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1 **Core outcome domains for clinical trials on somatic symptom disorder, bodily**
2 **distress disorder and functional syndromes: Euronet-SOMA recommendations**

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12
13 On behalf of the Euronet-SOMA Group (all Members of the Euronet-SOMA Group
14 see end of manuscript)

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1 **Abstract**

2 Objective: The harmonization of core outcome domains in clinical trials facilitates
3 comparison and pooling of data, and simplifies the preparation and review of
4 research projects, and comparison of risks and benefits of treatments. Therefore we
5 provide recommendations for the core outcome domains that should be considered in
6 clinical trials on the efficacy and effectiveness of interventions for somatic symptom
7 disorder, bodily distress disorder, and functional syndromes.

8 Methods: The **European Network on somatic** symptom disorders group (EURONET-
9 Soma) of more than 20 experts in the field met twice in Hamburg to discuss issues of
10 assessment and intervention research in somatic symptom disorder, bodily distress
11 disorder, and functional syndromes. The consensus meetings identified core
12 outcome domains that should be considered in clinical trials evaluating treatments for
13 somatic symptom disorder and associated functional syndromes.

14 Results : The following core domains should be considered when defining
15 ascertainment methods in clinical trials: (1) classification of somatic symptom
16 disorder/bodily distress disorder, associated functional syndromes, and comorbid
17 mental disorders (using structured clinical interviews), duration of symptoms, medical
18 morbidity, and prior treatments (2) location, intensity, and interference of somatic
19 symptoms, (3) associated psychobehavioral features and biological markers, (4)
20 illness consequences (quality of life, disability, health care utilization, health care
21 costs), (5) global improvement, treatment satisfaction, and (6) unwanted negative
22 effects.

23 Conclusions: The proposed criteria are intended to improve synergies of clinical trials
24 and to facilitate decision making when comparing different treatment approaches.
25 These recommendations should not result in inflexible guidelines, but increase
26 consistency across investigations in this field.

27 Words: 250

28 Key Words: somatization, somatoform, bodily distress, functional somatic syndromes,
29 fibromyalgia, irritable bowel syndrome.

30

31 **Abbreviations:**

32 BDD Bodily Distress Disorder

33 BDS Bodily Distress Syndrome Checklist

34 CIDI Composite International Diagnostic Interview

35 DSM Diagnostic and Statistical Manual for Mental Disorders

36 EMA Ecological Momentary Assessment

- 1 EuroQoL European Quality of Life Group
- 2 HrQoL health related quality of life
- 3
- 4 IBS: Irritable Bowel Syndrome
- 5
- 6 IDCL International Diagnostic Check List
- 7
- 8 NAS Numeric Analogue Scale
- 9
- 10 IMMPACT Initiative on Methods, Measurement, and Pain Assessment in Clinical
- 11 Trials
- 12
- 13 PHQ Patient Health Questionnaire
- 14
- 15 QALY: Quality adjusted Life years
- 16 SCAN [Schedules for Clinical Assessment in Neuropsychiatry](#)
- 17
- 18 SCID Structured Clinical Interview for DSM-IV/DSM-5 disorders
- 19 SCL Symptom Check List
- 20 SOMS-7 Screening for Somatoform Symptoms, last 7 days
- 21 SSD Somatic Symptom Disorder
- 22 SSD-12 Somatic Symptom Disorder Scale
- 23

1 Ascertainment methods, addressed domains and outcome reports in intervention
2 trials on bodily distress disorder (BDD), somatic symptom disorder
3 (SSD)/somatoform disorders and functional syndromes vary substantially. This has
4 impeded evaluations of the efficacy and effectiveness of suggested treatment
5 approaches. Current interventions on somatic symptom and associated disorders
6 reveal moderate effect sizes for psychological interventions (1, 2), but also for
7 pharmacological interventions like tricyclic antidepressants (3), which can be a result
8 of moderately effective treatments, but also of flaws of assessment strategies.
9 Agglomeration of results of intervention trials (e.g., in meta-analyses) is blurred by
10 assessment tools that are not sufficiently evaluated about their sensitivity to assess
11 change, by a large variability of assessment tools, by a lack of including relevant core
12 domains for comparability, and other factors (2, 4).

