undertaken in English-speaking countries. Although a fully-powered RCT is clearly required to establish the effectiveness of Morita Therapy, given the novelty of Morita Therapy in the UK a number of clinical, methodological and procedural uncertainties[36] prevented us from immediately undertaking such a trial.

Here, we report the results of a pilot RCT, comprising part of a mixed methods programme of research undertaken to prepare for the design and conduct of a fully-powered RCT of Morita Therapy plus treatment as usual (TAU) versus TAU alone, or to determine that such a trial is not appropriate and/or feasible. Our pilot RCT was designed to address the uncertainties associated with conducting a definitive trial by gathering information on (i) likely rates of recruitment, retention and treatment adherence and (ii) variance in participant outcomes and how these correlate with baseline scores, in order to inform future sample size calculations. It follows on from a programme of work conducted with patients and therapists to develop our Morita Therapy clinical protocol[37]. Findings from qualitative and mixed methods work undertaken alongside the trial, to explore the acceptability of Morita Therapy and how this relates to treatment adherence, are reported elsewhere.

Research questions

1. What proportion of participants approached to take part in a trial of Morita Therapy for depression will agree to do so?

2. What proportion of participants who agree to take part in the trial will remain in the trial at four month follow-up?

3. What proportion of participants who agree to take part in Morita Therapy will adhere to a pre-defined per-protocol dose of Morita Therapy?

4. What is the variance in participant outcomes following Morita Therapy plus TAU and TAU alone, and how do they correlate with participants' baseline scores?

5. What are the estimated between-group differences (and 95% confidence intervals) in participant outcomes following Morita Therapy plus TAU and TAU alone?

METHODS

Trial design

The Morita Trial was a mixed methods feasibility study encompassing a pilot trial and embedded qualitative interviews. The trial, reported here, used a parallel group randomised controlled design.

Participants

We recruited people aged ≥18 with Diagnostic and Statistical Manual of Mental Disorders (DSM)[38] Major Depressive Disorder, with or without accompanying DSM anxiety disorder(s), assessed using standard clinical interview (Structured Clinical Interview for DSM-IV-TR Axis Disorders, Clinical Trials Version[39]) (SCID). We excluded people who were cognitively impaired, had bipolar disorder or psychosis/psychotic symptoms, were substance dependent, were currently in receipt of psychological therapy, and those whose risk of suicide was sufficiently acute to demand immediate management by a specialist mental health crisis team.

We recruited participants through record searches at eight General Practices in Devon, UK, to identify potential participants from depression Read Codes. Practice staff contacted potentially eligible patients to seek permission for researcher contact. Adverts were also placed on the websites of the University of Exeter Medical School and Mood Disorders Centre (MDC) Accessing Evidence-Based Psychological Therapies (AccEPT) Clinic; leaflets and flyers were placed in the waiting rooms of consenting Devon General Practices; an email invitation was circulated to former MDC participants who had consented to such contact. People who responded to these invitations/ adverts were interviewed by the study team who provided detailed information on the study, assessed eligibility and took informed written consent. The study received ethical approval from the National Research Ethics Service South West – Frenchay (reference 15/SW/0103). The protocol has been published previously[40].

<insert link to Supplementary File 1 here>

Interventions

Morita Therapy plus treatment as usual

Participants allocated to the intervention group were asked not to engage in other formal courses of psychological therapy during the course of their treatment. Otherwise, they were free to access any other usual care and medication in liaison with their GP.

Morita Therapy consisted of eight to twelve one hour face-to-face weekly sessions delivered at the University of Exeter's MDC AccEPT clinic (http://www.exeter.ac.uk/mooddisorders/acceptclinic/) by two professionally accredited research therapists experienced in the delivery of psychological interventions, including experimental treatments. Therapists were trained in Morita Therapy over 6 months. Training included background reading, attending presentations, involvement in the development of the UK Morita Therapy outpatient protocol[37], and practical training led by DAR, a clinically qualified academic with ten-years' membership of the Japanese Society for Morita Therapy. Practical training was experiential: role plays, diary examples, additional reading and peer support as per a tailored therapist training programme developed by the study team[37].

Therapists followed the UK Morita Therapy outpatient protocol developed by the study team[37]. DAR provided fortnightly supervision of cases together with advice and support. A qualitative checklist highlighting the key components of Morita Therapy, and key discussions to be held in facilitating patients' engagement with the treatment phases, was used as an aide memoir to structure supervision discussions and the assessment of fidelity. With the patient's consent, all therapy sessions were audio recorded for use in supervision.

During therapy, patients progressed through Morita Therapy's four phases of rest and increasing action-taking in order to address fatigue, expand peripheral attention and move from a mood-oriented to purpose- and action-oriented lifestyle. Therapists aided patients in re-appraising their symptoms as part of the natural ecology of human experience; recognising the vicious cycle of symptom aggravation created by fixation on symptoms, contradictions between the 'real' and 'ideal', and attempts to fight or control otherwise inevitable emotions; and moving from a position of preoccupation with symptoms to acceptance of spontaneous affective experiences. Therapists continually reinforced the patient's shift from self-reflection towards a

focus on constructive action and the external environment. Patients completed daily diaries in which therapists wrote comments to increase communication and the opportunity for therapeutic reinforcement.

Treatment as usual alone

For the control group, no specific recommendation or requirement to alter the usual treatment received by depressed patients in the UK was made, and no restrictions were placed on the treatment options available to these participants. GPs were free to treat and refer participants as would be their normal practice and participants were free to access any other care and services, including formal courses of psychological therapy such as CBT.

All participants, irrespective of their allocation, were free to choose whether they took antidepressant medication.

Outcomes

We collected demographic data including SCID diagnoses at baseline assessment. We collected the following self-reported data at baseline and four months post-baseline: severity of depressive symptoms (PHQ-9); severity of generalised anxiety symptoms (Generalised Anxiety Disorder questionnaire 7 (GAD-7)[41]); quality of life (Short Form 36 Health Survey Questionnaire (SF-36)[42] and Work and Social Adjustment Scale (WSAS)[43]). We measured participants' attitudes towards themselves and their symptoms using a questionnaire developed for Morita Therapy-specific outcomes (Morita Attitudinal Scale for Arugamama (MASA)[44]).

We collected data on the flow of participants through the trial. For Morita Therapy participants, therapists also informed the study researchers of the number of therapy sessions attended and reason for ending treatment.

Trial success criteria

We defined criteria which should be met in order to determine if a fully-powered trial would be feasible or not[36, 40]. These were:

1. Participant recruitment and retention: we can recruit and retain sufficient participants to populate a fully-powered trial, i.e. at a recruitment rate of 12% of those invited and an attrition rate no higher than 20% of those randomised, in line with other UK National Institute of Health Research (NIHR) mental health trials[45, 46].

2. Participants will engage with and adhere to Morita Therapy at a rate on a par with other UK NIHR mental health trials[45], i.e. at least 65% of participants allocated to Morita Therapy attend the per-protocol minimum of ≥five sessions out of a maximum of twelve available sessions.

In terms of decision-making against these criteria, should we have fallen below any of these rates in our pilot trial we would consider whether protocol modification or close monitoring during a fully-powered RCT would address any failure to meet these criteria, or decide that a fully-powered trial would not be feasible[36].

Sample size

A conventional power calculation is inappropriate for the purpose of a pilot trial[36]. However, informed by our criteria above and guidance on using pilot studies to reliably estimate variance for participant outcomes[36, 47], we aimed to invite 570 potential participants, recruit 72 participants and follow-up 60 participants (30 in each arm). These figures were sufficient to estimate (i) participation rates (as percentage of subjects invited) of 10% with a margin of error of +/- 2.46%, or 12% with a margin of error of +/- 2.67%, or 15% with a margin of error of +/- 2.93%, based on 95% confidence intervals (CI); (ii) follow-up rates (as percentage of participants randomised) of 80% with a margin of error of +/- 9.24% or 85% with a margin of error of +/- 8.25%, based on 95% CI; (iii) the standard deviation (SD) of continuous outcomes to within 22% of their true value based on the upper limit of the 95% CI; (iv) a Pearson's correlation coefficient between baseline and follow-up scores with a margin of error of +/- 0.1 if the true correlation is 0.8, or +/- 0.14 if the true correlation is 0.7, or +/- 0.17 if the true correlation is 0.6.

Randomisation

We randomised participants in a 1:1 ratio to the intervention or control arm using a computer-generated random allocation sequence at the Exeter Clinical Trials Unit (ExeCTU). We stratified randomisation according to participants' symptom severity on the PHQ-9 and minimised allocation to balance the stratification variable across the two arms. To ensure allocation concealment, we randomised using an externally administered, password-protected randomisation website independently developed and maintained by ExeCTU. Allocation occurred on completion of an eligible participants' baseline assessment. Subsequently, the study researchers informed the participant and their GP, via standard letter, of the outcome and, for those randomised to the intervention group, passed participant details to the clinic to arrange treatment.

It was not possible to blind participants or clinicians to group allocation due to the nature of the intervention. The study researchers were not blinded to group allocation due to resource limitations. However, baseline and follow-up data were self-reported and all research measures were applied equally to both groups to reduce potential detection bias.

Statistical methods

We undertook all analyses on an intention to treat basis and did not impute missing data. We report recruitment, retention, treatment adherence and baseline characteristics using descriptive statistics: means and SDs for continuous variables; numbers and percentages for categorical variables. We report the SDs of the outcome measures (all continuous) with 95% CI for each trial arm at baseline and four months. We estimated the correlations between participants' scores on these measures at baseline and four months to inform the sample size calculation for a fully-powered trial. Although insufficiently powered to make inferential statements or calculate p-values, we report the observed differences between the intervention and control groups on the mean changes in these measures (with 95% CI), as well as proportions of participants recovering (follow-up PHQ-9 and GAD-7 scores <10[16, 41]) and responding to treatment (≥50% reduction in PHQ-9 and GAD-7 scores from baseline to follow-up) in each trial arm.

RESULTS

Participant flow

Participant flow through the trial is summarised in Figure 1.

We randomised 68 participants into the trial between October 2015 and September 2016: 34 (50%) to each trial arm. 146 potential participants gave permission for study researcher contact ('opted in'). We excluded 55/140 (39.3%) of those who could be contacted for telephone screen (24 did not meet inclusion criteria; 26 declined to participate; 5 were unable to arrange a baseline assessment) and 17/85 (20%) of those who attended baseline interview (15 did not meet inclusion criteria; 2 declined to participate). We randomised 68/146 (46.6%) of those who opted into the study. The 690 study invitations sent to potentially eligible patients identified via GP record search resulted in 35 participants randomised into the trial, a rate of 5.1% (95% CI 3.4% to 6.6%), with an additional 33 participants recruited from alternative sources such as advertising.

From January 2016 to January 2017, we collected four month follow-up data from 64/68 (94%) participants (95% CI 88.3% to 99.7%): 33/34 (97%) in the intervention arm and 31/34 (91%) in the control arm. In the intervention arm, one participant could not be contacted for follow-up; in the control arm, two participants could not be contacted for follow-up and one withdrew on the basis that they had not received active treatment. An additional control participant, after attending follow-up, revoked consent for their data to be included in the trial. Thus, whilst they are included within the participant flow figures, their data have not been included in the analysis of baseline characteristics or outcomes.

<insert Figure 1 (CONSORT diagram) here>

Baseline data

Baseline characteristics are summarised in Table 1.

Table 1. Participant baseline characteristics

	Intervention (n=34)	Control (n=33*)	Total (n=67)
Gender			
Female	22 (64.7)	19 (57.6)	41 (61.2)
Age (years)			
Mean (SD)	49.8 (14.8)	48.6 (15.9)	49.2 (15.2)
Ethic origin			
White British	31 (91.2)	30 (90.9)	61 (91.0)
White other	2 (5.9)	0 (0.0)	2 (3.0)
Mixed other	0 (0.0)	2 (6.1)	2 (3.0)
Asian Indian	0 (0.0)	1 (3.0)	1 (1.5)
Asian other	1 (2.9)	0 (0.0)	1 (1.5)
Education			
No qualifications	3 (8.8)	2 (6.1)	5 (7.5)
GCSE or O Level	7 (20.6)	6 (18.2)	13 (19.4)
Post GCSE or O Level	7 (20.6)	8 (24.2)	15 (22.4)
Undergraduate degree	9 (26.5)	10 (30.3)	19 (28.4)
Postgraduate qualification or higher	8 (23.5)	7 (21.2)	15 (22.4)
Marital status			
Married or cohabiting	23 (67.6)	16 (48.5)	39 (58.2)
Number of children			
Mean (SD)	1 (1)	1 (1)	1 (1)
History of depression			
One or more previous episodes	29 (85.3)	25 (75.8)	54 (80.6)
Age of onset (mean (SD))	28.9 (17.8)	25.2 (17.4)	27.1 (17.6)
Duration of current episode in months (mean (SD))	13.1 (12.8)	30.3 (43.8)	21.3 (32.4)
PHQ-9 (depression) score			
Mean (SD)	17.4 (4.7)	16.1 (4.5)	16.8 (4.6)
GAD-7 (anxiety) score			
Mean (SD)	13.3 (4.8)	12.2 (4.0)	12.7 (4.4)
Secondary SCID diagnoses (current)			
Any anxiety disorder	21 (61.8)	28 (84.8)	49 (73.1)
Generalised anxiety disorder	13 (38.2)	17 (51.5)	30 (44.8)
Social phobia	5 (14.7)	11 (33.3)	16 (23.9)
Panic disorder with agoraphobia	6 (17.6)	8 (24.2)	14 (20.9)
Panic disorder without agoraphobia	7 (20.6)	3 (12.6)	10 (14.9)
Post-traumatic stress disorder	3 (8.8)	7 (21.2)	10 (14.9)
Obsessive Compulsive Disorder	2 (5.9)	5 (15.2)	7 (10.4)

Specific phobia	1 (2.9)	4 (12.1)	5 (7.5)
Agoraphobia without panic disorder	1 (2.9)	1 (3.0)	2 (3.0)
Antidepressant treatment			
Currently prescribed antidepressants	20 (58.8)	20 (60.6)	40 (59.7)
Previous psychotherapy/ counselling (at least one course of)			
Any psychotherapy (not including counselling)	23 (67.6)	26 (78.8)	49 (73.1)
Cognitive Behavioural Therapy	20 (58.8)	21 (63.6)	41 (61.2)
Mindfulness-based Cognitive Therapy	8 (23.5)	6 (18.2)	14 (20.9)
Behavioural Activation	1 (2.9)	3 (9.1)	4 (6.0)
Eye Movement Desensitization and Reprocessing	2 (5.9)	2 (6.1)	4 (6.0)
Counselling	15 (44.1)	14 (42.4)	29 (43.3)
Other psychotherapy	9 (26.5)	10 (30.3)	19 (28.4)

Notes: data are number (%) unless stated otherwise; SD=standard deviation; percentages may not always total 100 due to rounding; *34 participants were randomised into the control arm, with 33 participants' characteristics included due to one participant revoking consent to include data.

Receipt of Morita Therapy

No participants in the intervention group declined to start Morita Therapy and 24/34 (70.6%) adhered to a per-protocol minimum (≥five sessions). The mean number of sessions attended for all participants was 7.7 (range 1-14; SD 4.0); the mean number attended for those who did and did not adhere to the minimum dose was 9.8 (range 5-14; SD 2.5) and 2.6 (range 1-4; SD 1.0) respectively.

Outcomes and estimation

The SD of the outcomes at baseline and follow-up by trial arm, with 95% CI, are reported in Table 2. At follow-up, the pooled SD around the mean PHQ-9 score (the primary outcome in any definitive trial) was 6.4 (95% CI 5.5% to 7.8%). The correlations between baseline and four month scores by trial arm, with 95% CI, are reported in Table 3.

Table 2. Variability in outcomes at baseline and four month follow-up

Outcome	Intervention				Control				All participants			
	n	Mean	SD	95% CI	n	Mean	SD	95% CI	n	Mean	SD	95% CI
PHQ-9 baseline	34	17.4	4.7	3.8 to 6.2	33	16.1	4.5	3.6 to 6.0	67	16.8	4.6	3.9 to 5.6
PHQ-9 4 months	33	8.4	6.5	5.2 to 8.6	30	12.4	5.7	4.6 to 7.7	63	10.3	6.4	5.5 to 7.8
GAD-7 baseline	34	13.3	4.8	3.9 to 6.4	33	12.2	4.0	3.2 to 5.3	67	12.7	4.4	3.8 to 5.3
GAD-7 4 months	32	6.8	5.2	4.2 to 7.0	30	8.7	4.7	3.7 to 6.3	62	7.7	5.0	4.3 to 6.1
WSAS baseline	34	22.7	7.9	6.3 to 10.3	33	22.1	7.4	6.0 to 9.8	67	22.4	7.6	6.5 to 9.2
WSAS 4 months	32	13.5	11.0	8.9 to 14.7	30	18.0	9.4	7.5 to 12.7	62	15.7	10.5	8.9 to 12.7
MASA baseline	34	80.7	29.3	23.6 to 38.5	33	72.7	23.0	18.5 to 30.5	67	76.8	26.5	22.6 to 31.9
MASA 4 months	32	114.4	40.3	32.3 to 53.6	30	91.8	27.7	22.1 to 37.3	62	103.5	36.3	30.9 to 44.2
SF-36 PCS baseline	34	49.6	12.3	10.0 to 16.2	33	52.2	10.6	8.5 to 14.0	67	50.9	11.5	9.8 to 13.9
SF-36 PCS 4 months	33	47.9	13.0	10.5 to 17.2	30	51.1	10.8	8.6 to 14.5	63	49.4	12.0	10.2 to 14.6
SF-36 MCS baseline	34	25.0	8.8	7.1 to 11.6	33	23.8	6.6	5.3 to 8.7	67	24.4	7.8	6.6 to 9.3
SF-36 MCS 4 months	33	39.8	11.9	9.6 to 15.7	30	30.1	11.0	8.8 to 14.8	63	35.2	12.4	10.5 to 15.0

Notes: SD=standard deviation of the mean; 95% CI = 95% confidence intervals around the standard deviation.

Table 3. Correlation between participant scores at baseline and four months

Association	Participants	n	Rho	95% CI	p
PHQ-9 at baseline and 4 months	All	63	0.42	0.19 to 0.61	<0.001
	Intervention	33	0.37	0.04 to 0.64	0.032
	Control	30	0.71	0.47 to 0.85	<0.001
GAD-7 at baseline and 4 months	All	62	0.40	0.17 to 0.59	0.001
	Intervention	32	0.40	0.07 to 0.66	0.022
	Control	30	0.51	0.18 to 0.73	0.004
WSAS at baseline and 4 months	All	62	0.52	0.31 to 0.68	<0.001
	Intervention	32	0.45	0.12 to 0.69	0.009
	Control	30	0.76	0.55 to 0.88	<0.001
MASA at baseline and 4 months	All	62	0.58	0.39 to 0.73	<0.001
	Intervention	32	0.45	0.12 to 0.69	0.009
	Control	30	0.73	0.50 to 0.86	<0.001
SF-36 PCS at baseline and 4 months	All	63	0.68	0.52 to 0.80	<0.001
	Intervention	33	0.78	0.59 to 0.88	<0.001
	Control	30	0.58	0.27 to 0.78	<0.001
SF-36 MCS at baseline and 4 months	All	63	0.42	0.20 to 0.61	<0.001
	Intervention	33	0.43	0.10 to 0.67	0.012
	Control	30	0.39	0.04 to 0.66	0.033

Notes: Rho=Spearman's Rho; 95% CI = 95% confidence intervals around Spearman's Rho.

Outcomes in the intervention and control arms at baseline and follow-up, with observed between-group differences in changes from baseline to follow-up (with 95% CI), are summarised in Table 4. Depressive symptoms reduced from baseline to follow-up by an average of 9 PHQ-9 points in the intervention group and an average of 3.5 PHQ-9 points in the control group.

Table 4. Treatment outcomes at baseline and four month follow-up with between-group differences

Outcome measure	Participants	Baseline			4 months			Change from baseline to 4 months			Between-group difference	
		n	Mean	SD	n	Mean	SD	n	Mean	SD	Mean	95% CI
PHQ-9	All	67	16.8	4.6	63	10.3	6.4	63	-6.3	5.8	-5.5	-8.1 to -2.9
	Intervention	34	17.4	4.7	33	8.4	6.5	33	-9.0	5.9		
	Control	33	16.1	4.5	30	12.4	5.7	30	-3.5	4.2		
GAD-7	All	67	12.7	4.4	62	7.7	5.0	62	-5.0	5.2	-3.3	-5.8 to -0.7
	Intervention	34	13.3	4.8	32	6.8	5.2	32	-6.6	5.6		
	Control	33	12.2	4.0	30	8.7	4.7	30	-3.3	4.3		
WSAS	All	67	22.4	7.6	62	15.7	10.5	62	-6.8	8.8	-5.9	-10.1 to -1.7
	Intervention	34	22.7	7.9	32	13.5	11.0	32	-9.7	9.7		
	Control	33	22.1	7.4	30	18.0	9.4	30	-3.7	6.5		
MASA	All	67	76.8	26.5	62	103.5	36.3	62	25.3	30.6	15.5	0.4 to 30.7
	Intervention	34	80.7	29.3	32	114.4	40.3	32	32.8	37.2		
	Control	33	72.7	23.0	30	91.8	27.7	30	17.2	19.0		
SF-36 PCS	All	67	50.9	11.5	63	49.4	12.0	63	-1.9	7.5	0.6	-3.2 to 4.4
	Intervention	34	49.6	12.3	33	47.9	13.0	33	-1.7	6.6		
	Control	33	52.2	10.6	30	51.1	10.8	30	-2.2	8.5		
SF-36 MCS	All	67	24.4	7.8	63	35.2	12.4	63	10.8	11.5	8.1	2.7 to 13.6
	Intervention	34	25.0	8.8	33	39.8	11.9	33	14.7	11.3		
	Control	33	23.8	6.6	30	30.1	11.0	30	6.6	10.3		

Notes: SD=standard deviation of the mean; 95% CI = 95% confidence intervals around the mean between-group difference.

Proportions of recovery and response on the PHQ-9 (depressive symptoms) and GAD-7 (anxiety symptoms) by trial arm are summarised in Table 5. At follow-up, 22/33 participants in the intervention group (66.7%) scored below the threshold for moderate depression (PHQ-9 <10) with 9/30 controls (30.0%) similarly recovering. Depressive symptoms reduced by ≥50% from baseline to follow-up for 22/33 participants in the intervention group (66.7%) and 4/30 controls (13.3%).

Table 5. Proportions of recovery and response at four month follow-up

			Recovery	Response	
Outcome measure	**Participants**	**n**	**n (%) scoring <10 at follow-up**	**n (%) showing 50% reduction**	**n (%) either showing 50% reduction or scoring <10 at follow-up**
PHQ-9	All	63	31 (49.2)	26 (41.3)	32 (50.8)
	Intervention	33	22 (66.7)	22 (66.7)	23 (69.7)
	Control	30	9 (30.0)	4 (13.3)	9 (30.0)
GAD-7	All	62	40 (64.5)	27 (43.5)	40 (64.5)
	Intervention	32	24 (75.0)	17 (53.1)	24 (75.0)
	Control	30	16 (53.3)	10 (33.3)	16 (53.3)

DISCUSSION

In this pilot RCT we have demonstrated that it is possible to recruit UK-based people with depression into a trial of Morita Therapy, and to retain them at four month follow-up at a rate which is equivalent to or exceeds that found in other trials in the field[e.g. 25, 46, 48, 49]. Participants' adherence to the minimum dose of Morita Therapy was on a par with other psychological therapies in similar trials[e.g. 25]. Furthermore, depressive symptoms reduced from baseline to follow-up by an average of 9 PHQ-9 points in the intervention group and 3.5 points in the control group: a between-group difference exceeding the PHQ-9 minimum clinically important difference (MCID)[50]. Rates of recovery and response to Morita Therapy (66.7%) were at least as good as those achieved by leading evidence-based psychological therapies[17, 18, 20-26].

Strengths and limitations

A key strength of this trial is that it represents not only the first study of Morita Therapy in the UK but the first randomised controlled trial of Morita Therapy for depression within English-speaking countries. Whilst the findings are consistent with previous studies which suggest possible benefits of Morita Therapy[35, 51, 52] (Minami, M. 2011), this study provides a valuable contribution in terms of applying Morita Therapy to a UK population, and by employing a rigorous methodology in

preparation for a fully-powered trial. The methods utilised were suitable for a feasibility study: the study purpose and research questions accorded with The National Institute for Health Research Evaluation Trials and Studies' definition of a feasibility study[53], endorsed by Arain et. al.[54]; the trial was designed to address key uncertainties associated with a large-scale trial; criteria for success were specified a priori[36].

Due to resource limitations, the study researchers were not blinded to group allocation. Whilst baseline and follow-up data were self-reported, and all research measures were applied equally to both groups, it is possible that this introduced detection bias into the study[55, 56] and blinding of study researchers would be ensured in any future definitive trial.

Implications and future research

We can now estimate the parameters necessary in order to design a fully-powered trial based on the 95% confidence intervals around our current data: we estimate that (i) the randomisation rate (as percentage of patients invited via GP record searches alone) would be between 3.4% and 6.6%; (ii) the retention rate would be between 88.3% and 99.7%; (iii) the pooled SD on the PHQ-9 score at follow-up would be between 5.5 and 7.8. Using our pilot trial data alongside the most conservative estimate of the between-group difference based on the published PHQ-9 MCID (2.59)[50], we also estimate that 133 participants per group would be required to provide 90% power based on a two-sided 5% significance level and allowing for 20% attrition. Our previous experience leads us to assert that we could reasonably expect to recruit such numbers into a future trial.

We specified two criteria for success[36] for proceeding to a fully-powered trial. Our pilot trial attrition rate of 6% fulfils the specified standard (no higher than 20%), as does the treatment adherence rate of 70.6% (at least 65%). Whilst the recruitment rate from GP record searches alone (5.1%) was lower than anticipated, this is slightly higher than that found in other trials in the field[e.g. 48, 49]. In a fully-powered trial, recruitment might be maximised by identifying additional participants through advertising and utilising research registers (as per our current study) and by modifying the pilot trial protocol to include measures known to improve recruitment

rates, such as telephone reminders to non-responding patients invited via GP record search[57-59]. We therefore anticipate that a sufficient number of participants to populate a fully-powered trial can be recruited, albeit with additional procedures, and conclude that a fully-powered trial is feasible with minor modifications to the pilot trial protocol in relation to our recruitment activities.

