# Research protocol

# Group schema-focused therapy enriched with psychomotor therapy for older adults with personality disorders in specialized mental health care: A (cost-)effectiveness study

**(Version 5)**

**PROTOCOL TITLE**

**Group schema-focused therapy enriched with psychomotor therapy for older adults with personality disorders in specialized mental health care: a (cost-)effectiveness study**

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## LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

| | |
|---|---|
| **AE** | **Adverse Event** |
| **AUDIT** | **Alcohol Use Disorder Identification Test** |
| **BIA** | **Budget Impact Analysis** |
| **BKZ** | **Budgettair Kader Zorg** |
| **BSI** | **Brief Symptom Inventory** |
| **CEA** | **Cost-Effectiveness Analysis** |
| **CONSORT** | **Consolidated Standards of Reporting Trials** |
| **DSM** | **Diagnostic and Statistical Manual of Mental Disorders** |
| **ES** | **Effect Size** |
| **EMS** | **Early Maladaptive Schemes** |
| **EQ-5D-5L** | **EuroQoL assessment of health related quality of life** |
| **GP** | **General Practitioner** |
| **gSFT+PMT** | **Group Schema Focused Therapy enriched with Psycho-Motor Therapy** |
| **ICER** | **Incremental Cost-Effectiveness Ratio** |
| **ISPOR** | |
| **LASA** | **Logitudinal Aging Study Amsterdam** |
| **MAIA** | **Multidimensional Assessment of Interoceptive Awareness** |
| **METC** | **Medical research ethics committee (MREC); in Dutch: medisch ethische toetsing commissie (METC)** |
| **MINI-Plus** | **MINI International Neuropsychiatric Interview – Plus version** |
| **MoCA** | **Montreal Cognitive Assessment** |
| **NEMESIS** | **Netherlands Mental Health Survey and Incidence Study** |
| **PID-5-SF** | **Personality Inventory for DSM5 - Short Form** |
| **PMT** | **Psycho-Motor Therapy** |
| **QALYs** | **Quality-Adjusted Life-Years** |
| **RCT** | **Randomized Clinical Trial** |
| **RGOc** | **Rob Giel Research center of Mental Health Services** |
| **ROMGPS** | **Routine Outcome Monitoring for Geriatric Psychiatry & Science** |
| **(S)AE** | **(Serious) Adverse Event** |
| **SCID-II** | **Structured Clinical Interview for DSM-IV axis II personality disorders** |
| **SCL-90** | **Symptom Checklist-90** |
| **SFT** | **Schema Focused Therapy** |
| **SIPP-SF** | **Severity Indices of Personality Functioning – Short Form** |
| **SMI** | **Schema Mode Inventory** |

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| **Sponsor** | **The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.** |
| **TAU** | **Treatment As Usual** |
| **Wbp** | **Personal Data Protection Act (in Dutch: Wet Bescherming Persoonsgevens)** |
| **WEMWBS** | **Warwick-Edinburgh Mental Well-being Scale** |
| **WMO** | **Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen** |
| **YSQ** | **Young Schema Questionnaire** |

## SUMMARY

**Rationale:** The disease burden due to personality disorders is high for patients (lowered quality of life, high levels of psychological distress) and society (increased medical consumption and informal care). A personality disorder is found in more than one third of geriatric psychiatric outpatients, and presence of a comorbid personality disorder worsens treatment outcome for affective disorders. For long, personality disorders were considered treatment resistant, but the past decades several psychological therapies – including schema-focused therapy - have been proven successful. However, personality disorders often remain undiagnosed in geriatric psychiatry, and specific treatment for personality disorders is often not available. Patients are therefore commonly offered treatment for symptoms of depression, anxiety or somatization, leaving their underlying personality pathology untreated.

**Objective:** To study the (cost-)effectiveness of group schema-focused therapy enriched with psychomotor therapy (gSFT+PMT) in specialized mental health care for older adults. It is hypothesized that gSFT+PMT is cost-effective and superior to treatment as usual (TAU) in reducing psychological distress and improving quality of life.

**Study design:** A multicenter, randomized trial, with one-year follow-up, comparing the treatment effect of gSFT+PMT to that of TAU.

**Study population:** Older persons (60 years or older) with a cluster B or C personality disorder or meeting the general criteria for a personality disorder, who are treated in specialized mental health care.

**Intervention (if applicable)**:Twenty sessions of gSFT+PMT delivered in groups of 4 through 8 older patients over a 6-month period.

**Main study parameters/endpoints:** Primary outcome is general psychological distress (Brief Symptom Inventory; BSI-53). Cost-effectiveness analysis will be performed from a societal perspective (based on EQ-5D-5L and structured cost-interviews).

**Nature and extent of the burden and risks associated with participation, benefit and group relatedness:**
Before patients can participate in the study, eligibility is checked in a 90 minutes diagnostic interview with a local researcher (psychologist).
gSFT+PMT treatment consists of 20 three-hour sessions (2 hours psychotherapy and 1 hour PMT) over a 6-month period. Outcome assessment in both study groups consist of questionnaires (taking approximately 1 hour to complete), a brief questionnaire by smartphone or tablet (taking approximately 2 minutes, three times a day during one week), and telephone interviews (one week after the questionnaires, and taking approximately 30 minutes) are administered at the start and end of treatment, and 6 and 12 months post-treatment. These latter questionnaires assess psychological distress and quality of life, and the telephone interviews inquire about treatment related contacts and activities for the cost-effectiveness analyses.
gSFT is a specific form of psychotherapy, aimed at reducing current and future psychological distress, and PMT is added to enhance treatment effect by experiential – bodily - techniques. PMT will be adapted to the physical abilities of individual participants. We do not expect any risk associated with participation in the study, and therefore applied for exemption from the compulsory insurance for study participants.