13 The development of a core set of outcome domains and quality criteria has been
14 shown to improve comparison and pooling of data of intervention trials, while leaving
15 investigators free to extend the core set with other instruments of their choice. In pain
16 research, the introduction of the so-called IMMPACT criteria (5-7) led to a substantial
17 improvement of the comparability and potential for accumulation of clinical trials. The
18 introduction of quality criteria for intervention studies, such as the CONSORT criteria
19 or the quality criteria of Cochrane analyses substantially improved the average
20 quality of published clinical trials, and reduced the risk of publication of false-positive
21 results. In the field of BDD, SSD and functional syndromes, the development of a
22 recommended core set of outcome domains is still lacking, although assessment
23 recommendations for single functional somatic syndromes have been published (e.g.,
24 for fibromyalgia (8)). Therefore the European Network on somatic symptom disorders
25 (Euronet-SOMA) aimed to find a consensus for core domains to be assessed in the
26 evaluation of interventions in the general field of somatic symptoms and associated
27 disorders.

28

29 **Methods**

30 Two meetings of more than 20 European experts took place in Hamburg (Germany),
31 and were organized by Bernd Löwe and his team in 2016. Several subgroups
32 addressed different topics of research in somatic symptom disorder. Members of this
33 subgroup were experienced in the conduct of clinical trials, and aggregation of
34 different trial results. During the first session, we defined the clinical conditions of
35 interest. After discussing different options, a consensus was reached to address
36 somatic symptom disorder, bodily distress disorder, and associated functional
37 syndromes. Reasons for this decision were the fact that these syndromes pretend to
38 describe specific clinical conditions, although they are highly overlapping. The
39 concept of somatic symptom disorder is defined in DSM-5; bodily distress disorder
40 was originally defined by the Danish group of Per Fink, and it was shown that this
41 definition covers most forms of somatization and functional somatic syndromes (9,
42 10). For several functional somatic syndromes, current definitions and classification

1 criteria exist (e.g., ROME-III criteria for irritable bowel syndrome (11); fibromyalgia
2 criteria (12)). To develop a consensus for assessment domains, we analyzed the
3 IMMPACT criteria, results of Cochrane and other meta-analyses in the field of SSD
4 or BDD, recommendations for outcome measurement in specific syndromes, such as
5 irritable bowel syndrome and fibromyalgia, general recommendations about the
6 assessment of change in psychosomatic, psychiatric and psychological research, as
7 well as specific results on the quality of assessing change of various assessment
8 tools (e.g.,(13)).All participants of this specific working group were invited to name
9 existing recommendations for outcome measurements of the corresponding groups.
10 These nominations were collected and grouped to domains. The resulting proposal of
11 domains was presented during the second meeting, and further discussed. These
12 discussions led to further adaptations. After the second meeting, the resulting
13 proposal was circulated twice to find a general agreement. Afterwards, this
14 agreement was further circulated to the overall group, and finally harmonized. The
15 final proposal was accepted by all group members. Of note, while recommendations
16 for the assessment of trait variables and current state variables of somatic symptoms
17 in particular for epidemiological research have been published elsewhere (4), more
18 specific challenges of selecting tools for the assessment of change are addressed in
19 this paper.

20

21 **Results**

22 All clinical trials of this field should consider reporting in agreement with the general
23 quality criteria for clinical trials, such as the CONSORT criteria, with their specific
24 recommendations. In particular, the description of interventions, the selection of
25 participants, inclusion and exclusion criteria, the definition of concurrent treatments,
26 the assessment of treatments during follow-up periods, randomization and blinding
27 procedures, statistical management of missing values and drop-outs, adherence to
28 treatment guidelines etc. are crucial pre-requisites to evaluate scientific rigor and
29 clinical implications of these trials.