The level of participant adherence to Morita Therapy suggests that it is as acceptable to participants as other psychological treatments[25]. Whilst it is not the purpose of this paper to assess the effectiveness of Morita Therapy and the study was not powered to enable inferential statements to be made, our findings also suggest promising possible effects of Morita Therapy plus TAU versus TAU alone[60]. The observed between-group difference in reduction in depressive symptoms (PHQ-9) from baseline to follow-up, and indeed the lower margin of error on this figure, exceeds the PHQ-9 MCID. Furthermore, the rates of recovery and treatment response found in this study are comparable to or exceed those found for current NICE recommended treatments for depression[17, 18, 20-26]. This data supports the potential value of Morita Therapy as a treatment for depression and, given the contrast between Morita Therapy and established Western approaches[31], as a treatment option which might provide patients with a meaningfully distinct alternative in the future.

Conclusions

We have determined that it is feasible to conduct a large-scale trial of Morita Therapy with minor modifications to the pilot trial protocol in order to maximise recruitment. Our findings indicate that Morita Therapy shows promise in the treatment of depression, supporting the potential of Morita Therapy to provide patients in the UK with a distinct and meaningful alternative to current treatment options.

FOOTNOTES

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions and acknowledgements

DAR proposed the study; HVRS as chief investigator and study researcher designed the study with the involvement of DAR and JF; HVRS drafted the study protocol and materials and obtained National Health Service ethical approval and research and development governance assurance; HVRS was responsible for project management, data collection and analysis; HVRS and DAR developed the UK Morita Therapy outpatient protocol; DAR supervised the study therapists. HVRS drafted the manuscript. All other authors contributed to editing of the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figure legend:

Figure 1. CONSORT diagram

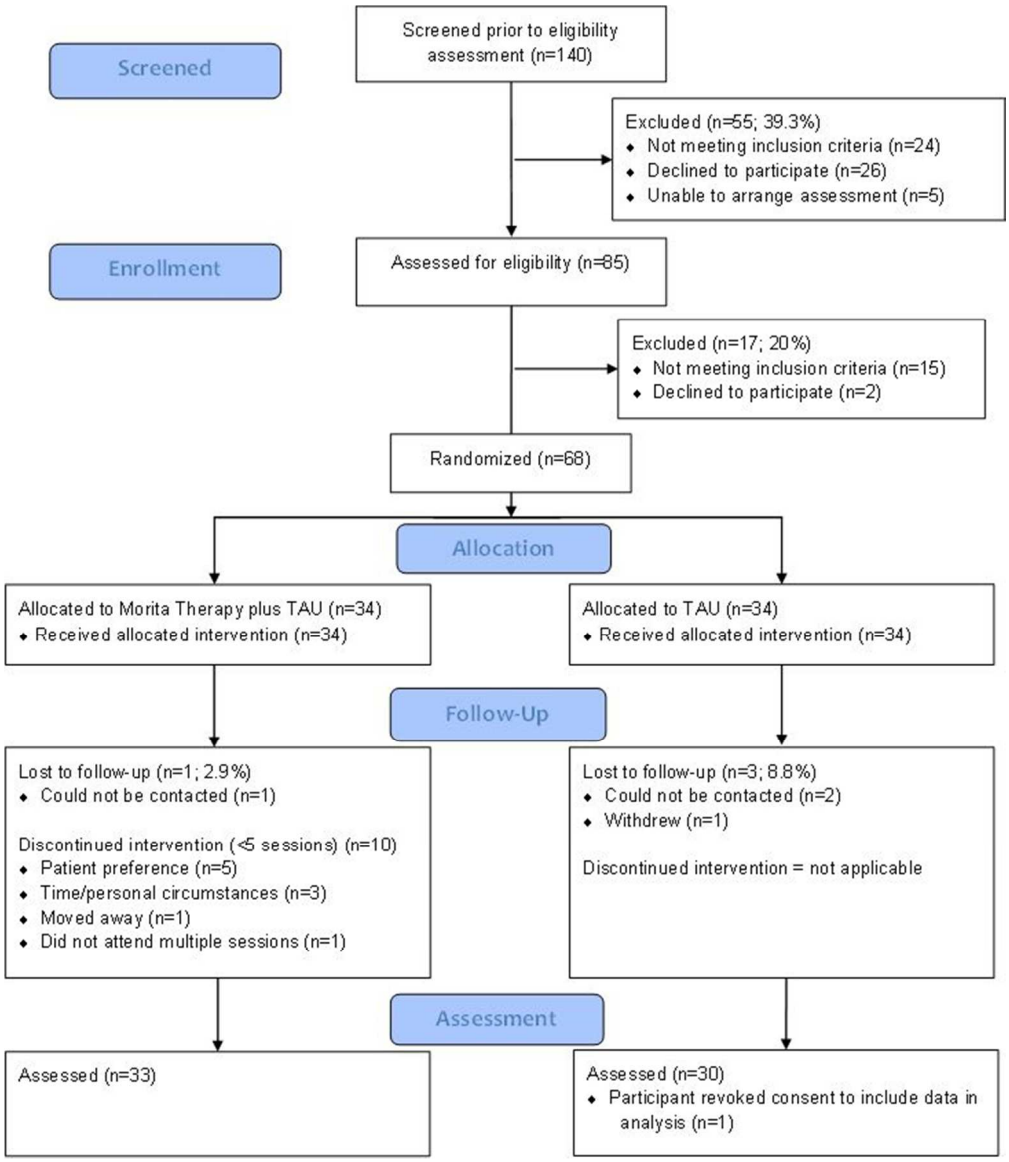

Figure 1. CONSORT diagram

61x71mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	1-2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	3-5
	2b	Specific objectives or research questions for pilot trial	5
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
	4c	How participants were identified and consented	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-8
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	8-9
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	9
Sample size	7a	Rationale for numbers in the pilot trial	9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	10
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	10

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	10
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	10
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	11
	13b	For each group, losses and exclusions after randomisation, together with reasons	11
Recruitment	14a	Dates defining the periods of recruitment and follow-up	11
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	12-13
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	14-17
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14-17
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	17-18
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	17-19
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	17-19
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	18-19
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	2
Protocol	24	Where the pilot trial protocol can be accessed, if available	6
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19-20
	26	Ethical approval or approval by research review committee, confirmed with reference number	6

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

BMJ Open

Morita Therapy for depression (Morita Trial): a pilot randomised controlled trial

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Secondary Subject Heading:	Health services research
Keywords:	Morita Therapy, Depression & mood disorders < PSYCHIATRY, Major Depressive Disorder, Feasibility study, Pilot randomised controlled trial

Morita Therapy for depression (Morita Trial): a pilot randomised controlled trial

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Word count 4683

Keywords

Morita Therapy; Depression; Major Depressive Disorder; Feasibility study; Pilot randomised controlled trial

Abstract

Objective. To address uncertainties prior to conducting a fully-powered randomised controlled trial of Morita Therapy plus treatment as usual (TAU) versus TAU alone, or to determine that such a trial is not appropriate and/or feasible.

Design. Pilot parallel group randomised controlled feasibility trial.

Setting and participants. Participants aged ≥18 with DSM-IV Major Depressive Disorder, with or without DSM-IV anxiety disorder(s), recruited from General Practice record searches in Devon, UK.

Interventions. We randomised participants on a 1:1 basis stratified by symptom severity, concealing allocation using a secure independent web-based system, to receive TAU (Control) or eight to twelve sessions of Morita Therapy, a Japanese psychological therapy, plus TAU (Intervention).

Outcomes. Rates of recruitment, retention and treatment adherence; variance and estimated between-group differences in follow-up scores (on the PHQ-9 (depressive symptoms); GAD-7 (anxiety symptoms); SF-36/ WSAS (quality of life); MASA (attitudes)) and their correlation with baseline scores.

Results. We recruited 68 participants, 5.1% (95% CI 3.4% to 6.6%) of those invited (34 Control; 34 Intervention); 64/68 (94%; 95% CI 88.3% to 99.7%) provided four month follow-up data. Participants had a mean age of 49 and mean PHQ-9 score of 16.8; 61% were female. 24/34 (70.6%) adhered to the minimum treatment dose. The follow-up PHQ-9 (future primary outcome measure) pooled SD was 6.4 (95% CI 5.5 to 7.8); the magnitude of correlation between baseline and follow-up PHQ-9 scores was 0.42 (95% CI 0.19 to 0.61). 66.7% and 30.0% of participants recovered in the intervention and control groups respectively; 66.7% and 13.3% responded to treatment in the intervention and control groups respectively.

Conclusions. A large-scale trial of Morita Therapy would require 133 participants per group and is feasible with minor modifications to the pilot trial protocol. Morita Therapy shows promise in treating depression and may provide patients with a distinct alternative to current treatments.

Trial registration. Current Controlled Trials ISRCTN17544090.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first randomised controlled trial of Morita Therapy for depression in English-speaking countries.
- Our pilot trial used mixed methods to address the procedural, methodological and clinical uncertainties associated with a large-scale trial.
- Criteria for success were specified a priori.
- The patients, clinicians and researchers were not blinded to group allocation, although self-report measures were used to reduce detection bias.

INTRODUCTION AND OBJECTIVES

Globally, depression is the leading cause of disability, affecting 350 million people worldwide[1]. In the UK, depression has a lifetime prevalence of 16.2%[2]. For individuals, depression is often chronic and recurrent, and rates of comorbidity and risk for suicide are high[2-5]. Furthermore, the comorbidity between depression and anxiety disorders, such as generalised anxiety disorder (GAD), makes a strong contribution to the total disability attributed to mental disorders[6-8]. Overall, the cost of depression and anxiety in the UK is significant at an annual rate of £17bn in lost output and direct health care costs [9].

Medication and Cognitive Behavioural Therapy (CBT) have the strongest evidence-base for treating depression, with each recommended by the National Institute for Health and Care Excellence (NICE)[10]. However, many people are resistant to such interventions[11]. Indeed, current treatments appear to have had little impact on the prevalence of common mental disorders in the UK, and depression remains a chronic disorder despite the available interventions[6, 12]. Recovery (defined as Patient Health Questionnaire 9 (PHQ-9)[13] score <10) is reached by fewer than 50% of patients who complete a NICE recommended psychological therapy within the 'Improving Access to Psychological Therapies' (IAPT) service, thereby increasing patients' risk of future relapses and the maintenance of chronic and recurring problems[14-16] Similarly, studies suggest that between one third and half of depressed patients treated with psychotherapy or antidepressant medication do not respond to treatment (typically defined as a 50% reduction in symptoms)[17-23]. Thus, there is scope to develop and test new potentially effective treatments for depression.

Morita Therapy is a Japanese psychotherapy developed by Dr Shōma Morita in 1919, and informed by Zen Buddhist principles[24, 25]. It is a holistic approach aiming to improve everyday functioning rather than targeting specific symptoms[26]. Through conceptualising unpleasant emotions as part of the natural ecology of human experience, Morita Therapy seeks to re-orientate patients in the natural world and potentiate their natural healing capacity. Morita therapists thus help patients to move away from symptom preoccupation and combat, which are considered to exacerbate symptoms and interfere with this natural recovery process[27]. By helping patients to accept symptoms as natural phenomena which

ebb and flow as a matter of course, Morita Therapy is in sharp contrast to the focus of established Western approaches on symptom reduction and control[28]. In Morita Therapy, patients are taught to live with, rather than be without, their symptoms.

Whilst other psychological therapies (such as Acceptance and Commitment Therapy[29]) also foster patients' acceptance of symptoms, through Morita's four experiential stages of rest and increasing action-taking, acceptance has a uniquely active, spontaneous and paradoxical quality: it cannot be brought about by deliberate cognitive reappraisal or meditative exercises (as per other approaches), only through everyday behavioural experience[26, 30, 31]. Indeed, according to Morita's unique method of shifting patients' attention away from self-reflection and immersing them in their environments, any efforts to consciously accept symptoms are considered counter-productive: maintaining focus on and therefore exacerbating symptoms[26, 31]. Thus, Morita Therapy is a unique psychotherapy with the potential to provide patients in the UK with a distinct and meaningful alternative to current treatment options.

Originally developed as an inpatient treatment for psychological problems similar to GAD, Morita Therapy is now applied to a wider range of conditions, including depression, and is considered a potentially pan-diagnostic approach given the absence of symptom-focus[26]. The approach is practiced in Japan and applied to a limited degree in countries including Australia, China, North America, Russia and Rwanda[26]. Initial evidence for the efficacy of Morita Therapy is largely based on case studies, predominantly conducted in Japan[32] (Minami, M. 2011). A limited number of randomised controlled trials (RCTs) in China and the USA provide mixed evidence for the effectiveness of inpatient Morita Therapy for post-schizophrenic depression[33] and in/outpatient Morita Therapy for anxiety[34-38]. However, Morita Therapy is untested within the UK, to date no RCTs of Morita Therapy for depression have been undertaken in English-speaking countries, and to our knowledge no RCTs of outpatient Morita Therapy for depression have been undertaken worldwide. Although a fully-powered RCT is clearly required to establish the effectiveness of Morita Therapy, given the novelty of Morita Therapy

in the UK a number of clinical, methodological and procedural uncertainties[39] prevented us from immediately undertaking such a trial.

Here, we report the results of a pilot RCT, comprising part of a mixed methods programme of research undertaken to prepare for the design and conduct of a fully-powered RCT of Morita Therapy plus treatment as usual (TAU) versus TAU alone, or to determine that such a trial is not appropriate and/or feasible. Our pilot RCT was designed to address the uncertainties associated with conducting a definitive trial by gathering information on (i) likely rates of recruitment, retention and treatment adherence and (ii) variance in participant outcomes and how these correlate with baseline scores, in order to inform future sample size calculations. It follows on from a programme of work conducted with patients and therapists to develop our Morita Therapy clinical protocol[40]. Findings from qualitative and mixed methods work undertaken alongside the trial, to explore the acceptability of Morita Therapy and how this relates to treatment adherence, are reported elsewhere.

Research questions

1. What proportion of participants approached to take part in a trial of Morita Therapy for depression will agree to do so?

2. What proportion of participants who agree to take part in the trial will remain in the trial at four month follow-up?

3. What proportion of participants who agree to take part in Morita Therapy will adhere to a pre-defined per-protocol dose of Morita Therapy?

4. What is the variance in participant outcomes (depressive symptoms; anxiety symptoms; qualitative of life; attitudes towards symptoms) following Morita Therapy plus TAU and TAU alone, and how do they correlate with participants' baseline scores?

5. What are the estimated between-group differences (and 95% confidence intervals) in participant outcomes (depressive symptoms; anxiety symptoms;

qualitative of life; attitudes towards symptoms) following Morita Therapy plus TAU and TAU alone?

METHODS

Trial design

The Morita Trial was a mixed methods feasibility study encompassing a pilot trial and embedded qualitative interviews. The trial, reported here, used a parallel group randomised controlled design.

Participants

We recruited people aged ≥18 with Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[41] Major Depressive Disorder, with or without DSM-IV anxiety disorder(s), assessed using standard clinical interview (Structured Clinical Interview for DSM-IV-TR Axis Disorders, Clinical Trials Version[42]) (SCID). We excluded people who were cognitively impaired, had bipolar disorder or psychosis/psychotic symptoms, were substance dependent, were currently in receipt of psychological therapy, and those whose risk of suicide was sufficiently acute to demand immediate management by a specialist mental health crisis team.

We recruited participants through record searches at eight General Practices in Devon, UK, to identify potential participants from depression Read Codes. Practice staff contacted potentially eligible patients to seek permission for researcher contact. Adverts were also placed on the websites of the University of Exeter Medical School and Mood Disorders Centre (MDC) Accessing Evidence-Based Psychological Therapies (AccEPT) Clinic; leaflets and flyers were placed in the waiting rooms of consenting Devon General Practices; an email invitation was circulated to former MDC participants who had consented to such contact. People who responded to these invitations/ adverts were interviewed by the study team who provided detailed information on the study, assessed eligibility and took informed written consent. The study received ethical approval from the National Research Ethics Service South West – Frenchay (reference 15/SW/0103). The protocol has been published previously[43] (see supplementary file 1).

Interventions

Morita Therapy plus treatment as usual

Participants allocated to the intervention group were asked not to engage in other formal courses of psychological therapy during the course of their treatment. Otherwise, they were free to access any other usual care and medication in liaison with their GP.

Morita Therapy consisted of eight to twelve one hour face-to-face weekly sessions delivered at the University of Exeter's MDC AccEPT clinic (http://www.exeter.ac.uk/mooddisorders/acceptclinic/) by two professionally accredited research therapists experienced in the delivery of psychological interventions, including experimental treatments. Therapists were trained in Morita Therapy over 6 months. Training included background reading, attending presentations, involvement in the development of the UK Morita Therapy outpatient protocol[40], and practical training led by the second author (DAR), a clinically qualified academic with ten-years' membership of the Japanese Society for Morita Therapy. Practical training was experiential: role plays, diary examples, additional reading and peer support as per a tailored therapist training programme developed by the study team[40].

Therapists followed the UK Morita Therapy outpatient protocol developed by the study team[40]. DAR provided fortnightly supervision of cases together with advice and support. A qualitative checklist highlighting the key components of Morita Therapy, and key discussions to be held in facilitating patients' engagement with the treatment phases, was used as an aide memoir to structure supervision discussions and the assessment of fidelity. With the patient's consent, all therapy sessions were audio recorded for use in supervision.

During therapy, patients progressed through Morita Therapy's four phases of rest and increasing action-taking in order to address fatigue, expand peripheral attention and move from a mood-oriented to purpose- and action-oriented lifestyle. Therapists aided patients in re-appraising their symptoms as part of the natural ecology of human experience; recognising the vicious cycle of symptom aggravation created by

fixation on symptoms, contradictions between the 'real' and 'ideal', and attempts to fight or control otherwise inevitable emotions; and moving from a position of preoccupation with symptoms to acceptance of spontaneous affective experiences. Therapists continually reinforced the patient's shift from self-reflection towards a focus on constructive action and the external environment. Patients completed daily diaries in which therapists wrote comments to increase communication and the opportunity for therapeutic reinforcement.

Treatment as usual alone

For the control group, no intervention (nor 'waiting-list' option) was offered by the study team. No specific recommendation or requirement to alter the usual treatment received by depressed patients in the UK was made, and no restrictions were placed on the treatment options available to these participants. GPs were free to treat and refer participants as would be their normal practice and participants were free to access any other care and services, including formal courses of psychological therapy such as CBT.

All participants, irrespective of their allocation, were free to choose whether they took antidepressant medication. For all participants, we informed their GP of their participation in the study and group allocation.

Outcomes

We collected demographic data including SCID diagnoses at baseline assessment. We collected the following self-reported data at baseline and four months post-baseline: severity of depressive symptoms (PHQ-9); severity of generalised anxiety symptoms (Generalised Anxiety Disorder questionnaire 7 (GAD-7)[44]); quality of life (Short Form 36 Health Survey Questionnaire (SF-36)[45] and Work and Social Adjustment Scale (WSAS)[46]). We measured participants' attitudes towards themselves and their symptoms using a questionnaire developed for Morita Therapy-specific outcomes (Morita Attitudinal Scale for Arugamama (MASA)[47]).

We collected data on the flow of participants through the trial. For Morita Therapy participants, therapists also informed the study researchers of the number of therapy sessions attended and reason for ending treatment.

Trial success criteria

We defined criteria which should be met in order to determine if a fully-powered trial would be feasible or not[39, 43]. These were:

1. Participant recruitment and retention: we can recruit and retain sufficient participants to populate a fully-powered trial, i.e. at a recruitment rate of 12% of those invited and an attrition rate no higher than 20% of those randomised, in line with other UK National Institute of Health Research (NIHR) mental health trials[22, 48].

2. Participants will engage with and adhere to Morita Therapy at a rate on a par with other UK NIHR mental health trials[22], i.e. at least 65% of participants allocated to Morita Therapy attend the per-protocol minimum of ≥five sessions out of a maximum of twelve available sessions.

In terms of decision-making against these criteria, should we have fallen below any of these rates in our pilot trial we would consider whether protocol modification or close monitoring during a fully-powered RCT would address any failure to meet these criteria, or decide that a fully-powered trial would not be feasible[39].

Sample size

A conventional power calculation is inappropriate for the purpose of a pilot trial[39]. However, informed by our criteria above and guidance on using pilot studies to reliably estimate variance for participant outcomes[39, 49], we aimed to invite 570 potential participants, recruit 72 participants and follow-up 60 participants (30 in each arm). These figures were sufficient to estimate (i) participation rates (as percentage of subjects invited) of 10% with a margin of error of +/- 2.46%, or 12% with a margin of error of +/- 2.67%, or 15% with a margin of error of +/- 2.93%, based on 95% confidence intervals (CI); (ii) follow-up rates (as percentage of participants randomised) of 80% with a margin of error of +/- 9.24% or 85% with a margin of error

of +/- 8.25%, based on 95% CI; (iii) the standard deviation (SD) of continuous outcomes to within 22% of their true value based on the upper limit of the 95% CI; (iv) a Pearson's correlation coefficient between baseline and follow-up scores with a margin of error of +/- 0.1 if the true correlation is 0.8, or +/- 0.14 if the true correlation is 0.7, or +/- 0.17 if the true correlation is 0.6.

Randomisation

We randomised participants in a 1:1 ratio to the intervention or control arm using a computer-generated random allocation sequence at the Exeter Clinical Trials Unit (ExeCTU). We stratified randomisation according to participants' symptom severity on the PHQ-9 and minimised allocation to balance the stratification variable across the two arms. To ensure allocation concealment, we randomised using an externally administered, password-protected randomisation website independently developed and maintained by ExeCTU. Allocation occurred on completion of an eligible participants' baseline assessment. Subsequently, the study researchers informed the participant and their GP, via standard letter, of the outcome and, for those randomised to the intervention group, passed participant details to the clinic to arrange treatment.

It was not possible to blind participants or clinicians to group allocation due to the nature of the intervention. The study researchers were not blinded to group allocation due to resource limitations. However, baseline and follow-up data were self-reported and all research measures were applied equally to both groups to reduce potential detection bias.

Statistical methods

We undertook all analyses on an intention to treat basis and did not impute missing data. We applied pairwise deletion to each measure in order to maximise the data available. Where a questionnaire item was missing (which occurred only at follow-up), pairwise deletion was applied to that follow-up measure for that participant. We report recruitment, retention, treatment adherence and baseline characteristics using descriptive statistics: means and SDs for continuous variables; numbers and percentages for categorical variables. We report the SDs of the outcome measures

(all continuous) with 95% CI for each trial arm at baseline and four months. We estimated the correlations between participants' scores on these measures at baseline and four months to inform the sample size calculation for a fully-powered trial. Although insufficiently powered to make inferential statements or calculate p-values, we report the observed differences between the intervention and control groups on the mean changes in these measures (with 95% CI), as well as proportions of participants recovering (follow-up PHQ-9 and GAD-7 scores <10[13, 44]) and responding to treatment (≥50% reduction in PHQ-9 and GAD-7 scores from baseline to follow-up) in each trial arm.

Patient and Public Involvement

The Morita Trial follows on from an iterative programme of work conducted to develop our Morita Therapy clinical protocol, whereby we optimised Morita Therapy according to the views of potential patients and therapists[40]. The patient materials were developed on the basis of consultation with a Public and Patient Involvement (PPI) expert and similar materials used in other mental health trials which had received feedback from PPI groups (e.g. PenPIG http://clahrc-peninsula.nihr.ac.uk/). A former trial participant, who expressed an interest in supporting our research and will be involved in the further dissemination of results, has co-written a summary sheet explaining our results in lay terms which has been sent to consenting former trial participants.

RESULTS

Participant flow

Participant flow through the trial is summarised in Figure 1.

We randomised 68 participants into the trial between October 2015 and September 2016: 34 (50%) to each trial arm. 146 potential participants gave permission for study researcher contact ('opted in'). We excluded 55/140 (39.3%) of those who could be contacted for telephone screen (24 did not meet inclusion criteria; 26 declined to participate; 5 were unable to arrange a baseline assessment) and 17/85 (20%) of those who attended baseline interview (15 did not meet inclusion criteria; 2

declined to participate). We randomised 68/146 (46.6%) of those who opted into the study. The 690 study invitations sent to potentially eligible patients identified via GP record search resulted in 35 participants randomised into the trial, a rate of 5.1% (95% CI 3.4% to 6.6%), with an additional 33 participants recruited from alternative sources such as advertising.

From January 2016 to January 2017, we collected four month follow-up data from 64/68 (94%) participants (95% CI 88.3% to 99.7%): 33/34 (97%) in the intervention arm and 31/34 (91%) in the control arm. In the intervention arm, one participant could not be contacted for follow-up; in the control arm, two participants could not be contacted for follow-up and one withdrew on the basis that they had not received active treatment. An additional control participant, after attending follow-up, revoked consent for his data to be included in the trial. Thus, whilst this participant is included within the participant flow figures, his data have not been included in the analysis of baseline characteristics or outcomes.

<insert Figure 1 (CONSORT diagram) here>

Baseline data

Baseline characteristics are summarised in Table 1.

