

BMJ Open Affective disorders: eliminate WArning signs and REstore functioning—AWARE—a randomised controlled multimodule intervention study, presentation of design and intervention

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ABSTRACT

Introduction Affective disorders are associated with impaired overall functioning and quality of life (QoL). Despite different medical and psychological treatment options, the prognosis remains largely unchanged. Consequently, the field needs new intervention strategies especially targeting patient groups with impaired functioning. This study aims to improve functioning and QoL in patients with affective disorders using a comprehensive 360° intervention.

Methods and analysis Affective disorders: eliminate WArning signs And REstore (AWARE) functioning is a randomised, controlled, parallel-group design study. Participants will be 120 outpatients, men or women, aged 18–65 years, with a diagnosis of bipolar disorder or major depressive disorder. Inclusion requires an objectively rated impaired functioning defined as a score ≥ 11 according to the Functioning Assessment Short Test. Participants will be randomised to 6-month AWARE intervention or treatment as usual (TAU). The AWARE intervention is a 360° multimodal intervention based on the International Classification of Functioning Brief Core Set for bipolar and unipolar disorder targeting functioning. The primary outcome is improvement of observation-based activities of daily living (ADL) ability using Assessment of Motor and Process Skills. Secondary outcomes are changes from baseline to endpoint in functioning, QoL, stress, cognition and physical health. Our hypothesis is that the AWARE treatment in comparison with TAU will improve observed ability to perform ADL, patients self-perceived level of functioning and QoL.

Status: currently recruiting patients.

Ethics and dissemination Ethical approval has been obtained from The Regional Ethics Committee in the Capital Region of Denmark. All patients will be provided oral and written information about the trial before informed consent is obtained. The study results will be disseminated by peer-review publications. If the present AWARE intervention shows beneficial effects, the goal is to use it as a template for future interventions addressing disability in patients with affective disorders as well as for patients within other diagnostic categories.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The trial is an open label randomised multimodule intervention study with blinded outcome assessment, which is designed to evaluate the effect of a 360° multimodal intervention on functioning and quality of life in patients with bipolar and unipolar disorder.
- ⇒ A considerable strength of the study is the comprehensive assessment and intervention, targeting most well-known factors contributing to impaired functioning.
- ⇒ Observer-based measures of activities of daily living ability as part of functioning conducted in the patients' homes and thereby everyday life.
- ⇒ A limitation is that some patients might be unwilling to participate due to assessment/observations in patients' home surroundings at baseline and endpoint.
- ⇒ Another limitation is the duration of the intervention, which is limited to 6 months.

Trial registration number NCT04701827; Clinicaltrials.gov.

INTRODUCTION

Unipolar disorder (UD) and bipolar disorder (BD) have a major impact on patients' functioning and quality of life (QoL) and are among the leading cause of lost years of work.¹ Measured by disability-adjusted life year, these affective disorders are among the 10 leading causes of disability globally.² The total costs of BD in the USA in 2015 were estimated to be more than US\$202.1 billion,³ and it is estimated that one-third of the expenses for sickness leave in the European Union is due to severe mental illness with affective disorders accounting for the largest proportion of this cost.⁴ Affective disorders are also associated with major somatic

disorders⁵ mainly cardiovascular disorders,⁶ obesity⁷ and non-insulin-dependent diabetes.⁸ Putative reasons for these conditions and the increased mortality observed in patients with affective disorders⁹ include a more sedentary lifestyle¹⁰ as well as abnormal sleep patterns,^{11 12} leading to disturbed diurnal rhythm that also impact daily functioning.¹³

