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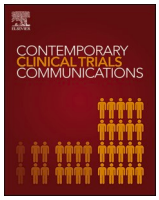

Internet-delivered treatment for patients suffering from severe functional somatic disorders: Protocol for a randomized controlled trial

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ABSTRACT

Background: Functional somatic disorders (FSDs) with symptoms from multiple organs, i.e., multi-system type, are common in the general population and may lead to disability and reduced quality of life. Evidence for efficient treatment programs has been established, however, there is a need for making treatments accessible to a larger group of patients. Internet-delivered therapy has become prevalent and has proven as effective as face-to-face therapy, while providing a flexible and easily accessible treatment alternative. The aim of the current study is to compare the efficacy of the therapist-assisted internet-delivered treatment program One step at a time (OneStep) with the internet-delivered self-help program Get started (GetStarted).

Methods: A total of 166 participants aged 18–60 years diagnosed with multi-system FSD will be assessed and randomized to either 1) OneStep: a 14-week program consisting of 11 treatment modules based on principles from cognitive behavioural therapy or 2) GetStarted consisting of 1 module on psychoeducation. The primary outcome is physical health, assessed by a Short Form Health Survey (SF-36) aggregate score of the subscales vitality, physical functioning, and bodily pain 3 months after end-of-treatment and self-reported improvement assessed by the Clinical Global Improvement Scale. Secondary outcomes include symptom load, depression, anxiety, and illness worry. Process measures include emotional distress, illness perception, illness behaviour, and symptom interference.

Conclusions: This study is the first study to test an internet-delivered treatment program for FSD, multi-system type and has the potential to show the importance of making evidence-based internet-delivered treatment for FSD more accessible.

1. Background

Functional somatic disorders (FSDs) are conditions in which the patients suffer from impairing physical symptoms from various bodily systems. The diagnosis is based on the identification of a characteristic symptom pattern as no diagnostic blood tests or other paraclinical tests, exist [1,2]. Co-occurring physical and psychiatric conditions should be considered. The conditions are common, disabling and emotionally distressing for patients, and costly for society [3–5].

In the healthcare system, patients frequently receive medical specialty-specific syndrome diagnoses (FSS) such as fibromyalgia, chronic widespread pain, chronic fatigue syndrome, and irritable bowel syndrome [6,7]. Nevertheless, a substantial overlap of symptoms has been shown between the various types of FSS, indicating that the syndromes are not entirely independent conditions but different representations of a family of related disorders [8]. In order to meet this issue, the unifying research diagnostic construct *bodily distress syndrome* (BDS) has been proposed [3,9,10]. Thus, patients who report symptoms from 3 or more organ systems are classified as having *multi-organ* BDS. For patients reporting symptoms from only one or two organ system, the term *single-organ* BDS has been proposed. The BDS diagnosis may be considered an operationalization of the FSD construct, with specific diagnostic criteria. For the remaining paper, the term FSD multi-organ type will be used when referring to patients diagnosed with multi-organ BDS.

FSD multi-organ type affects an estimated 2% of the general population in Denmark and represents patients moderately to severely impaired by their illness [11,12]. The condition causes suffering and

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Abbreviations:

FSD	Functional somatic disorders
FSS	Functional somatic syndromes
RCT	Randomized controlled trial
CBT	Cognitive Behavioural Therapy
DeFuD	The Department for Functional Disorders
AUH	Aarhus University Hospital
PHC	Pain and Headache Clinic
CFD	Center for Functional Disorders
SCAN	Schedules for Clinical Assessment in Neuropsychiatry
ACT	Acceptance and Commitment Therapy
GET	Graded Exercise Therapy
MBSR	Mindfulness Based Stress Reduction
CFT	Compassion Focused Therapy
FU	Follow-up

reduced quality of life and is associated with substantial socioeconomic costs, involving expensive diagnostic examinations, sick leave, and long-term disability [2,13,14]. The course of FSD multi-organ type is often chronic as only few patients receive treatment [2,15,16].