Table 1. Participant baseline characteristics

	Intervention (n=34)	Control (n=33*)	Total (n=67)
Gender			
Female	22 (64.7)	19 (57.6)	41 (61.2)
Age (years)			
Mean (SD)	49.8 (14.8)	48.6 (15.9)	49.2 (15.2)
Ethic origin			
White British	31 (91.2)	30 (90.9)	61 (91.0)
White other	2 (5.9)	0 (0.0)	2 (3.0)
Mixed other	0 (0.0)	2 (6.1)	2 (3.0)
Asian Indian	0 (0.0)	1 (3.0)	1 (1.5)
Asian other	1 (2.9)	0 (0.0)	1 (1.5)
Education			
No qualifications	3 (8.8)	2 (6.1)	5 (7.5)

GCSE or O Level	7 (20.6)	6 (18.2)	13 (19.4)
Post GCSE or O Level	7 (20.6)	8 (24.2)	15 (22.4)
Undergraduate degree	9 (26.5)	10 (30.3)	19 (28.4)
Postgraduate qualification or higher	8 (23.5)	7 (21.2)	15 (22.4)
Marital status			
Married or cohabiting	23 (67.6)	16 (48.5)	39 (58.2)
Number of children			
Mean (SD)	1 (1)	1 (1)	1 (1)
History of depression			
One or more previous episodes	29 (85.3)	25 (75.8)	54 (80.6)
Age of onset (mean (SD))	28.9 (17.8)	25.2 (17.4)	27.1 (17.6)
Duration of current episode in months (mean (SD))	13.1 (12.8)	30.3 (43.8)	21.3 (32.4)
PHQ-9 (depression) score			
Mean (SD)	17.4 (4.7)	16.1 (4.5)	16.8 (4.6)
GAD-7 (anxiety) score			
Mean (SD)	13.3 (4.8)	12.2 (4.0)	12.7 (4.4)
Secondary SCID diagnoses (current)			
Any anxiety disorder	21 (61.8)	28 (84.8)	49 (73.1)
Generalised anxiety disorder	13 (38.2)	17 (51.5)	30 (44.8)
Social phobia	5 (14.7)	11 (33.3)	16 (23.9)
Panic disorder with agoraphobia	6 (17.6)	8 (24.2)	14 (20.9)
Panic disorder without agoraphobia	7 (20.6)	3 (12.6)	10 (14.9)
Post-traumatic stress disorder	3 (8.8)	7 (21.2)	10 (14.9)
Obsessive Compulsive Disorder	2 (5.9)	5 (15.2)	7 (10.4)
Specific phobia	1 (2.9)	4 (12.1)	5 (7.5)
Agoraphobia without panic disorder	1 (2.9)	1 (3.0)	2 (3.0)
Antidepressant treatment			
Currently prescribed antidepressants	20 (58.8)	20 (60.6)	40 (59.7)
Previous psychotherapy/ counselling (at least one course of)			
Any psychotherapy (not including counselling)	23 (67.6)	26 (78.8)	49 (73.1)
Cognitive Behavioural Therapy	20 (58.8)	21 (63.6)	41 (61.2)
Mindfulness-based Cognitive Therapy	8 (23.5)	6 (18.2)	14 (20.9)
Behavioural Activation	1 (2.9)	3 (9.1)	4 (6.0)
Eye Movement Desensitization and Reprocessing	2 (5.9)	2 (6.1)	4 (6.0)
Counselling	15 (44.1)	14 (42.4)	29 (43.3)
Other psychotherapy	9 (26.5)	10 (30.3)	19 (28.4)

Notes: data are number (%) unless stated otherwise; SD=standard deviation; percentages may not always total 100 due to rounding; *34 participants were randomised into the control arm, with 33 participants' characteristics included due to one participant revoking consent to include data.

Receipt of Morita Therapy

No participants in the intervention group declined to start Morita Therapy and 24/34 (70.6%) adhered to a per-protocol minimum (≥five sessions). The mean number of sessions attended for all participants was 7.7 (range 1-14; SD 4.0); the mean number attended for those who did and did not adhere to the minimum dose was 9.8 (range 5-14; SD 2.5) and 2.6 (range 1-4; SD 1.0) respectively.

Outcomes and estimation

The SD of the outcomes at baseline and follow-up by trial arm, with 95% CI, are reported in Table 2. At follow-up, the pooled SD around the mean PHQ-9 score (the primary outcome in any definitive trial) was 6.4 (95% CI 5.5% to 7.8%). The correlations between baseline and four month scores by trial arm, with 95% CI, are reported in Table 3.

Table 2. Treatment outcomes at baseline and four month follow-up with variability and between-group differences

Outcome measure	Participants	Baseline				4 months				Change from baseline to 4 months			Between-group difference	
		n	Mean	SD	95% CI[1]	n	Mean	SD	95% CI[1]	n	Mean	SD	Mean	95% CI[2]
PHQ-9	All	67	16.8	4.6	3.9 to 5.6	63	10.3	6.4	5.5 to 7.8	63	-6.3	5.8		
	Intervention	34	17.4	4.7	3.8 to 6.2	33	8.4	6.5	5.2 to 8.6	33	-9.0	5.9	-5.5	-8.1 to -2.9
	Control	33	16.1	4.5	3.6 to 6.0	30	12.4	5.7	4.6 to 7.7	30	-3.5	4.2		
GAD-7	All	67	12.7	4.4	3.8 to 5.3	62	7.7	5.0	4.3 to 6.1	62	-5.0	5.2		
	Intervention	34	13.3	4.8	3.9 to 6.4	32	6.8	5.2	4.2 to 7.0	32	-6.6	5.6	-3.3	-5.8 to -0.7
	Control	33	12.2	4.0	3.2 to 5.3	30	8.7	4.7	3.7 to 6.3	30	-3.3	4.3		
WSAS	All	67	22.4	7.6	6.5 to 9.2	62	15.7	10.5	8.9 to 12.7	62	-6.8	8.8		
	Intervention	34	22.7	7.9	6.3 to 10.3	32	13.5	11.0	8.9 to 14.7	32	-9.7	9.7	-5.9	-10.1 to -1.7
	Control	33	22.1	7.4	6.0 to 9.8	30	18.0	9.4	7.5 to 12.7	30	-3.7	6.5		
MASA	All	67	76.8	26.5	22.6 to 31.9	62	103.5	36.3	30.9 to 44.2	62	25.3	30.6		
	Intervention	34	80.7	29.3	23.6 to 38.5	32	114.4	40.3	32.3 to 53.6	32	32.8	37.2	15.5	0.4 to 30.7
	Control	33	72.7	23.0	18.5 to 30.5	30	91.8	27.7	22.1 to 37.3	30	17.2	19.0		
SF-36 PCS	All	67	50.9	11.5	9.8 to 13.9	63	49.4	12.0	10.2 to 14.6	63	-1.9	7.5		
	Intervention	34	49.6	12.3	10.0 to 16.2	33	47.9	13.0	10.5 to 17.2	33	-1.7	6.6	0.6	-3.2 to 4.4
	Control	33	52.2	10.6	8.5 to 14.0	30	51.1	10.8	8.6 to 14.5	30	-2.2	8.5		
SF-36 MCS	All	67	24.4	7.8	6.6 to 9.3	63	35.2	12.4	10.5 to 15.0	63	10.8	11.5		
	Intervention	34	25.0	8.8	7.1 to 11.6	33	39.8	11.9	9.6 to 15.7	33	14.7	11.3	8.1	2.7 to 13.6
	Control	33	23.8	6.6	5.3 to 8.7	30	30.1	11.0	8.8 to 14.8	30	6.6	10.3		

Notes: SD=standard deviation of the mean; [1]95% CI = 95% confidence intervals around the standard deviation; [2]95% CI = 95% confidence intervals around the mean between-group difference.

Table 3. Correlation between participant scores at baseline and four months

Association	Participants	n	Rho	95% CI	
PHQ-9 at baseline and 4 months	All	63	0.42	0.19 to 0.61	
	Intervention	33	0.37	0.04 to 0.64	
	Control	30	0.71	0.47 to 0.85	
GAD-7 at baseline and 4 months	All	62	0.40	0.17 to 0.59	
	Intervention	32	0.40	0.07 to 0.66	
	Control	30	0.51	0.18 to 0.73	
WSAS at baseline and 4 months	All	62	0.52	0.31 to 0.68	
	Intervention	32	0.45	0.12 to 0.69	
	Control	30	0.76	0.55 to 0.88	
MASA at baseline and 4 months	All	62	0.58	0.39 to 0.73	
	Intervention	32	0.45	0.12 to 0.69	
	Control	30	0.73	0.50 to 0.86	
SF-36 PCS at baseline and 4 months	All	63	0.68	0.52 to 0.80	
	Intervention	33	0.78	0.59 to 0.88	
	Control	30	0.58	0.27 to 0.78	
SF-36 MCS at baseline and 4 months	All	63	0.42	0.20 to 0.61	
	Intervention	33	0.43	0.10 to 0.67	
	Control	30	0.39	0.04 to 0.66	

Notes: Rho=Spearman's Rho; 95% CI = 95% confidence intervals around Spearman's Rho.

Outcomes in the intervention and control arms at baseline and follow-up, with observed between-group differences in changes from baseline to follow-up (with 95% CI), are summarised in Table 2. Depressive symptoms reduced from baseline to follow-up by an average of 9 PHQ-9 points in the intervention group and an average of 3.5 PHQ-9 points in the control group.

Proportions of recovery and response on the PHQ-9 (depressive symptoms) and GAD-7 (anxiety symptoms) by trial arm are summarised in Table 4. At follow-up, 22/33 participants in the intervention group (66.7%) scored below the threshold for moderate depression (PHQ-9 <10) with 9/30 controls (30.0%) similarly recovering. Depressive symptoms reduced by ≥50% from baseline to follow-up for 22/33 participants in the intervention group (66.7%) and 4/30 controls (13.3%).

Table 4. Proportions of recovery and response at four month follow-up

			Recovery	Response	
Outcome measure	**Participants**	**n**	**n (%) scoring <10 at follow-up**	**n (%) showing 50% reduction**	**n (%) either showing 50% reduction or scoring <10 at follow-up**
PHQ-9	All	63	31 (49.2)	26 (41.3)	32 (50.8)
	Intervention	33	22 (66.7)	22 (66.7)	23 (69.7)
	Control	30	9 (30.0)	4 (13.3)	9 (30.0)
GAD-7	All	62	40 (64.5)	27 (43.5)	40 (64.5)
	Intervention	32	24 (75.0)	17 (53.1)	24 (75.0)
	Control	30	16 (53.3)	10 (33.3)	16 (53.3)

Service use

Participants' use of health services (in addition to Morita Therapy) since baseline assessment is presented in Table 5. These data were collected in order to characterise TAU in preparation for costing a large-scale trial. Service use was comparable across the two arms with the exception of psychological therapy and counselling, which were proscribed in the Morita Therapy arm (0% in the Morita Therapy arm; 26% (n=8) in TAU). Compared to baseline assessment, antidepressant medication use reduced in both groups (58.8% (20/34) to 43.8% (14/32) and 60.6% (20/33) to 45.2% (14/31) in the intervention and control groups respectively).

Table 5. Service use at four month follow-up

Service	Participants	n	%	No. contacts		Duration of contacts (minutes)	
				Mean	SD	Mean	SD
Antidepressant medication (continuing at follow-up)	Morita Therapy (n=32) TAU (n=31)	14 14	43.8 45.2				
Psychological therapy	Morita Therapy (n=32) TAU (n=31)	0 5	0.0 16.1	- 5.4	- 4.4	- 68.0	- 47.6
Counselling	Morita Therapy (n=32) TAU (n=31)	0 3	0.0 9.7	- 6.3	- 2.1	- 60.0	- 0.0
Hospital admission	Morita Therapy (n=33) TAU (n=31)	2 1	6.1 3.2	1.5 1.0	0.7 0.0		
Hospital outpatient appointment	Morita Therapy (n=32) TAU (n=31)	9 9	28.1 29.0	2.1 2.1	1.5 3.0		
A&E attendance	Morita Therapy (n=32) TAU (n=31)	3 3	9.4 9.7	1.0 1.3	0.0 0.6		
GP appointment	Morita Therapy (n=32) TAU (n=31)	20 17	62.5 54.8	4.8 2.5	4.0 2.0	12.0 12.8	2.4 6.2
GP home visit	Morita Therapy (n=32) TAU (n=31)	2 0	6.3 0.0	1.0 -	0.0 -	12.5 -	3.5 -
GP telephone contact	Morita Therapy (n=32) TAU (n=31)	10 5	31.3 16.1	3.5 2.4	5.0 1.7	6.9 5.0	4.5 3.1
Practice nurse	Morita Therapy (n=32) TAU (n=31)	7 10	21.9 32.3	3.6 1.6	5.3 1.1	9.3 12.0	6.7 5.8
Psychiatrist	Morita Therapy (n=32) TAU (n=31)	0 1	0.0 3.2	- 12	- 0.0	- 50.0	- 0.0
Occupational therapist	Morita Therapy (n=32) TAU (n=31)	2 1	6.3 3.2	2.5 5.0	0.7 0.0	35.0 45.0	35.4 0.0
Social worker	Morita Therapy (n=32) TAU (n=31)	1 0	3.1 0.0	5.0 -	0.0 -	60.0 -	0.0 -
Advice service	Morita Therapy (n=32) TAU (n=31)	2 1	6.3 3.2	1.0 1.0	0.0 0.0	75.0 60.0	21.2 0.0
Helpline	Morita Therapy (n=32) TAU (n=31)	1 2	3.1 6.5	1.0 25.0	0.0 0.0	60.0 30.0	0.0 0.0
Chiropractor	Morita Therapy (n=32) TAU (n=31)	5 3	15.6 9.7	3.8 2.0	3.0 1.7	29.0 41.7	17.5 10.4
Acupuncture	Morita Therapy (n=32) TAU (n=31)	1 1	3.1 3.2	1.0 9.0	0.0 0.0	30.0 60.0	0.0 0.0
Physiotherapist	Morita Therapy (n=32) TAU (n=31)	1 1	3.1 3.2	3.0 4.0	0.0 0.0	60.0 60.0	0.0 0.0
Mental Health support worker	Morita Therapy (n=32) TAU (n=31)	1 1	3.1 3.2	1.0 6.0	0.0 0.0	60.0 60.0	0.0 0.0

Notes: SD=standard deviation of the mean; TAU=treatment as usual; A&E=Accident and Emergency; GP=General Practitioner

DISCUSSION

In this pilot RCT we have demonstrated that it is possible to recruit UK-based people with depression into a trial of Morita Therapy, and to retain them at four

month follow-up at a rate which is equivalent to or exceeds that found in other trials in the field[e.g. 22, 48, 50, 51]. Participants' adherence to the minimum dose of Morita Therapy was on a par with other psychological therapies in similar trials[e.g. 22]. Furthermore, depressive symptoms reduced from baseline to follow-up by an average of 9 PHQ-9 points in the intervention group and 3.5 points in the control group: a between-group difference exceeding the PHQ-9 minimum clinically important difference (MCID)[52]. Rates of recovery and response to Morita Therapy (66.7%) were at least as good as those achieved by leading evidence-based psychological therapies[14, 15, 17-23].

Strengths and limitations

A key strength of this trial is that it represents not only the first study of Morita Therapy in the UK but the first randomised controlled trial of Morita Therapy for depression within English-speaking countries. Whilst the findings are consistent with previous studies which suggest possible benefits of Morita Therapy[32, 38, 53] (Minami, M. 2011), this study provides a valuable contribution in terms of applying Morita Therapy to a UK population, and by employing a rigorous methodology in preparation for a fully-powered trial. The methods utilised were suitable for a feasibility study: the study purpose and research questions accorded with The National Institute for Health Research Evaluation Trials and Studies' definition of a feasibility study[54], endorsed by Arain et. al.[55]; the trial was designed to address key uncertainties associated with a large-scale trial; criteria for success were specified a priori[39].

Due to resource limitations, the study researchers were not blinded to group allocation. Whilst baseline and follow-up data were self-reported, and all research measures were applied equally to both groups, it is possible that this introduced detection bias into the study[56, 57] and blinding of study researchers would be ensured in any future definitive trial.

Implications and future research

We can now estimate the parameters necessary in order to design a fully-powered trial based on the 95% confidence intervals around our current data: we estimate

that (i) the randomisation rate (as percentage of patients invited via GP record searches alone) would be between 3.4% and 6.6%; (ii) the retention rate would be between 88.3% and 99.7%; (iii) the pooled SD on the PHQ-9 (the primary outcome measure in a definitive trial) score at follow-up would be between 5.5 and 7.8. Using our pilot trial data alongside the most conservative estimate of the between-group difference based on the published PHQ-9 MCID (2.59)[52], we also estimate that 133 participants per group would be required to provide 90% power based on a two-sided 5% significance level and allowing for 20% attrition. Our previous experience leads us to assert that we could reasonably expect to recruit such numbers into a future trial.

We specified two criteria for success[39] for proceeding to a fully-powered trial. Our pilot trial attrition rate of 6% fulfils the specified standard (no higher than 20%), as does the treatment adherence rate of 70.6% (at least 65%). Whilst the recruitment rate from GP record searches alone (5.1%) was lower than anticipated, this is slightly higher than that found in other trials in the field[e.g. 50, 51]. To recruit 266 participants into a fully-powered trial, based on our pilot data 51 average sized General Practices would need to participate in record searches. This could be achieved in a similar timeframe to the pilot trial by conducting the trial over three sites (as opposed to one site) and with an increased workforce to recruit participants. Recruitment might also be maximised by identifying additional participants through advertising and utilising research registers (as per our current study) and by modifying the pilot trial protocol to include measures known to improve recruitment rates, such as telephone reminders to non-responding patients invited via GP record search[58-60]. We therefore anticipate that a sufficient number of participants to populate a fully-powered trial can be recruited, albeit with additional procedures, and conclude that a fully-powered trial is feasible with minor modifications to the pilot trial protocol in relation to our recruitment activities.

The level of participant adherence to Morita Therapy suggests that it is as acceptable to participants as other psychological treatments[22]. Whilst it is not the purpose of this paper to assess the effectiveness of Morita Therapy and the study was not powered to enable inferential statements to be made, our findings also suggest promising possible effects of Morita Therapy plus TAU versus TAU

alone[61]. The observed between-group difference in reduction in depressive symptoms (PHQ-9) from baseline to follow-up, and indeed the lower margin of error on this figure, exceeds the PHQ-9 MCID. Furthermore, the rates of recovery and treatment response found in this study are comparable to or exceed those found for current NICE recommended treatments for depression[14, 15, 17-23]. Whilst these findings suggest that Morita Therapy may be equivalent in effectiveness to other psychological therapies, supporting the potential value of Morita Therapy as a treatment for depression, our qualitative and mixed methods findings (reported elsewhere) provide early indications of which patients might benefit most from Morita Therapy, which will be incorporated into a process evaluation in a fully-powered trial[62].

In line with this, given that treatment effectiveness varies at an individual if not population level, it is argued that research should focus on matching patient characteristics to treatment type[63-66]. In order to facilitate such work, it makes sense to test treatments which are qualitative distinct from current options. Given the contrast between Morita Therapy and established Western approaches[28], Morita Therapy may prove a valuable addition to current treatment options by providing a meaningful alternative which may be particularly suited to patients for whom current treatments are not suitable. As such, Morita Therapy may facilitate both true patient choice (as enshrined in the forthcoming NICE guidelines for depression[67]) and the future 'matching' of patients to treatments, and potentially provide patients for whom current NICE-recommended therapies have failed a qualitatively different approach towards mental health.

Conclusions

We have determined that it is feasible to conduct a large-scale trial of Morita Therapy with minor modifications to the pilot trial protocol in order to maximise recruitment. Our findings indicate that Morita Therapy shows promise in the treatment of depression, supporting the potential of Morita Therapy to provide patients in the UK with a distinct and meaningful alternative to current treatment options.

FOOTNOTES

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions and acknowledgements

DAR proposed the study; HVRS as chief investigator and study researcher designed the study with the involvement of DAR and JF; HVRS drafted the study protocol and materials and obtained National Health Service ethical approval and research and development governance assurance; HVRS was responsible for project management, data collection and analysis; HVRS and DAR developed the UK Morita Therapy outpatient protocol; DAR supervised the study therapists. HVRS drafted the manuscript. All other authors contributed to editing of the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figure legend:

Figure 1. CONSORT diagram

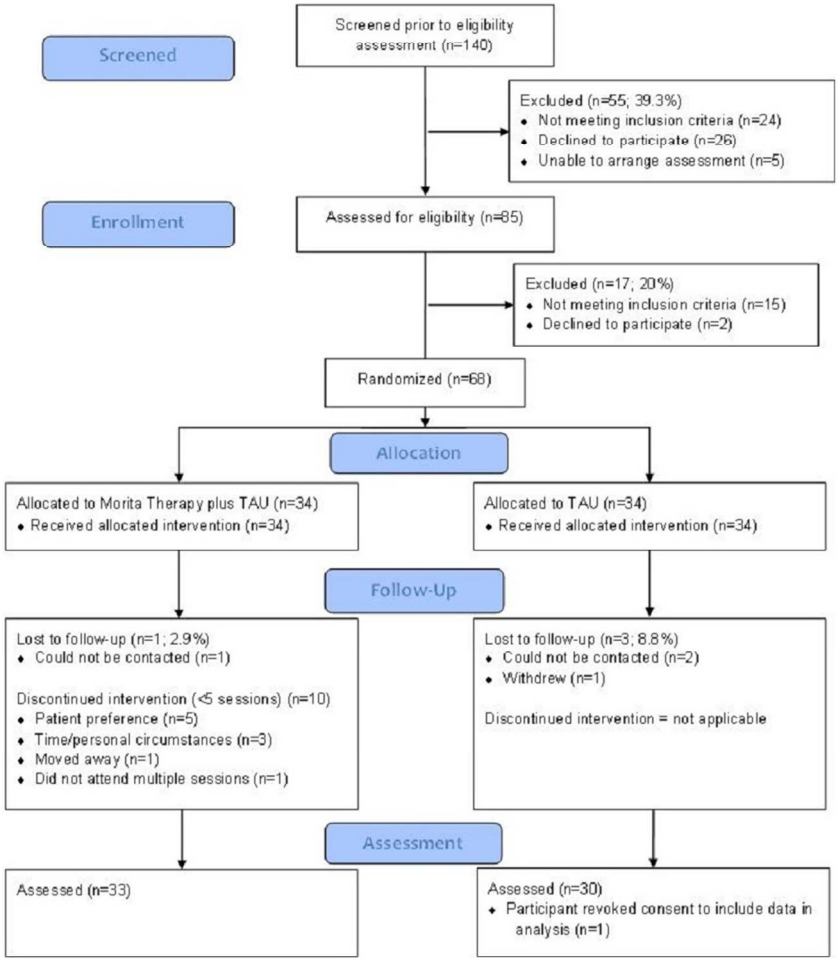

Figure 1. CONSORT diagram

91x102mm (300 x 300 DPI)

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Trials

STUDY PROTOCOL

Open Access

Morita therapy for depression and anxiety (Morita Trial): study protocol for a pilot randomised controlled trial

Holly Victoria Rose Sugg*, David A. Richards and Julia Frost

Abstract

Background: Morita Therapy, a psychological therapy for common mental health problems, is in sharp contrast to established western psychotherapeutic approaches in teaching that undesired symptoms are natural features of human emotion rather than something to control or eliminate. The approach is widely practiced in Japan, but untested and little known in the UK. A clinical trial of Morita Therapy is required to establish the effectiveness of Morita Therapy for a UK population. However, a number of methodological, procedural and clinical uncertainties associated with such a trial first require addressing.

Methods/Design: The Morita Trial is a mixed methods study addressing the uncertainties associated with an evaluation of Morita Therapy compared with treatment as usual for depression and anxiety. We will undertake a pilot randomised controlled trial with embedded qualitative study. Sixty participants with major depressive disorder, with or without anxiety disorders, will be recruited predominantly from General Practice record searches and randomised to receive Morita Therapy plus treatment as usual or treatment as usual alone. Morita Therapy will be delivered by accredited psychological therapists. We will collect quantitative data on depressive symptoms, general anxiety, attitudes and quality of life at baseline and four month follow-up to inform future sample size calculations; and rates of recruitment, retention and treatment adherence to assess feasibility. We will undertake qualitative interviews in parallel with the trial, to explore people's views of Morita Therapy. We will conduct separate and integrated analyses on the quantitative and qualitative data.

Discussion: The outcomes of this study will prepare the ground for the design and conduct of a fully-powered evaluation of Morita Therapy plus treatment as usual versus treatment as usual alone, or inform a conclusion that such a trial is not feasible and/or appropriate. We will obtain a more comprehensive understanding of these issues than would be possible from either a quantitative or qualitative approach alone.

Trial registration: Current Controlled Trials ISRCTN17544090 registered on 23 July 2015.

Keywords: Morita therapy, Major depressive disorder, Mixed methods, Feasibility study

Background

Clinical depression and generalised anxiety disorder are the two most common mental health disorders [1], with one in six people in the UK experiencing such a disorder each year [2]. Together, depression and anxiety are estimated to cost the UK economy £17bn in lost output and direct health care costs annually, with a £9bn impact on the Exchequer through benefit payments and lost tax receipts [3].

Depression accounts for the greatest burden of disease among all mental health problems, and is the second-highest among all general health problems [4]. The lifetime prevalence of depression has been estimated at 16.2 %, and rates of co-morbidity and risk for suicide are high [5–7]. Depression is also recurrent, with over three quarters of people who recover from one episode experiencing at least one more [8].

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Generalised Anxiety Disorder (GAD) affects between 2–5 % of the UK population at any one time, and accounts for up to 30 % of the mental health problems presented to General Practitioners (GPs) [2]. The lifetime prevalence of GAD has been estimated at 5.7 % [9]. Furthermore, the comorbidity between anxiety and depression make a strong contribution to the total disability attributed to mental disorders [1].

Medication and Cognitive Behavioural Therapy have the strongest evidence-base for treating these conditions, and are each recommended by the National Institute for Health and Care Excellence (NICE) [10, 11]. However, many patients are refractory to such interventions [12], with both depression and anxiety remaining chronic disorders despite treatment [1]. Recovery is only reached by 55–56 % of people receiving treatment through the large-scale UK initiative to provide NICE recommended psychological therapies ('Improving Access to Psychological Therapies' (IAPT)) [13, 14], thereby increasing the risk of future relapse and the maintenance of recurring and chronic problems [15].

Thus, it is important to develop and test new potentially effective treatments for depression and anxiety in order to treat a wider range of patients [15] and provide patients in the UK with choice alternatives.

Morita Therapy

Morita Therapy is a psychotherapy developed in Japan by Dr Shoma Morita in 1919 [16] used for the treatment of common mental health problems. Morita Therapy was originally developed in inpatient settings for patients with particular psychological problems, including but not limited to GAD [17]. More recently, Morita Therapy has been applied to a wider range of conditions, including depression, and guidelines for practicing outpatient Morita Therapy have been developed [17]. Morita Therapy is now widely practiced in Japan, and has branches in various other countries including North America, Australia, China, Russia and Rwanda [18].