Despite different medical and psychological treatment options, the prognosis for affective disorder remains largely unchanged for many patients.¹⁴ Consequently, the field needs new intervention strategies especially targeting the patient groups having impaired functioning. Therefore, our group conducted a pilot study using a performance-based assessment tool, including patients with BD in remission assessed in their home surroundings. These patients (mean age 35 years) had an observed ability to perform activities of daily living (ADL) below the mean of healthy persons at the same age,¹⁵ and their ADL ability was equivalent to healthy persons between 60 and 85 years. Thus, having an ADL ability as being 30 years older, they exhibited increased physical effort, clumsiness or fatigue and/or efficiency, leading to concern for safe task performance.¹⁵ Furthermore, concerning cognition, impaired processing speed was significant associated with more difficulties in performing ADL.¹⁶ Finally, a similar pattern has been observed among patients with UD.^{17–19}

The International Classification of Functioning, Disability and Health (ICF)^{20 21} is recommended as a conceptual model to describe functioning and disability within mental health in general.^{22–24} Most research on functioning and disability has focused on the component *body functions and body structures*, that is, cognition. Fewer studies have addressed the component *activities and participation*,²² including self-care and domestic life, also termed ADL, including tasks such as personal hygiene, eating, reading and more complex home maintenance tasks for example, cleaning, cooking and shopping.^{20 25} Studies assessing ADL ability show that patients with affective disorders have limited ability to perform ADL tasks.^{26–28} This ability is required for independent living and represents the basis for other activities, including work and leisure. Accordingly, interventions targeting functioning should address many aspects of disability: activity limitations and participation restrictions, physical activity and metabolic abnormalities, disturbed circadian rhythm, cognitive impairment and finally daily perceived stress.

The main focus of Affective disorders: eliminate Warning signs And REstore functioning (AWARE) is to improve functioning and QoL in patients with affective disorders in everyday life using a comprehensive multimodal 360° intervention. The AWARE intervention represents an integrated treatment avenue to improve functioning in patients with affective disorders.²⁹ Including the experiences from our previous randomised studies^{30 31} and the described pilot study,¹⁶ we have established a manual used for the present intervention (Decker L, Schwarz R, Vinberg M, AWARE, *Intervention manual*, Unpublished). Currently,

other multimodal studies, including patients in the more *impaired stages of the disorders* are scarce.

METHODS AND ANALYSIS

Aim

This pragmatically randomised controlled trial aims to investigate the effect of a 360° multimodal intervention based on the ICF Brief Core Set for BD³² and UD³³ targeting functioning in the AWARE arm in comparison with treatment as usual (TAU). See online supplemental figure 1 for a flow diagram of the trial.

Main hypothesis

It is hypothesised that the AWARE arm in comparison with TAU will: (1) improve observed ADL ability assessed with the Assessment of Motor and Process Skills (AMPS)²⁵ (primary outcome), (2) improve functioning assessed with Functioning Assessment Short Test (FAST)³⁴ and WHO Disability Assessment Schedule V.2.0 (WHODAS)³⁵ and QoL measured with WHO Quality of life questionnaire (WHOQoL)³⁶ (secondary outcomes). In addition, exploratory analyses will involve investigation of the effects of AWARE on cognition and physical health (tertiary outcomes).

Participants

Study participants will be 120 outpatients. Inclusion criteria are

- ▶ men or women, age 18–65 years with a diagnosis of BD or major depressive disorder by WHO International Classification of Disease 10th edition (ICD-10) diagnostic criteria.
- ▶ Current state of remission or partial remission (defined as Hamilton Depression Rating Scale, 17-items (HDRS-17)³⁷ and Young Mania Rating Scale (YMRS)³⁸ scores of ≤14).
- ▶ Impaired functioning defined as a score ≥11 according to the FAST.³⁴
- ▶ Participants must be able to participate in two-thirds of the planned visits.

During the intervention, ongoing psychotherapy and outpatient medical treatments are all allowed.

Due to the pragmatic clinical design chosen to obtain high generalisability of results from the trial, bearing in mind the potential of translating the present results into everyday clinical settings, only a few exclusion criteria are applied. Exclusion criteria are;

- ▶ Severe somatic disorder interfering with daily living.
- ▶ Ongoing alcohol or substance abuse.
- ▶ Electroconvulsive therapy treatment within last 3 month before inclusion.
- ▶ Dementia or inability to cooperate with the study, including inability to speak and read Danish.