## 1. INTRODUCTION AND RATIONALE

The disease burden due to personality disorders is high for patients (lowered quality of life, high levels of psychological distress) as well as society (increased medical consumption and informal care) [1, 2]. For long, personality disorders were considered treatment resistant. The past decades, however, several psychological therapies have been proven successful [3, 4]. Schema-focused therapy (SFT) is considered most relevant for geriatric practice due to its favourable effects on comorbid, often longstanding affective disorders [5]. In geriatric psychiatry, however, treatment for personality disorders is rather exceptional [6], while standardized diagnostic assessment identifies (comorbid) personality disorders in 33 - 58% of older patients receiving outpatient mental health care [6-10]. Therefore, it's imperative to examine the (cost-) effectiveness of schema-focused therapy among older patients.

HEALTH CARE EFFICIENCY PROBLEM

The largest population-based survey with rigorous methodology has reported a prevalence rate of personality disorders of 8% among older persons [11]. Among community-dwelling older persons suffering from an axis 1 psychiatric disorder, prevalence rates increase up to 25% [9, 10]. In the Netherlands, we found a prevalence rate of 26.3% among older patients treated in specialized mental health care [12]. This latter estimate is conservative, since personality disorders in later life often remain undiagnosed in routine clinical care [8]. Standardized assessment of personality disorders among outpatient geriatric psychiatry services have revealed prevalence rates of 33% [7], 53% [6], and 58% [8], respectively. According to the Statistics Netherlands the actual number as well as the proportion of people aged 60 years and older will increase over the next 25 years, i.e. from 4.1 million in 2016 through 5.7 million in 2040, respectively 24.4% and 31.7% of the population in those years [13]. The increasing ageing population in the Netherlands will raise healthcare costs. Among older persons, maladaptive personality traits will increase somatic healthcare consumption by 16 – 30% [14, 15].

Personality disorders often remain undiagnosed in geriatric psychiatry [8, 16]. The life-time prevalence of comorbid psychiatric disorders in older persons with a personality disorder in the community is 67.1% [11], and this proportion is probably even higher in specialized mental health care. Treatment of these patients is targeted at actual psychological symptoms and/or comorbid psychiatric disorders. Strikingly, the presence of a personality disorder significantly worsens treatment outcome of affective disorders [17]. Schema-focused therapy has not only emerged as an effective treatment for personality disorders, but also for patients suffering from chronic and/or treatment resistant mood and anxiety disorders [18, 19].

USUAL CARE

Pilot data of the Routine Outcome Monitoring for Geriatric Psychiatry & Science (ROM-GPS) project conducted in the Northern Netherlands (RGOc network) shows that 78.5% (153/195) referrals to outpatient mental health clinics for older persons consist of patients suffering from affective disorders, encompassing mood-, anxiety and somatic-symptom disorders. Ideally, these patients should be treated according to the multidisciplinary guidelines for axis I disorders in the Netherlands. Psychotherapy has a prominent place -often as a first-choice treatment- in the Dutch multidisciplinary guidelines. Nonetheless, less than a quarter of young adults receive psychotherapy for depression [20] or personality disorders [21]. The situation is even worse in old age.

Compared to younger adults, older adults are less likely to be treated with psychotherapy and more likely to receive benzodiazepines as treatment [22]. Specific treatment for personality disorders is often not available and rarely offered in old age psychiatry services. So the majority of older patients with personality disorders receive pharmacotherapy with or without nurse-led supportive care for affective disorders, while psychotherapy is preferred [23]. A situation that needs to be improved.

RELEVANCE FOR PRACTICE

Remarkably, the Dutch multidisciplinary guidelines for personality disorders do not even have a paragraph on personality disorders in later life [24]. In Dutch specialized mental health care, 25 - 50% of all older patients suffer from a personality disorder [6, 12]. These patients are commonly offered treatment for symptoms of depression, anxiety or somatization, leaving underlying personality pathology untreated. This predisposes them for treatment resistance and relapse [12], unnecessarily resulting in long-term supportive care.
Furthermore, treatment of personality disorders substantially lessens medical consumption [1] and informal care [2], which is especially relevant in later life.

EXISTING EVIDENCE OF EFFECTIVENESS

Last year, our group has published a systematic review on the epidemiology and treatment of older adults suffering from personality disorders [16]. This systematic review has identified only two uncontrolled studies of SFT among older adults [5, 25]. Repeating the search strategy on February 4th, 2016, did not reveal any new studies.
Review studies on SFT for personality disorders in adults up to 60 years have concluded that SFT improves in quality of life above and beyond recovery from psychological symptoms [26] and cost-saving compared to usual care [4]. Although most studies focus on borderline personality disorder [3], effectiveness has also been reported for avoidant personality disorder [19], mixed group personality disorders [27], and chronic mood- and anxiety disorders [28]. SFT delivered in groups is supposed to speed up and amplify the treatment effects of individual SFT [29].
Randomized controlled trials of SFT in older patients are not available [16]. Nonetheless, in a Dutch, multicenter randomized controlled trial on the effectiveness of SFT for adults with borderline personality disorders (mean age 53 years, range 18 - 65 years), effectiveness of the intervention increased with age [30]. The two uncontrolled trials among older patients [5, 25], point in the same direction. Among 51 depressed inpatients SFT led to improvement of depressive symptoms, anxiety and five out of seven early maladaptive schemes (EMS) [25]. Among 31 Dutch older outpatients, SFT improved psychological distress with effect-sizes similar to those reported in younger patient [5]. Moreover, pre-treatment to mid-treatment changes in schema severity predicted symptom improvement from mid- to end-of-treatment [5]. This implies that EMS change as process variable mediates changes in psychological distress. Subsequent qualitative studies among participants of SFT stress the potential of non-verbal, experiential techniques in older patients. In our own pilot study in older adults, enrichment of SFT with psychomotor therapy was highly valued by patients themselves. In conclusion, the existing data on SFT for older adults suffering from personality disorders show promising results on both personality pathology as well as psychological distress and affective symptoms. A critical mark is that relevant studies were conducted in younger age groups and differ with respect to methodology, i.e. the type of personality disorder included (borderline versus mixed), the severity of the personality disorder (disorder or features only), personality disorders versus long-standing axis I psychiatric disorders, duration of treatment (long-term or protocolled short-term treatment) and finally delivering individually versus group format). Despite these differences, all studies have shown promising results. Therefore, one may expect also good results in older adults suffering from personality disorders, albeit it is too soon to draw firm conclusions.