Morita Therapy is a holistic approach, aiming to improve functioning in everyday life, rather than an approach targeting specific symptoms [18]. The underlying premise is that unpleasant symptoms are part of the natural ecology of the human experience. Morita Therapy thus helps patients to re-orientate themselves in the natural world and takes a restorative approach to potentiate their natural healing capacity. Morita therapists help patients to move away from symptom preoccupation and combat, which it is conceptualised both interfere with this natural recovery process and lead to preoccupation with and worsening of symptoms [17]. By helping patients to accept that undesired symptoms are natural features of human emotion rather than something to control or eliminate, and that emotions ebb and flow as a matter of course and can be lived with, Morita Therapy is in sharp contrast to established western psychotherapeutic approaches with their focus on symptom elimination. In Morita Therapy, patients are taught to live with, rather than be without, unpleasant emotions.

Uncertainties: The need for a mixed methods feasibility study

As with the development of many other treatments to date [15], initial evidence for Morita Therapy's efficacy is largely based on case studies, predominantly conducted in Japan. A narrative review of forty-nine such studies and four quasi-experimental studies indicated that Morita Therapy has been reported as effective for a diverse range of issues, but that further work is required to both standardise its delivery and investigate its efficacy in controlled trials (personal communications: Minami, M).

Furthermore, Morita Therapy is currently little known in the UK. Thus, evidence of the efficacy of Morita Therapy based on truly experimental studies, and evidence of the effectiveness of Morita Therapy specifically for a UK population, has not yet been established. Whilst a fully-powered UK randomised controlled trial (RCT) of Morita Therapy versus treatment as usual is needed to establish the effects of Morita Therapy, a number of clinical, procedural and methodological uncertainties currently prevent us moving immediately to such a trial.

With respect to clinical uncertainties, the operationalisability of the UK Morita Therapy outpatient protocol, and the acceptability of both the protocol specifically and Morita Therapy in general, is unknown. Gathering data on these uncertainties is essential to ensure that the treatment administered in a large-scale trial is deliverable by therapists, and acceptable to both therapists and patients.

With respect to procedural uncertainties, information is required on the likely rates of recruitment to and retention in a trial of Morita Therapy, and of treatment adherence, in order to assess the feasibility of a trial and inform the required sample size. With respect to methodological uncertainties, estimates of the variance in participant outcomes and information on how these correlate with baseline scores are also required to inform future sample size calculations.

In line with the Medical Research Council (MRC) framework for the development and evaluation of complex interventions [19], all such uncertainties are appropriate to address within a pilot trial and feasibility study [20]. In order to both collect the required quantitative data and understand people's views of Morita Therapy, qualitative work will be embedded in a pilot randomised controlled trial of Morita Therapy compared to treatment as usual, and merged with quantitative data on treatment adherence to potentially help explain variability in participants' therapeutic engagement.

Study purpose

The purpose of this study is to prepare the ground for the design and conduct of a fully-powered RCT of Morita Therapy plus treatment as usual versus treatment as usual alone, or to conclude that such a trial is not appropriate and/or feasible.

Research questions

1. What proportion of participants approached to take part in the trial will agree to do so?
2. What proportion of participants who agree to take part in the trial will remain in the trial at four month follow-up?
3. What proportion of participants who agree to take part in Morita Therapy will adhere to a pre-defined per-protocol dose of Morita Therapy?
4. What is the variance in participant outcomes following Morita Therapy plus treatment as usual and treatment as usual alone, and how do they correlate with participants' baseline scores?
5. What are the estimated between-group differences (and 95 % confidence intervals) in participant outcomes following Morita Therapy plus treatment as usual and treatment as usual alone?
6. How acceptable is Morita Therapy to participants and therapists?
7. How do participants' views about Morita Therapy relate to the variability in the number of treatment sessions they attend?

Criteria for success

The criteria to be met in order to deem a fully-powered RCT feasible as is [20] are:

1. A sufficient number of participants to populate a fully-powered trial are likely to be recruited and retained, i.e. we recruit at the rate anticipated in the pilot trial (12 % of those invited) and experience an attrition rate no higher than 20 % of those randomised, in line with our other National Institute of Health Research (NIHR) mental health trials [21–23]. We will consider whether protocol modification or close monitoring during a fully-powered RCT will address any failure to meet these criteria [20].
2. The levels of engagement with and adherence to Morita Therapy are likely to be on par with our other NIHR mental health trials [23], i.e. at least 65 % of patients allocated to Morita Therapy attend at least 40 % of treatment sessions. Any failure to meet this criterion will be considered in the light of participants' views on the acceptability of Morita Therapy in order to determine whether protocol modification or close monitoring are sufficient to deem a fully-powered RCT feasible [20].
3. It is likely that a Morita Therapy outpatient protocol can be produced which is acceptable to patients and therapists, and deliverable by therapists, as defined by responses to qualitative interviewing.

Methods/Design

Study design

We will incorporate exploratory and explanatory components in a mixed methods embedded design [24]. Thus, we will embed semi-structured qualitative interviews within a pilot randomised controlled trial of Morita Therapy plus treatment as usual versus treatment as usual alone for people with depression, with or without anxiety disorders. We will give quantitative and qualitative components equal priority and mix them interactively at the design level within a program-objective framework [24]. For these two components, we will collect data concurrently and analyse data simultaneously. We will use quantitative data to assess the feasibility of trial recruitment, retention and treatment adherence, and to inform any future sample size calculations. We will collect qualitative data on participants' and therapists' views of Morita Therapy. By merging qualitative and quantitative data, we aim to explain variability in participants' treatment adherence and develop a richer understanding of the feasibility, acceptability and appropriateness of Morita Therapy (Table 1).

Philosophical assumptions

Our decision to use a mixed methods design is driven by the primary importance we give to addressing the uncertainties associated with running a fully-powered RCT. Thus, we are guided by a pragmatic philosophy: we prioritise our research objectives and the methods which will lead to the best evidence with regards to those objectives [25]. Consistent with a pragmatic worldview, we will also approach the objectives from a pluralistic perspective, combine deductive and inductive modes of reasoning, and allow for a singular view and multiple views of reality in how we come to understand and interpret our findings [25].

Pilot Randomised Controlled Trial

Sample size

A conventional power calculation is inappropriate for the purpose of a pilot trial [20]. Instead, we have calculated the sample size in order to provide useful information about the aspects of the study being assessed for feasibility [20]. Thus, we have constructed confidence intervals based on certain criteria for success [20], specifically: recruiting at a rate of 12 % of those invited and experiencing an attrition rate no higher than 20 % of those randomised. We expect to invite a total of 570 participants to

Table 1 World Health Organization Trial Registration Data Set

Data category	Information
Primary registry and trial identifying number	Current Controlled Trials database
	ISRCTN17544090
Date of registration in primary registry	23-Jul-15
Secondary identifying numbers	N/A
Source(s) of monetary or material support	University of Exeter Medical School, UK
Primary sponsor	University of Exeter, UK
Secondary sponsor(s)	N/A
Contact for public queries	Holly Victoria Rose Sugg
	University of Exeter Medical School, UK
	h.v.s.sugg@exeter.ac.uk
Contact for scientific queries	Holly Victoria Rose Sugg
	University of Exeter Medical School, UK
	h.v.s.sugg@exeter.ac.uk
Public title	The Morita Trial
Scientific title	Morita Therapy for Depression and Anxiety: A Feasibility and Pilot Study
Countries of recruitment	UK
Health condition(s) or problem(s) studied	Depression
Intervention(s)	Morita Therapy
	Treatment as usual
Key inclusion and exclusion criteria	Ages eligible for study: ≥18 years;
	Sexes eligible for study: both;
	Accepts healthy volunteers: no
	Inclusion criteria: adult patient (≥18 years), current DSM Major Depressive Disorder
	Exclusion criteria: cognitive impairment, bipolar disorder or psychosis/psychotic symptoms, substance dependence, acute suicidal risk, current psychological therapy
Study type	Interventional
	Allocation: randomised intervention model
	Primary purpose: treatment
	Phase II
Date of first enrolment	Sep-15
Target sample size	72
Recruitment status	Recruiting
Primary outcome(s)	Depressive symptoms, generalised anxiety symptoms, quality of life, attitudes (at four-month follow-up); qualitative exploration of acceptability.
Key secondary outcomes	N/A

participate in the trial. Thus, we expect to recruit 72 participants into the trial, and follow-up 60 participants (30 in each trial arm).

Inviting 570 participants is sufficient to estimate a participation rate (as percentage of subjects invited) of 10 % with a margin of error of +/− 2.46 %, or to estimate a participation rate of 12 % with a margin of error of +/− 2.67 %, or to estimate a participation rate of 15 % with a margin of error of +/− 2.93 %, based on 95 % confidence intervals. Recruiting 72 participants is sufficient to estimate a follow-up rate (as percentage of participants randomised) of 80 % with a margin of error of +/− 9.24 %, or to estimate a follow-up rate of 85 % with a margin of error of +/− 8.25 %, based on 95 % confidence intervals.

In addition, we will calculate the standard deviation of participant outcomes and the correlation between baseline and four month follow-up scores, which can be used to refine future sample size calculations to incorporate the additional precision obtained from adjusting for baseline scores when comparing outcome scores between the trial arms. 30 participants in each group is sufficient to estimate: (i) the standard deviation of continuous outcomes to within 22 % of their true value based on the upper limit of the 95 % confidence interval; (ii) a Pearson's correlation coefficient between baseline and follow-up scores with a margin of error of +/− 0.1 if the true correlation is 0.8, or with a margin of error of +/− .14 if the true correlation is 0.7, or with a margin of error of +/− 0.17 if the true correlation is 0.6.

30 participants per group is also in line with the general rule of thumb for using pilot studies to reliably estimate variance for participant outcomes [26]. With these factors in mind, we consider 60 participants at follow-up to be both sufficient to provide useful information and reasonable to recruit for within the constraints of our pilot trial and have, therefore, selected 72 as our target sample size, inflating our sample by 20 % to take account of predicted attrition.

Participant inclusion criteria

Eligible participants will be aged 18 or over with Diagnostic and Statistical Manual of Mental Disorders (DSM) Major Depressive Disorder, with or without accompanying DSM anxiety disorder(s).

Participant exclusion criteria

Given the exploratory nature of this trial (and any fully-powered evaluation), and thus the requirement for reasonable internal validity with a homogenous and tightly defined population, we will identify and exclude people who are cognitively impaired, have bipolar disorder or psychosis/psychotic symptoms, or are substance dependent. Cognitive impairment will be determined using the Mini-Cog, whereby a score of 0, or 1–2 with an abnormal clock-face, would indicate sufficient cognitive impairment to be excluded [27]. Bipolar disorder,

psychosis and substance dependence will be established according to the DSM.

We will also exclude participants whose risk of suicide is sufficiently acute to demand immediate management by a specialist mental health crisis team, and those who are currently in receipt of psychological therapy. Psychological therapy includes any formal standard course of psychological (talking) therapy, such as Cognitive Behavioural Therapy. Ad hoc contact with a therapist or counsellor will not be considered to meet this exclusion criterion. Participants will be eligible regardless of whether they are in receipt of antidepressant medication or have received psychological therapy in the past.

Participant identification and recruitment

Our main method of recruitment will be through searches of General Practice records, conducted by Practice staff. We will recruit six GP Practices in Devon. All GP Practices who are able to access the University of Exeter's Mood Disorders Centre (MDC) Accessing Evidence-Based Psychological Therapies (AccEPT) Clinic (those within the National Health Service Northern, Eastern and Western Devon Clinical Commissioning Group) will be eligible.

Practice record searches will be limited to patients aged 18 or over and seen within the past three months for depression. The resulting patient names will be screened by the GP with whom the patient is registered for any patients known to meet exclusion criteria or for whom the GP considers the trial unsuitable. The remaining patients will be sent invitations to participate in the trial by Practice staff.

We will also place adverts on websites of the University of Exeter Medical School and AccEPT Clinic, place leaflets in the waiting rooms of consenting Devon General Practices and circulate an email invitation to former MDC participants who have consented to such contact. All invitations and adverts will include a study summary sheet [see Additional file 1] and permission to contact form [see Additional file 2] (Figs. 1 and 2).

Screening and baseline

We will telephone all people who return their permission to contact form to the study team to assess possible eligibility using a standard two-question case-finding instrument for depression [28] and arrange baseline interviews with potentially eligible and willing participants who will be sent a confirmation letter and full participant information leaflet [see Additional file 3]. We will hold baseline interviews at University of Exeter premises or the participant's home, depending on participant preference. At interview, we will explain the study in full and assess eligibility according to the Mini-Cog [27] (to screen for cognitive impairment) and standard clinical interview (Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Clinical Trials Version [29]). If eligible and once fully informed, participants will be asked to complete a consent form [see Additional file 4] and entered into the trial. Ineligible participants will be returned to the care of their GP.

Randomisation, allocation concealment and blinding

We will allocate participants in a 1:1 ratio to either Morita Therapy plus treatment as usual or treatment as usual alone, stratified according to their symptom severity on the nine item version of the Patient Health Questionnaire (PHQ-9) [30], specifically whether they score below 19 or

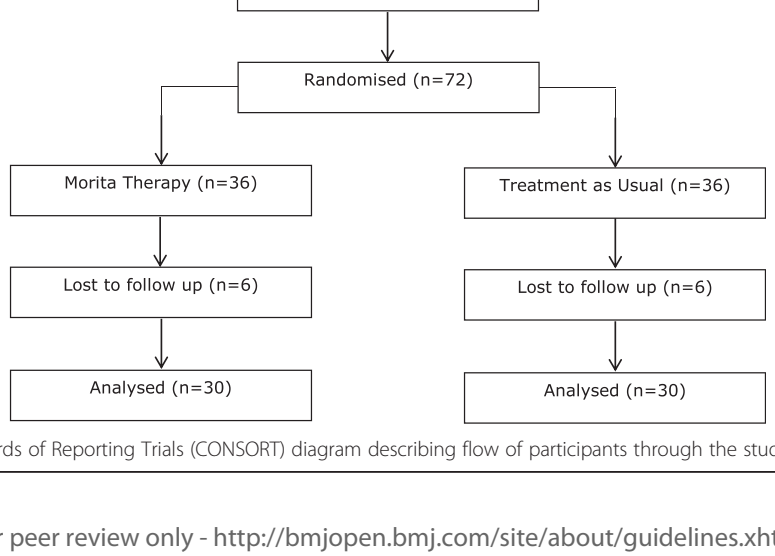

Fig. 1 Consolidated Standards of Reporting Trials (CONSORT) diagram describing flow of participants through the study

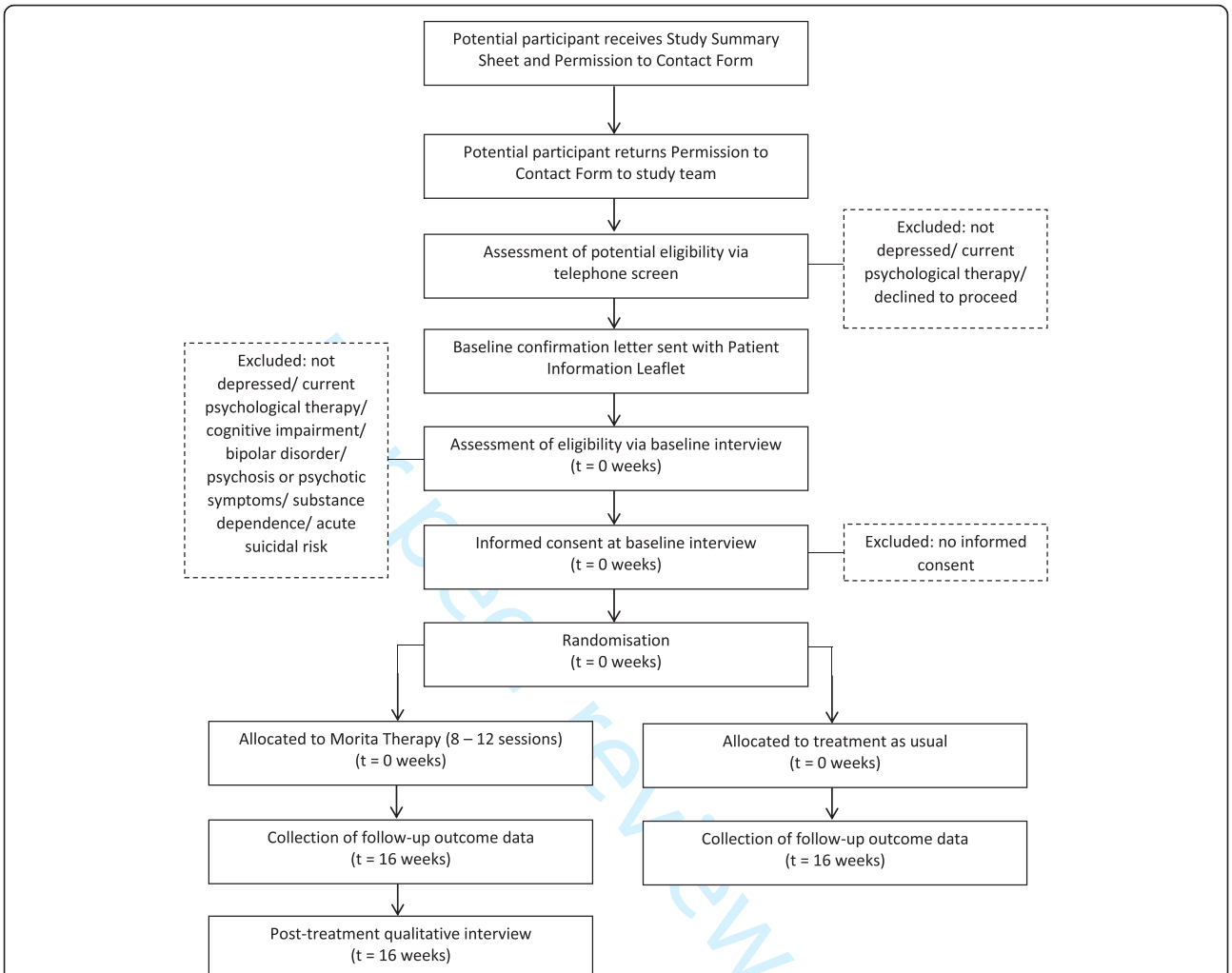

Fig. 2 Schematic diagram describing timeline for participants in the study

19 and above, given that a score of 19 is the median score of depressed participants in our previous research [21, 23]. Allocation will be minimised to maximise the likelihood of balance in the stratification variable across the two trial arms. To ensure allocation concealment, we will undertake randomisation through the use of an externally administered, password-protected randomisation website independently developed and maintained by the Exeter Clinical Trials Unit.

The researchers will not be blinded to allocation due to the different pathways to be followed for each trial arm. Baseline and follow-up data will be self-reported and the risk of bias related to lack of blinding will be both minimal and tolerable.

Trial interventions

Morita Therapy plus treatment as usual We will ask participants in the Morita Therapy plus treatment as usual trial arm not to engage in other formal courses of psychological therapy elsewhere during the course of their treatment. Otherwise, these participants will be free to access any other usual care and medication in liaison with their GP.

Morita Therapy will consist of eight to twelve one hour face-to-face weekly sessions and be delivered at the University of Exeter's MDC AccEPT clinic [31] by two research therapists trained in Morita Therapy and experienced in both the delivery of complex psychological interventions and adopting different modes of treatment, including experimental treatments. Therapist training took place over 6 months and included background reading, attending presentations, involvement in the development and review of the UK Morita Therapy outpatient protocol, and practical training led by DAR, a clinically qualified academic and 10 year member of the Japanese Society for Morita Therapy. Practical training was experiential, involving role plays, diary examples, additional reading and peer support.

The therapists are not accredited as there is no accreditation process for Morita Therapy within the UK.

Therapists will follow the UK Morita Therapy outpatient protocol developed by the study researchers from multiple sources of literature on the delivery and practice of Morita Therapy [16–18, 32–35] and by considering the views of potential participants and therapists about Morita Therapy, as explored in qualitative interviews, in order to enhance the suitability of Morita Therapy for a UK population. DAR will provide fortnightly supervision of cases together with advice and support. A qualitative checklist highlighting the key components of Morita Therapy will be used as an aide memoir to structure supervision discussions and the assessment of adherence and fidelity. With the patient's consent, all therapy sessions will be audio recorded. We will use the first two recordings for each therapist to confirm their adherence to the Morita Therapy outpatient protocol and a further 10 %, stratified by length of time in treatment, to evaluate fidelity to the protocol, which will inform therapist supervision.

During therapy, patients will progress through four stages of rest and increasing action taking in order to address fatigue, expand peripheral attention and move from a mood-oriented to purpose-oriented and action-based lifestyle. Therapists will aid patients in re-appraising their symptoms as part of the natural ecology of human experience; recognising the vicious cycle of symptom aggravation created by fixation on symptoms, contradictions between reality and the ideal, and attempts to fight or control otherwise inevitable emotions; and moving from a position of preoccupation with symptoms to the acceptance of spontaneous affective experiences. Therapists will continually reinforce the patient's shift from self-reflection towards a focus on constructive action and the external environment. Throughout therapy, patients will also complete a daily diary for therapists to comment on, to increase communication and the opportunity for therapist reinforcement.

Treatment as usual alone

We have selected treatment as usual as our trial comparator as a reflection of the trial comparator which would be selected for a fully-powered RCT, in which our key interest would be whether Morita Therapy plus treatment as usual has superior or equivalent effectiveness to current clinical practice in the UK, in which people have access to GP care and a range of other treatments. Thus, a large scale RCT would be a pragmatic trial embedded within the healthcare environment in which Morita Therapy would be delivered, seeking to establish whether Morita Therapy could be useful in addition to the options currently available to depressed patients in the UK.

Thus, in this pilot trial we will replicate 'treatment as usual' by making no specific patient-level recommendation or requirement to alter the usual treatment received by depressed patients in the UK, and the study will not place any restrictions on the treatment options available to these participants. GPs will treat and refer participants as would be their normal practice and participants in this trial arm are free to access any other care and services, including formal courses of psychological therapy such as Cognitive Behavioural Therapy. All participants, irrespective of their allocation, are free to choose whether they take antidepressant medication or not. We will record the treatments received in the course of participants' treatment as usual.

Outcomes

Given this is a feasibility study with a range of different aims, there is no single primary outcome measure. Rather, we will collect a variety of data at baseline interview and four months post-randomisation: severity of depressive symptoms (PHQ-9 [30]), severity of generalised anxiety symptoms (seven item Generalised Anxiety Disorder questionnaire: GAD-7 [36]), quality of life (Short Form 36 Health Survey Questionnaire: SF-36 [37]; Work and Social Adjustment Scale: WSAS [38]), and attitudes (The Morita Attitudinal Scale for Arugamama: MASA [39]). At four months post-randomisation, we anticipate that treatment for participants in the Morita Therapy plus treatment as usual trial arm will be complete. We will hold follow-ups at University of Exeter premises or the participant's home, depending on participant preference, and apply all research measures to both groups of participants equally.

We will also collect data on the flow of participants through the trial. For participants in the Morita Therapy plus treatment as usual trial arm, therapists will also inform the researcher of the number of therapy sessions attended and the reason for ending treatment. We will not conduct an economic evaluation as part of this pilot trial, although at follow-up we will incorporate methods for collecting data on participants' use of health and social care services as used in our recent mental health trials [23] (whereby we will establish the rates and nature of hospital visits; use of community, social and complementary services; and use of psychotropic medication since baseline assessment), in order to characterise treatment as usual and calculate the cost of each trial arm for a large-scale RCT.

Semi-structured Interviews

Sample and setting

We will invite all participants who are allocated to Morita Therapy plus treatment as usual for a post-treatment

semi-structured interview, thus selecting as diverse a sample as possible within this pilot trial. This will provide a maximum of 30 participants (all those retained in the Morita Therapy trial arm). We will also invite the two therapists providing Morita Therapy to interview. We will hold participant interviews at University of Exeter premises or the participant's home, depending on participant preference. Therapist interviews will be conducted at the AccEPT Clinic.

Recruitment

We will explain the purpose and content of the interview to participants in the participant information leaflet, and determine their consent to participate at baseline interview. We will send therapists an interviewee information leaflet explaining the interview prior to a pre-trial meeting, and establish their consent to participate during this meeting. Upon completion of Morita Therapy (delivery, for therapists), we will contact participants to establish whether they are still willing to be interviewed, remind them of what will be involved and answer any questions. For willing participants, we will arrange an interview no sooner than 48 hours later and send an interview confirmation letter explaining the opportunity to rearrange or cancel the interview at any time.

Interview process and questions

We will undertake semi-structured interviews to allow participants to describe their views of Morita Therapy. This method will enable us to investigate the meaning of participants' responses, both exploring views on our predefined topics of interest and eliciting more detail on any emerging themes [40]. Interviews are expected to last up to one hour and will be audio-recorded with the participant's consent. The interviewer will also take field notes during and after the interview.

We will follow topic guides established on the basis of our recent mental health trials addressing similar research questions [21, 23, 41] (which ask about participants' views and experiences of treatment, any barriers to treatment, and the impact of treatment) and existing Morita Therapy literature. To explore the acceptability of Morita Therapy, we will ask participants to describe their understanding of Morita Therapy, explore their views and experiences of Morita Therapy and investigate potential barriers to/facilitating factors in engaging with Morita Therapy. In particular, we will explore participant's views and experiences of the defining features of Morita Therapy in practice, such as the four stages and daily diaries. To explore the feasibility and appropriateness of our trial procedures, we will explore participants' views on the support provided throughout the trial; procedures for recruitment, monitoring and data collection; and use of the MASA questionnaire. We aim to identify both procedures that facilitated the efficient running of the trial and any considered problematic.

Analysis

We will first analyse the quantitative and qualitative data separately before integrating both types of information in a mixed methods analysis.

Quantitative analysis

Following double data entry into STATA v.11 [42], we will analyse recruitment, retention, treatment adherence and estimates of the participant-related data to inform the feasibility of and sample size calculation for a fully-powered trial. Thus, we will emphasise quantification and estimation rather than hypothesis testing. All analyses will be on an intention to treat basis and we will not impute missing data, although we will report outcome data that are missing in each trial arm and the reasons for missing data where possible.