Patients will be invited to participate in the study following referral from the Psychiatric Centers in the Capital Region of Denmark, private practitioners and advertising through patients' advocacy.

Screening

The trial staff will establish the first contact via the patients' therapists. The patients will be given a booklet and the therapist refers to the project and the project manager. A researcher contacts interested patients and they will have a brief screening by telephone, in which basic study inclusion and exclusion criteria are reviewed. Eligible patient will be invited to an in-person conversation about the study, where participant information will be elaborated and where they can ask questions. The reflection time between the oral/written information and the later signature on the consent form will be estimated to a few days, but as noted in the participant information, according to the individual's needs.

Patient and public involvement

No patient involved.

Experimental design

The participants will be on inclusion, be randomised to participate in either 6 months of AWARE treatment or TAU. The control group will receive TAU consisting of the standard out patient mental health service routines in The Capital Region of Denmark, that is, treatment at their general practitioner, private psychiatrists or psychologists or the local community mental health Centre.

Randomisation and blinding

A total of 120 patients (completers 104, see 'Power calculation' section) will be randomised, and stratification is done for age (18–34 years vs 35–65 years), sex and diagnosis (BD vs UD) using Research Electronic Data Capture (REDCap).³⁹ The method used for randomisation is block randomisation to ensure a balance in sample size across groups. Block sizes are randomly varied intermittently between sizes of 2, 4 and 6, with randomly varying order of treatment allocation within blocks, to ensure the sequence from becoming predictable and avoiding possible selection bias.

The study is outcome-assessor-blind, and the allocation will under no circumstances be revealed to the outcome assessors. Allocation is done by the therapist, who will perform the randomisation in REDCap following each eligibility assessment. The allocation coding file in REDCap is accessible to neither the therapist performing the randomisation, the outcome assessors or anyone involved in the project, as user rights to access the coding file in REDCap are not granted. Participants will be instructed not to disclose any information concerning their treatment allocation during endpoint assessments.

Diagnostic interview and ratings

Participants will be rated in a face-to-face interview using semistructured interviews: to verify the psychiatric diagnosis, the participants will undergo a diagnostic interview using The Mini International Neuropsychiatric Interview.⁴⁰ The FAST is an interviewer-administered interview covering six areas of functioning: autonomy, occupational functioning, cognition, financial issues, interpersonal

relationships and leisure time.³⁴ A FAST total score above 11 indicates functional impairment, with the thresholds of severity being: no impairment in functioning (scores between 0 and 11), mild impairment (scores between 12 and 20), moderate impairment (scores between 20 and 40) and severe impairment (scores between 40 and 72).⁴¹ The FAST interview is used as initial screening regarding the functioning of participant candidates and is also administered at baseline and endpoint. A neuropsychological battery previous used by our group will be conducted at baseline and endpoint,¹⁶ using Screen for Cognitive Impairment in Psychiatry—Danish version (SCIP-D),^{42 43} Danish Adult Reading Test⁴⁴ and Trail Making Test A, Trail Making Test B.⁴⁵

AMPS is a standardised observation-based assessment providing measures of the quality of ADL task performance.²⁵ The AMPS ADL ability measures are found valid and reliable across diagnostic groups, including mental disorders, and has high interrater reliability and are found to be sensitive over time to changes in ADL ability.^{46 47} The procedure of administrating the AMPS is: during an interview, the patient selects two ADL tasks to perform. The tasks must be well known, meaningful and challenging for the patient to perform. In the manual, there are currently 125 standardised tasks calibrated in terms of the severity of the task. The ADL motor ability measure indicates how much effort or clumsiness the patient demonstrates, and the ADL process ability skills measure how timely and well organised the patient was during the observation. Both scales also reflect safety (risk of personal injury or environmental damage) and independence (need for physical or verbal assistance).