INNOVATIVE CHARACTER

This proposal replicates uncontrolled findings in a RCT comparing SFT with usual care for older patients. Based on clinical experience and multiple pilot studies, we have developed a format for delivering SFT in groups consisting of patients with mixed personality disorders enriched with experiential techniques facilitating age-related barriers.

## 2. OBJECTIVES

Aim of the present study is to better identify and treat cluster B and C personality disorders among older patients referred to specialized mental health care (geriatric psychiatry). We focus specifically on cluster B and C personality disorders for two reasons: 1) Cluster B and C disorders are most prevalent in later life and 2) evidence for SFT is limited to these subgroups, while cluster A personality disorders are supposed to need other kind of treatment.

The research question studied is: What is the (cost-)effectiveness of group schema-focused therapy (gSFT+PMT) compared to treatment as usual (TAU) in specialized mental health care (geriatric psychiatry) for adults aged 60 years and over who suffer from a cluster B or C personality disorder, or meet the general diagnostic criteria for a personality disorder?

We hypothesize that gSFT+PMT enriched with psychomotor therapy delivered to older patients (aged 60 years or over) suffering from a cluster B or C personality disorder is superior to TAU with respect to psychological distress and quality of life as well as cost-effective from a health care and societal perspective during a one- year follow-up. Since affective disorders, including depressive-, anxiety- and somatoform disorders are highly interwoven and often comorbid with personality disorder, especially in geriatric patients, we expect better outcome with respect to both these affective disorders as well as the personality disorder itself. For these reasons, we have chosen for a general outcome measure of psychological distress.

## 3. STUDY DESIGN

Multi-centre randomized trial with two parallel treatment groups: 1) group Schema-Focused Therapy enriched with Psychomotor Therapy (gSFT+PMT), and 2) treatment as usual (TAU) in specialized mental health care for older adults.

Primary outcomes are: 1) psychological distress (on which power calculations were based), 2) health related quality of life, and 3) medical consumption and costs. These are assessed at baseline (start of treatment for experimental group), 6 months (end of treatment for experimental group) and 12 and 18 months.

A total of 140 older adults (= 60 years) suffering from a cluster B or C personality disorder or meeting the general criteria for a personality disorder will be recruited from the participating mental health centres.

Additional qualitative research will be conducted in the experimental arm of the study, in order to examine how the patients and therapists evaluate the group Schema-Focused Therapy in general and the contribution of the Psychomotor Therapy in particular. This research will consist of interviews with patients who give additional informed consent for such interviews, and focus groups with the therapists who provided the therapy. This additional qualitative research is described in section 8.5.

## 4. STUDY POPULATION

### 4.1 Population (base)

Older adults (60 years or older) treated by the participating specialized mental health care centres for personality pathology, affective disorders encompassing mood-, anxiety and somatic-symptom disorders, adjustment disorders or psychosocial adversity, will be screened for eligibility for the study. If the treatment provider suspects a personality disorder, the patient will be informed about the study (both orally and in writing) by the treatment provider and will be asked to give written informed consent for the study. Patients will be given at least one week to consider participation.
The eligibility for the study will be formally evaluated by a researcher (psychologist) for all patients who provided written informed consent. This evaluation includes the Structured Clinical Interview for DSM-IV axis II personality disorders (SCID-II) [31], MINI International Neuropsychiatric Interview – Plus version (MINI-Plus) [32, 33] and Montreal Cognitive Assessment (MoCa) [34]. As some of these instruments may be included in regular care procedures, the researcher (psychologist) may take recent data on these instruments from the medical files. In other cases, the researcher (psychologist) will administer these interviews for the evaluation of study eligibility. Only for patients who meet the criteria for study participation, will information from the instruments included in the eligibility evaluation procedure be passed on to the research database.

### 4.2 Inclusion criteria

- Age: 60 years or older.
- Cluster B or C personality disorder confirmed by the SCID-II [31]. Since the criterion threshold for diagnosing a personality disorder is too strict for older patients [35, 36], we will also include older patients meeting the general diagnostic criteria for a personality disorder falling short one content criterion for a specific cluster B or C personality disorder. Older patients generally endorse fewer specific personality disorder criteria than younger age groups (29% of the criteria contain measurement bias in older age groups), while the latent variable structure for each personality disorders suggest a similar severity level of personality pathology [31].
- Mentally able to adhere to the group schema-focused treatment schedule and to fill out the schema (mode) questionnaires.
- Informed consent after having received oral and written information.

### 4.3 Exclusion criteria

- Severe mental illness, including current bipolar disorder, psychosis, or substance abuse disorder needing clinical detoxification.
- An established neurodegenerative disorder or cognitive impairment defined as a MoCA sum score below 24 points [34].
- Prior schema-focused therapy, received in the previous year or during the present episode of illness.
- Immediate suicide risk interfering with adequate treatment delivery.

Physical restraints or physical frailty is no exclusion criterion, as even within a group format, the psychomotor therapy will be individually adapted. So even the frailest elderly are able to participate.

### 4.4 Sample size calculation

The only RCT comparing group SFT with TAU (younger adults with borderline personality disorder), found a between group Cohen's d effect size (ES) of 2.0 based on the BSI-53 [37]. In our power analysis we tuned down this ES to 0.5 (medium effect) for two reasons. First, the

ES of 2.0 was partly due to a none-effect of TAU [37], while meta-analysis in geriatric psychiatry shows an average pre-post ES of 0.4 for TAU [38]. Second, an open study on group SFT reported a pre-post Cohen's d ES of 0.8 among adults with mixed cluster B and C personality disorders [5]. Applying a 2-sided alpha of 0.05 and a power of 80%, this requires 63 patients per arm. Although we have not to compensate for dropout, as we will conduct intention-to-treat analyses as per CONSORT, we aim to include 140 patients in order to compensate for 10% early dropouts (between giving Informed Consent and starting the group therapy).