We will use count data with calculated estimated margins of error, expressed as a percentage of both the total number of participants invited and in relation to the preceding step in recruitment, to quantify the flow of the participants through the trial. For each trial arm, we will quantify the number of participants who withdrew, could not be contacted or did not provide follow-up data for another reason. We will also express data as a percentage of the total number of participants in each trial arm. We will follow CONSORT guidelines, including the forthcoming pilot and feasibility extension [43], in reporting all data including the number of participants exiting the trial at each step and from whom we are unable to collect follow-up data. Descriptive statistics will also be used to describe the number of Morita Therapy sessions attended by participants allocated to Morita Therapy plus treatment as usual.

To measure the variance in participant outcomes, we will estimate the standard deviation around the mean PHQ-9, GAD-7, SF-36, WSAS and MASA scores at baseline and four months for both groups. We will also estimate the correlation between participants' scores on these measures at baseline and at four months, which can be used to refine the sample size calculation for any fully-powered evaluation. Although we do not have the power to make inferential statements on between (or within) group differences and as such no p values will be calculated, we will also calculate and report the observed differences between Morita Therapy plus treatment as usual and treatment as usual alone on the mean changes in these measures from baseline to four month follow-up, and the 95 % confidence intervals around these figures.

Qualitative analysis

With participants' permission, we will record and transcribe interviews verbatim. We will use NVivo10 [44] to organise the data and conduct a systematic analysis of interviews and field notes, using Framework analysis [45] to allow for the combination of both inductive and deductive approaches in the development of analytic categories. In line with this, an initial thematic framework will be developed as preliminary analysis is undertaken and subsequently as batches of transcriptions are analysed, iteratively combining our topic guide and the overall impression of the narratives in context. Using this framework, transcripts will be coded at the level of individual participants and then analysed thematically across the whole dataset as well as in the context of each participant's interview using a constant comparison approach [46], whereby each piece of data (e.g. one statement or one theme) is compared with others for similarities and differences [47]. As we formulate explanations in this way, negative cases will be explored and explanations of variance provided [48], thus incorporating all observations relevant to our research question. Data collection and analysis will be iterative: we will amend our interviewing style to respond to emerging themes and explore deviant cases further in subsequent interviews as appropriate.

Mixed methods analysis

Our mixed methods analysis will be guided by both the nature of the quantitative and qualitative data that we ultimately obtain and the inferences that arise from our separate analysis of each [41]. Thus, the analysis we eventually undertake may differ to the analysis we propose [41]. Analytical techniques have been proposed below based on the methods summarised by Creswell and Plano Clark [24].

To explore how the qualitative data on the acceptability of Morita Therapy explains the quantitative findings on treatment adherence, we will merge these two types of data. Firstly, we will develop typologies of participants' different views on the acceptability of Morita Therapy from the qualitative data, and for each typology we will present data on treatment adherence for participants to whom the typology applies [41]. Alongside this, we will also present data on fidelity to the therapy protocol if the qualitative data relates to particular sections of the protocol or stages of therapy. This will allow us to explore whether any issues with the acceptability of Morita Therapy relate to the treatment itself or the therapists' delivery of treatment and thus aid us in identifying any 'fatal flaws' [49] of Morita Therapy requiring refinement in the future. Secondly, we will identify categories of participants defined by their treatment adherence and explore similar and different views on acceptability within and between categories [41].

We will consider the use of joint displays to summarise the quantitative data in relation to the qualitative themes for both of these purposes [41]. We will also integrate data on acceptability and treatment adherence in a case-oriented merged analysis display that will position cases (participants) on a scale of treatment adherence along with their qualitative data on acceptability [41].

Ethical issues

We will conduct this trial in such a way as to protect the human rights and dignity of the participants, as reflected in the Helsinki Declaration [50]. The study has received ethical approval from the National Research Ethics Service South West – Frenchay (reference 15/SW/0103) and governance assurance from the National Health Service Research and Development Directorate (reference CG/JL), and has been approved by the University of Exeter Medical School following independent peer review.

Participants will not receive any financial inducement to participate. We will conform to Good Clinical Practice Guidelines, data protection and freedom of information acts. All data will be stored securely and anonymised wherever possible. All identifiable participant information will be stored separately to questionnaire data which will be coded by a trial ID number only. No published material will contain identifiable participant information.

Informed consent and withdrawal

The study researchers will be fully trained and supervised by senior academic and clinically qualified staff. All our information leaflets and consent forms have been produced using the current Health Research Authority's online guidance for writing such documents [51], and are based on similar materials used in our other mental health trials as informed by Patient and Public Involvement.

Informed consent will be determined by a two phase process. Potential participants will receive a study summary sheet and a form on which to complete their contact details and confirm their permission for a researcher to contact them. We will telephone those who return this form to us, to assess their potential eligibility and answer any questions. For those who are eligible and willing, we will send a participant information leaflet and arrange a baseline interview at least 48 hours later, to allow the participant time to reflect on their decision to participate and change their mind if they so wish. Full informed consent will only be obtained at this interview where the information leaflet will be fully explained and the opportunity to ask questions given.

Consent to participate in the qualitative interview is optional; participants may participate in the pilot RCT only. We will explain the purpose and content of the interview in the participant information leaflet

(or interviewee information sheet, for therapists), and note that a decision not to be interviewed will not affect participation in the trial. At baseline interview (for participants) and the pre-trial meeting (for therapists), we will answer any questions, explain the opportunity to stop and/or withdraw from the interview at any time and clarify steps to maintain confidentiality. We will ask willing participants to indicate their decision on a consent from. Consent for audio recording of the interview and/or therapy sessions is also optional.

We will treat informed consent as an ongoing process whereby participants may withdraw their consent to participate at any time, and set up communication and recording systems to enable us to monitor and act on such wishes. When obtaining consent, we will advise participants of this fact and that they may be asked to give a reason for their withdrawal but will not have to provide one. Participants allocated to Morita Therapy plus treatment as usual may withdraw from therapy and continue their involvement in the trial through participation in the follow-up and qualitative interview if they wish.

Should it come to our attention that a participant loses capacity to consent during the study according to the Mental Capacity Act 2005 [52], we will withdraw them from the study as per information provided to participants in the participant information leaflet. Within this leaflet, we will also inform participants that if they should withdraw or be withdrawn from the study, we will retain any data already provided to be used confidentially in relation to the purpose for which consent was sought.

Anticipated risks and benefits

No treatment will be withheld from participants taking part in this trial. All participants will remain under the care of their GP and will have access to primary care services in the usual way. Participants allocated to treatment as usual alone will be returned to the care of their GP with no restrictions placed on treatment options. Participants allocated to Morita Therapy plus treatment as usual will be asked not to engage in other formal courses of psychological therapy during their treatment, as it is not considered good practice to engage in more than one psychological therapy at once. Should participants in this trial arm wish to engage in other psychological therapy elsewhere, a discussion will be held with their therapist to establish which therapy option is in the participant's best interests.

Participants allocated to Morita Therapy plus treatment as usual will take part in an alternative therapeutic approach to psychopathology which is widely practiced in Japan and somewhat elsewhere. Morita Therapy has been practiced since the 1920s and is not known to be associated with any risks to patients. It is possible that participation in therapy focused on psychopathology may cause distress to some participants, however participants in the Morita Therapy trial arm will receive an intensive level of monitoring so that any worsening or at suicidal risk will be identified and directed to appropriate care. Similarly, we will address any impact of potentially distressing questions within our assessment and outcome measures by following our protocols for responding to risk and directing participants to appropriate care. Additionally, we will report any serious adverse events reported to a therapist or researcher which are thought to be treatment related to the trial sponsor, Research Ethics Committee and independent oversight clinician (see section on study oversight).

The patient information leaflet will explain that participants allocated to Morita Therapy plus treatment as usual will no longer be offered such therapy once they have received a full "dose" (up to twelve sessions), but will be referred back to their GP with whom they could consider access to other treatments. We will ensure participants are reminded of these factors throughout the trial.

The University of Exeter has insurance to cover the potential legal liability for any harm to participants arising from the management of this trial. We will also provide potential participants with information about the possible benefits and risks of taking part in the trial in the participant information leaflet, and give them the opportunity to discuss this issue with us before consenting. We will inform participants in writing if new information comes to light which may affect their willingness to participate in the trial.

Managing risk of suicide

Inherent in the nature of the population under scrutiny is the risk of suicide. We will follow good clinical practice in monitoring for suicide risk during all appointments and explain to participants that we will contact their GP or specialist if deemed necessary in line with our risk protocol. If an acute risk is present, we will seek advice from the participant's GP (or the duty GP) immediately and/or follow locally established suicide management plans. All clinicians and researchers will be familiar with established risk protocols used in our previous research trials and/or within the AccEPT Clinic, specifically trained in risk assessment and supervised by experienced clinicians. We will put in place systems to ensure that senior academic and clinically qualified staff are notified should there be any risk to a participant's safety.

Patient and public involvement

We have developed the patient materials on the basis of both consultation with a Public and Patient Involvement Expert and similar materials used in our other mental health trials which received feedback from Public and

Patient Involvement groups such as the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South West Peninsula (PenCLAHRC) [53] Patient and Public Involvement Group (PenPIG). This feedback has helped us to ensure that our research respects the rights, safety and dignity of participants. Ensuring that our research materials are sensitive and consistent with the views of people with depression will also aid us in recruitment and participants' engagement in and openness during interviews.

Following completion of the pilot trial, to ensure that our results reach our former trial participants and people with mental health issues in a way that is meaningful and accessible, we will establish an advisory group comprising members of PenPIG and follow national good practice guidance for researchers on public involvement in research and the paying of representatives [53]. The group will be involved in the dissemination of the results to the public and patients using accessible channels and their own conference and group meetings. Training in presentation skills will be arranged for members of the group should they consider this helpful. We will also consult the advisory group on the development of a summary sheet explaining the results of the study and their implications in lay terms, to be sent to consenting former trial participants.

Dissemination protocol

In addition to the above details on the dissemination of results to the public and former trial participants, we will disseminate the results of this study in a full internal report and intend to publish our results in a peer reviewed scientific journal. Authors will be those considered to have made a substantive intellectual contribution to the study. The main output from this study will be the information required to design and seek funding to conduct a definitive trial of Morita Therapy. Thus, in the long term we aim to contribute to national guidelines for the treatment of depression and anxiety.

The investigators and relevant authorities will have access to the trial dataset. Furthermore, we will store anonymised research data and outputs in the University of Exeter's Open Research Exeter repository [54] in order to facilitate open access to, and the impact of, our research.

Study oversight

This research forms part of the first author and Chief Investigator's (HVRS) PhD programme of studies for which she is supervised by DAR and JF. Trial conduct will be discussed between the Chief Investigator and her supervisors at monthly supervision meetings.

Although the convention of a formal Data Monitoring and Ethics Committee is not appropriate for the scale of this study, an independent clinician will act in this capacity in order to review serious adverse events which are thought to be treatment related, and any substantive protocol amendments. All such amendments will be communicated to the relevant authorities as deemed necessary.

Forecast execution dates

The preparatory period started in October 2014. Recruitment is running from September 2015 for approximately ten months. Follow-up and qualitative data will be collected from January 2016 to November 2016. Data analysis and reporting are expected to take another nine months. The total duration of the study will be 24 months.

Discussion

By preparing the ground for the design and conduct of a large-scale RCT, this study will contribute important information towards the development and subsequent evaluation of Morita Therapy for the treatment of depression and anxiety for the first time in the UK. One strength of our study design is that the proposed methods are appropriate for undertaking a feasibility study [41]. Our study purpose and research questions are in line with the National Institute for Health Research Trials and Studies' definition of a feasibility study [55] endorsed by Arain and colleagues [56]. We have calculated the RCT sample size based on the key feasibility objectives around recruitment and retention rates, and will calculate the variance in participant outcomes and their correlation with baseline scores to inform future sample size calculations. We will also calculate the observed differences between Morita Therapy plus treatment as usual and treatment as usual alone on the mean changes in outcome measures, although we will not make inferential statements or evaluate these outcomes. Rather than identifying a primary outcome measure, we have designed both the pilot trial and qualitative interviews to allow us to test the uncertainties associated with designing and running a large-scale fully-powered RCT of Morita Therapy plus treatment as usual versus treatment as usual alone.

To embrace the complexity of developing and evaluating interventions and provide a comprehensive understanding of the intervention in question, no one method will suffice [25]. Thus, a further strength of this study is our explicit commitment to a mixed methods approach and transparent description of the way in which quantitative and qualitative components will be integrated [41, 57]. We have carefully considered guidance on maximising the impact of qualitative research in feasibility studies

[49] and described our proposal in line with recommendations for Good Reporting of a Mixed Methods Study [57], which we will continue to follow in our future reporting. Our embedded mixed methods design reflects key decisions we have reached on the levels of interaction, priority, timing and procedures in the mixing of the quantitative and qualitative components [24, 41]. Thus, we will interactively mix the two components before final interpretation, at both the design and analysis levels, by embedding qualitative interviews within the pilot RCT in a program-objective framework; give the two components equal priority; undertake the pilot trial and qualitative interviews concurrently; and analyse data from the two components simultaneously.

We have specified research question seven to frame the integration of results from the quantitative and qualitative strands, to help explain variability in treatment adherence and thus facilitate a more complex picture of the acceptability of Morita Therapy [24]. By qualitatively exploring the acceptability of both Morita Therapy and our trial procedures, and integrating the qualitative and quantitative data, we will facilitate both the interpretation of our pilot trial findings and the feasibility and/or efficiency of any large-scale RCT, thus allowing us to optimise both our intervention and trial conduct in the future [58]. The integration of quantitative and qualitative methods will enable us to address both exploratory and explanatory research questions simultaneously, and help to reduce the limitations of each individual method whilst retaining their strengths [25]. Ultimately, by implementing an embedded mixed methods design, this study will better prepare the ground for a large-scale fully-powered RCT of Morita Therapy plus treatment as usual versus treatment as usual alone than would be possible from either a quantitative or qualitative approach alone [25, 41].

Trial status

Recruitment commenced in September 2015 and is ongoing.

Additional files

Additional file 1: Study Summary Sheet. (PDF 222 kb)
Additional file 2: Permission to contact form. (PDF 160 kb)
Additional file 3: Participant Information Leaflet. (PDF 766 kb)
Additional file 4: Model Consent Form. (PDF 246 kb)

Abbreviations

GAD: Generalised Anxiety Disorder; GPs: General Practitioners; NICE: National Institute for Health and Care Excellence; IAPT: Improving Access to Psychological Therapies; RCT: Randomised Controlled Trial; MRC: Medical Research Council; NIHR: National Institute for Health Research; DSM: Diagnostic and Statistical Manual of Mental Disorders; MDC: Mood Disorders Centre; AccEPT: Accessing Evidence Based Psychological Therapies; PHQ-9: nine item version of the Patient Health Questionnaire; GAD-7: seven item Generalised Anxiety Disorder questionnaire; SF-36: Short Form 36 Health Survey Questionnaire; WSAS: Work and Social Adjustment Scale; MASA: The Morita Attitudinal Scale for Arugamama; CLAHRC: National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care; PenCLAHRC: National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula; PenPIG: National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula Patient and Public Involvement Group.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

DAR proposed the study; HVRS as chief investigator and study researcher designed the study with the involvement of DAR and JF; JF provided additional guidance and support in relation to the qualitative aspects of the study; HVRS drafted the study protocol and materials and obtained National Health Service ethical approval and research and development governance assurance; HVRS is responsible for project management, data collection and analysis; HVRS and DAR developed the UK Morita Therapy outpatient protocol; DAR supervises the study therapists. HVRS drafted the manuscript. All other authors contributed to editing of the final manuscript. All authors read and approved the final manuscript.

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CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	1-2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	3-5
	2b	Specific objectives or research questions for pilot trial	5-6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
	4c	How participants were identified and consented	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-8
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	8-9
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	9
Sample size	7a	Rationale for numbers in the pilot trial	9-10
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	10
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	10

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	10
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	11-12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11-12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	11
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	12-13
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	14-18
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14-18
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	19-21
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	19-21
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	19-21
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	2
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	22
	26	Ethical approval or approval by research review committee, confirmed with reference number	6

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.
*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

BMJ Open

Morita Therapy for depression (Morita Trial): a pilot randomised controlled trial

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Secondary Subject Heading:	Health services research
Keywords:	Morita Therapy, Depression & mood disorders < PSYCHIATRY, Major Depressive Disorder, Feasibility study, Pilot randomised controlled trial

Morita Therapy for depression (Morita Trial): a pilot randomised controlled trial

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Abstract

Objective. To address uncertainties prior to conducting a fully-powered randomised controlled trial of Morita Therapy plus treatment as usual (TAU) versus TAU alone, or to determine that such a trial is not appropriate and/or feasible.

Design. Pilot parallel group randomised controlled feasibility trial.

Setting and participants. Participants aged ≥18 with DSM-IV Major Depressive Disorder, with or without DSM-IV anxiety disorder(s), recruited from General Practice record searches in Devon, UK.

Interventions. We randomised participants on a 1:1 basis stratified by symptom severity, concealing allocation using a secure independent web-based system, to receive TAU (Control) or eight to twelve sessions of Morita Therapy, a Japanese psychological therapy, plus TAU (Intervention).

Outcomes. Rates of recruitment, retention and treatment adherence; variance and estimated between-group differences in follow-up scores (on the PHQ-9 (depressive symptoms); GAD-7 (anxiety symptoms); SF-36/ WSAS (quality of life); MASA (attitudes)) and their correlation with baseline scores.

Results. We recruited 68 participants, 5.1% (95% CI 3.4% to 6.6%) of those invited (34 Control; 34 Intervention); 64/68 (94%; 95% CI 88.3% to 99.7%) provided four month follow-up data. Participants had a mean age of 49 and mean PHQ-9 score of 16.8; 61% were female. 24/34 (70.6%) adhered to the minimum treatment dose. The follow-up PHQ-9 (future primary outcome measure) pooled SD was 6.4 (95% CI 5.5 to 7.8); the magnitude of correlation between baseline and follow-up PHQ-9 scores was 0.42 (95% CI 0.19 to 0.61). 66.7% and 30.0% of participants recovered in the intervention and control groups respectively; 66.7% and 13.3% responded to treatment in the intervention and control groups respectively.

Conclusions. A large-scale trial of Morita Therapy would require 133 participants per group and is feasible with minor modifications to the pilot trial protocol. Morita Therapy shows promise in treating depression and may provide patients with a distinct alternative to current treatments.

Trial registration. Current Controlled Trials ISRCTN17544090.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This is the first randomised controlled trial of Morita Therapy for depression in English-speaking countries.
- Our pilot trial used mixed methods to address the procedural, methodological and clinical uncertainties associated with a large-scale trial.
- Criteria for success were specified a priori.
- The patients, clinicians and researchers were not blinded to group allocation, although self-report measures were used to reduce detection bias.

INTRODUCTION AND OBJECTIVES

Globally, depression is the leading cause of disability, affecting 350 million people worldwide[1]. In the UK, depression has a lifetime prevalence of 16.2%[2]. For individuals, depression is often chronic and recurrent, and rates of comorbidity and risk for suicide are high[2-5]. Furthermore, the comorbidity between depression and anxiety disorders, such as generalised anxiety disorder (GAD), makes a strong contribution to the total disability attributed to mental disorders[6-8]. Overall, the cost of depression and anxiety in the UK is significant at an annual rate of £17bn in lost output and direct health care costs[9].

Medication and Cognitive Behavioural Therapy (CBT) have the strongest evidence-base for treating depression, with each recommended by the National Institute for Health and Care Excellence (NICE)[10]. However, many people are resistant to such interventions[11]. Indeed, current treatments appear to have had little impact on the prevalence of common mental disorders in the UK, and depression remains a chronic disorder despite the available interventions[6, 12]. Recovery (defined as Patient Health Questionnaire 9 (PHQ-9)[13] score <10) is reached by fewer than 50% of patients who complete a NICE recommended psychological therapy within the 'Improving Access to Psychological Therapies' (IAPT) service, thereby increasing patients' risk of future relapses and the maintenance of chronic and recurring problems[14-16] Similarly, studies suggest that between one third and half of depressed patients treated with psychotherapy or antidepressant medication do not respond to treatment (typically defined as a 50% reduction in symptoms)[17-23]. Thus, there is scope to develop and test new potentially effective treatments for depression.

Morita Therapy is a Japanese psychotherapy developed by Dr Shōma Morita in 1919, and informed by Zen Buddhist principles[24, 25]. It is a holistic approach aiming to improve everyday functioning rather than targeting specific symptoms[26]. Through conceptualising unpleasant emotions as part of the natural ecology of human experience, Morita Therapy seeks to re-orientate patients in the natural world and potentiate their natural healing capacity. Morita therapists thus help patients to move away from symptom preoccupation and combat, which are considered to exacerbate symptoms and interfere with this natural recovery process[27]. By helping patients to accept symptoms as natural phenomena which

ebb and flow as a matter of course, Morita Therapy is in sharp contrast to the focus of established Western approaches on symptom reduction and control[28]. In Morita Therapy, patients are taught to live with, rather than be without, their symptoms.

Whilst other psychological therapies (such as Acceptance and Commitment Therapy[29]) also foster patients' acceptance of symptoms, through Morita's four experiential stages of rest and increasing action-taking, acceptance has a uniquely active, spontaneous and paradoxical quality: it cannot be brought about by deliberate cognitive reappraisal or meditative exercises (as per other approaches), only through everyday behavioural experience[26, 30, 31]. Indeed, according to Morita's unique method of shifting patients' attention away from self-reflection and immersing them in their environments, any efforts to consciously accept symptoms are considered counter-productive: maintaining focus on and therefore exacerbating symptoms[26, 31]. Thus, Morita Therapy is a unique psychotherapy with the potential to provide patients in the UK with a distinct and meaningful alternative to current treatment options.

Originally developed as an inpatient treatment for psychological problems similar to GAD, Morita Therapy is now applied to a wider range of conditions, including depression, and is considered a potentially pan-diagnostic approach given the absence of symptom-focus[26]. The approach is practiced in Japan and applied to a limited degree in countries including Australia, China, North America, Russia and Rwanda[26]. Initial evidence for the efficacy of Morita Therapy is largely based on case studies, predominantly conducted in Japan[32] (Minami, M. 2011). A limited number of randomised controlled trials (RCTs) in China and the USA provide mixed evidence for the effectiveness of inpatient Morita Therapy for post-schizophrenic depression[33] and in/outpatient Morita Therapy for anxiety[34-38]. However, to our knowledge, outpatient Morita Therapy for depression has not been tested using a randomised controlled design. Furthermore, no RCTs of any form of Morita Therapy for depression have been undertaken in English-speaking countries, and Morita Therapy is untested within the UK. Although a fully-powered RCT is clearly required to establish the effectiveness of Morita Therapy, given the novelty of

Morita Therapy in the UK a number of clinical, methodological and procedural uncertainties[39] prevented us from immediately undertaking such a trial.

Here, we report the results of a pilot RCT, comprising part of a mixed methods programme of research undertaken to prepare for the design and conduct of a fully-powered RCT of outpatient Morita Therapy plus treatment as usual (TAU) versus TAU alone for the treatment of depression, or to determine that such a trial is not appropriate and/or feasible. Our pilot RCT was designed to address the uncertainties associated with conducting a definitive trial by gathering information on (i) likely rates of recruitment, retention and treatment adherence and (ii) variance in participant outcomes and how these correlate with baseline scores, in order to inform future sample size calculations. It follows on from a programme of work conducted with patients and therapists to develop our Morita Therapy clinical protocol[40]. Findings from qualitative and mixed methods work undertaken alongside the trial, to explore the acceptability of Morita Therapy and how this relates to treatment adherence, are reported elsewhere.

Research questions

1. What proportion of participants approached to take part in a trial of Morita Therapy for depression will agree to do so?

2. What proportion of participants who agree to take part in the trial will remain in the trial at four month follow-up?

3. What proportion of participants who agree to take part in Morita Therapy will adhere to a pre-defined per-protocol dose of Morita Therapy?

4. What is the variance in participant outcomes (depressive symptoms; anxiety symptoms; qualitative of life; attitudes towards symptoms) following Morita Therapy plus TAU and TAU alone, and how do they correlate with participants' baseline scores?

5. What are the estimated between-group differences (and 95% confidence intervals) in participant outcomes (depressive symptoms; anxiety symptoms;

qualitative of life; attitudes towards symptoms) following Morita Therapy plus TAU and TAU alone?

METHODS

Trial design

The Morita Trial was a mixed methods feasibility study encompassing a pilot trial and embedded qualitative interviews. The trial, reported here, used a parallel group randomised controlled design.

Participants

We recruited people aged ≥18 with Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[41] Major Depressive Disorder, with or without DSM-IV anxiety disorder(s), assessed using standard clinical interview (Structured Clinical Interview for DSM-IV-TR Axis Disorders, Clinical Trials Version[42]) (SCID). We excluded people who were cognitively impaired, had bipolar disorder or psychosis/psychotic symptoms, were substance dependent, were currently in receipt of psychological therapy, and those whose risk of suicide was sufficiently acute to demand immediate management by a specialist mental health crisis team.

We recruited participants through record searches at eight General Practices in Devon, UK, to identify potential participants from depression Read Codes. Practice staff contacted potentially eligible patients to seek permission for researcher contact. Adverts were also placed on the websites of the University of Exeter Medical School and Mood Disorders Centre (MDC) Accessing Evidence-Based Psychological Therapies (AccEPT) Clinic; leaflets and flyers were placed in the waiting rooms of consenting Devon General Practices; an email invitation was circulated to former MDC participants who had consented to such contact. People who responded to these invitations/ adverts were interviewed by the study team who provided detailed information on the study, assessed eligibility and took informed written consent. The study received ethical approval from the National Research Ethics Service South West – Frenchay (reference 15/SW/0103). The protocol has been published previously[43] (see supplementary file 1).

Interventions

Morita Therapy plus treatment as usual

Participants allocated to the intervention group were asked not to engage in other formal courses of psychological therapy during the course of their treatment. Otherwise, they were free to access any other usual care and medication in liaison with their GP.