Participants' ADL task performance is assessed with AMPS at baseline and endpoint. In addition, participants perceived quality of ADL task performance is assessed at baseline and endpoint using the activities of daily living interview.⁴⁸ Affective symptoms are assessed using HDRS-17 and YMRS at baseline and after the intervention. Participants in the intervention group are further assessed after 3 months of the intervention using FAST, HDRS-17 and YMRS. Participants will undergo Standardised Assessment of Personality-Abbreviated Scale⁴⁹ at baseline. For further overview of the timing of the assessments, interviews and questionnaires, please see [table 1](#).

Physical assessment

Physical assessment includes height and weight, waist circumference, blood pressure, pulse, assessment for medical side effects using a validated scale⁵⁰ and blood sampling biomarkers related to glucose and fat metabolism and inflammation. The latter includes plasma/serum concentrations of triglyceride, haemoglobin A1c and high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, total cholesterol, lipid fraction and C reactive protein, and also including routine blood samples; haemoglobin, leucocytes, thrombocytes, sodium, potassium, creatinine, blood calcium,

Table 1 Schedule of enrolment and assessment

Timepoint	Preintervention	Baseline (preallocation) day 0	Midway 3 months	Endpoint 6 months	Follow-up 24 month
Enrolment:					
Project information; written and oral	X				
Written informed consent	X				
Eligibility assessment	X				
Assessments:					
Mood ratings	X	X	X	X	X
Primary outcome					
AMPS		X		X	
Secondary outcome					
FAST	X	X	X	X	X
PSS		X		X	X
WHODAS		X		X	X
WHOQoL		X		X	X
Tertiary outcome					
SCIP-D		X		X	X
TMT-A		X		X	X
TMT-B		X		X	X
Physical health		X		X	X
Other measures					
ADL-I		X			
CISS		X		X	X
COBRA		X		X	X
CTQ		X			
DART		X			
EPQ		X			
IPAQ		X		X	X
Life event questionnaire		X		X	X
OASIS		X		X	X
PSQI		X		X	X
SAPAS		X			
VSSS-54				X	

ADL-I, Activities of Daily Living Interview; AMPS, Assessment of Motor and Process Skills; CISS, Coping Inventory for Stressful Situations; COBRA, Cognitive Complaints in Bipolar Disorder Rating Assessment; CTQ, Childhood Trauma Questionnaire; DART, Danish Adult Reading Test; EPQ, Eysenck Personality Questionnaire Inventory; FAST, Functional Assessment Short Test; IPAQ, International Physical Activity Questionnaire; OASIS, Overall Anxiety Severity and Impairment Scale; PSQI, The Pittsburgh Sleep Quality Index; PSS, Cohen's Perceived Stress Scale; SAPAS, Standardised Assessment of Personality—Abbreviated Scale; SCIP-D, Screen for Cognitive Impairment in Psychiatry—Danish version; TMT-A, Trail Making Test A; TMT-B, Trail making Test B; VSSS-54, Verona Satisfaction Scale-Affective Disorder; WHODAS, WHO Disability Assessment Schedule 2.0; WHOQoL, WHO Quality of Life.

aspartate aminotransferase, bilirubin, alkaline phosphatase and thyroid-stimulating hormone (TSH).