30

31 The CONSORT criteria suggest defining specific primary outcome variables. In
32 addition to identifying the primary outcome of a trial, present recommendations add a
33 broad variety of assessment domains relevant to SSRD/BDD, to facilitate the
34 comparison and agglomeration of different clinical intervention effects. To accomplish
35 this goal, we had to consider the broad variety of diagnoses, concepts, and
36 approaches of this clinical group. We recommend the following domains to be
37 addressed in clinical trials (for an overview see **Table 1**):

38 **(1) Classification of disorder, comorbid mental and physical conditions**

39 In a field where differing terminologies and classifications have all too often
40 hampered transparency and comparability, a clear definition of the disorder in
41 question and its comorbid aspects is of prime importance. While DSM-5 and/or

1 ICD-11 diagnoses should be adequately addressed, broader and/or additional
2 ways of classification can be useful considering the limited duration of validity of
3 current classification systems. For the purpose of classification, structured clinical
4 interviews are the current gold standard of assessments in particular for mental
5 disorders. Various evaluated methods exist with specific strength and limitations,
6 such as the structured clinical interview for DSM classification SCID (14), the
7 Composite International Diagnostic Interview (CIDI) (15), the Schedules for
8 Clinical Assessment in Neuropsychiatry (SCAN) (16), among other interviews. A
9 semi-structured approach such as the International Diagnostic Check Lists (IDCL)
10 (17) can offer an economic alternative. In any case, a clear description of the
11 selected sample and consideration of inclusion and exclusion criteria requires the
12 use of one of these types of instruments. While a clear description of inclusion
13 criteria is a prerequisite of high quality trials, investigators should be aware of the
14 tremendous overlap of symptom profiles and other characteristics of functional
15 somatic syndromes (10, 18). Therefore it is crucial to use broad-spectrum
16 assessments for multiple symptoms or multi-symptomatic syndromes in addition
17 to focusing on any particular symptom profile. Symptom onset, symptom duration,
18 and treatment pre-experiences should be additionally investigated. A re-
19 assessment at end-of-treatment and/or follow-up is strongly recommended. In
20 combination with potential expert disability ratings (see below), these ratings
21 should be done by raters blinded to the treatment selected for this patient - this
22 could lead to expert ratings of remission and response rates.

23 The diagnosis of Somatic Symptom Disorder according to DSM-5 as well as the
24 current ICD-11 proposal of Bodily Distress Disorder do not exclude the existence
25 of comorbid medical conditions. SSD can be used as a diagnosis even if *all*
26 somatic symptoms are explained on the background of a medical disease, such
27 as cancer, because for the SSD diagnosis the burden of the symptoms is more
28 relevant than the postulated etiology. Several functional somatic syndromes
29 require that their core symptoms (e.g. abdominal pain in case of irritable bowel
30 syndrome) are not mainly explained by a general medical disease. Nevertheless,
31 also these functional syndromes often co-occur with physical diseases. Moreover,
32 co-occurring medical conditions influence other relevant clinical outcome
33 measures and health care use (19) Therefore it is crucial to assess the co-
34 occurrence of physical diseases carefully. Binary checklists for somatic illnesses,
35 such as the WHO checklist of chronic diseases in the SCAN (16) help to ensure
36 that a comprehensive description of the somatic and psychological dimensions of
37 the patient's medical status is given. In more severely affected or inpatient
38 samples, the updated Charlson comorbidity index could also be relevant (20).
39 Depending on the research question, repeated measurement could be useful.

42 (2) Assessment of somatic symptoms

43 While DSM-5 has shifted the focus of classification from the assessment of
44 somatic symptoms to the consideration of concurrent psychosocial factors, clinical

1 trials should continue to assess the different facets of somatic symptoms (e.g.,
2 multiplicity of symptoms, location and type of symptoms, intensity, occurrence,
3 duration, interference with daily activities) as change in symptoms will continue to
4 be a central outcome feature of treatments for patients and physicians/ therapists
5 alike. Although more sophisticated assessment tools are additionally necessary,
6 we recommend the use of two numerical rating scales (NRS; see **Table 2**) to
7 assess

- 8 • Symptom intensity
- 9 • Symptom interference with daily activities

10
11 The field of pain research has strongly benefited from using these two simple to
12 use NRS. It allows comparing the efficiency of interventions between clinical trials.
13 NRS have been shown to be sensitive to the assessment of change, valid, and
14 simple to use (21). A commonly used time frame for assessing somatic
15 symptoms with a NRS is 7 days.