Morita Therapy consisted of eight to twelve one hour face-to-face weekly sessions delivered at the University of Exeter's MDC AccEPT clinic (http://www.exeter.ac.uk/mooddisorders/acceptclinic/) by two professionally accredited research therapists experienced in the delivery of psychological interventions, including experimental treatments. Therapists were trained in Morita Therapy over 6 months. Training included background reading, attending presentations, involvement in the development of the UK Morita Therapy outpatient protocol[40], and practical training led by the second author (DAR), a clinically qualified academic with ten-years' membership of the Japanese Society for Morita Therapy. Practical training was experiential: role plays, diary examples, additional reading and peer support as per a tailored therapist training programme developed by the study team[40].

Therapists followed the UK Morita Therapy outpatient protocol developed by the study team[40]. DAR provided fortnightly supervision of cases together with advice and support. A qualitative checklist highlighting the key components of Morita Therapy, and key discussions to be held in facilitating patients' engagement with the treatment phases, was used as an aide memoir to structure supervision discussions and the assessment of fidelity. With the patient's consent, all therapy sessions were audio recorded for use in supervision.

During therapy, patients progressed through Morita Therapy's four phases of rest and increasing action-taking in order to address fatigue, expand peripheral attention and move from a mood-oriented to purpose- and action-oriented lifestyle. Therapists aided patients in re-appraising their symptoms as part of the natural ecology of human experience; recognising the vicious cycle of symptom aggravation created by

fixation on symptoms, contradictions between the 'real' and 'ideal', and attempts to fight or control otherwise inevitable emotions; and moving from a position of preoccupation with symptoms to acceptance of spontaneous affective experiences. Therapists continually reinforced the patient's shift from self-reflection towards a focus on constructive action and the external environment. Patients completed daily diaries in which therapists wrote comments to increase communication and the opportunity for therapeutic reinforcement.

Treatment as usual alone

For the control group, no intervention (nor 'waiting-list' option) was offered by the study team. No specific recommendation or requirement to alter the usual treatment received by depressed patients in the UK was made, and no restrictions were placed on the treatment options available to these participants. GPs were free to treat and refer participants as would be their normal practice and participants were free to access any other care and services, including formal courses of psychological therapy such as CBT.

All participants, irrespective of their allocation, were free to choose whether they took antidepressant medication. For all participants, we informed their GP of their participation in the study and group allocation.

Outcomes

We collected demographic data including SCID diagnoses at baseline assessment. We collected the following self-reported data at baseline and four months post-baseline: severity of depressive symptoms (PHQ-9); severity of generalised anxiety symptoms (Generalised Anxiety Disorder questionnaire 7 (GAD-7)[44]); quality of life (Short Form 36 Health Survey Questionnaire (SF-36)[45] and Work and Social Adjustment Scale (WSAS)[46]). We measured participants' attitudes towards themselves and their symptoms using a questionnaire developed for Morita Therapy-specific outcomes (Morita Attitudinal Scale for Arugamama (MASA)[47]).

We collected data on the flow of participants through the trial. For Morita Therapy participants, therapists also informed the study researchers of the number of therapy sessions attended and reason for ending treatment.

Trial success criteria

We defined criteria which should be met in order to determine if a fully-powered trial would be feasible or not[39, 43]. These were:

1. Participant recruitment and retention: we can recruit and retain sufficient participants to populate a fully-powered trial, i.e. at a recruitment rate of 12% of those invited and an attrition rate no higher than 20% of those randomised, in line with other UK National Institute of Health Research (NIHR) mental health trials[22, 48].

2. Participants will engage with and adhere to Morita Therapy at a rate on a par with other UK NIHR mental health trials[22], i.e. at least 65% of participants allocated to Morita Therapy attend the per-protocol minimum of ≥five sessions out of a maximum of twelve available sessions.

In terms of decision-making against these criteria, should we have fallen below any of these rates in our pilot trial we would consider whether protocol modification or close monitoring during a fully-powered RCT would address any failure to meet these criteria, or decide that a fully-powered trial would not be feasible[39].

Sample size

A conventional power calculation is inappropriate for the purpose of a pilot trial[39]. However, informed by our criteria above and guidance on using pilot studies to reliably estimate variance for participant outcomes[39, 49], we aimed to invite 570 potential participants, recruit 72 participants and follow-up 60 participants (30 in each arm). These figures were sufficient to estimate (i) participation rates (as percentage of subjects invited) of 10% with a margin of error of +/- 2.46%, or 12% with a margin of error of +/- 2.67%, or 15% with a margin of error of +/- 2.93%, based on 95% confidence intervals (CI); (ii) follow-up rates (as percentage of participants randomised) of 80% with a margin of error of +/- 9.24% or 85% with a margin of error

of +/- 8.25%, based on 95% CI; (iii) the standard deviation (SD) of continuous outcomes to within 22% of their true value based on the upper limit of the 95% CI; (iv) a Pearson's correlation coefficient between baseline and follow-up scores with a margin of error of +/- 0.1 if the true correlation is 0.8, or +/- 0.14 if the true correlation is 0.7, or +/- 0.17 if the true correlation is 0.6.

Randomisation

We randomised participants in a 1:1 ratio to the intervention or control arm using a computer-generated random allocation sequence at the Exeter Clinical Trials Unit (ExeCTU). We stratified randomisation according to participants' symptom severity on the PHQ-9 and minimised allocation to balance the stratification variable across the two arms. To ensure allocation concealment, we randomised using an externally administered, password-protected randomisation website independently developed and maintained by ExeCTU. Allocation occurred on completion of an eligible participants' baseline assessment. Subsequently, the study researchers informed the participant and their GP, via standard letter, of the outcome and, for those randomised to the intervention group, passed participant details to the clinic to arrange treatment.

It was not possible to blind participants or clinicians to group allocation due to the nature of the intervention. The study researchers were not blinded to group allocation due to resource limitations. However, baseline and follow-up data were self-reported and all research measures were applied equally to both groups to reduce potential detection bias.

Statistical methods

We undertook all analyses on an intention to treat basis and did not impute missing data. We applied pairwise deletion to each measure in order to maximise the data available. Where a questionnaire item was missing (which occurred only at follow-up), pairwise deletion was applied to that follow-up measure for that participant. We report recruitment, retention, treatment adherence and baseline characteristics using descriptive statistics: means and SDs for continuous variables; numbers and percentages for categorical variables. We report the SDs of the outcome measures

(all continuous) with 95% CI for each trial arm at baseline and four months. We estimated the correlations between participants' scores on these measures at baseline and four months to inform the sample size calculation for a fully-powered trial. Although insufficiently powered to make inferential statements or calculate p-values, we report the observed differences between the intervention and control groups on the mean changes in these measures (with 95% CI), as well as proportions of participants recovering (follow-up PHQ-9 and GAD-7 scores <10[13, 44]) and responding to treatment (≥50% reduction in PHQ-9 and GAD-7 scores from baseline to follow-up) in each trial arm.

Patient and Public Involvement

The Morita Trial follows on from an iterative programme of work conducted to develop our Morita Therapy clinical protocol, whereby we optimised Morita Therapy according to the views of potential patients and therapists[40]. The patient materials were developed on the basis of consultation with a Public and Patient Involvement (PPI) expert and similar materials used in other mental health trials which had received feedback from PPI groups (e.g. PenPIG http://clahrc-peninsula.nihr.ac.uk/). A former trial participant, who expressed an interest in supporting our research and will be involved in the further dissemination of results, has co-written a summary sheet explaining our results in lay terms which has been sent to consenting former trial participants.

RESULTS

Participant flow

Participant flow through the trial is summarised in Figure 1.

We randomised 68 participants into the trial between October 2015 and September 2016: 34 (50%) to each trial arm. 146 potential participants gave permission for study researcher contact ('opted in'). We excluded 55/140 (39.3%) of those who could be contacted for telephone screen (24 did not meet inclusion criteria; 26 declined to participate; 5 were unable to arrange a baseline assessment) and 17/85 (20%) of those who attended baseline interview (15 did not meet inclusion criteria; 2

declined to participate). We randomised 68/146 (46.6%) of those who opted into the study. The 690 study invitations sent to potentially eligible patients identified via GP record search resulted in 35 participants randomised into the trial, a rate of 5.1% (95% CI 3.4% to 6.6%), with an additional 33 participants recruited from alternative sources such as advertising.

From January 2016 to January 2017, we collected four month follow-up data from 64/68 (94%) participants (95% CI 88.3% to 99.7%): 33/34 (97%) in the intervention arm and 31/34 (91%) in the control arm. In the intervention arm, one participant could not be contacted for follow-up; in the control arm, two participants could not be contacted for follow-up and one withdrew on the basis that they had not received active treatment. An additional control participant, after attending follow-up, revoked consent for his data to be included in the trial. Thus, whilst this participant is included within the participant flow figures, his data have not been included in the analysis of baseline characteristics or outcomes.

<insert Figure 1 (CONSORT diagram) here>

Baseline data

Baseline characteristics are summarised in Table 1.

Table 1. Participant baseline characteristics

	Intervention (n=34)	Control (n=33*)	Total (n=67)
Gender			
Female	22 (64.7)	19 (57.6)	41 (61.2)
Age (years)			
Mean (SD)	49.8 (14.8)	48.6 (15.9)	49.2 (15.2)
Ethic origin			
White British	31 (91.2)	30 (90.9)	61 (91.0)
White other	2 (5.9)	0 (0.0)	2 (3.0)
Mixed other	0 (0.0)	2 (6.1)	2 (3.0)
Asian Indian	0 (0.0)	1 (3.0)	1 (1.5)
Asian other	1 (2.9)	0 (0.0)	1 (1.5)
Education			
No qualifications	3 (8.8)	2 (6.1)	5 (7.5)

GCSE or O Level	7 (20.6)	6 (18.2)	13 (19.4)
Post GCSE or O Level	7 (20.6)	8 (24.2)	15 (22.4)
Undergraduate degree	9 (26.5)	10 (30.3)	19 (28.4)
Postgraduate qualification or higher	8 (23.5)	7 (21.2)	15 (22.4)
Marital status			
Married or cohabiting	23 (67.6)	16 (48.5)	39 (58.2)
Number of children			
Mean (SD)	1 (1)	1 (1)	1 (1)
History of depression			
One or more previous episodes	29 (85.3)	25 (75.8)	54 (80.6)
Age of onset (mean (SD))	28.9 (17.8)	25.2 (17.4)	27.1 (17.6)
Duration of current episode in months (mean (SD))	13.1 (12.8)	30.3 (43.8)	21.3 (32.4)
PHQ-9 (depression) score			
Mean (SD)	17.4 (4.7)	16.1 (4.5)	16.8 (4.6)
GAD-7 (anxiety) score			
Mean (SD)	13.3 (4.8)	12.2 (4.0)	12.7 (4.4)
Secondary SCID diagnoses (current)			
Any anxiety disorder	21 (61.8)	28 (84.8)	49 (73.1)
Generalised anxiety disorder	13 (38.2)	17 (51.5)	30 (44.8)
Social phobia	5 (14.7)	11 (33.3)	16 (23.9)
Panic disorder with agoraphobia	6 (17.6)	8 (24.2)	14 (20.9)
Panic disorder without agoraphobia	7 (20.6)	3 (12.6)	10 (14.9)
Post-traumatic stress disorder	3 (8.8)	7 (21.2)	10 (14.9)
Obsessive Compulsive Disorder	2 (5.9)	5 (15.2)	7 (10.4)
Specific phobia	1 (2.9)	4 (12.1)	5 (7.5)
Agoraphobia without panic disorder	1 (2.9)	1 (3.0)	2 (3.0)
Antidepressant treatment			
Currently prescribed antidepressants	20 (58.8)	20 (60.6)	40 (59.7)
Previous psychotherapy/ counselling (at least one course of)			
Any psychotherapy (not including counselling)	23 (67.6)	26 (78.8)	49 (73.1)
Cognitive Behavioural Therapy	20 (58.8)	21 (63.6)	41 (61.2)
Mindfulness-based Cognitive Therapy	8 (23.5)	6 (18.2)	14 (20.9)
Behavioural Activation	1 (2.9)	3 (9.1)	4 (6.0)
Eye Movement Desensitization and Reprocessing	2 (5.9)	2 (6.1)	4 (6.0)
Counselling	15 (44.1)	14 (42.4)	29 (43.3)
Other psychotherapy	9 (26.5)	10 (30.3)	19 (28.4)

Notes: data are number (%) unless stated otherwise; SD=standard deviation; percentages may not always total 100 due to rounding; *34 participants were randomised into the control arm, with 33 participants' characteristics included due to one participant revoking consent to include data.

Receipt of Morita Therapy

No participants in the intervention group declined to start Morita Therapy and 24/34 (70.6%) adhered to a per-protocol minimum (≥five sessions). The mean number of sessions attended for all participants was 7.7 (range 1-14; SD 4.0); the mean number attended for those who did and did not adhere to the minimum dose was 9.8 (range 5-14; SD 2.5) and 2.6 (range 1-4; SD 1.0) respectively.

Outcomes and estimation

The SD of the outcomes at baseline and follow-up by trial arm, with 95% CI, are reported in Table 2. At follow-up, the pooled SD around the mean PHQ-9 score (the primary outcome in any definitive trial) was 6.4 (95% CI 5.5% to 7.8%). The correlations between baseline and four month scores by trial arm, with 95% CI, are reported in Table 3.

Table 2. Treatment outcomes at baseline and four month follow-up with variability and between-group differences

Outcome measure	Participants	Baseline				4 months				Change from baseline to 4 months			Between-group difference	
		n	Mean	SD	95% CI[1]	n	Mean	SD	95% CI[1]	n	Mean	SD	Mean	95% CI[2]
PHQ-9	All	67	16.8	4.6	3.9 to 5.6	63	10.3	6.4	5.5 to 7.8	63	-6.3	5.8		
	Intervention	34	17.4	4.7	3.8 to 6.2	33	8.4	6.5	5.2 to 8.6	33	-9.0	5.9	-5.5	-8.1 to -2.9
	Control	33	16.1	4.5	3.6 to 6.0	30	12.4	5.7	4.6 to 7.7	30	-3.5	4.2		
GAD-7	All	67	12.7	4.4	3.8 to 5.3	62	7.7	5.0	4.3 to 6.1	62	-5.0	5.2		
	Intervention	34	13.3	4.8	3.9 to 6.4	32	6.8	5.2	4.2 to 7.0	32	-6.6	5.6	-3.3	-5.8 to -0.7
	Control	33	12.2	4.0	3.2 to 5.3	30	8.7	4.7	3.7 to 6.3	30	-3.3	4.3		
WSAS	All	67	22.4	7.6	6.5 to 9.2	62	15.7	10.5	8.9 to 12.7	62	-6.8	8.8		
	Intervention	34	22.7	7.9	6.3 to 10.3	32	13.5	11.0	8.9 to 14.7	32	-9.7	9.7	-5.9	-10.1 to -1.7
	Control	33	22.1	7.4	6.0 to 9.8	30	18.0	9.4	7.5 to 12.7	30	-3.7	6.5		
MASA	All	67	76.8	26.5	22.6 to 31.9	62	103.5	36.3	30.9 to 44.2	62	25.3	30.6		
	Intervention	34	80.7	29.3	23.6 to 38.5	32	114.4	40.3	32.3 to 53.6	32	32.8	37.2	15.5	0.4 to 30.7
	Control	33	72.7	23.0	18.5 to 30.5	30	91.8	27.7	22.1 to 37.3	30	17.2	19.0		
SF-36 PCS	All	67	50.9	11.5	9.8 to 13.9	63	49.4	12.0	10.2 to 14.6	63	-1.9	7.5		
	Intervention	34	49.6	12.3	10.0 to 16.2	33	47.9	13.0	10.5 to 17.2	33	-1.7	6.6	0.6	-3.2 to 4.4
	Control	33	52.2	10.6	8.5 to 14.0	30	51.1	10.8	8.6 to 14.5	30	-2.2	8.5		
SF-36 MCS	All	67	24.4	7.8	6.6 to 9.3	63	35.2	12.4	10.5 to 15.0	63	10.8	11.5		
	Intervention	34	25.0	8.8	7.1 to 11.6	33	39.8	11.9	9.6 to 15.7	33	14.7	11.3	8.1	2.7 to 13.6
	Control	33	23.8	6.6	5.3 to 8.7	30	30.1	11.0	8.8 to 14.8	30	6.6	10.3		

Notes: SD=standard deviation of the mean; [1]95% CI = 95% confidence intervals around the standard deviation; [2]95% CI = 95% confidence intervals around the mean between-group difference.

Table 3. Correlation between participant scores at baseline and four months

Association	Participants	n	Rho	95% CI
PHQ-9 at baseline and 4 months	All	63	0.42	0.19 to 0.61
	Intervention	33	0.37	0.04 to 0.64
	Control	30	0.71	0.47 to 0.85
GAD-7 at baseline and 4 months	All	62	0.40	0.17 to 0.59
	Intervention	32	0.40	0.07 to 0.66
	Control	30	0.51	0.18 to 0.73
WSAS at baseline and 4 months	All	62	0.52	0.31 to 0.68
	Intervention	32	0.45	0.12 to 0.69
	Control	30	0.76	0.55 to 0.88
MASA at baseline and 4 months	All	62	0.58	0.39 to 0.73
	Intervention	32	0.45	0.12 to 0.69
	Control	30	0.73	0.50 to 0.86
SF-36 PCS at baseline and 4 months	All	63	0.68	0.52 to 0.80
	Intervention	33	0.78	0.59 to 0.88
	Control	30	0.58	0.27 to 0.78
SF-36 MCS at baseline and 4 months	All	63	0.42	0.20 to 0.61
	Intervention	33	0.43	0.10 to 0.67
	Control	30	0.39	0.04 to 0.66

Notes: Rho=Spearman's Rho; 95% CI = 95% confidence intervals around Spearman's Rho.

Outcomes in the intervention and control arms at baseline and follow-up, with observed between-group differences in changes from baseline to follow-up (with 95% CI), are summarised in Table 2. Depressive symptoms reduced from baseline to follow-up by an average of 9 PHQ-9 points in the intervention group and an average of 3.5 PHQ-9 points in the control group.

Proportions of recovery and response on the PHQ-9 (depressive symptoms) and GAD-7 (anxiety symptoms) by trial arm are summarised in Table 4. At follow-up, 22/33 participants in the intervention group (66.7%) scored below the threshold for moderate depression (PHQ-9 <10) with 9/30 controls (30.0%) similarly recovering. Depressive symptoms reduced by ≥50% from baseline to follow-up for 22/33 participants in the intervention group (66.7%) and 4/30 controls (13.3%).

Table 4. Proportions of recovery and response at four month follow-up

			Recovery	Response	
Outcome measure	**Participants**	**n**	**n (%) scoring <10 at follow-up**	**n (%) showing 50% reduction**	**n (%) either showing 50% reduction or scoring <10 at follow-up**
PHQ-9	All	63	31 (49.2)	26 (41.3)	32 (50.8)
	Intervention	33	22 (66.7)	22 (66.7)	23 (69.7)
	Control	30	9 (30.0)	4 (13.3)	9 (30.0)
GAD-7	All	62	40 (64.5)	27 (43.5)	40 (64.5)
	Intervention	32	24 (75.0)	17 (53.1)	24 (75.0)
	Control	30	16 (53.3)	10 (33.3)	16 (53.3)

Service use

Participants' use of health services (in addition to Morita Therapy) since baseline assessment is presented in Table 5. These data were collected in order to characterise TAU in preparation for costing a large-scale trial. Service use was comparable across the two arms with the exception of psychological therapy and counselling, which were proscribed in the Morita Therapy arm (0% in the Morita Therapy arm; 26% (n=8) in TAU). Compared to baseline assessment, antidepressant medication use reduced in both groups (58.8% (20/34) to 43.8% (14/32) and 60.6% (20/33) to 45.2% (14/31) in the intervention and control groups respectively).

Table 5. Service use at four month follow-up

Service	Participants	n	%	No. contacts		Duration of contacts (minutes)	
				Mean	SD	Mean	SD
Antidepressant medication (continuing at follow-up)	Morita Therapy (n=32) TAU (n=31)	14 14	43.8 45.2				
Psychological therapy	Morita Therapy (n=32) TAU (n=31)	0 5	0.0 16.1	- 5.4	- 4.4	- 68.0	- 47.6
Counselling	Morita Therapy (n=32) TAU (n=31)	0 3	0.0 9.7	- 6.3	- 2.1	- 60.0	- 0.0
Hospital admission	Morita Therapy (n=33) TAU (n=31)	2 1	6.1 3.2	1.5 1.0	0.7 0.0		
Hospital outpatient appointment	Morita Therapy (n=32) TAU (n=31)	9 9	28.1 29.0	2.1 2.1	1.5 3.0		
A&E attendance	Morita Therapy (n=32) TAU (n=31)	3 3	9.4 9.7	1.0 1.3	0.0 0.6		
GP appointment	Morita Therapy (n=32) TAU (n=31)	20 17	62.5 54.8	4.8 2.5	4.0 2.0	12.0 12.8	2.4 6.2
GP home visit	Morita Therapy (n=32) TAU (n=31)	2 0	6.3 0.0	1.0 -	0.0 -	12.5 -	3.5 -
GP telephone contact	Morita Therapy (n=32) TAU (n=31)	10 5	31.3 16.1	3.5 2.4	5.0 1.7	6.9 5.0	4.5 3.1
Practice nurse	Morita Therapy (n=32) TAU (n=31)	7 10	21.9 32.3	3.6 1.6	5.3 1.1	9.3 12.0	6.7 5.8
Psychiatrist	Morita Therapy (n=32) TAU (n=31)	0 1	0.0 3.2	- 12	- 0.0	- 50.0	- 0.0
Occupational therapist	Morita Therapy (n=32) TAU (n=31)	2 1	6.3 3.2	2.5 5.0	0.7 0.0	35.0 45.0	35.4 0.0
Social worker	Morita Therapy (n=32) TAU (n=31)	1 0	3.1 0.0	5.0 -	0.0 -	60.0 -	0.0 -
Advice service	Morita Therapy (n=32) TAU (n=31)	2 1	6.3 3.2	1.0 1.0	0.0 0.0	75.0 60.0	21.2 0.0
Helpline	Morita Therapy (n=32) TAU (n=31)	1 2	3.1 6.5	1.0 25.0	0.0 0.0	60.0 30.0	0.0 0.0
Chiropractor	Morita Therapy (n=32) TAU (n=31)	5 3	15.6 9.7	3.8 2.0	3.0 1.7	29.0 41.7	17.5 10.4
Acupuncture	Morita Therapy (n=32) TAU (n=31)	1 1	3.1 3.2	1.0 9.0	0.0 0.0	30.0 60.0	0.0 0.0
Physiotherapist	Morita Therapy (n=32) TAU (n=31)	1 1	3.1 3.2	3.0 4.0	0.0 0.0	60.0 60.0	0.0 0.0
Mental Health support worker	Morita Therapy (n=32) TAU (n=31)	1 1	3.1 3.2	1.0 6.0	0.0 0.0	60.0 60.0	0.0 0.0

Notes: SD=standard deviation of the mean; TAU=treatment as usual; A&E=Accident and Emergency; GP=General Practitioner

DISCUSSION

In this pilot RCT we have demonstrated that it is possible to recruit UK-based people with depression into a trial of Morita Therapy, and to retain them at four

month follow-up at a rate which is equivalent to or exceeds that found in other trials in the field[e.g. 22, 48, 50, 51]. Participants' adherence to the minimum dose of Morita Therapy was on a par with other psychological therapies in similar trials[e.g. 22]. Furthermore, depressive symptoms reduced from baseline to follow-up by an average of 9 PHQ-9 points in the intervention group and 3.5 points in the control group: a between-group difference exceeding the PHQ-9 minimum clinically important difference (MCID)[52]. Rates of recovery and response to Morita Therapy (66.7%) were at least as good as those achieved by leading evidence-based psychological therapies[14, 15, 17-23].

Strengths and limitations

A key strength of this trial is that it represents not only the first study of Morita Therapy in the UK but the first randomised controlled trial of Morita Therapy for depression within English-speaking countries. Whilst the findings are consistent with previous studies which suggest possible benefits of Morita Therapy[32, 38, 53] (Minami, M. 2011), this study provides a valuable contribution in terms of applying Morita Therapy to a UK population, and by employing a rigorous methodology in preparation for a fully-powered trial. The methods utilised were suitable for a feasibility study: the study purpose and research questions accorded with The National Institute for Health Research Evaluation Trials and Studies' definition of a feasibility study[54], endorsed by Arain et. al.[55]; the trial was designed to address key uncertainties associated with a large-scale trial; criteria for success were specified a priori[39].

Due to resource limitations, the study researchers were not blinded to group allocation. Whilst baseline and follow-up data were self-reported, and all research measures were applied equally to both groups, it is possible that this introduced detection bias into the study[56, 57] and blinding of study researchers would be ensured in any future definitive trial.

Implications and future research

We can now estimate the parameters necessary in order to design a fully-powered trial based on the 95% confidence intervals around our current data: we estimate

that (i) the randomisation rate (as percentage of patients invited via GP record searches alone) would be between 3.4% and 6.6%; (ii) the retention rate would be between 88.3% and 99.7%; (iii) the pooled SD on the PHQ-9 (the primary outcome measure in a definitive trial) score at follow-up would be between 5.5 and 7.8. Using our pilot trial data alongside the most conservative estimate of the between-group difference based on the published PHQ-9 MCID (2.59)[52], we also estimate that 133 participants per group would be required to provide 90% power based on a two-sided 5% significance level and allowing for 20% attrition. Our previous experience leads us to assert that we could reasonably expect to recruit such numbers into a future trial.

We specified two criteria for success[39] for proceeding to a fully-powered trial. Our pilot trial attrition rate of 6% fulfils the specified standard (no higher than 20%), as does the treatment adherence rate of 70.6% (at least 65%). Whilst the recruitment rate from GP record searches alone (5.1%) was lower than anticipated, this is slightly higher than that found in other trials in the field[e.g. 50, 51]. To recruit 266 participants into a fully-powered trial, based on our pilot data 51 average sized General Practices would need to participate in record searches. This could be achieved in a similar timeframe to the pilot trial by conducting the trial over three sites (as opposed to one site) and with an increased workforce to recruit participants. Recruitment might also be maximised by identifying additional participants through advertising and utilising research registers (as per our current study) and by modifying the pilot trial protocol to include measures known to improve recruitment rates, such as telephone reminders to non-responding patients invited via GP record search[58-60]. We therefore anticipate that a sufficient number of participants to populate a fully-powered trial can be recruited, albeit with additional procedures, and conclude that a fully-powered trial is feasible with minor modifications to the pilot trial protocol in relation to our recruitment activities.