Questionnaires

For an overview of the used questionnaires and timing, please see [table 1](#). Patients reported outcome measures obtained via surveys at baseline and after 6-month intervention (or TAU) are: general health (a modified version of the Danish National Health Profile survey,⁵¹ QoL (WHO Quality of life (WHOQoL),³⁶ disability (WHODAS),³⁵ stress (Cohen's Perceived Stress Scale (PSS),⁵² anxiety (Overall Anxiety Severity and Impairment Scale),⁵³ cognitive impairment (Cognitive complaints in bipolar disorder rating assessment),⁵⁴ sleep (Pittsburgh Sleep

Quality Index),⁵⁵ physical activity and exercise (International Physical Activity Questionnaire),⁵⁶ coping strategies (Coping Inventory for Stressful Situations),⁵⁷ recent and former severe life events (Life event questionnaire used by Kendler and colleagues (Danish version)),⁵⁸ depressive symptoms (Major Depression Inventory),⁵⁹ manic symptoms (Altman Self-Rating Mania Scale)⁶⁰ and, at follow-up, the Verona Satisfaction Scale-Affective Disorder⁶¹ measuring level of satisfaction with resent psychiatric treatment. At baseline, only personality dimensions will be assessed using the Eysenck Personality Inventory⁶² and childhood traumas using the Childhood Trauma Questionnaire.⁶³ These questionnaires will help

us to cover the 360° assessment and to evaluate the intervention. The questionnaires are used in clinical settings, translated into validated Danish versions and used in previous studies from our group.^{16 64}

The intervention

The present intervention targets multiple aspects of the described enhancers of functioning based on the ICF Brief Core Set: (1) ADL ability as a part of carrying out daily routines, (2) mood symptoms, medication and side effects, (3) social, relatives and network, (4) physical health, including body mass index (BMI), biomarkers and exercise, (5) cognition, circadian rhythm measured as sleep quality and coping (stress reduction). Based on the assessments, a transdisciplinary group of clinical experts (medical professionals, nurses, social workers and occupational therapists) within the field of affective disorders will conduct a targeted individual intervention profile based on the five described pillars of ICF. The group is headed by MV (psychiatrist). The goals for the intervention are based on the areas where the patients have the lowest scores (most severe impairment). An intervention manual is developed and targets the described enhancers of functioning based on the comprehensive assessment procedure (see the Introduction section).

The AWARE intervention will include 6–14 visits. Visits 1–2: feedback on the 360° baseline assessments, including the results of all the questionnaires, the ADL observation and the physical and cognitive evaluation. Based on these goals, the individualised AWARE intervention will be set. Participants at first visit are the patient, a medical professional, an occupational therapist and other transdisciplinary professionals. This transdisciplinary group will conduct a targeted individual intervention profile, which will be discussed and shaped with the patients aiming to select one to three main goals (eg, problems with performing daily routines and mood symptoms). Visits 3–13: intervention sessions; the intervention will address the prioritised treatment goals following the intervention manual that describes each area in detail, and at each intervention visit, either a medical professional or an occupational therapist will be present. If relevant, relatives are involved in one or more intervention visits. A midway evaluation meeting with the patient will be held after 3 months of intervention, with an assessment of functioning (FAST) and mood symptoms (HDRS-17 and YMRS). There will be a transdisciplinary session after visit 13 aiming to perform a status and a treatment plan involving the relevant actors in the further treatment, for example, relatives, social workers, the general practitioner or psychiatrist. Visit 14. The last visit; the patient's evaluation of the intervention and the achieved goals. The patient is required to participate in two-thirds of the planned visits during the intervention period to complete the intervention. The intervention will be optimised following the template for intervention description and replication checklist and guide.⁶⁵

Outcomes

The primary outcome is changes in ADL motor and process ability measures from baseline to endpoint according to scores on the AMPS. Patients will be observed and rated at baseline and after 6 months endpoint by blinded personnel trained in AMPS assessment.

Secondary outcomes are changes from baseline to endpoint in functioning using FAST and WHODAS V.2.0. and in QoL and stress using WHOQoL and PSS. Tertiary outcomes are cognition using a composite score assessed at baseline and after endpoint by blinded raters, and physical health change in observed side effects, BMI and biomarkers related to glucose and fat metabolism and inflammation.