16 Self-rating scales should be used that are specifically evaluated to assess
17 changes of somatic symptoms. While the Patient Health Questionnaire PHQ-15 is
18 one of the most frequently used instruments to identify people at risk for
19 somatization, its sensitivity to assess change was only sparsely evaluated (22).
20 However, it has shown treatment effects in some evaluation trials (e.g., (23)). The
21 somatization subscale of the Symptom Checklist SCL-90R is also frequently
22 used, albeit its specificity for somatic symptom disorder is less clear (24). The
23 Screening for Somatoform Symptoms (SOMS-7) has been evaluated for the
24 sensitivity to assess change (25), but represents a very broad assessment tool.
25 The Bradford Somatic Inventory (BSI) claims to be valid for multiple ethnic groups
26 (26), which is an aspect that was frequently neglected during assessment tool
27 evaluation. The Bodily Distress Syndrome Checklist (BDS) has been validated as
28 a screening tool for bodily distress syndrome (27), but its sensitivity to assess
29 change needs further evaluation.

30 In contrast to pain research, symptom diaries and other experience sampling
31 methods are less frequently used in the field of SSD or BDD. However, they could
32 provide information that goes far beyond self-rating scales, and new technologies
33 are further facilitating their application (28)(e.g., ecological momentary
34 assessments EMA). Multiple assessments allow the analysis of patterns of
35 change, and the use of time-lag analyses. If diaries are used, it is recommended
36 not only to use “negative” items (e.g., current symptom intensity), but also to
37 address positive features (e.g., current ability to cope with symptoms, current
38 ability to enjoy life despite of symptoms) (29).

39 40 **(3) Psychobehavioral features**

41 DSM-5 introduced classification-relevant psychobehavioral features of SSD, such
42 as health anxiety, illness worry, excessive time and energy spent on the
43 symptoms or health concerns. Therefore these features are part of the
44 classification process (domain #1), but often they also determine significant parts

1 of the overall suffering of patients, and they also belong to potential mechanisms
2 of symptom development and symptom maintenance. Therefore they also
3 constitute a core outcome domain. Several assessment tools have been
4 developed to investigate these features. The frequently used Whiteley-Index WI is
5 a well-established and economic instrument to assess health anxiety (30), but
6 also other instruments have demonstrated sensitivity to assess change in this
7 field (31). New developments try to cover the full spectrum of the B-criteria of
8 somatic symptom disorder (i.e., the cognitive, affective and behavioral impact of
9 symptoms), e.g. the Somatic Symptom Disorder Scale (SSD-12) (32). Again, their
10 sensitivity to assess change has to be further evaluated.

11 Anxiety and depression are frequently co-occurring psychopathological
12 phenomena. Therefore the assessment of broader psychopathology beyond
13 somatization is strongly recommended. Typical assessment tools are the SCL-
14 90R, the anxiety and depression subscales of the Patient Health Questionnaire
15 PHQ (33-35), or other self- and expert ratings on psychopathology (36, 37)