The level of participant adherence to Morita Therapy suggests that it is as acceptable to participants as other psychological treatments[22]. Whilst it is not the purpose of this paper to assess the effectiveness of Morita Therapy and the study was not powered to enable inferential statements to be made, our findings also suggest promising possible effects of Morita Therapy plus TAU versus TAU

alone[61]. The observed between-group difference in reduction in depressive symptoms (PHQ-9) from baseline to follow-up, and indeed the lower margin of error on this figure, exceeds the PHQ-9 MCID. Furthermore, the rates of recovery and treatment response found in this study are comparable to or exceed those found for current NICE recommended treatments for depression[14, 15, 17-23]. Whilst these findings suggest that Morita Therapy may be equivalent in effectiveness to other psychological therapies, supporting the potential value of Morita Therapy as a treatment for depression, our qualitative and mixed methods findings (reported elsewhere) provide early indications of which patients might benefit most from Morita Therapy, which will be incorporated into a process evaluation in a fully-powered trial[62].

In line with this, given that treatment effectiveness varies at an individual if not population level, it is argued that research should focus on matching patient characteristics to treatment type[63-66]. In order to facilitate such work, it makes sense to test treatments which are qualitatively distinct from current options. Given the contrast between Morita Therapy and established Western approaches[28], Morita Therapy may prove a valuable addition to current treatment options by providing a meaningful alternative which may be particularly suited to patients for whom current treatments are not suitable. As such, Morita Therapy may facilitate both true patient choice (as enshrined in the forthcoming NICE guidelines for depression[67]) and the future 'matching' of patients to treatments, and potentially provide patients for whom current NICE-recommended therapies have failed a qualitatively different approach towards mental health.

Conclusions

We have determined that it is feasible to conduct a large-scale trial of Morita Therapy with minor modifications to the pilot trial protocol in order to maximise recruitment. Our findings indicate that Morita Therapy shows promise in the treatment of depression, supporting the potential of Morita Therapy to provide patients in the UK with a distinct and meaningful alternative to current treatment options.

FOOTNOTES

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions

DAR proposed the study; HVRS as chief investigator and study researcher designed the study with the involvement of DAR and JF; HVRS drafted the study protocol and materials and obtained National Health Service ethical approval and research and development governance assurance; HVRS was responsible for project management, data collection and analysis; HVRS and DAR developed the UK Morita Therapy outpatient protocol; DAR supervised the study therapists. HVRS drafted the manuscript. All other authors contributed to editing of the final manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figure legend:

Figure 1. CONSORT diagram

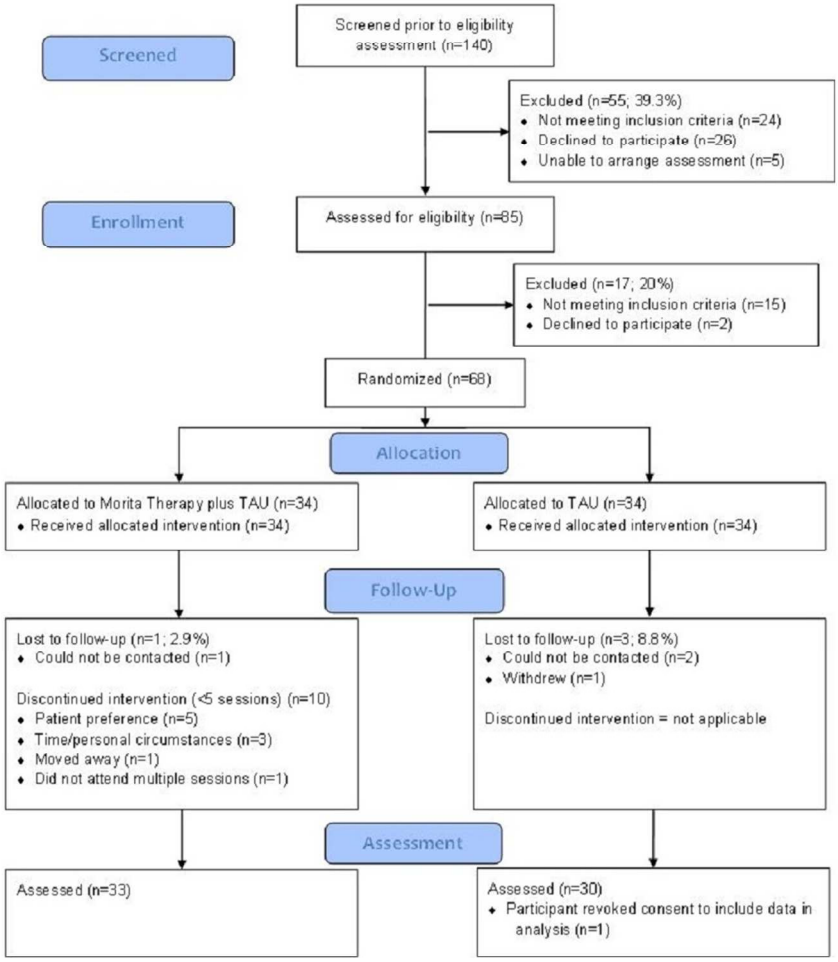

Figure 1. CONSORT diagram

91x102mm (300 x 300 DPI)

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Trials

STUDY PROTOCOL

Open Access

Morita therapy for depression and anxiety (Morita Trial): study protocol for a pilot randomised controlled trial

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Abstract

Background: Morita Therapy, a psychological therapy for common mental health problems, is in sharp contrast to established western psychotherapeutic approaches in teaching that undesired symptoms are natural features of human emotion rather than something to control or eliminate. The approach is widely practiced in Japan, but untested and little known in the UK. A clinical trial of Morita Therapy is required to establish the effectiveness of Morita Therapy for a UK population. However, a number of methodological, procedural and clinical uncertainties associated with such a trial first require addressing.

Methods/Design: The Morita Trial is a mixed methods study addressing the uncertainties associated with an evaluation of Morita Therapy compared with treatment as usual for depression and anxiety. We will undertake a pilot randomised controlled trial with embedded qualitative study. Sixty participants with major depressive disorder, with or without anxiety disorders, will be recruited predominantly from General Practice record searches and randomised to receive Morita Therapy plus treatment as usual or treatment as usual alone. Morita Therapy will be delivered by accredited psychological therapists. We will collect quantitative data on depressive symptoms, general anxiety, attitudes and quality of life at baseline and four month follow-up to inform future sample size calculations; and rates of recruitment, retention and treatment adherence to assess feasibility. We will undertake qualitative interviews in parallel with the trial, to explore people's views of Morita Therapy. We will conduct separate and integrated analyses on the quantitative and qualitative data.

Discussion: The outcomes of this study will prepare the ground for the design and conduct of a fully-powered evaluation of Morita Therapy plus treatment as usual versus treatment as usual alone, or inform a conclusion that such a trial is not feasible and/or appropriate. We will obtain a more comprehensive understanding of these issues than would be possible from either a quantitative or qualitative approach alone.

Trial registration: Current Controlled Trials ISRCTN17544090 registered on 23 July 2015.

Keywords: Morita therapy, Major depressive disorder, Mixed methods, Feasibility study

Background

Clinical depression and generalised anxiety disorder are the two most common mental health disorders [1], with one in six people in the UK experiencing such a disorder each year [2]. Together, depression and anxiety are estimated to cost the UK economy £17bn in lost output and direct health care costs annually, with a £9bn impact on the Exchequer through benefit payments and lost tax receipts [3].

Depression accounts for the greatest burden of disease among all mental health problems, and is the second-highest among all general health problems [4]. The lifetime prevalence of depression has been estimated at 16.2 %, and rates of co-morbidity and risk for suicide are high [5–7]. Depression is also recurrent, with over three quarters of people who recover from one episode experiencing at least one more [8].

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Generalised Anxiety Disorder (GAD) affects between 2–5 % of the UK population at any one time, and accounts for up to 30 % of the mental health problems presented to General Practitioners (GPs) [2]. The lifetime prevalence of GAD has been estimated at 5.7 % [9]. Furthermore, the comorbidity between anxiety and depression make a strong contribution to the total disability attributed to mental disorders [1].

Medication and Cognitive Behavioural Therapy have the strongest evidence-base for treating these conditions, and are each recommended by the National Institute for Health and Care Excellence (NICE) [10, 11]. However, many patients are refractory to such interventions [12], with both depression and anxiety remaining chronic disorders despite treatment [1]. Recovery is only reached by 55–56 % of people receiving treatment through the large-scale UK initiative to provide NICE recommended psychological therapies ('Improving Access to Psychological Therapies' (IAPT)) [13, 14], thereby increasing the risk of future relapse and the maintenance of recurring and chronic problems [15].

Thus, it is important to develop and test new potentially effective treatments for depression and anxiety in order to treat a wider range of patients [15] and provide patients in the UK with choice alternatives.

Morita Therapy

Morita Therapy is a psychotherapy developed in Japan by Dr Shoma Morita in 1919 [16] used for the treatment of common mental health problems. Morita Therapy was originally developed in inpatient settings for patients with particular psychological problems, including but not limited to GAD [17]. More recently, Morita Therapy has been applied to a wider range of conditions, including depression, and guidelines for practicing outpatient Morita Therapy have been developed [17]. Morita Therapy is now widely practiced in Japan, and has branches in various other countries including North America, Australia, China, Russia and Rwanda [18].

Morita Therapy is a holistic approach, aiming to improve functioning in everyday life, rather than an approach targeting specific symptoms [18]. The underlying premise is that unpleasant symptoms are part of the natural ecology of the human experience. Morita Therapy thus helps patients to re-orientate themselves in the natural world and takes a restorative approach to potentiate their natural healing capacity. Morita therapists help patients to move away from symptom preoccupation and combat, which it is conceptualised both interfere with this natural recovery process and lead to preoccupation with and worsening of symptoms [17]. By helping patients to accept that undesired symptoms are natural features of human emotion rather than something to control or eliminate, and that emotions ebb and flow as a matter of course and can be lived with, Morita Therapy is in sharp contrast to established western psychotherapeutic approaches with their focus on symptom elimination. In Morita Therapy, patients are taught to live with, rather than be without, unpleasant emotions.

Uncertainties: The need for a mixed methods feasibility study

As with the development of many other treatments to date [15], initial evidence for Morita Therapy's efficacy is largely based on case studies, predominantly conducted in Japan. A narrative review of forty-nine such studies and four quasi-experimental studies indicated that Morita Therapy has been reported as effective for a diverse range of issues, but that further work is required to both standardise its delivery and investigate its efficacy in controlled trials (personal communications: Minami, M).

Furthermore, Morita Therapy is currently little known in the UK. Thus, evidence of the efficacy of Morita Therapy based on truly experimental studies, and evidence of the effectiveness of Morita Therapy specifically for a UK population, has not yet been established. Whilst a fully-powered UK randomised controlled trial (RCT) of Morita Therapy versus treatment as usual is needed to establish the effects of Morita Therapy, a number of clinical, procedural and methodological uncertainties currently prevent us moving immediately to such a trial.

With respect to clinical uncertainties, the operationalisability of the UK Morita Therapy outpatient protocol, and the acceptability of both the protocol specifically and Morita Therapy in general, is unknown. Gathering data on these uncertainties is essential to ensure that the treatment administered in a large-scale trial is deliverable by therapists, and acceptable to both therapists and patients.

With respect to procedural uncertainties, information is required on the likely rates of recruitment to and retention in a trial of Morita Therapy, and of treatment adherence, in order to assess the feasibility of a trial and inform the required sample size. With respect to methodological uncertainties, estimates of the variance in participant outcomes and information on how these correlate with baseline scores are also required to inform future sample size calculations.

In line with the Medical Research Council (MRC) framework for the development and evaluation of complex interventions [19], all such uncertainties are appropriate to address within a pilot trial and feasibility study [20]. In order to both collect the required quantitative data and understand people's views of Morita Therapy, qualitative work will be embedded in a pilot randomised controlled trial of Morita Therapy compared to treatment as usual, and merged with quantitative data on treatment adherence to potentially help explain variability in participants' therapeutic engagement.

Study purpose

The purpose of this study is to prepare the ground for the design and conduct of a fully-powered RCT of Morita Therapy plus treatment as usual versus treatment as usual alone, or to conclude that such a trial is not appropriate and/or feasible.

Research questions

1. What proportion of participants approached to take part in the trial will agree to do so?
2. What proportion of participants who agree to take part in the trial will remain in the trial at four month follow-up?
3. What proportion of participants who agree to take part in Morita Therapy will adhere to a pre-defined per-protocol dose of Morita Therapy?
4. What is the variance in participant outcomes following Morita Therapy plus treatment as usual and treatment as usual alone, and how do they correlate with participants' baseline scores?
5. What are the estimated between-group differences (and 95 % confidence intervals) in participant outcomes following Morita Therapy plus treatment as usual and treatment as usual alone?
6. How acceptable is Morita Therapy to participants and therapists?
7. How do participants' views about Morita Therapy relate to the variability in the number of treatment sessions they attend?

Criteria for success

The criteria to be met in order to deem a fully-powered RCT feasible as is [20] are:

1. A sufficient number of participants to populate a fully-powered trial are likely to be recruited and retained, i.e. we recruit at the rate anticipated in the pilot trial (12 % of those invited) and experience an attrition rate no higher than 20 % of those randomised, in line with our other National Institute of Health Research (NIHR) mental health trials [21–23]. We will consider whether protocol modification or close monitoring during a fully-powered RCT will address any failure to meet these criteria [20].
2. The levels of engagement with and adherence to Morita Therapy are likely to be on par with our other NIHR mental health trials [23], i.e. at least 65 % of patients allocated to Morita Therapy attend at least 40 % of treatment sessions. Any failure to meet this criterion will be considered in the light of participants' views on the acceptability of Morita Therapy in order to determine whether protocol modification or close monitoring are sufficient to deem a fully-powered RCT feasible [20].
3. It is likely that a Morita Therapy outpatient protocol can be produced which is acceptable to patients and therapists, and deliverable by therapists, as defined by responses to qualitative interviewing.

Methods/Design

Study design

We will incorporate exploratory and explanatory components in a mixed methods embedded design [24]. Thus, we will embed semi-structured qualitative interviews within a pilot randomised controlled trial of Morita Therapy plus treatment as usual versus treatment as usual alone for people with depression, with or without anxiety disorders. We will give quantitative and qualitative components equal priority and mix them interactively at the design level within a program-objective framework [24]. For these two components, we will collect data concurrently and analyse data simultaneously. We will use quantitative data to assess the feasibility of trial recruitment, retention and treatment adherence, and to inform any future sample size calculations. We will collect qualitative data on participants' and therapists' views of Morita Therapy. By merging qualitative and quantitative data, we aim to explain variability in participants' treatment adherence and develop a richer understanding of the feasibility, acceptability and appropriateness of Morita Therapy (Table 1).

Philosophical assumptions

Our decision to use a mixed methods design is driven by the primary importance we give to addressing the uncertainties associated with running a fully-powered RCT. Thus, we are guided by a pragmatic philosophy: we prioritise our research objectives and the methods which will lead to the best evidence with regards to those objectives [25]. Consistent with a pragmatic worldview, we will also approach the objectives from a pluralistic perspective, combine deductive and inductive modes of reasoning, and allow for a singular view and multiple views of reality in how we come to understand and interpret our findings [25].

Pilot Randomised Controlled Trial

Sample size

A conventional power calculation is inappropriate for the purpose of a pilot trial [20]. Instead, we have calculated the sample size in order to provide useful information about the aspects of the study being assessed for feasibility [20]. Thus, we have constructed confidence intervals based on certain criteria for success [20], specifically: recruiting at a rate of 12 % of those invited and experiencing an attrition rate no higher than 20 % of those randomised. We expect to invite a total of 570 participants to

Table 1 World Health Organization Trial Registration Data Set

Data category	Information
Primary registry and trial identifying number	Current Controlled Trials database
	ISRCTN17544090
Date of registration in primary registry	23-Jul-15
Secondary identifying numbers	N/A
Source(s) of monetary or material support	University of Exeter Medical School, UK
Primary sponsor	University of Exeter, UK
Secondary sponsor(s)	N/A
Contact for public queries	Holly Victoria Rose Sugg
	University of Exeter Medical School, UK
	h.v.s.sugg@exeter.ac.uk
Contact for scientific queries	Holly Victoria Rose Sugg
	University of Exeter Medical School, UK
	h.v.s.sugg@exeter.ac.uk
Public title	The Morita Trial
Scientific title	Morita Therapy for Depression and Anxiety: A Feasibility and Pilot Study
Countries of recruitment	UK
Health condition(s) or problem(s) studied	Depression
Intervention(s)	Morita Therapy
	Treatment as usual
Key inclusion and exclusion criteria	Ages eligible for study: ≥18 years;
	Sexes eligible for study: both;
	Accepts healthy volunteers: no
	Inclusion criteria: adult patient (≥18 years), current DSM Major Depressive Disorder
	Exclusion criteria: cognitive impairment, bipolar disorder or psychosis/psychotic symptoms, substance dependence, acute suicidal risk, current psychological therapy
Study type	Interventional
	Allocation: randomised intervention model
	Primary purpose: treatment
	Phase II
Date of first enrolment	Sep-15
Target sample size	72
Recruitment status	Recruiting
Primary outcome(s)	Depressive symptoms, generalised anxiety symptoms, quality of life, attitudes (at four-month follow-up); qualitative exploration of acceptability.
Key secondary outcomes	N/A

participate in the trial. Thus, we expect to recruit 72 participants into the trial, and follow-up 60 participants (30 in each trial arm).

Inviting 570 participants is sufficient to estimate a participation rate (as percentage of subjects invited) of 10 % with a margin of error of +/− 2.46 %, or to estimate a participation rate of 12 % with a margin of error of +/− 2.67 %, or to estimate a participation rate of 15 % with a margin of error of +/− 2.93 %, based on 95 % confidence intervals. Recruiting 72 participants is sufficient to estimate a follow-up rate (as percentage of participants randomised) of 80 % with a margin of error of +/− 9.24 %, or to estimate a follow-up rate of 85 % with a margin of error of +/− 8.25 %, based on 95 % confidence intervals.

In addition, we will calculate the standard deviation of participant outcomes and the correlation between baseline and four month follow-up scores, which can be used to refine future sample size calculations to incorporate the additional precision obtained from adjusting for baseline scores when comparing outcome scores between the trial arms. 30 participants in each group is sufficient to estimate: (i) the standard deviation of continuous outcomes to within 22 % of their true value based on the upper limit of the 95 % confidence interval; (ii) a Pearson's correlation coefficient between baseline and follow-up scores with a margin of error of +/− 0.1 if the true correlation is 0.8, or with a margin of error of +/− .14 if the true correlation is 0.7, or with a margin of error of +/− 0.17 if the true correlation is 0.6.

30 participants per group is also in line with the general rule of thumb for using pilot studies to reliably estimate variance for participant outcomes [26]. With these factors in mind, we consider 60 participants at follow-up to be both sufficient to provide useful information and reasonable to recruit for within the constraints of our pilot trial and have, therefore, selected 72 as our target sample size, inflating our sample by 20 % to take account of predicted attrition.

Participant inclusion criteria

Eligible participants will be aged 18 or over with Diagnostic and Statistical Manual of Mental Disorders (DSM) Major Depressive Disorder, with or without accompanying DSM anxiety disorder(s).

Participant exclusion criteria

Given the exploratory nature of this trial (and any fully-powered evaluation), and thus the requirement for reasonable internal validity with a homogenous and tightly defined population, we will identify and exclude people who are cognitively impaired, have bipolar disorder or psychosis/psychotic symptoms, or are substance dependent. Cognitive impairment will be determined using the Mini-Cog, whereby a score of 0, or 1–2 with an abnormal clock-face, would indicate sufficient cognitive impairment to be excluded [27]. Bipolar disorder,

psychosis and substance dependence will be established according to the DSM.

We will also exclude participants whose risk of suicide is sufficiently acute to demand immediate management by a specialist mental health crisis team, and those who are currently in receipt of psychological therapy. Psychological therapy includes any formal standard course of psychological (talking) therapy, such as Cognitive Behavioural Therapy. Ad hoc contact with a therapist or counsellor will not be considered to meet this exclusion criterion. Participants will be eligible regardless of whether they are in receipt of antidepressant medication or have received psychological therapy in the past.

Participant identification and recruitment

Our main method of recruitment will be through searches of General Practice records, conducted by Practice staff. We will recruit six GP Practices in Devon. All GP Practices who are able to access the University of Exeter's Mood Disorders Centre (MDC) Accessing Evidence-Based Psychological Therapies (AccEPT) Clinic (those within the National Health Service Northern, Eastern and Western Devon Clinical Commissioning Group) will be eligible.

Practice record searches will be limited to patients aged 18 or over and seen within the past three months for depression. The resulting patient names will be screened by the GP with whom the patient is registered for any patients known to meet exclusion criteria or for whom the GP considers the trial unsuitable. The remaining patients will be sent invitations to participate in the trial by Practice staff.

We will also place adverts on websites of the University of Exeter Medical School and AccEPT Clinic, place leaflets in the waiting rooms of consenting Devon General Practices and circulate an email invitation to former MDC participants who have consented to such contact. All invitations and adverts will include a study summary sheet [see Additional file 1] and permission to contact form [see Additional file 2] (Figs. 1 and 2).

Screening and baseline

We will telephone all people who return their permission to contact form to the study team to assess possible eligibility using a standard two-question case-finding instrument for depression [28] and arrange baseline interviews with potentially eligible and willing participants who will be sent a confirmation letter and full participant information leaflet [see Additional file 3]. We will hold baseline interviews at University of Exeter premises or the participant's home, depending on participant preference. At interview, we will explain the study in full and assess eligibility according to the Mini-Cog [27] (to screen for cognitive impairment) and standard clinical interview (Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Clinical Trials Version [29]). If eligible and once fully informed, participants will be asked to complete a consent form [see Additional file 4] and entered into the trial. Ineligible participants will be returned to the care of their GP.

Randomisation, allocation concealment and blinding

We will allocate participants in a 1:1 ratio to either Morita Therapy plus treatment as usual or treatment as usual alone, stratified according to their symptom severity on the nine item version of the Patient Health Questionnaire (PHQ-9) [30], specifically whether they score below 19 or

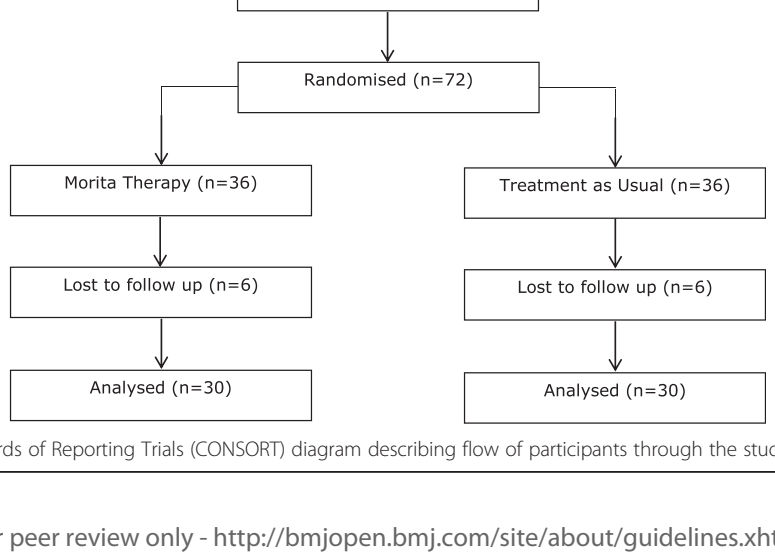

Fig. 1 Consolidated Standards of Reporting Trials (CONSORT) diagram describing flow of participants through the study

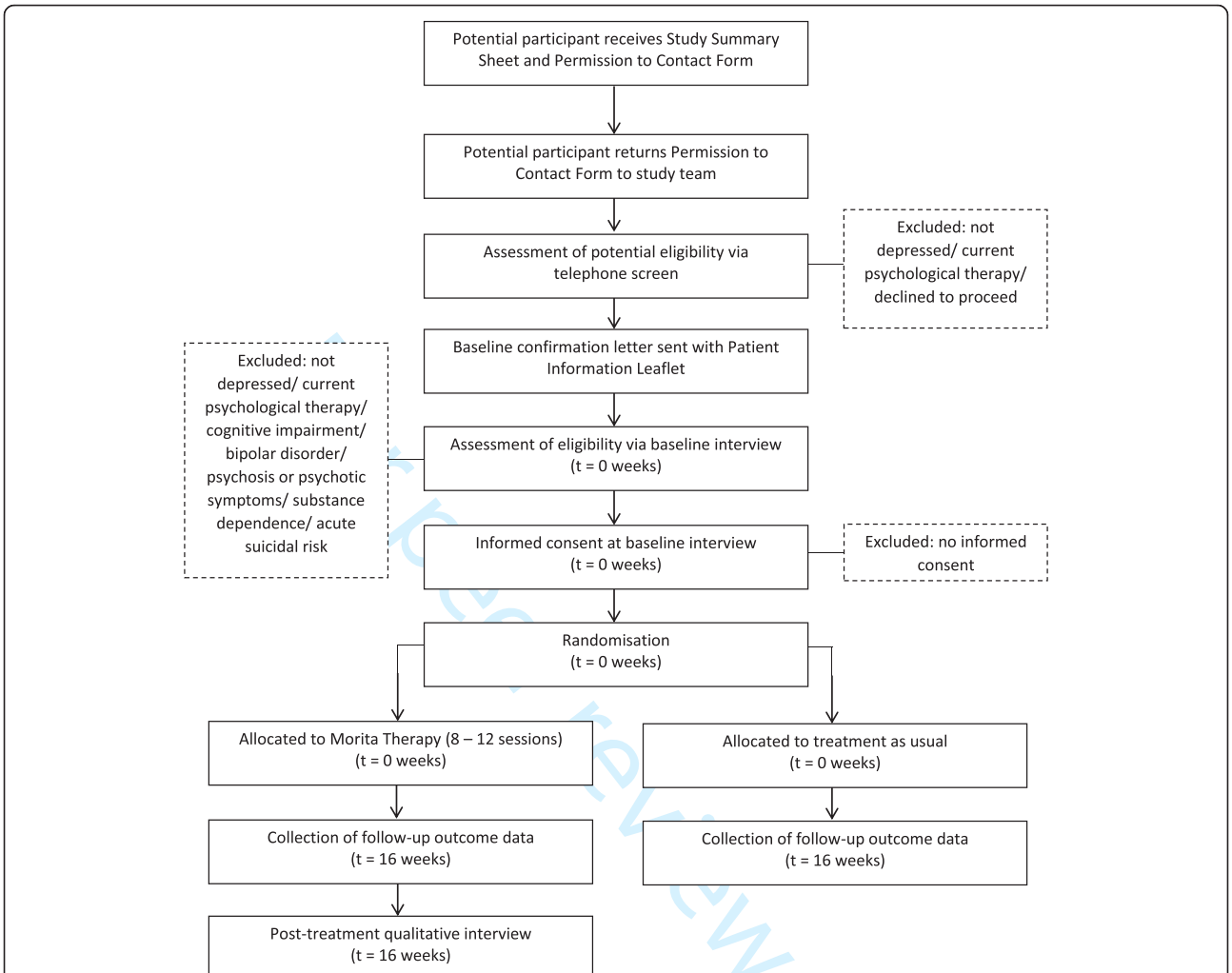

Fig. 2 Schematic diagram describing timeline for participants in the study

19 and above, given that a score of 19 is the median score of depressed participants in our previous research [21, 23]. Allocation will be minimised to maximise the likelihood of balance in the stratification variable across the two trial arms. To ensure allocation concealment, we will undertake randomisation through the use of an externally administered, password-protected randomisation website independently developed and maintained by the Exeter Clinical Trials Unit.