A number of clinical trials have provided evidence for an effect of psychological interventions for FSD multi-organ type [17–19]. Furthermore, a psychoeducation intervention tailored to FSD multi-organ type resulted in symptom improvement and reduced illness worry and was found highly acceptable by the patients [20]. The introduction to graded exercise as a means of moderating maladaptive illness behaviour and increasing physical function is also considered an important element in the treatment and has been found effective for chronic fatigue syndrome [21]. However, only few treatments are currently available and often only in specialized settings. Since the FSD multi-organ type is a condition with a major public health impact, there is a need for treatment programs that are accessible, feasible, and effective and can be provided on a larger scale. Assisted internet-delivered treatment programs in which patients log in to an online treatment program supported by a therapist provide an opportunity to offer treatment to a wider range of patients in a more flexible format.

Internet-delivered treatment programs have become more prevalent [22] and have shown to be as effective as face-to-face therapy for a range of psychiatric and somatic disorders [23]. Studies focusing on internet-delivered therapy for patients with medical speciality FSSs such as irritable bowel syndrome [24–26], fibromyalgia [27], chronic pain [28,29] and non-cardiac chest pain [30], as well as somatic symptom distress [31] have shown promising results for internet-delivered treatments compared with waiting list or active control conditions. However, to our knowledge, no studies have yet developed and tested an internet-delivered treatment for FSD multi-organ type, that is for patients, who could potentially fulfill diagnostic criteria for several medical speciality FSS. Being able to just complete one program tailored for the phenomenon of presenting with a variety of symptoms (FSD multi-organ type) could potentially help patients to identify more with the given treatment and limit the use of health care services.

Therefore, a therapist-assisted internet-based treatment program One step at a time (OneStep) was developed for patients with FSD multi-organ type in collaboration with clinical experts in FSD and leading researchers in internet-based interventions at the Department of Functional Disorders (DeFuD), Aarhus University Hospital (AUH). The format of the program is modelled on an existing internet-delivered treatment program for severe health anxiety [32]. The content of the program is inspired by the face-to-face patient education program offered at the DeFuD [20] and is founded on principles from Cognitive Behavioural Therapy (CBT) with the addition of elements from Acceptance and Commitment Therapy (ACT) [17,19].

2. Purpose and aim

The purpose of this study protocol is to present the rationale and methods of the OneStep trial, a multi-center randomized controlled trial for patients with FSD multi-organ type. The aim of the trial is to test the efficacy of a therapist-guided internet-delivered treatment program OneStep in comparison with a non-guided self-help program Get started (GetStarted) using a randomized controlled trial (RCT) design.

Primary hypothesis: A statistically significant higher proportion of patients receiving OneStep will report a clinically relevant improvement in self-reported physical health at the 3-month follow-up after end-of-treatment compared with those receiving GetStarted, and a higher proportion receiving the OneStep will report a subjectively rated improvement at the 3-month follow-up compared with those receiving GetStarted.

Secondary hypotheses: We expect a statistical significant difference in the development over time for OneStep compared to GetStarted in secondary outcomes, specifically in terms of increasing helpful illness perceptions and behaviours, and reducing illness worry from baseline to the 3-month after end-of-treatment (end-point), and we expect OneStep to be superior to GetStarted at end-of-point for the secondary outcomes.

Further, we hypothesize illness perceptions, illness behaviour and, emotional distress to mediate change in health status as measured by the primary outcome, the aggregate score.

3. Methods

3.1. Study design

The study is a two-armed randomized controlled clinical superiority trial where participants are randomized to a 14-week internet-delivered and therapist-assisted treatment program OneStep or to a self-help program GetStarted (1:1). The study is registered at www.clinicaltrials.gov, (ID NCT05525598) and is approved by the Central Region Denmark Ethics Review Committee (Case number: 1-10-72-361-21).

3.2. Setting

The trial is being conducted as a multi-center trial led by the DeFuD based at AUH, Denmark (www.functionaldisorders.dk). This clinic has been operating since 1999 and offers assessment and specialized treatment to patients with FSD multi-organ type. In addition, the Pain and Headache Clinic (PHC) based at AUH and the Center for Functional Disorders (CFD) based at the Hospital Lillebælt in the Southern Region Denmark will participate. All three clinics will take part in the assessment and recruitment of patients, however, the project is led by researchers at the DeFuD, and the treatment will be conducted by trained psychologists at the DeFuD.