## 5. TREATMENT OF SUBJECTS

Schema therapy has been developed as an individual psychotherapy for the treatment of borderline personality disorder [39], and recently been elaborated for the treatment of other complex psychiatric disorders [40]. Schema therapy is an effective treatment for adults suffering from either personality disorders or chronic mood and anxiety disorders [18, 19]. Even short-term group schema-focused therapy [41] is associated with improvements in affective symptoms as well as personality pathology, both in adults with personality disorder features as well as with long-standing mood disorders [28] and adolescents with personality disorder features [42].

Group Schema Focused Therapy enriched with psychomotor therapy (gSFT+PMT) will be delivered as an eighteen weekly and two booster sessions program (at 22 and 26 weeks), consisting of 1.5h group SFT and 1h psychomotor therapy (PMT). Group-SFT is particularly effective for relapsing mood, chronic adjustment and anxiety disorders which are intermingled with comorbid personality disorders or features. During gSFT, we particularly focus on the cognitive behavioural techniques of schema therapy. Patients will be educated about the schema model, their most prominent early maladaptive schemes (EMS) and modes, and subsequently asked to respond to situations that triggered their EMS in a more adaptive manner. Understanding the potential origin of feelings and physical sensations is an important intermediate therapeutic stage of SFT.
The group will be encouraged to explore EMS triggering as it occurs naturally in the group setting and to discuss it openly. The protocolled gSFT can be criticized for its relatively short duration and emphasize on cognitive and behavioural techniques. In later life, however, a shorter duration and emphasize on behavioural techniques probably increase the feasibility. Moreover, to overcome the limitations of verbal therapy only, we have added PMT. During PMT, the psychomotor therapist sets up physical exercises to facilitate the experience of patients' schemas and modi. Exercises have to be performed individually as well as in the group. The psychomotor therapist observes physical appearance, posture, attitude, and emotions as well as interaction between group members and taking up positions in the group. Observations during PMT will be further analysed within the verbal sessions. Experiential techniques are considered to be more powerful at changing early maladaptive schemes [43]. Participants of the uncontrolled study [5], pointed out the potential surplus of extending the verbal therapy with experiential techniques, during their post-treatment focus group interviews. For this reason, we extended the gSFT with PMT. Evaluation of our two pilot groups indeed revealed that PMT was deemed extremely valuable by the participants; even by a patient bound to a wheelchair.
Treatment as usual (TAU) will be unrestricted and involve whatever the multidisciplinary team thinks is best for the patient consistent with the Dutch guidelines. Treatment most likely will include psychotropic drug use, supportive-care delivered by specialized mental health nurses or social workers and even disorder specific or protocolled cognitive-behavioural therapy for mood- or anxiety disorders delivered by psychologists. As pointed out before (see Introduction and Rationale) TAU is generally less optimal than current guidelines may suggest.

## 6. INVESTIGATIONAL PRODUCT

Not applicable.

## 7. NON-INVESTIGATIONAL PRODUCT

Not applicable.

## 8. METHODS

### 8.1 Study parameters/endpoints

All study outcome measures described in the paragraphs 8.1.1 end 8.1.2 are assessed in both study groups at baseline (start of treatment for experimental group), 6 months (end of treatment for experimental group) and 12 and 18 months. In order to examine mediation of the intervention effect, the study parameters described in paragraph 8.1.3 will additionally be assessed in the experimental group at baseline, 3, 6, and 12 months. Finally, the study parameters listed in paragraph 8.1.4 will be assessed at baseline in both study groups, and will be used to describe the study sample, test baseline differences between the study groups, and control for confounding in the outcome analyses. Figure 1 gives an overview of the study parameters assessed in both study groups, and figure 2 of the additional parameters assessed in the experimental group only.

#### 8.1.1 Main study parameter/endpoint

Primary outcomes are: 1) psychological distress (assessed with the *Brief Symptom Inventory-53 item version;* BSI-53), 2) health related quality of life (*EuroQoL;* EQ-5D-5L), and 3) medical consumption and costs.

The BSI-53 is a shorter version of the Symptom Checklist-90 (SCL-90), and consists of 53items [44, 45]. The BSI-53 sum score reflects the overall level of psychopathology over the past week. The reliability of the Dutch BSI subscales is good and the convergent and divergent validity has been found to be satisfactory [45]. Moreover, the BSI is validated for older adults and preferred in this age group because it is less lengthy than the SCL-90 [46].

Health related quality of life will be evaluated using the EQ-5D-5L, as prescribed in the new Dutch guidelines for economic evaluation [47]. The EQ-5D-5L is a self-report questionnaire consisting of five health-state dimensions on which respondents indicate their perception of their health-related well-being [see www.euroqol.org].The Dutch EQ-5D-5L tariff will be used to calculate Quality-Adjusted Life-Years (QALYs) [47].

Medical consumption and other cost data will be collected by means of structured interviews by independent research assistants trained for this task, as previously done in this particular patient group by our group [33]. Formal registries such as hospital information systems or insurer's databases are considered to be incomplete, since a considerable amount of resource use is situated outside (mental) healthcare institutions [2]. Therefore, patient-reported prospective cost diaries [48], or retrospective cost interviews [49], are the preferred instruments covering all relevant events. We chose a 3-month recall interview [50], since a prospective cost diary is expected to lead to more missing items, given the patient characteristics.
The independent research assistants conducting the telephone interviews will be blind about the treatment condition of the interviewee and will not be involved in the intervention, TAU or study analyses in any way. Furthermore, they will be extensively trained in how to conduct the interviews, and during training their scoring of interviews will be systematically evaluated, compared and discussed, in order to generate consensus. Clear rules for scoring will be developed. After training, telephone interview assessments will – if the interviewee agrees - be recorded and systematically sampled and discussed with the interviewer trainer.