16 The assessment of psychological features of the disorders should also
17 address potential *mechanisms of change/mediators*. Somatosensory amplification
18 (38) describes the vicious circle of illness anxieties, attention focusing, and
19 amplified perception of symptoms, and catastrophizing of symptoms (39). This
20 mechanism shows close relationships with bodily vigilance (40). Fear avoidance
21 has been shown to be one of the most powerful predictors of the development of
22 symptom persistence/chronicity (41), and it is considered to be a major
23 maintaining factor for these types of symptoms (42). Patients can show
24 dysfunctional illness behavior that contributes to the maintenance of symptoms.
25 Many interventions try to improve symptom coping skills, and reduction in fear
26 avoidance or symptom catastrophizing partially mediates treatment effects across
27 various syndromes (43, 44). These variables should be addressed accordingly.
28 Illness beliefs in general, such as assumptions about the etiology of symptoms,
29 suspected medical explanations, expected course and treatment responses are
30 examples of components of illness beliefs. Some of these components can be
31 dysfunctional (e.g. in contributing to high health expenditures (45)), and need to
32 be changed during interventions. A typical instrument to assess these illness
33 beliefs is the Illness Perception Questionnaire (46), which is also available in a
34 shortened version (47). However, depending on the rationale of the treatment
35 approach, other mechanisms of change can be postulated, and should be
36 assessed accordingly (e.g., emotion regulation, attachment insecurity (48),
37 reduction of avoidance behavior, reduction of symptom reinforcement via
38 relatives, increase of acceptance and mindfulness, and communication skills).
39 The assessment of mediators could be complemented with the evaluation of
40 potential moderators (e.g., personality traits such as neuroticism or negative
41 affectivity, gender, age).

42 43 **(4) Illness consequences (Quality of life and disability assessment)**

1 Health related quality of life (HrQoL) is the most relevant outcome domain in this
2 field, and its assessment should address issues such as physical functioning,
3 psychological and emotional functioning, but also functioning in social roles. The
4 most frequently used assessment tool for HrQoL is the Short Form SF-36 or its
5 abbreviated version SF-12 (49, 50). This has been specifically adapted for the use
6 in the field of SSD (51). As an alternative or extension to the assessment of
7 HrQoL, assessments of disability are highly recommended. A frequently used
8 assessment tool that is both economic and valid to assess change is the Pain
9 Disability Inventory, which has been adapted to somatic symptoms in general
10 (52). Also frequently used are the Sheehan Disability Scales (53). Finally, health
11 care costs and health care utilization are considered to be of pivotal relevance in
12 somatization syndromes, in particular because a substantial subgroup of patients
13 is characterized by continuous health-care seeking. Although variables of health
14 care use and costs are notoriously associated with statistical distribution and
15 evaluation problems, their financial relevance should motivate to address this
16 issue in clinical trials. In combination with health economic research questions,
17 the assessment of quality-adjusted life years (QALY) is needed. For this purpose
18 instruments such as the EuroQol (EQ-5D; (54)) or the SF-6D (55) can be used as
19 an alternative to the SF-36. Recently, the reQOL has been developed which has
20 been validated to give a better assessment of QOL in mental disorders
21 (www.reqol.org.uk/p/overview.html).

22

23 **(5) Consumer satisfaction**

24 A global rating on treatment success from the perspective of the patient is also
25 highly recommended. It is obvious that the definition of improvement by a patient
26 can substantially differ from the improvements shown in symptom scales, or as
27 evaluated via clinical expert ratings. Additionally, treatment satisfaction can also
28 represent a variable that is of substantial relevance, but not identical to other
29 suggested variables. The “recommendation item” (“Would you recommend this
30 treatment to another person/a friend with similar problems?”) is one possible
31 simple item that could be used in all clinical trials to assess treatment satisfaction.
32 Consumer satisfaction scales have been developed for other clinical fields (56),
33 but can be easily adapted to the focus group of this manuscript.

34 The effect of psychological interventions strongly depends on factors such as
35 credibility of treatment, therapeutic relationship, and expectation of improvement.
36 Therefore their assessment is recommended if psychological interventions are
37 compared and evaluated. A brief scale to address these topics has been
38 suggested (57). For the assessment of the quality of the therapeutic relationship,
39 several screeners have been published (e.g. (58, 59)).