3.3. Study population and recruitment

A total of 166 patients aged 18–60 years with FSD multi-organ type, operationalized as severe multi-organ BDS, will be included in the study over an estimated 2-year period between January 2023 and December 2024. Patients meeting inclusion criteria will be recruited consecutively and identified at the first contact at the clinics during assessment. Fig. 1 presents the flow of participants throughout the study.

3.4. Inclusion criteria

Patients aged 18–60 years fulfilling the criteria for FSD multi-organ type, operationalized as multi-organ BDS [10] and with a symptom duration >6 months, are eligible for inclusion. Furthermore, participants should have had an affiliation to the labour market or educational

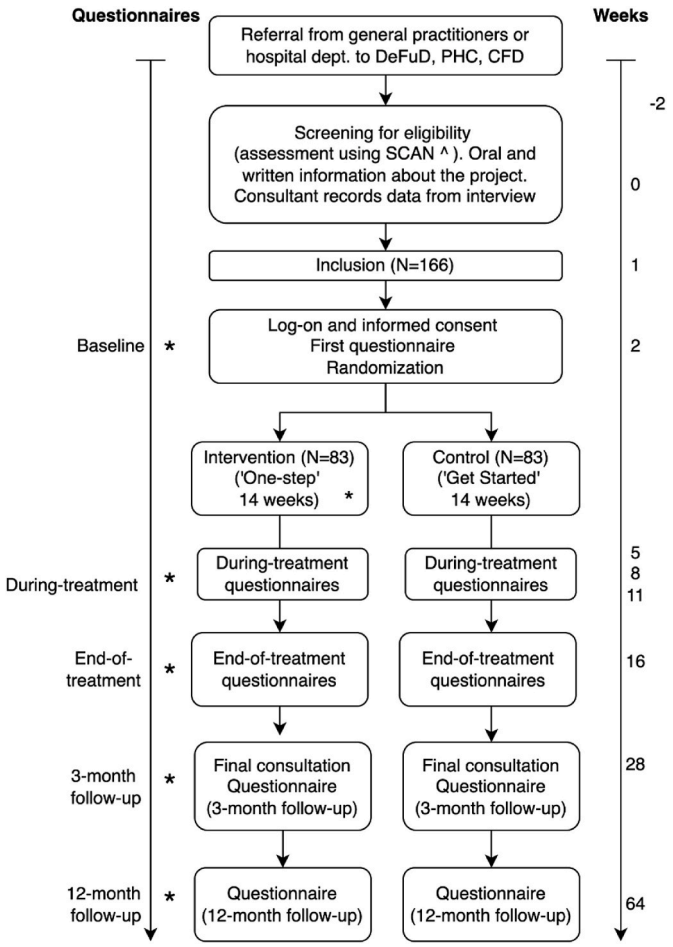

Fig. 1. Flowchart
^ Schedules for Clinical Assessment in Neuropsychiatry (SCAN) [33]* The intervention group will answer questions regarding the treatment every week.

system for at least 12 months during the last 2 years (at least part time (18.5 h/week). Patients must also have access to a computer or a tablet with internet connection, and understand, read, and write Danish fluently.

3.5. Exclusion criteria

Patients are excluded from participation if they present with severe comorbid somatic or psychiatric disorders that are insufficiently treated at the time of assessment and considered to be a potential barrier for engaging in the treatment. Patients are also excluded if they are treated with benzodiazepines or opioids. Other psychoactive medications should be stable. Further exclusion criteria are lack of motivation for engaging with internet-delivered treatment, poor self-reported IT skills, and lack of informed consent.

3.6. Diagnostic assessment and informed consent

All patients are assessed by a diagnostic interview before entering treatment at the three recruiting clinics. The diagnostic interview is based on SCAN [33], which is a thorough semi-structured interview recommended by the WHO as a diagnostic assessment of psychiatric and physical diseases. The diagnostic interviews are performed by medical doctors trained in this interview method, using either an electronic or a paper version. At the clinical assessment, patients receive verbal and written information about the study. When patients have received a diagnosis and given oral consent to participate, they will receive a link via secure email to the treatment platform. Here they can log in using their personal NemID/MitID to sign a written consent and answer the baseline questionnaire. Following this, they will automatically be randomized to one of the two treatments. Up to two reminders are sent to patients at weeks 1 and 2 after the first contact if they have not signed the written consent and completed baseline questionnaire. If they do not respond to the reminders, patients will receive a phone call in week 3. The same reminder procedure is used for the end-of-treatment and 3-month follow-ups. All data is collected and stored via REDCap, which is hosted at Aarhus University. The questionnaires are described under the measures section and displayed in Table 1.