The researchers will not be blinded to allocation due to the different pathways to be followed for each trial arm. Baseline and follow-up data will be self-reported and the risk of bias related to lack of blinding will be both minimal and tolerable.

Trial interventions

Morita Therapy plus treatment as usual We will ask participants in the Morita Therapy plus treatment as usual trial arm not to engage in other formal courses of psychological therapy elsewhere during the course of their treatment. Otherwise, these participants will be free to access any other usual care and medication in liaison with their GP.

Morita Therapy will consist of eight to twelve one hour face-to-face weekly sessions and be delivered at the University of Exeter's MDC AccEPT clinic [31] by two research therapists trained in Morita Therapy and experienced in both the delivery of complex psychological interventions and adopting different modes of treatment, including experimental treatments. Therapist training took place over 6 months and included background reading, attending presentations, involvement in the development and review of the UK Morita Therapy outpatient protocol, and practical training led by DAR, a clinically qualified academic and 10 year member of the Japanese Society for Morita Therapy. Practical training was experiential, involving role plays, diary examples, additional reading and peer support.

The therapists are not accredited as there is no accreditation process for Morita Therapy within the UK.

Therapists will follow the UK Morita Therapy outpatient protocol developed by the study researchers from multiple sources of literature on the delivery and practice of Morita Therapy [16–18, 32–35] and by considering the views of potential participants and therapists about Morita Therapy, as explored in qualitative interviews, in order to enhance the suitability of Morita Therapy for a UK population. DAR will provide fortnightly supervision of cases together with advice and support. A qualitative checklist highlighting the key components of Morita Therapy will be used as an aide memoir to structure supervision discussions and the assessment of adherence and fidelity. With the patient's consent, all therapy sessions will be audio recorded. We will use the first two recordings for each therapist to confirm their adherence to the Morita Therapy outpatient protocol and a further 10 %, stratified by length of time in treatment, to evaluate fidelity to the protocol, which will inform therapist supervision.

During therapy, patients will progress through four stages of rest and increasing action taking in order to address fatigue, expand peripheral attention and move from a mood-oriented to purpose-oriented and action-based lifestyle. Therapists will aid patients in re-appraising their symptoms as part of the natural ecology of human experience; recognising the vicious cycle of symptom aggravation created by fixation on symptoms, contradictions between reality and the ideal, and attempts to fight or control otherwise inevitable emotions; and moving from a position of preoccupation with symptoms to the acceptance of spontaneous affective experiences. Therapists will continually reinforce the patient's shift from self-reflection towards a focus on constructive action and the external environment. Throughout therapy, patients will also complete a daily diary for therapists to comment on, to increase communication and the opportunity for therapist reinforcement.

Treatment as usual alone

We have selected treatment as usual as our trial comparator as a reflection of the trial comparator which would be selected for a fully-powered RCT, in which our key interest would be whether Morita Therapy plus treatment as usual has superior or equivalent effectiveness to current clinical practice in the UK, in which people have access to GP care and a range of other treatments. Thus, a large scale RCT would be a pragmatic trial embedded within the healthcare environment in which Morita Therapy would be delivered, seeking to establish whether Morita Therapy could be useful in addition to the options currently available to depressed patients in the UK.

Thus, in this pilot trial we will replicate 'treatment as usual' by making no specific patient-level recommendation or requirement to alter the usual treatment received by depressed patients in the UK, and the study will not place any restrictions on the treatment options available to these participants. GPs will treat and refer participants as would be their normal practice and participants in this trial arm are free to access any other care and services, including formal courses of psychological therapy such as Cognitive Behavioural Therapy. All participants, irrespective of their allocation, are free to choose whether they take antidepressant medication or not. We will record the treatments received in the course of participants' treatment as usual.

Outcomes

Given this is a feasibility study with a range of different aims, there is no single primary outcome measure. Rather, we will collect a variety of data at baseline interview and four months post-randomisation: severity of depressive symptoms (PHQ-9 [30]), severity of generalised anxiety symptoms (seven item Generalised Anxiety Disorder questionnaire: GAD-7 [36]), quality of life (Short Form 36 Health Survey Questionnaire: SF-36 [37]; Work and Social Adjustment Scale: WSAS [38]), and attitudes (The Morita Attitudinal Scale for Arugamama: MASA [39]). At four months post-randomisation, we anticipate that treatment for participants in the Morita Therapy plus treatment as usual trial arm will be complete. We will hold follow-ups at University of Exeter premises or the participant's home, depending on participant preference, and apply all research measures to both groups of participants equally.

We will also collect data on the flow of participants through the trial. For participants in the Morita Therapy plus treatment as usual trial arm, therapists will also inform the researcher of the number of therapy sessions attended and the reason for ending treatment. We will not conduct an economic evaluation as part of this pilot trial, although at follow-up we will incorporate methods for collecting data on participants' use of health and social care services as used in our recent mental health trials [23] (whereby we will establish the rates and nature of hospital visits; use of community, social and complementary services; and use of psychotropic medication since baseline assessment), in order to characterise treatment as usual and calculate the cost of each trial arm for a large-scale RCT.

Semi-structured Interviews

Sample and setting

We will invite all participants who are allocated to Morita Therapy plus treatment as usual for a post-treatment

semi-structured interview, thus selecting as diverse a sample as possible within this pilot trial. This will provide a maximum of 30 participants (all those retained in the Morita Therapy trial arm). We will also invite the two therapists providing Morita Therapy to interview. We will hold participant interviews at University of Exeter premises or the participant's home, depending on participant preference. Therapist interviews will be conducted at the AccEPT Clinic.

Recruitment

We will explain the purpose and content of the interview to participants in the participant information leaflet, and determine their consent to participate at baseline interview. We will send therapists an interviewee information leaflet explaining the interview prior to a pre-trial meeting, and establish their consent to participate during this meeting. Upon completion of Morita Therapy (delivery, for therapists), we will contact participants to establish whether they are still willing to be interviewed, remind them of what will be involved and answer any questions. For willing participants, we will arrange an interview no sooner than 48 hours later and send an interview confirmation letter explaining the opportunity to rearrange or cancel the interview at any time.

Interview process and questions

We will undertake semi-structured interviews to allow participants to describe their views of Morita Therapy. This method will enable us to investigate the meaning of participants' responses, both exploring views on our predefined topics of interest and eliciting more detail on any emerging themes [40]. Interviews are expected to last up to one hour and will be audio-recorded with the participant's consent. The interviewer will also take field notes during and after the interview.

We will follow topic guides established on the basis of our recent mental health trials addressing similar research questions [21, 23, 41] (which ask about participants' views and experiences of treatment, any barriers to treatment, and the impact of treatment) and existing Morita Therapy literature. To explore the acceptability of Morita Therapy, we will ask participants to describe their understanding of Morita Therapy, explore their views and experiences of Morita Therapy and investigate potential barriers to/facilitating factors in engaging with Morita Therapy. In particular, we will explore participant's views and experiences of the defining features of Morita Therapy in practice, such as the four stages and daily diaries. To explore the feasibility and appropriateness of our trial procedures, we will explore participants' views on the support provided throughout the trial; procedures for recruitment, monitoring and data collection; and use of the MASA questionnaire. We aim to identify both procedures that facilitated the efficient running of the trial and any considered problematic.

Analysis

We will first analyse the quantitative and qualitative data separately before integrating both types of information in a mixed methods analysis.

Quantitative analysis

Following double data entry into STATA v.11 [42], we will analyse recruitment, retention, treatment adherence and estimates of the participant-related data to inform the feasibility of and sample size calculation for a fully-powered trial. Thus, we will emphasise quantification and estimation rather than hypothesis testing. All analyses will be on an intention to treat basis and we will not impute missing data, although we will report outcome data that are missing in each trial arm and the reasons for missing data where possible.

We will use count data with calculated estimated margins of error, expressed as a percentage of both the total number of participants invited and in relation to the preceding step in recruitment, to quantify the flow of the participants through the trial. For each trial arm, we will quantify the number of participants who withdrew, could not be contacted or did not provide follow-up data for another reason. We will also express data as a percentage of the total number of participants in each trial arm. We will follow CONSORT guidelines, including the forthcoming pilot and feasibility extension [43], in reporting all data including the number of participants exiting the trial at each step and from whom we are unable to collect follow-up data. Descriptive statistics will also be used to describe the number of Morita Therapy sessions attended by participants allocated to Morita Therapy plus treatment as usual.

To measure the variance in participant outcomes, we will estimate the standard deviation around the mean PHQ-9, GAD-7, SF-36, WSAS and MASA scores at baseline and four months for both groups. We will also estimate the correlation between participants' scores on these measures at baseline and at four months, which can be used to refine the sample size calculation for any fully-powered evaluation. Although we do not have the power to make inferential statements on between (or within) group differences and as such no p values will be calculated, we will also calculate and report the observed differences between Morita Therapy plus treatment as usual and treatment as usual alone on the mean changes in these measures from baseline to four month follow-up, and the 95 % confidence intervals around these figures.

Qualitative analysis

With participants' permission, we will record and transcribe interviews verbatim. We will use NVivo10 [44] to organise the data and conduct a systematic analysis of interviews and field notes, using Framework analysis [45] to allow for the combination of both inductive and deductive approaches in the development of analytic categories. In line with this, an initial thematic framework will be developed as preliminary analysis is undertaken and subsequently as batches of transcriptions are analysed, iteratively combining our topic guide and the overall impression of the narratives in context. Using this framework, transcripts will be coded at the level of individual participants and then analysed thematically across the whole dataset as well as in the context of each participant's interview using a constant comparison approach [46], whereby each piece of data (e.g. one statement or one theme) is compared with others for similarities and differences [47]. As we formulate explanations in this way, negative cases will be explored and explanations of variance provided [48], thus incorporating all observations relevant to our research question. Data collection and analysis will be iterative: we will amend our interviewing style to respond to emerging themes and explore deviant cases further in subsequent interviews as appropriate.

Mixed methods analysis

Our mixed methods analysis will be guided by both the nature of the quantitative and qualitative data that we ultimately obtain and the inferences that arise from our separate analysis of each [41]. Thus, the analysis we eventually undertake may differ to the analysis we propose [41]. Analytical techniques have been proposed below based on the methods summarised by Creswell and Plano Clark [24].

To explore how the qualitative data on the acceptability of Morita Therapy explains the quantitative findings on treatment adherence, we will merge these two types of data. Firstly, we will develop typologies of participants' different views on the acceptability of Morita Therapy from the qualitative data, and for each typology we will present data on treatment adherence for participants to whom the typology applies [41]. Alongside this, we will also present data on fidelity to the therapy protocol if the qualitative data relates to particular sections of the protocol or stages of therapy. This will allow us to explore whether any issues with the acceptability of Morita Therapy relate to the treatment itself or the therapists' delivery of treatment and thus aid us in identifying any 'fatal flaws' [49] of Morita Therapy requiring refinement in the future. Secondly, we will identify categories of participants defined by their treatment adherence and explore similar and different views on acceptability within and between categories [41].

We will consider the use of joint displays to summarise the quantitative data in relation to the qualitative themes for both of these purposes [41]. We will also integrate data on acceptability and treatment adherence in a case-oriented merged analysis display that will position cases (participants) on a scale of treatment adherence along with their qualitative data on acceptability [41].

Ethical issues

We will conduct this trial in such a way as to protect the human rights and dignity of the participants, as reflected in the Helsinki Declaration [50]. The study has received ethical approval from the National Research Ethics Service South West – Frenchay (reference 15/SW/0103) and governance assurance from the National Health Service Research and Development Directorate (reference CG/JL), and has been approved by the University of Exeter Medical School following independent peer review.

Participants will not receive any financial inducement to participate. We will conform to Good Clinical Practice Guidelines, data protection and freedom of information acts. All data will be stored securely and anonymised wherever possible. All identifiable participant information will be stored separately to questionnaire data which will be coded by a trial ID number only. No published material will contain identifiable participant information.

Informed consent and withdrawal

The study researchers will be fully trained and supervised by senior academic and clinically qualified staff. All our information leaflets and consent forms have been produced using the current Health Research Authority's online guidance for writing such documents [51], and are based on similar materials used in our other mental health trials as informed by Patient and Public Involvement.

Informed consent will be determined by a two phase process. Potential participants will receive a study summary sheet and a form on which to complete their contact details and confirm their permission for a researcher to contact them. We will telephone those who return this form to us, to assess their potential eligibility and answer any questions. For those who are eligible and willing, we will send a participant information leaflet and arrange a baseline interview at least 48 hours later, to allow the participant time to reflect on their decision to participate and change their mind if they so wish. Full informed consent will only be obtained at this interview where the information leaflet will be fully explained and the opportunity to ask questions given.

Consent to participate in the qualitative interview is optional; participants may participate in the pilot RCT only. We will explain the purpose and content of the interview in the participant information leaflet

(or interviewee information sheet, for therapists), and note that a decision not to be interviewed will not affect participation in the trial. At baseline interview (for participants) and the pre-trial meeting (for therapists), we will answer any questions, explain the opportunity to stop and/or withdraw from the interview at any time and clarify steps to maintain confidentiality. We will ask willing participants to indicate their decision on a consent from. Consent for audio recording of the interview and/or therapy sessions is also optional.

We will treat informed consent as an ongoing process whereby participants may withdraw their consent to participate at any time, and set up communication and recording systems to enable us to monitor and act on such wishes. When obtaining consent, we will advise participants of this fact and that they may be asked to give a reason for their withdrawal but will not have to provide one. Participants allocated to Morita Therapy plus treatment as usual may withdraw from therapy and continue their involvement in the trial through participation in the follow-up and qualitative interview if they wish.

Should it come to our attention that a participant loses capacity to consent during the study according to the Mental Capacity Act 2005 [52], we will withdraw them from the study as per information provided to participants in the participant information leaflet. Within this leaflet, we will also inform participants that if they should withdraw or be withdrawn from the study, we will retain any data already provided to be used confidentially in relation to the purpose for which consent was sought.

Anticipated risks and benefits

No treatment will be withheld from participants taking part in this trial. All participants will remain under the care of their GP and will have access to primary care services in the usual way. Participants allocated to treatment as usual alone will be returned to the care of their GP with no restrictions placed on treatment options. Participants allocated to Morita Therapy plus treatment as usual will be asked not to engage in other formal courses of psychological therapy during their treatment, as it is not considered good practice to engage in more than one psychological therapy at once. Should participants in this trial arm wish to engage in other psychological therapy elsewhere, a discussion will be held with their therapist to establish which therapy option is in the participant's best interests.

Participants allocated to Morita Therapy plus treatment as usual will take part in an alternative therapeutic approach to psychopathology which is widely practiced in Japan and somewhat elsewhere. Morita Therapy has been practiced since the 1920s and is not known to be associated with any risks to patients. It is possible that participation in therapy focused on psychopathology may cause distress to some participants, however participants in the Morita Therapy trial arm will receive an intensive level of monitoring so that any worsening or at suicidal risk will be identified and directed to appropriate care. Similarly, we will address any impact of potentially distressing questions within our assessment and outcome measures by following our protocols for responding to risk and directing participants to appropriate care. Additionally, we will report any serious adverse events reported to a therapist or researcher which are thought to be treatment related to the trial sponsor, Research Ethics Committee and independent oversight clinician (see section on study oversight).

The patient information leaflet will explain that participants allocated to Morita Therapy plus treatment as usual will no longer be offered such therapy once they have received a full "dose" (up to twelve sessions), but will be referred back to their GP with whom they could consider access to other treatments. We will ensure participants are reminded of these factors throughout the trial.

The University of Exeter has insurance to cover the potential legal liability for any harm to participants arising from the management of this trial. We will also provide potential participants with information about the possible benefits and risks of taking part in the trial in the participant information leaflet, and give them the opportunity to discuss this issue with us before consenting. We will inform participants in writing if new information comes to light which may affect their willingness to participate in the trial.

Managing risk of suicide

Inherent in the nature of the population under scrutiny is the risk of suicide. We will follow good clinical practice in monitoring for suicide risk during all appointments and explain to participants that we will contact their GP or specialist if deemed necessary in line with our risk protocol. If an acute risk is present, we will seek advice from the participant's GP (or the duty GP) immediately and/or follow locally established suicide management plans. All clinicians and researchers will be familiar with established risk protocols used in our previous research trials and/or within the AccEPT Clinic, specifically trained in risk assessment and supervised by experienced clinicians. We will put in place systems to ensure that senior academic and clinically qualified staff are notified should there be any risk to a participant's safety.

Patient and public involvement

We have developed the patient materials on the basis of both consultation with a Public and Patient Involvement Expert and similar materials used in our other mental health trials which received feedback from Public and

Patient Involvement groups such as the National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South West Peninsula (PenCLAHRC) [53] Patient and Public Involvement Group (PenPIG). This feedback has helped us to ensure that our research respects the rights, safety and dignity of participants. Ensuring that our research materials are sensitive and consistent with the views of people with depression will also aid us in recruitment and participants' engagement in and openness during interviews.

Following completion of the pilot trial, to ensure that our results reach our former trial participants and people with mental health issues in a way that is meaningful and accessible, we will establish an advisory group comprising members of PenPIG and follow national good practice guidance for researchers on public involvement in research and the paying of representatives [53]. The group will be involved in the dissemination of the results to the public and patients using accessible channels and their own conference and group meetings. Training in presentation skills will be arranged for members of the group should they consider this helpful. We will also consult the advisory group on the development of a summary sheet explaining the results of the study and their implications in lay terms, to be sent to consenting former trial participants.

Dissemination protocol

In addition to the above details on the dissemination of results to the public and former trial participants, we will disseminate the results of this study in a full internal report and intend to publish our results in a peer reviewed scientific journal. Authors will be those considered to have made a substantive intellectual contribution to the study. The main output from this study will be the information required to design and seek funding to conduct a definitive trial of Morita Therapy. Thus, in the long term we aim to contribute to national guidelines for the treatment of depression and anxiety.

The investigators and relevant authorities will have access to the trial dataset. Furthermore, we will store anonymised research data and outputs in the University of Exeter's Open Research Exeter repository [54] in order to facilitate open access to, and the impact of, our research.

Study oversight

This research forms part of the first author and Chief Investigator's (HVRS) PhD programme of studies for which she is supervised by DAR and JF. Trial conduct will be discussed between the Chief Investigator and her supervisors at monthly supervision meetings.

Although the convention of a formal Data Monitoring and Ethics Committee is not appropriate for the scale of this study, an independent clinician will act in this capacity in order to review serious adverse events which are thought to be treatment related, and any substantive protocol amendments. All such amendments will be communicated to the relevant authorities as deemed necessary.

Forecast execution dates

The preparatory period started in October 2014. Recruitment is running from September 2015 for approximately ten months. Follow-up and qualitative data will be collected from January 2016 to November 2016. Data analysis and reporting are expected to take another nine months. The total duration of the study will be 24 months.

Discussion

By preparing the ground for the design and conduct of a large-scale RCT, this study will contribute important information towards the development and subsequent evaluation of Morita Therapy for the treatment of depression and anxiety for the first time in the UK. One strength of our study design is that the proposed methods are appropriate for undertaking a feasibility study [41]. Our study purpose and research questions are in line with the National Institute for Health Research Trials and Studies' definition of a feasibility study [55] endorsed by Arain and colleagues [56]. We have calculated the RCT sample size based on the key feasibility objectives around recruitment and retention rates, and will calculate the variance in participant outcomes and their correlation with baseline scores to inform future sample size calculations. We will also calculate the observed differences between Morita Therapy plus treatment as usual and treatment as usual alone on the mean changes in outcome measures, although we will not make inferential statements or evaluate these outcomes. Rather than identifying a primary outcome measure, we have designed both the pilot trial and qualitative interviews to allow us to test the uncertainties associated with designing and running a large-scale fully-powered RCT of Morita Therapy plus treatment as usual versus treatment as usual alone.

To embrace the complexity of developing and evaluating interventions and provide a comprehensive understanding of the intervention in question, no one method will suffice [25]. Thus, a further strength of this study is our explicit commitment to a mixed methods approach and transparent description of the way in which quantitative and qualitative components will be integrated [41, 57]. We have carefully considered guidance on maximising the impact of qualitative research in feasibility studies

[49] and described our proposal in line with recommendations for Good Reporting of a Mixed Methods Study [57], which we will continue to follow in our future reporting. Our embedded mixed methods design reflects key decisions we have reached on the levels of interaction, priority, timing and procedures in the mixing of the quantitative and qualitative components [24, 41]. Thus, we will interactively mix the two components before final interpretation, at both the design and analysis levels, by embedding qualitative interviews within the pilot RCT in a program-objective framework; give the two components equal priority; undertake the pilot trial and qualitative interviews concurrently; and analyse data from the two components simultaneously.

We have specified research question seven to frame the integration of results from the quantitative and qualitative strands, to help explain variability in treatment adherence and thus facilitate a more complex picture of the acceptability of Morita Therapy [24]. By qualitatively exploring the acceptability of both Morita Therapy and our trial procedures, and integrating the qualitative and quantitative data, we will facilitate both the interpretation of our pilot trial findings and the feasibility and/or efficiency of any large-scale RCT, thus allowing us to optimise both our intervention and trial conduct in the future [58]. The integration of quantitative and qualitative methods will enable us to address both exploratory and explanatory research questions simultaneously, and help to reduce the limitations of each individual method whilst retaining their strengths [25]. Ultimately, by implementing an embedded mixed methods design, this study will better prepare the ground for a large-scale fully-powered RCT of Morita Therapy plus treatment as usual versus treatment as usual alone than would be possible from either a quantitative or qualitative approach alone [25, 41].

Trial status

Recruitment commenced in September 2015 and is ongoing.

Additional files

Additional file 1: Study Summary Sheet. (PDF 222 kb)
Additional file 2: Permission to contact form. (PDF 160 kb)
Additional file 3: Participant Information Leaflet. (PDF 766 kb)
Additional file 4: Model Consent Form. (PDF 246 kb)

Abbreviations

GAD: Generalised Anxiety Disorder; GPs: General Practitioners; NICE: National Institute for Health and Care Excellence; IAPT: Improving Access to Psychological Therapies; RCT: Randomised Controlled Trial; MRC: Medical Research Council; NIHR: National Institute for Health Research; DSM: Diagnostic and Statistical Manual of Mental Disorders; MDC: Mood Disorders Centre; AccEPT: Accessing Evidence Based Psychological Therapies; PHQ-9: nine item version of the Patient Health Questionnaire; GAD-7: seven item Generalised Anxiety Disorder questionnaire; SF-36: Short Form 36 Health Survey Questionnaire; WSAS: Work and Social Adjustment Scale; MASA: The Morita Attitudinal Scale for Arugamama; CLAHRC: National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care; PenCLAHRC: National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula; PenPIG: National Institute for Health Research Collaboration for Leadership in Applied Health Research and Care South West Peninsula Patient and Public Involvement Group.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

DAR proposed the study; HVRS as chief investigator and study researcher designed the study with the involvement of DAR and JF; JF provided additional guidance and support in relation to the qualitative aspects of the study; HVRS drafted the study protocol and materials and obtained National Health Service ethical approval and research and development governance assurance; HVRS is responsible for project management, data collection and analysis; HVRS and DAR developed the UK Morita Therapy outpatient protocol; DAR supervises the study therapists. HVRS drafted the manuscript. All other authors contributed to editing of the final manuscript. All authors read and approved the final manuscript.

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CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	1-2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	3-5
	2b	Specific objectives or research questions for pilot trial	5-6
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
	4c	How participants were identified and consented	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	7-8
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	8-9
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	N/A
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	9
Sample size	7a	Rationale for numbers in the pilot trial	9-10
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	10
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	10
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	10

Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	10
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	10
	11b	If relevant, description of the similarity of interventions	N/A
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	11-12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11-12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	11
	14b	Why the pilot trial ended or was stopped	N/A
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	12-13
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	14-18
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	14-18
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	N/A
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
	19a	If relevant, other important unintended consequences	N/A
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	19
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	19-21
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	19-21
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	19-21
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	2
Protocol	24	Where the pilot trial protocol can be accessed, if available	7
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	22
	26	Ethical approval or approval by research review committee, confirmed with reference number	6

Citation: Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. BMJ. 2016;355.
*We strongly recommend reading this statement in conjunction with the CONSORT 2010, extension to randomised pilot and feasibility trials, Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.