Power calculation

Power calculation is based on changes in ADL ability on AMPS during the 6 months of study period. A clinically relevant difference between the two groups in change is defined as ≥ 0.3 logits with a mean SD of 0.3 logits. The statistic power to detect a clinically relevant improvement of ≥ 0.3 logits in the treatment group is 95% with $\alpha=0.05$ for two-sample comparison of means including 104 patients. <https://www.dssresearch.com/KnowledgeCenter/toolkitcalculators/statisticalpowercalculators.aspx>. Assuming a 10%–15% dropout rate from baseline to treatment completion, we will recruit 120 participants to achieve a full 6-month completion and data set for 104 patients. The current dropout rate at endpoint (6 months) is 9% based on the first 11 patients.

Statistical analyses

Data from the randomised patients will be collected until dropout or the end of the study period. Differences from baseline (T_0) to after six months intervention (T_6) will be analysed, first unadjusted and then adjusted for age, sex, diagnosis, previously number of affective episodes and significant differences in current medication if these variables present with a $p \leq 0.1$ in univariate analyses (independent t tests). All comparative analyses between the treatment groups will be intention-to-treat using the last observation carried forward for missing values. Data will be analysed using repeated measures analyses of covariance with treatment group (AWARE vs TAU) as the between-group factor, time (baseline to 6 months) as the within-subject factor and adjustment for stratification variables (age, gender and diagnosis) to minimise effects of any baseline imbalances. The statistical threshold for significance is $p \leq 0.05$ (two tailed).

Data management

Personal information is obtained during the assessment of the participants, and data from patient records can be obtained as well if needed. Signed consent forms are uploaded to REDCap and kept in paper form in a locked filing cabinet. Data from neuropsychological test, questionnaires, demographics and interviews are entered into the REDCap database. The database REDCap meets the Good Clinical Practice requirements for data management and

storing. On exclusion or withdrawal from the study, the reason will be recorded. The Danish Data Protection Agency can conduct inspections to ensure that data management is handled in agreement with the legislation. The Danish Data Protection Agency operates independently of the study.

DISCUSSION

The present study investigates the effect of multimodal 360° intervention on ADL, functioning and QoL of BD and UD patients in remission or partial remission. Functioning is increasingly recognised as a central outcome in these patient groups and might even be considered more important than the syndromal outcome.

A recent review article suggests functional outcomes as a primary outcome in future studies of BD and finds a current lag of intervention studies specifically targeting functioning.⁶⁶ To the best of our knowledge, previous available intervention studies have primarily focused on cognitive aspects of functioning.^{67 68} Several psychosocial interventions in adjunct to psychopharmacology have shown effectiveness in the treatment of BD, but none specifically targeting functioning as a primary outcome in patients in a remitted state.⁶⁹

Strengths

A considerable strength of the AWARE study is the comprehensive 360° assessment, including the most known factors contributing to impaired functioning in BD and UD.⁶⁶ Therefore, we can base the individualised intervention on understanding the specific factors associated with, and causing, the impaired functioning of each patient. Considering the shortcomings of current available treatments and the scarcity of multimodal intervention studies as previously mentioned, we consider the AWARE intervention of great relevance in affective disorders.

To assess the participants' ability to perform ADL, we have explicitly chosen a performance-based assessment (AMPS) conducted in the patient's home surroundings. These observations are likely a better proxy to understand the daily hassles patients encounter than assessments conducted in clinical settings, and they might contribute to a greater focus on improving functioning.⁷⁰ In addition to AMPS and FAST, patients self-perceived level of functioning and ADL ability is assessed using WHODAS and ADL-I. Few previous studies include more than one measure of functioning, with some using observer-based measures and others using self-reported measures.⁶⁶ When assessing impairment in patients with BD, correlation between patients' subjective experience and objective measures is not present in all cases. This discrepancy might result from patients' own experience of impairment being influenced by subclinical depressive symptoms.¹⁶

The study has few exclusion criteria, making the study representative of, and applicable to, 'real-life' patient populations.

The randomised, controlled design of the study with blinded outcome assessment is an advantage as it reduces experimental bias.