3.7. Randomization

Randomization to one of the two arms in the study: OneStep or GetStarted takes place immediately after the patient has completed the baseline questionnaire. Thus, the assessor is blinded to the allocation. Eligible patients are randomly assigned to OneStep or GetStarted in a 1:1 computer-generated block randomization with block sizes randomly varying from 10 to 16 with no restrictions or matching. The randomization happens continuously, and treatment onset will take place no later than 1 month after the diagnostic interview.

4. Treatment

4.1. OneStep

OneStep consists of 11 internet-delivered modules delivered over 14 weeks that are based on previous treatment manuals for group-based psychoeducation and treatment for FSD multi-organ type [17–20]. The core treatment elements are based on CBT and psychoeducation to facilitate illness understanding and awareness of the interaction between thoughts, emotions, symptoms, and behaviour. In addition, the treatment includes Graded Exercise Therapy (GET) and elements from third wave therapies such as ACT, Mindfulness Based Stress Reduction (MBSR), and Compassion Focused Therapy (CFT).

Treatment content and the flow of treatment throughout the 14-week period is displayed in Fig. 2. Each module has a specific theme and contains on average 8 pages with elements such as psychoeducation; videos of former patients sharing their narrative and treatment experience; videos of health professionals on FSD, symptom understanding, and illness behaviour; interactive and graded exposure exercises; and videos of guided physical stretching and mindfulness exercises. Furthermore, the program holds information and specific advice on diet, physical activity, and sleep, as well as access to mindfulness and stretching exercises. Patients can access this information on an as-needed basis.

The treatment is assisted by a therapist with the purpose of motivating the patient to engage in the program, answer questions, and provide suggestions for graded exercises. The contact is primarily written and takes place in an embedded secured message system on the platform. Patients are encouraged to give a short status at the end of each week on their self-evaluated progress and experience of the treatment, which is recorded using standardized items. Patients will receive written feedback from their therapist on this status as well as written exercises once a week and may expect an answer on written text messages within 48 h on weekdays. Furthermore, patients are offered 3 supportive telephone consultations during the treatment: 1) A start-up consultation within the first 2 weeks, 2) a mid-term consultation after module 5 focusing on their progress and a possibility to adjust treatment goals, and 3) an end-of treatment consultation on relapse prevention and self-management after treatment.

Patients are encouraged to invite close relatives to access a module for relatives during treatment. The module consists of information on FSD, how to support patient during treatment, and how to take care of yourself while also being supportive of your spouse/other. The content

Table 1
Registration and outcome measures.

	Preassessment	Post-assessment	Baseline	Weekly status	Midterm 1	Midterm 2	Midterm 3	End of treatment	3-month FU	12-month FU
Patient evaluation										
Consent			X							
Contact info			X							
Sociodemographics	x		X							
Bodily distress syndrome checklist (BDS-25)			X					X	x	x
Numeric rating scale (NRS)			X		X	X	x	X	x	x
36-item Short Survey Form (SF-36)	x		X					X	x	x
36-item Short Survey Form (aggregate score)					X	X	x			
Symptomchecklist 90 (SCL-90)	x		X					X	x	x
Symptomchecklist 90 (Distress subscale)					X	X	x			
Brief Illness perception questionnaire (bIPQ)	x		X		X	X	x	X	x	x
Behavioural response to illness questionnaire (BRIQ)	x		X		X	X	x	X	x	x
Illness worry (WI-6-R)	x		X					X	x	x
Sources of meaning (SoMe)			X					X	x	x
European Quality of life - 5 dimensions (EQ-5D-5L)			X					X	x	x
Costs associated with Psychiatric Illness (TIC-P)			X					X	x	x
Experiences of satisfaction questionnaire (ESQ)								X		
Inventory of negative effects of psychotherapy (INEP)								X		
Internet evaluation and utility questionnaire (iEUQ)								X		
Clinical global improvement (CGI-I)								X	x	x
Working Alliance inventory (WAI)					X					
Emotional approach coping scale (EACS)			X					X	x	x
Toronto alexitymia Scale 20 (TAS-20)			X					X	x	x
Interoceptive Sensitivity and Awareness Questionnaire (ISAQ)			X					X	x	x
Experiences in close relations (ECR)			X							
Amsterdam resting state questionnaire (ARSQ)			X					X	x	x
Status on motivation and satisfaction with the treatment				X						
Consultant evaluation										
Diagnosis		X								
Inclusion/exclusion criteria		X								
Psychiatric comorbidity		X								
Patient motivation		X								
Patient medication		X								
Patient's illness perception		X								
Patient's barriers for engaging in treatment		X								
Treatment progress								X		
Fullfill diagnostic criteria								X		
Therapist evaluation										
Amount of phone conversations			X	X	X	X	X	X		
Themes of conversations			X	X	X	X	X	X		
Evaluation of patient engagement								X		
Evaluation of treatment effect								X		
Barriers for engaging in treatment								X		