40

41 **(6) Unwanted negative treatment effects**

42 A scientifically-based treatment recommendation requires an evaluation of the
43 expected positive treatment effects in relation to potential negative outcomes.
44 However, even in pharmacology research, side effects are frequently assessed

1 with unsatisfactory methods (60, 61). Over the last century, psychotherapy
2 research has also neglected the issue of unwanted negative effects (62).
3 However, considering the vulnerable states of many patients with SSD/BDD as
4 well as the many problematic experiences that patients report from past
5 treatments, it is strongly recommended to assess unwanted negative effects
6 during and after treatment. It is not considered sufficient just to add one or two
7 open questions, and to rate their answers by experts about their relevance, as
8 was frequently done in pharmacology research (63). More systematic
9 assessments for negative effects are required both in psychological intervention
10 trials and pharmacological intervention trials; just recently, assessment tools to
11 ascertain negative effects of psychotherapy have been developed, although this
12 field is just at the beginning of validating corresponding instruments (64, 65). In
13 pharmacological trials, systematic and structured assessments should
14 complement registrations that are more spontaneous and observation-based (65,
15 66).

17 **Discussion**

18 In this manuscript, we present consensus recommendations on which domains
19 should be covered when planning the assessment tools in clinical trials in the field of
20 SSD, BDD, and functional syndromes. While such a multidimensional approach
21 should not replace other quality criteria of clinical trials (such as the definition of
22 primary outcome variables), it should facilitate the comparability between clinical
23 trials and help optimize the accumulation of results from different trials, e.g. in meta-
24 analyses or Cochrane analyses.

25 A harmonization of assessments between clinical trials has the potential to not only
26 substantially improve trial quality per se, but also the synergistic potentials between
27 trials. It would be extremely helpful to have at least one or two very simple
28 assessment methods that should be part of most clinical trials such as two suggested
29 NRS on symptom intensity and interference with daily activities respectively (domain
30 #2). Moreover, the definition of domains should also help to decrease the notorious
31 lack of information, as soon as other than the primary variables are analyzed in meta-
32 analyses. When features such as comorbid emotional problems, psychobehavioral
33 features (domain #3) and illness consequences (quality of life and disability ; domain
34 #4) are subject of agglomeration of trials, often less than 30% of the original trials
35 provide full data (1). In such a situation, where the majority of published trials cannot
36 be used, scientific and clinical progress will be unnecessarily delayed, and most
37 conclusions from clinical trials must remain incomplete.. Moreover, a systematic
38 consideration of potential mediators and moderators of interventions offers a basis for
39 targeted treatment decisions. Therefore we expect a major breakthrough if these
40 recommendations are considered in future clinical trials.

1 While the IMMPACT criteria and CONSORT criteria offer stimulating and thoughtful
2 recommendations, a specific adaptation to the field of SSD, BDD, and functional
3 syndromes is necessary. CONSORT offers a general quality framework for all clinical
4 trials, which needed to be more specified for the field of interest of this paper.
5 Specific domains of necessary ascertainments beyond the definition of primary,
6 secondary outcome variables, and side effects are not specified in CONSORT
7 criteria, but in our paper. IMMPACT has a strong focus on specific pain syndromes.
8 While pain syndromes are also of relevance for many functional syndromes, the
9 scope has to be broadened up for SSD, BDD and functional syndromes, to address
10 the multiplicity of symptoms, the large overlap between different functional
11 syndromes, and considering that for some functional syndromes, non-pain symptoms
12 are crucial (e.g., chronic fatigue). Therefore, not surprisingly, some recommendations
13 of our approach show similarity to IMMPACT recommendations (e.g., physical and
14 emotional functioning; participant ratings of improvement and satisfaction with
15 treatment; symptoms and adverse events), while others are adapted to the field of
16 interest (e.g., classification issues; how to address somatic conditions; addressing
17 overlap between functional syndromes; distinction between illness consequences
18 and psychobehavioral mechanisms).

19
20 Another advantage of these recommendations is the inclusion of frequently
21 neglected, yet highly relevant variables. The neglect of assessing unexpected
22 negative effects in clinical trials investigating psychological interventions is one of the
23 most impressive examples of blind spots in clinical research. However, if
24 interventions increase the risk of somatic symptom turbulences, emotional crisis,
25 suicidal ideation, or if patients feel that they are not taken seriously, such an
26 intervention should be considered more critically compared to other interventions with
27 similar benefits, but fewer of these negative effects. Therefore an adequate benefit-
28 risk-evaluation requires not only the assessment of treatment advantages, but also of
29 treatment-related problems (domain #5). These unwanted treatment outcomes may
30 also influence patients' consumer satisfaction of the intervention, which is another
31 important outcome (domain #6)..