LIMITATIONS

The timeframe of the AWARE intervention in the present study is 6 months. Some of the included patients might have years or even decades with significant functional impairment. Nevertheless, 6 months is a limited span of the treatment, and more time might be necessary to gain noteworthy improvements in functioning. Even if the intervention group shows significant improvement in functioning and QoL after 6 months, the improvement might not be sustained. To address the long-term effects, a 24-month follow-up is planned.

Current, ongoing substance abuse is one of the few exclusion criteria. Previous studies have found substance abuse to be one of the factors associated with functional impairment.⁷¹ However, this is not addressed in the AWARE treatment programme, due to presumed problems with compliance and completion accompanying the substance abuse.

A crucial challenge for recruitment in this study is that some patients might be unwilling to participate due to the AMPS observation performed in the patients' home, which some may find 'intrusive'. So far, one of the 32 patients who has been screened for the trial has declined participation for this reason. Only two other patients have declined participation (one due to anxiety symptoms and the other because of lack of energy). In general, we expect patients to be positive towards participation, as the intervention targets vital areas of functioning persisting despite the patients' previous treatment/ treatments. The current participation rate is 91%.

ETHICS AND DISSEMINATION

The Regional Ethics Committee in the Capital Region of Denmark (protocol number H-20029748) approves the AWARE trial and the Danish Data protection agency (j. nr. P-2020-1216), and the trial was registered at Clinicaltrials.gov on 8 January 2021. The project is following the ethical aspects as declared in the Helsinki-Declaration 2. Important changes in the protocol will be reported to the Ethics Committee in the Capital Region of Denmark and the Danish Data Protection Agency. All potential participants will have written and oral information about the trial before informed consent is obtained. Participants are informed that they can withdraw from the trial at any time without this having any effect on their course of treatment thereafter. The Danish Data Protection Agency is at any given time entitled to audit trial conduct.

The study results will be disseminated by peer-review publications

If the present intervention shows a beneficial outcome for the AWARE arm, it can be used as a template for future treatment, addressing disability with a transdiagnostic approach (affective disorders, anxiety disorders and psychotic

disorders). This would support the use of specialised cross-disciplinary teams capable of bridging the different sectors to create a tailored individualised and cooperative intervention focusing on improving daily functioning.

There are no known or expected direct risks associated with participation in the study. Participants will be asked about adverse events at midway evaluation, endpoint interview, and in case of drop-out from the study. Data will be collected I REDCap.

Trial status

Enrollment of patients began on 1 February 2021. As of 1 October 2021, 32 patients were screened, and 29 patients included in the AWARE study. Recruitment completion is planned for 31 December 2022.

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Contributors All authors meet the four criteria for authorship, as stated by ICMJE. The primary areas of contribution from each of the authors are listed below. MV conceived the study together with LD. MV, LD and RS wrote the study protocol. MV obtained the required funding for the study along with LD. MV and LD developed the intervention program and LD, RS and MV wrote the intervention manual. KWM and LVK contributed to revising the study protocol. IS and RS set up the study, assessments and questionnaires in the REDCap program. RS is responsible for carrying out the treatment with assistance from occupational therapists and nurses at Psychiatric Centre North Zealand, and under supervision of MV. RS has the primary responsibility for recruitment, enrolment, data collection, data analysis and interpretation of the data under supervision of MV. All authors have read and approved the present manuscript.

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Disclaimer The foundations have not been involved in writing the present manuscript or in the design of the study, nor will they be involved in the data collection, analysis, interpretation of data, or other activities.

Competing interests KWM has received consultancy fees from Lundbeck and Janssen-Cilag in the past 3 years. LVK has within the last 3 years been a consultant for Lundbeck and Teva. MV discloses within the last three years consultancy fees from Lundbeck, Sunovion and Janssen-Cilag. RS has received consultancy fees from Lundbeck and in the past 3 years.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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