is presented as text as well as video material with health professionals and relatives of former patients.

Treatment is considered completed when the patient has worked actively with the first 5 modules of the treatment program. This was chosen because patients have received fundamental treatment elements such as psychoeducation on FSD, symptom understanding, and graded exercise at this point.

4.2. Quality control

Before the onset of the trial, all therapists will receive training in the program OneStep. A therapist manual will be distributed and the core

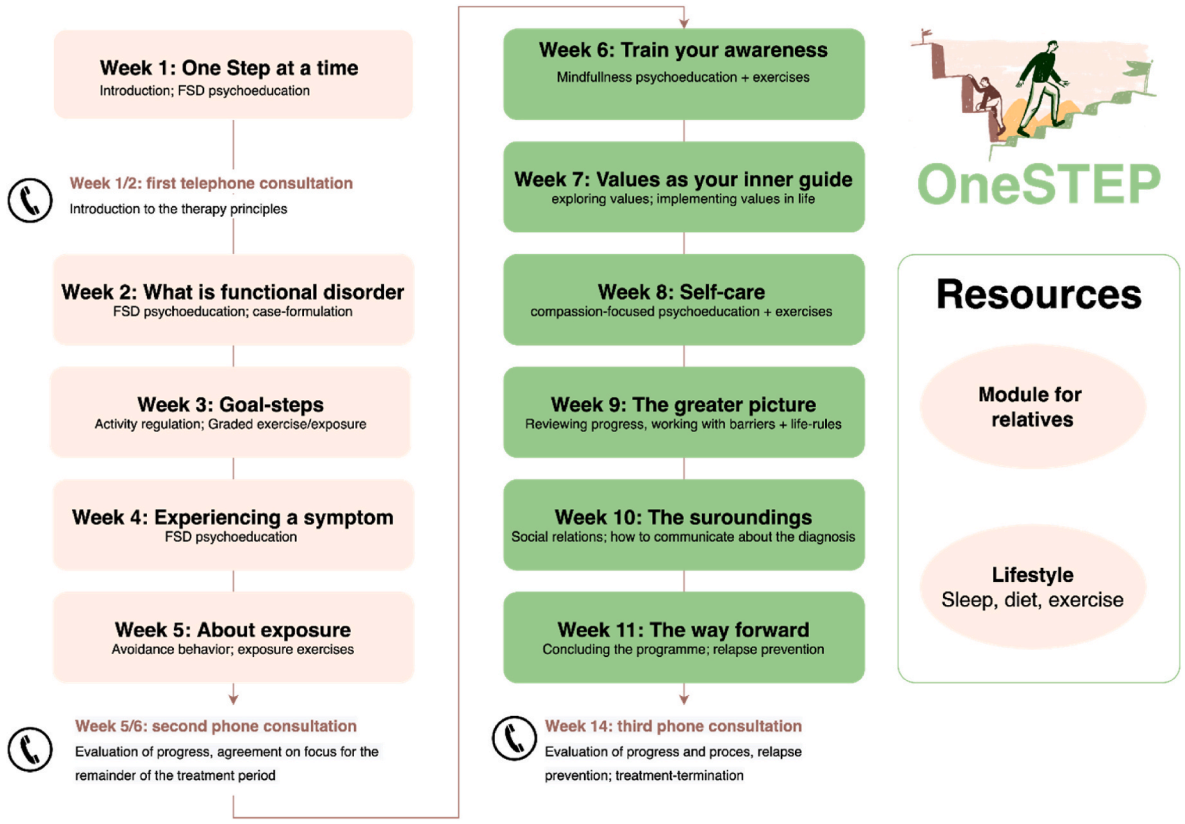

Fig. 2. Treatment content and flow.