**Figure 1: Assessment of outcomes and characteristics**

| | | Duration (min.) | Time of assessment | | | | |
|---|---|---|---|---|---|---|---|
| | | | Screening | Baseline | 6 months | 12 months | 18 months |
| ***Primary outcomes*** | | | | | | | |
| Psychological distress: BSI-53 | | 15 | | X | X | X | X |
| Health-related quality of life: EQ-5D-5L | | 5 | | X | X | X | X |
| Medical consumption & costs: telephone interview | | 30 | | (X) | (X) | (X) | (X) |
| ***Secondary outcomes*** | | | | | | | |
| Life satisfaction: Cantril's Ladder | | 2 | | X | X | X | X |
| Mental wellbeing: WEMWBS | | 5 | | X | X | X | X |
| Personality functioning: SIPP-SF | | 15 | | X | X | X | X |
| Interoceptive body awareness: MAIA | | 10 | | X | X | X | X |
| Psychotropic drug use & treatment received[1] | | - | | | | | |
| Mood variability: Mood-Zoom | | 21 X 2 | | (X) | (X) | (X) | (X) |
| ***Characteristics*** | | | | | | | |
| Personality disorders: SCID-II Cluster B & C | | 60 | X | | | | |
| Mental disorders: MINI-Plus | | 20 | X | | | | |
| Cognitive screening: MoCA | | 10 | X | | | | |
| Psychiatric treatment history: telephone interview | | 10 | | (X) | | | |
| Socio-demographics: telephone interview | | 10 | | (X) | | | |
| Chronic illnesses: LASA questionnaire | | 10 | | X | | | |
| Early life-events: NEMESIS questionnaire | | 10 | | X | | | |
| Alcohol use: AUDIT | | 5 | | X | | | |
| Current smoking: NEMESIS questions | | 2 | | X | | | |
| Physical activity: NEMESIS question | | 2 | | X | | | |
| Personality traits: PID-5-SF | | 20 | | X | | | |
| ***Duration*** | ***Screening & Questionnaire*** | | 90 | 101 | 52 | 52 | 52 |
| | ***Mood-Zoom*** | | | 42 | 42 | 42 | 42 |
| | ***Telephone interview*** | | | 50 | 30 | 30 | 30 |

1 Part of telephone interview on medical consumption

**Figure 2: Assessment of mediators in experimental group**

| | Duration (min.) | Time of assessment | | | | | |
|---|---|---|---|---|---|---|---|
| | | Baseline | Weekly during treatment | 3 months | 6 months | 12 months | 18 months |
| Early maladaptive schemes: YSQ L-2 | 30 | X | | X | X | X | |
| Schema modes: SMI | 20 | X | | X | X | X | |
| Severity scores | 2 | | X | | | | |
| ***Duration*** | | 50 | 40 | 50 | 50 | 50 | |

### *8.1.2 Secondary study parameters/endpoints*

Secondary outcome measures are: 1) life satisfaction, 2) mental wellbeing, 3) personality functioning, 4) interoceptive body awareness, 5) psychotropic drug use and treatment received, and 6) mood variability.

Life satisfaction is assessed with Cantril's ladder [51], which is a single question to rate one's current life situation on a scale ranging from 0 to 10, with 0 indicating 'the worst possible life for you' and 10 'the best possible life for you'. Life satisfaction is a conceptualization of subjective wellbeing which stresses the cognitive evaluation by a person of his or her life situation, in contrast for example to feelings such as feeling happy.

Mental wellbeing is assessed with the Warwick-Edinburgh Mental Well-being Scale (WEMWBS) [52]. This scale focusses on mental health in contrast to mental illness. Mental health and mental illness have been shown to related but distinct concepts [53], and reduction or absence of mental illness does not necessarily imply good mental health and wellbeing. The WEMWBS consists of 14 items covering positive affect, satisfying interpersonal relationships and positive functioning. The items inquire about frequency of positive feeling in the past two weeks, with 5 possible answers from 'none of the time' to 'all of the time'. A single total score is calculated, with higher scores indicating more mental wellbeing.

Impaired personality functioning and pathological personality traits constitute the two basic dimensions of the alternative dimensional model for personality disorders, included in the DSM5 beside the traditional categorical model. Changes in level of personality disorder severity may be more likely to be expressed by level of personality functioning than by the more descriptive level of personality style or traits [54, 55], and hence may be a more interesting outcome measure for therapy effect. In the present study, personality functioning is assessed with the Severity Indices of Personality Functioning – Short Form (SIPP-SF) [55]. This instrument covers both problems in self and interpersonal functioning, distinguished in the alternative personality disorders model. It assesses five core domains of (mal)adaptive personality functioning, namely: Identity Integration, Self-Control, Relational Functioning, Social Concordance and Responsibility. The 60-items of the questionnaire consists of propositions referring to the last three-months, which are answered on four-point Likert scales, ranging from fully agree to fully disagree. Higher scores imply more adaptive functioning. The SIPP-SF was specifically studied in an older, and was suggested to be a useful clinical tool to follow-up effects of therapy on levels of personality functioning [55].

Interoceptive body awareness is assessed with the Multidimensional Assessment of Interoceptive Awareness (MAIA) [56], which is a 32-item self-report measure divided over eight scales covering both the ability to notice bodily sensations and to regulate their influence on behaviour. The sensitivity of the MAIA to treatment change was recently shown in a study on the effect of a 3-months bodily focused contemplative training [57], which found improvements on five of the eight MAIA scales.

Psychotropic drug use and type and frequency of treatment received will be monitored with the aid of the structured interviews conducted to assess the medical consumption and costs, and will be cross-checked with the information in the medical record of the participant.