32 When summarizing these recommendations, it also became evident that cultural
33 adaptations of instruments are mostly lacking. This is all the more problematic, as
34 somatic symptoms are embedded and experienced in the context of culture and
35 language and thus differ in terms of type, location, intensity and ways of
36 communicating them. Most intervention trials included patients with diverse
37 backgrounds, and these effects of diversity can further add to uncontrolled variance if
38 instruments are used without cultural equivalence or adaptation.

39 Publishing recommendations always bears the risk of over-standardization, while
40 research progress needs some competition between conflicting approaches. Our aim
41 is to provide a set of domains which are advantageous to address, rather than setting
42 strict standards for future trials. Although we mention several specific assessment
43 tools, this is only done to highlight examples for the field, while the genuine

1 recommendations primarily cover the six core domains. It remains up to the
2 investigators to select assessment tools for these domains, but also to extend the
3 suggested domains with other fields of interest. However, we want to encourage the
4 use of multi-methodological approaches: the use of expert ratings can easily lead to
5 over-estimations of intervention effects, and should always be complemented with
6 validated self-ratings focusing on patient's perspective (67, 68).

7 Moreover we want to emphasize that in addition to statistical significance also clinical
8 significance should be considered. Clinical significance accounts for the clinical
9 relevance of individual patient's response to a treatment. There are many different
10 methods of analyzing clinical relevance. For continuous data the reliable change
11 index has been recommended since it incorporates the standard error of the
12 measurement depending on the measurement's reliability . However the cut-off of the
13 $RCI > 1.96$ indicating reliable change is not feasible for the assessment of change of
14 somatic symptom intensity, and is highly dependent on the variability of the
15 assessment tool as well as the correlation of the assessment tool over repeated
16 measures. For dichotomous data the number needed to treat for another beneficial
17 outcome (NNTB) is often used which is defined as the number of participants that
18 needed to be treated for one to benefit in a given time frame. Since clinical
19 significance regarding the outcome domains has not been examined sufficiently for
20 our field, empirical criteria of clinically significant change cannot be provided. We
21 refer to a recommendation by the Initiative on Methods, Measurement, and Pain
22 Assessment in Clinical Trials (IMMPACT) which provides provisional criteria for
23 interpreting the clinical importance of treatment outcomes in clinical trials of patients
24 with chronic pain (69). For example, a decrease of 30% on a 0-10 NRS measuring
25 pain intensity was defined as a moderately important change, and a decrease of
26 $\geq 50\%$ as a substantial improvement. The proposed multi-domain assessments will
27 enable investigation of whether such improvements are paralleled by changes in
28 other domains relevant to SSD, BDD and functional symptom disorders.

29 For the evaluation of clinical trials, there is no need to show improvements on all
30 recommended domains for a single intervention, and in most cases it will be essential
31 to establish an *a priori* primary outcome measure. However, it is important to realize
32 that treatment effects can differ substantially between the specific domains.
33 Treatments can substantially improve quality of life, although not change symptom
34 intensity (e.g., if the focus is on acceptance strategies). The relevance of specific
35 core domains can also vary depending on selection criteria and aim of the study: if,
36 for instance, patients with abnormal health care use are selected for treatments, the
37 effects on health care utilization can be of more relevance than the effect on
38 comorbid emotional problems. Moreover, the relevance of each domain partially
39 depends on one's theoretical perspective or clinical interest. For referring physicians,
40 the improvement of symptoms could be of major interest, whereas the reduction of
41 health care utilization could be more relevant for health care insurances. Similarly,
42 working ability and role functioning are crucial from a societal perspective; and for the
43 patient and significant others issues related to life satisfaction are likely to be

1 essential treatment outcomes. These examples highlight that the recommended core
2 domains reveal relevant and necessary information to evaluate a specific treatment
3 of interest in comparison to other treatments, and to reveal the relevant information
4 for the specific interest group.