treatment elements will be introduced. During the trial, therapists are supervised every week in which written material (exercises and text messages) are discussed to ensure adherence to protocol. Additionally, the treatment progress of the patients is discussed at these events, also including their clinical needs and potential adverse events. The therapists are asked to evaluate adherence with standardized instruments on a weekly basis. Protocol violations will be recorded.

4.3. Control condition: GetStarted

GetStarted is a brief internet-delivered non-guided self-help program consisting of one module on psycho-education about FSD multi-organ type and resources addressing the three life style factors sleep, diet, and physical activity. The program consists of written information as well as short videos with health professionals and former patients from the clinic, however the program offers no interactive exercises. The program provide specific advice based on CBT for insomnia [34], diet, and how to increase physical activity by applying graded exercise. Patients can work with all three domains during the treatment period, however they are encouraged to primarily focus on one thing at a time, either sleep, diet, or physical activity In this treatment modality patients are not nudged to provide a weekly status and no therapeutic assistance is provided. If patients experience deterioration during the treatment period, they are advised to seek help from their general practitioner. Thus, the aim of this program is to provide patients with a new illness understanding and support them in stabilising basic life style factors. This corresponds to initial standard care at our clinic, and corresponds to the first module plus the resources on sleep, diet, and physical activity in the active condition in this trial.

Both programs will be hosted on the platform "internetbehandling.dk", which utilizes the Drupal Content Management System (CMS) as a framework.

5. Data sources and effect measures

Data will be collected from various sources. Table 1 displays the instruments used, and at which time points they are collected. Self-reported data from the patients are obtained at 7 time points during the trial: at baseline (before the randomization), during treatment at weeks 5, 8, and 11, at end-of-treatment, at 3-month follow-up (FU, primary endpoint), and at the 12-month FU. Once a week, patients allocated to OneStep will be asked to evaluate self-reported treatment progress. Self-reported data will be collected via a prompt in the treatment platforms. The participants will receive a notification (text message) when a new questionnaire has been opened.

The medical doctors responsible for the assessment complete a short questionnaire after the assessment on inclusion and exclusion criteria, patient motivation, the patient's illness beliefs, and an assessment of potential barriers for the patient's adherence to treatment. The therapists responsible for the contact to patients allocated to OneStep complete a questionnaire immediately after end-of-treatment on patient motivation and evaluation of the treatment progress. Finally, the medical doctor completes a short questionnaire after the final consultation at the 3-month follow-up assessing the degree to which the patient has benefitted from treatment and if they still meet the diagnostic criteria for multi-organ BDS. All questionnaires are listed below. A more detailed display can be found in Table 1.

5.1. Primary outcomes

Two primary outcome measures will be used: First, an aggregate score based on the Short-Form Health Survey (SF-36), [35]. The SF-36 consists of 36 items, from which a score of physical health (PSC) can be derived from the SF-36. The PSC scale is often used as primary outcome. However, a study has suggested that some subscales of the PSC is not valid in patients with FSD [36], and therefore we have chosen to

use an aggregate score of SF-36, which measures physical health and is derived from the subscales PF (physical functioning), BP (bodily pain), and VT (vitality). These three widely used subscales cover key aspects of physical health that are commonly impaired in patients with FSD [37] and have also shown to be sensitive to change in this patient group [17–19]. The aggregate score ranges between 15 and 62, and a 4-point change which equals 0.5 sd. is considered a clinical relevant chance [38]. The primary end-point is defined as the measurement collected at 3-month after end-of-treatment.

Secondly, the self-reported Clinical Global Improvement Scale (CGI-I), which is a 5-point ordinal scale measuring patient-rated overall health improvement at end-point. Patients rate their general health as much worse, worse, unchanged, better, or much better in response to the following question: "How do you consider your health status now compared with when you first came to the clinic?" This simple scale correlates with other specific outcomes in this population, including physical functioning and symptom scores [39] and is chosen based on the recommendations from consensus groups in pain research and FSD [40,41]. The primary end-point is defined as the measurement collected at 3-month after end-of-treatment.