Mood variability is assessed with Mood Zoom, which is an experience sampling method for real-time mood assessment on a smartphone [58]. Participants are prompted by the phone to rate their current mood on a screen displaying six different moods which have to be scored on 7-point Likert scales. In the original study, participants were prompted once a day - at a pre-specified time convenient for each participant – over the study period of 3 to 12 months [58]. We will prompt participants three times a day, at variable time points, over a one week period

per measurement. Mood variability may be an interesting outcome for personality treatment, as reliable differences were found on Mood Zoom between patients with a borderline personality disorder and patients with a bipolar mood disorder, as well as between these patient groups and healthy controls [58].

### *8.1.3 Mediators*

The following parameters will be examined as mediators of the intervention effect, and will only be assessed in the experimental group. Mediators are: 1) Early Maladaptive Schemas (EMS) and 2) Schema Mode Inventory (SMI), which will be assessed at baseline, 3, 6 and 12 months, and 3) schemas and modes severity scores, which will be assessed during treatment on a weekly basis.

EMS are assessed with the Young Schema Questionnaire (YSQ L-2), which is the most commonly used EMS measure [59, 60]. The list consists of 205 items, which are phrased as a negative core belief and rated along a 6-point scale and measures 16 core beliefs [61]. The Dutch YSQ has good reliability and convergent and discriminant validity [62].

Schema modes are assessed with the SMI, which measures 16 modes [63,64]. These modes can be divided into 4 types of modes: healthy modes, parent modes, child modes and coping modes. This test consists of 118 items, which are rated along a 6-point scale. The Dutch SMI has excellent test-retest reliability and the convergent and divergent validity of the subscales are satisfactory [63].

The patients will score the severity scores of their schemas and modes on a weekly basis as part of the treatment. This takes two minutes each time. The first week patients rate the severity of their problematic schemas and modes. The subsequent 19 weeks the severity of their problematic schemas and modes will be compared to the previous week.

### *8.1.4 Control variables*

In both study groups, the following parameters will be assessed at baseline (as part of the screening procedure or regular baseline assessment), in order to describe the study sample, test for baseline differences between the study groups, and control for confounding in the outcome analyses: 1) personality disorders, 2) mental disorders, 3) cognitive functioning, 4) psychiatric treatment history, 5) socio-demographics, 6) chronic somatic illnesses, 7) early life events, 8) alcohol use, 9) current smoking, 10) physical activity, and 11) personality traits.

Personality disorders, according to the traditional categorical model, will be assessed with the Structured Clinical Interview for DSM-IV axis II personality disorders (SCID-II; 31), as part of the screening procedure (see paragraph 8.3). Cluster B or C personality disorders will be assessed, as well as the general diagnostic criteria for a personality disorder.

Mental disorders will also be assessed as part of the screening procedure, with the MINI International Neuropsychiatric Interview – Plus version (MINI-Plus) [32, 33], which is a structured diagnostic interview for DSM-IV and ICD-10 psychiatric disorders. The following section of the interview will be covering both lifetime and current diagnoses: Mood Disorders (Major Depressive Disorder, Dysthymic Disorder, Manic and Hypomanic Episodes, Bipolar Disorders type I and II), Anxiety Disorders (Generalized Anxiety Disorder, Panic Disorder, Agoraphobia, Social Phobia), Posttraumatic Stress Disorder, Obsessive Compulsive Disorder, Somatic Symptom Disorder, and Hypochondriasis.

The screening procedure will finally include screening for cognitive dysfunctioning with the Montreal Cognitive Assessment (MoCA) [34]. The MoCA assesses a broad range of cognitive domains.

The psychiatric history of the patient will be assessed by a brief structured interview taken form the ROMGPS-study [65] as part of the baseline telephone interview.

Socio-demographic characteristics of the participants will also be assessed as part of the baseline telephone interview, using a format taken from the ROMGPS-study [65]. Covered are, among other things, age, gender, education, religion, income, marital status and household composition.

Presence of chronic somatic illnesses is assessed by interview as part of baseline assessment, using a questionnaire derived from the LASA study [66].

Early traumatic life events are also assessed by interview at baseline with a questionnaire taken form the NEMESIS study [67]. Covered are, among other things, psychological, physical and sexual abuse.

Alcohol use is assessed with the Alcohol Use Disorder Identification Test (AUDIT) [68], which is a questionnaire inquiring about frequency and amount of alcohol use in the past year.

Smoking and amount smoked in the past four weeks are assessed by questions taken from the NEMESIS study [69].

Physical activity is assessed by a single question from the NEMESIS study on number of hours per week spent in physical exercise or sport lately, not counting passive pursuits such as chess or fishing [69].

Pathological personality traits, which – beside impaired personality functioning - constitutes the second dimension of the alternative dimensional model for personality disorders included in the DSM5, are assessed with the Personality Inventory for DSM5 - Short Form (PID-5-SF) [70]. The 100 items of the PID-5-SF cover the 25 pathological personality trait facets (4 items per facet) distinguished in the alternative dimensional personality model, and these facets are combined to obtain scores for the five higher-order domains distinguished. These facets and domains are related to traditional big five personality traits and to concepts from schema therapy [70]. Pathological personality traits and impaired personality functioning may be combined to obtain alternative DSM-5 model personality disorder diagnoses. The items of the PID-5-SF are rated on four-point Liker scales from 0 (very false or often false) to 3 (very true or often true).

### 8.2 Randomisation, blinding and treatment allocation

Randomisation will be stratified by study location and by meeting the diagnostic criteria of a particular personality disorder versus only meeting the general diagnostic criteria for personality disorders. Within study locations, blocks of 8 to 16 consecutive patients (depending on the speed of inclusion at that location, but always an even number of patients) will be randomised evenly over the study conditions. Randomisation will be performed centrally, by the principal investigator, who will be blind to patient characteristics.
After randomisation, neither the patient nor the therapists will be kept blind to the allocation of the patient to a particular study arm.

### 8.3 Study procedures

The study will be conducted among older adults treated by specialized mental health care centres for personality pathology, affective disorders encompassing mood-, anxiety and somatic-symptom disorders, adjustment disorders or psychosocial adversity. If their mental health provider suspects a personality disorder, patients will be informed - orally and in writing - about the study by their treatment provider and will be asked to give written informed consent for the study. Patients will be given at least one week to consider participation.