5.2. Power analysis for primary outcome

The power calculation is based on the proportion of patients experiencing a minimum 4-point increase in the aggregate score, from baseline to the 3-month follow-up, which may be regarded as a clinically relevant change [42], and has been used as an indicator of a clinically relevant response to treatment in FSD [17,19].

Based on previous studies, we estimate the proportion experiencing a minimum of a 4-point improvement at the primary outcome, the aggregate score, to be 35–50% in the intervention group and 10–25% in the active control group [17–20]. With a total sample size of $N = 150$ and a proportion experiencing a minimum of 4-point improvement in the control group equal to 15%, we will with a power of 81.4% be able to establish a difference between groups if the proportion experiencing a minimum of a 4-point improvement in the intervention group is at least 35%.

For the CGI-I, patients grade their health as much worse, worse, unchanged, better, or much better. In the analyses, much worse and worse will be collapsed into one category, and better and much better into one category, i.e., 3 outcomes in each category (worse, unchanged, and better). Power for different scenarios (based on previous trials [43]) of proportions of worse, unchanged, and better in the intervention group and control group respectively were simulated using a proportional odds model. With proportions of worse, unchanged, better being (10, 50, 40) in the intervention group versus (10, 70, 20) in the control group (resulting in an OR = 2.57), and 75 patients in each group, a power of 79.1% was achieved (assuming alpha level of 5%).

We expect an attrition rate of 10% in both groups. Therefore, we chose to include 16 additional patients to the number of patients needed (150).

5.3. Secondary measures

Illness severity is measured by two measures: 1) The Somatization Subscale from the Symptom Checklist Revised-90 (12 items, 5-point scale [44], and 2) the BDS Checklist [15] that covers 25 key symptoms of FSD in four symptom groups (25 items, 5-point scale).

Mental health will be measured by subscales of the Symptom Checklist Revised-90 [44], specifically subscales for anxiety (SCL-anx 4) and depression (SCL-depr 6) (10 items, 5-point scale). Whiteley-6-R (6 items, 5 point scale), was chosen to measure illness worry [45], which is prevalent in patients with FSD and considered a key element in the perpetuation of symptoms. Meaning in life is measured by the Meaning in Life Questionnaire [46,47], which is considered important for the recovery of patients with chronic disorders such as FSD (10 items, 6-point scale).

5.4. Process measures

The numeric rating scale (NRS, 2 items, 0–10 point scale will be used to measure the intensity and interference of symptoms [48]. Emotional distress (SCL-8, 8 items, 5-point scale) is measured by a subscale from the Symptom Checklist Revised-90 [44]. Illness perception is measured by the Brief IPQ (bIPQ) [49] (7 items, 10-point scale), and illness behaviour is measured by the BRIQ [50] (13 items, 5-point scale).

5.5. Other measures

5.5.1. Evaluation of treatment

Patients' expectancy of treatment effect is measured by the Credibility/Expectancy Questionnaire (CEQ) [51], (6-item, 10-point scale). The experience of working alliance will be measured by the Working Alliance Inventory-Short Revised (WAI-SR) [52] (12-items, 7- point scale). Furthermore, possible adverse events in therapy will be measured by the 39-item Inventory for the Balanced Assessment of Negative Effects of Psychotherapy (INEP) [53], and patient satisfaction with treatment is measured by selected items from the Experience of Service Questionnaire ESQ [54], and the Internet Evaluation and Utility Questionnaire (IEUQ) [55].

5.5.2. Moderators

To investigate possible moderating effect of trait-based features, attachment style will be assessed with the 9-item Experiences in Close Relationships-Revised questionnaire (ECR-RS) [56], covering anxiety and avoidance in close relationships, which may moderate the alliance between patient and therapist. Furthermore, spontaneous cognitions and feelings during resting state are measured by Amsterdam Resting-State Questionnaire [57]. Finally, emotional coping is measured by Emotional Approach Scale (EAS) [58], and interoception is measured by The Interoceptive Sensitivity and Attention Questionnaire (ISAQ) [59].