Before randomisation, an appointment will be made with a local researcher (psychologist) to check the in- and exclusion criteria. This evaluation includes the Structured Clinical Interview for DSM-IV axis II personality disorders (SCID-II) [31], MINI International Neuropsychiatric Interview – Plus version (MINI-Plus) [32, 33] and Montreal Cognitive Assessment (MoCa) [34]. As some of these instruments may be included in regular care procedures, the researcher (psychologist) may take recent data on these instruments from the medical files. In other cases, the researcher (psychologist) will administer these interviews for the evaluation of study eligibility. Only for patients who meet the criteria for study participation, will information from the instruments included in the eligibility evaluation procedure be passed on to the research database.

The therapy sessions in the experimental group will be audio recorded to assess the quality of the treatment provided. The audio files will be stored coded and encrypted. Only the researcher and the assessor will be able to open the files. The assessment is made by a therapist who takes part in the study, but from an other than the assessed site. The assessor will make an inventory of the extent to which the interventions have been carried out in accordance with the protocol.
Study participants will be reimbursed for travel or other costs specifically made to participate in the study. In addition, participants will receive 10 euro per completed study assessment, including the screening appointment and four outcome assessments (i.e. 50 euros in total).

Research data will be collected and stored digitally in the professional data-management service RoQua (https://roqua.nl/) of the Rob Giel Research center of the University Medical Center Groningen. Data will be stored anonymously, under a participant study number. All participating mental health care services will make a key to link the personal details of their participating patients to the study numbers of these patients. Only the treatment providers of these patients and the local clinician responsible for that study location will have access to the key. The key will be securely stored by the concerning mental health care service, together with the written informed consent documents. An anonymised digital copy of the written informed consent of all participating subjects, carrying their participant study number, will be sent to the coordinating investigator of the study and stored centrally. Handling of personal data will be in accordance with the Dutch Personal Data protection Act.

### 8.4 Withdrawal of individual subjects

Participants are free to leave the study at any time for any reason if they wish to do so without any consequences. These participants will not be replaced in the study.

### 8.5 Additional qualitative research

In order to examine how the patients and therapists evaluate the study therapy, and in particular the contribution of the Psychomotor Therapy, additional qualitative research will be conducted in the experimental arm of the study. This will consist of the below elements listed in paragraphs 8.5.1 to 8.5.2.

#### 8.5.1 Patient interviews

Patients in the experimental arm of the study will be asked additional informed consent for an interview about their experiences with the therapy. Open questions will be asked about these experiences (see Appendix 1: Patient Interview Questions) and the interview will last about 60 minutes. A researcher not involved in the therapy will conduct the interview, and the interview will be audio recorded and fully transcribed for later analysis. These transcripts will be analysed using a dedicated computer program for qualitative data analysis.
Patients will be informed orally and in writing about the additional interview (see Appendix 2: Patient Information for Additional Interview) in session 19, at week 22, of the therapy and will be asked to give written informed consent (see Appendix 3: Informed Consent Form for Additional Interview) in session 20, at week 26, if they are willing to participate.

#### 8.5.2 Focus groups of therapists

When all therapy groups at all study locations have ended, the therapists will be invited to participate in a focus group. Separate focus groups will be organized for schema-focused therapists and psychomotor therapists, to promote homogeneity of the groups. Only therapists who provided a substantial part of the treatment (10 sessions or more) will be invited. The focus groups will be conducted by two experienced panel chairmen who were involved in the development of the experimental therapy and are therefore well informed about its content. The focus groups will again be audio recorded and transcribed, and these transcripts will be analysed using a dedicated computer program for qualitative data analysis.

## 9. SAFETY REPORTING

### 9.1 Temporary halt for reasons of subject safety

In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise subject health or safety. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

### 9.2 AEs and SAEs

#### 9.2.1 Adverse events (AEs)

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the experimental intervention. All adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded.

#### 9.2.2 Serious adverse events (SAEs)

A serious adverse event is any untoward medical occurrence or effect that -
results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing inpatients' hospitalisation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect; or
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event.

The investigator will report all SAEs to the sponsor without undue delay after obtaining knowledge of the events.

The sponsor will report the SAEs through the web portal *ToetsingOnline* to the accredited METC that approved the protocol, within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete the initial preliminary report. All other SAEs will be reported within a period of maximum 15 days after the sponsor has first knowledge of the serious adverse events.

### 9.3 Follow-up of adverse events

All AEs will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist.
SAEs are reported till end of study within the Netherlands, as defined in the protocol

## 10. STATISTICAL ANALYSIS

Analyses will be conducted in agreement with the intention-to-treat principle as per the CONSORT statement. Differences in the scores between the intervention and control group on the various outcome measures (BSI-53, EQ-5D-5L, secondary outcomes) will be analysed using linear mixed-models accounting for missing data and relevant confounders.

COST-EFFECTIVENESS ANALYSIS (CEA)
General considerations: The cost-effectiveness analysis will be performed alongside the proposed clinical trial to assess the cost-effectiveness of gSFT+PMT versus TAU. The costeffectiveness analysis will result in two separate incremental cost-effectiveness ratios (ICERs) for gSFT+PMT as compared to TAU, i.e. incremental costs per additional point improvement on the BSI, and incremental costs per Quality Adjusted Life Year (QALY) gained. The analysis will be performed taking a societal perspective and with a time horizon of 1 year. Because the time horizon does not exceed 12 months, discounting for costs and effects is not necessary [47]. Univariate sensitivity analyses will investigate the impact of individual assumptions and parameters (e.g. costs of SFT and other elements). To quantify the combined effect of all uncertainty, bootstrap resampling will be performed. Results will be presented as tornado diagrams and cost-effectiveness acceptability curves, the latter representing the probability that gSFT+PMT is cost-effective given a certain value of 'willingness to pay' for a QALY (or one point improvement on the BSI).
In an additional analysis, the costs of identification of persons with an indication for this therapy will be added to the intervention costs. These will be estimated based on actual time costs of personnel involved.

Cost analysis: Included costs will be those of schema therapy, psychomotor therapy, other forms of psychotherapy, hospital admissions, medication, outpatient visits, GP visits, home care, out of pocket costs (for instance for over-the-counter medication) and informal care. Data are collected by means of structured interviews, administered by research assistants trained for this task. The interviews will take place at baseline, end of treatment, and at 6- and 12-month follow-up. Unit prices will be determined according to Dutch guidelines [47].

Patient outcome analysis: The cost-effectiveness analysis will include 2 outcome measures: QALYs and BSI. These outcomes will be measured and analysed as described in the outcome parameters section. According to the latest recommendations on economic evaluation in health care [47], we will use the 5 level version of the EQ-5D, and the accompanying Dutch value set (in press, see euroqol.org) to convert EQ-5D-5L scores into health state utilities.

BUDGET IMPACT ANALYSIS (BIA)
Based on the results of the cost-effectiveness analysis and using available epidemiological data, a budget impact analysis will be performed to inform decision makers on the financial consequences of the adoption and diffusion of gSTF+PMT in the Dutch health care system. The BIA will be performed according to the most recent principles of the ISPOR task force [71] and performed according to the specific chapter in the new guidelines for economic evaluation [47]. The trial results will be extrapolated to a time horizon of 5 years, and for the entire Dutch population concerned. Ageing of the population and therefore increasing size of the target population, namely older persons presenting with mental health problems in specialized mental health care) will be taken into account. Sensitivity analysis will explore several scenarios, regarding speed of uptake of the therapy in clinical practice and willingness to participate in the target population
The BIA will be conducted from various perspectives, including a societal perspective, a healthcare perspective (limited to "netto-BKZ-uitgaven"), and a third party payer/healthcare insurers perspective. The source of the unit prices will vary with the perspective, as described by the ZonMw guidance on BIA. Anticipated savings in costs of health care and informal care

will be based on the trial data. Extrapolation to a 5-year time horizon will reflect the uncertainty this inevitably brings by way of scenario analysis.

## 11. ETHICAL CONSIDERATIONS

### 11.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects Act (WMO). In accordance with this Act, the study will be presented to the Medical research ethics committee (METC) of the University Medical Center Groningen for approval.

### 11.2 Recruitment and consent

The study will be conducted among older adults treated by specialized mental health care centres for personality pathology, affective disorders encompassing mood-, anxiety and somatic-symptom disorders, adjustment disorders or psychosocial adversity. If their mental health provider suspects a personality disorder, patients will be informed - orally and in writing - about the study by their treatment provider. Patients interested to participate get an appointment with a local researcher (psychologist). This appointment serves two purposes: 1) a check of the in- and exclusion criteria of the study, which will include the Structured Clinical Interview for DSM-IV axis II personality disorders (SCID-II) [31], and 2) answering any remaining questions the patient has about the study. Patients eligible for the study, will be given another two weeks to consider participation. Patients willing to participate in the study, will be asked to give written informed consent. Only for patients who gave written informed consent and were included in the study, the data from the screening appointment, will be passed on – anonymously – for inclusion in de study database.

### 11.3 Compensation for injury

All participating mental health care services have a liability insurance, which is in accordance with article 7 of the WMO.

The sponsor applies to the METC for exemption from the compulsory insurance for study participants.

### 11.4 Incentives

Study participants will be reimbursed for travel or other costs specifically made to participate in the study and agreed upon with study management. In addition, participants will receive 10 euro per completed study assessment, including the screening appointment and four outcome assessments (i.e. 50 euros in total).

### 11.5 Burden, risks and benefits associated with study participation

Before patients can participate in the study, eligibility is checked in a 90 minutes diagnostic interview with a local researcher (psychologist).
gSFT+PMT treatment consists of 20 three-hour sessions (2 hours psychotherapy and 1 hour PMT) over a 6-month period. Outcome assessment in both study groups consist of questionnaires (also taking approximately 1 hour to complete) and telephone interviews (one week after the questionnaires, and taking approximately 30 minutes) are administered at the start and end of treatment, and 6 and 12 months post-treatment. These latter questionnaires assess psychological distress and quality of life, and the telephone interviews inquire about treatment related contacts and activities for the cost-effectiveness analyses.
gSFT is a specific form of psychotherapy, aimed at reducing current and future psychological distress, and PMT is added to enhance treatment effect by experiential – bodily - techniques. PMT will be adapted to the physical abilities of individual participants. We do not expect any risk associated with participation in the study, and therefore applied for exemption from the compulsory insurance for study participants.

## 12. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

### 12.1 Handling and storage of data and documents

Research data will be collected and stored digitally in the professional data-management service RoQua (https://roqua.nl/) of the Rob Giel Research center of the University Medical Center Groningen. Data will be stored anonymously, under a participant study number. All participating mental health care services will make a key to link the personal details of their participating patients to the study numbers of these patients. Only the treatment providers of these patients and the local clinician responsible for that study location will have access to the key. The key will be securely stored by the concerning mental health care service, together with the written informed consent documents. An anonymised digital copy of the written informed consent of all participating subjects, carrying their participant study number, will be sent to the coordinating investigator of the study and stored centrally. Handling of personal data will be in accordance with the Dutch Personal Data Protection Act (Wbp).

### 12.2 Amendments

Amendments are changes made to the research after a favourable opinion by the accredited METC has been given. All amendments will be notified to the METC that gave a favourable opinion.

### 12.3 Annual progress report

The investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments

### 12.4 Temporary halt and (prematurely) end of study report

The investigator will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's last visit.

The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action.

In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature termination.

Within one year after the end of the study, the investigator will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

### 12.5 Public disclosure and publication policy

After the main outcome and cost-effectiveness analysis have been published, all data will be freely available for other groups.

## 13. STRUCTURED RISK ANALYSIS

Not applicable.

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