5.5.3. Economic measures

Data from relevant registers such as the Danish National Patient Register (Landspatientregisteret), the Central Psychiatric Central Research Register (Det Psykiatriske Centralregister), the Danish Health Data Authority (Sygesikringsregisteret), the Danish Medicines Agency, (Lægemiddelstyrelsen), the Danish Register for Evaluation of Marginalization (Den Registerbaserede Evaluering Af Marginaliseringsomfanget (DREAM, a national database collecting information on social benefits), and FUNKdata (a clinical database collecting data before the assessment in the clinic) will be extracted enabling analyses on healthcare expenses, social benefits, and sick leave 1 year after end-of-treatment. We will assess QALYs, for health economic analysis using the European Quality of life 5-dimensions questionnaire (EQ-5D-5L) [60,61].

5.5.4. Data logging

To measure participants' engagement with the program, we will log certain usage metrics, including total time spent in program, total time spent on each module, total time per page, login frequency, frequency of completed modules, interactive activities engaged with in total and per module, (including movies started, text boxes written in, special features interacted with, e.g., value-sorting exercise), total word count in text boxes, and the textual content of all text boxes.

5.6. Analysis

The primary hypothesis will be analyzed using 1) binary regression model to compare the proportion of patients with a change in the aggregate score greater than 4 points and 2) proportional odds model for

the ordinal CGI-I. For the secondary hypotheses, mixed linear models will be used to investigate the development over time and for the comparison of measurements at the 3-month follow-up. An 'intention to treat' analysis and a 'completer analysis' will be performed. Furthermore, an adjusted analysis will be performed, and we will use directed acyclic graphs to determine the appropriate variables to adjust for.

Mediation analyses will be conducted to examine whether illness perceptions (bIPQ), illness behaviour (BRIQ), emotional distress (SCL-90-dist) mediate change in health status as measured by aggregate score. Mediation analyses will include data from baseline, mid-treatment measures (weeks 5, 8, and 11), end-of-treatment, and the 3-month follow-up. Mediation will be analyzed using parallel process latent growth curve models [62–65]. Results will be analyzed and reported according to the CONSORT statement [66]. A statistician is continuously involved in the project.

6. Discussion

This study protocol presents the design of a randomized controlled trial study with the aim of evaluating the effect of a therapist-assisted internet-based treatment program for patients with severe FSD multi-organ type. Previous studies have found positive effects of face-to-face psycho-therapy: however, there is a major need for more accessible evidence-based treatments for patients with severe multiple BDS/FSD. Often waiting list for specialized treatments are long and a prolonged period for receiving the right help and treatment may be a risk factor for severe deterioration. Thus, internet-based treatment may accommodate this need. This is the first internet-based treatment program for patients presenting with FSD of the multi-organ type. The intervention is expected to improve patients' illness understanding and facilitate a more adaptive illness behaviour, improve patients' symptom management, and promote positive adjustment of life style factors. The combination of these factors are hypothesized to lead to decreased illness worry, decreased symptom load, and improved health-related quality of life.

Perspectives

If proven effective and acceptable to patients, this program may offer an evidence-based first step of internet-based treatment for patients with FSD multi-organ type, many of which have no access to specialized face-to-face treatment. Finally, studies have indicated that internet-based treatments are more cost-efficient than face-to-face treatment [67]. Thus, it may allow a larger number of individuals to be treated at the same cost, thus increasing the availability of psychological treatment for individuals with FSD.

Ethical considerations

This study presents a low risk of patient harm since all patients are thoroughly assessed by a physician before referral to the study. Furthermore, patients allocated to the intervention (OneStep) are followed closely by a psychologist with access to assistance from a physician specialized in severe FSD. If patients report harmful events such as severe deterioration during treatment, the therapists are instructed to address this and if necessary stop the participation and offer face-to-face treatment instead. All patients are offered a consultation with a physician at the clinic 3 months after end-of-treatment. Patients allocated to the control condition GetStarted will be offered to participate in the treatment program OneStep or face-to-face treatment at the clinic after the 3-month follow-up period if needed. Further treatment may also be required for some of the patients who participated in OneStep. Patients without internet access or IT skills will not be able to participate, since the intervention is an internet-based treatment program. They will, however, be offered face-to-face treatment at one of the participating clinics.

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Author contribution

Heidi Frølund Pedersen: Conceptualization; Methodology; Funding acquisition; Project administration; Validation; Resources; Roles/Writing - original draft.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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