5 While the IMMPACT criteria of pain research stimulated the development of the
6 EuronetSOMA criteria, the later ones try to extend this proposal, and to tailor it
7 specifically to the field of somatic symptom disorder, bodily distress disorder, and
8 functional syndromes. Specific recommendations are included how to address the
9 diversity of included syndromes, how to address comorbid medical conditions, or how
10 to assess unwanted negative effects of interventions. Beyond these more specific
11 recommendations, the attempt to harmonize domains of evaluation methods is
12 expected to accelerate progress of intervention research in this field. Therefore, we
13 anticipate that the recommendations of core domains for outcome assessment in
14 clinical trials of somatic symptom disorder will result in more consistency in trial
15 design and output assessment with the goal of improving interpretability and
16 generalizability of clinical trials in this field.

17 **Conflict of Interest:**

18 WR declares that he was part of the group inventing the Screening for Somatoform
19 Symptoms SOMS-7 for outcome assessment in somatoform disorders, and of the
20 INEP to assess negative effects of psychotherapeutic interventions. PF and AS
21 invented the concept of bodily distress disorder, and PF was involved in the
22 development of the Bodily Distress Syndrome Checklist. AT, WR, PH and BL were
23 involved in the development of the SSI-12. All further authors declare no conflict of
24 interest that could have influenced the content of this manuscript.

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27

28 **Additional Members of the Euronet-SOMA Group** (in addition to authors on front 29 page):

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31 Harald Gündel, Paul Hüsing, Chris Kenedi, Ksenya Khohlova, Sebastian Kohlmann,
32 Claas Lahmann, Marco Lehmann, Nadine Pohontsch, Heribert Sattel, Omer van den
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- 1 **Table 1:** Overview on core domains to assess change in clinical trials on somatic
- 2 symptom and associated disorders

Domain	Specifications
Classification of disorder and comorbid mental problems	Validated structured clinical interview including specific criteria for the most important associated syndromes (fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, etc.). Duration/onset of symptoms. Pre-treatments.
Assessment of somatic symptoms	2 NRS (0..10; see Table 2): <ul style="list-style-type: none"> - Symptom Intensity - Symptom Interference Self-rating symptom scales, Symptom diaries, EMA
Psychobehavioral features	B-criteria of DSM-5 Psychopathology (Depression, Anxiety) Potential mechanisms (health anxiety, psychobiological markers, a.o.)
Illness consequences	Quality of Life; disability Health care use
Consumer satisfaction	Treatment satisfaction; recommendation item; Therapeutic relationship; Expectations
Unwanted negative effects	Worsening of problems Unexpected new problems and symptoms Systematic side effects assessments

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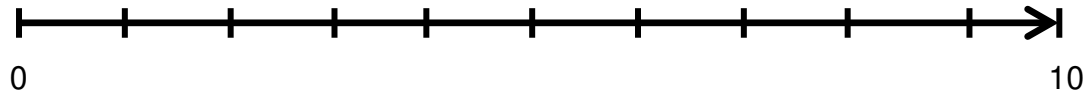
Table 2

Recommendations for 2 Numeric Analogue Scale Items to Be Used in Clinical Trials

Symptom Intensity:

During the last 7 days, the overall intensity of my bodily symptoms was:

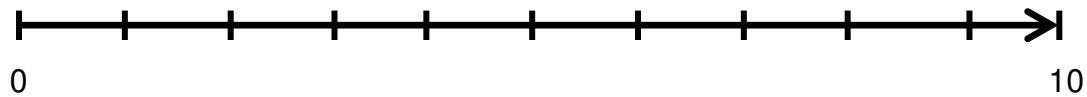
No Symptoms at all Worst possible symptoms



Symptom Interference:

During the last 7 days, my bodily symptoms interfered with daily life activities

Not at all Interfered completely



1 Appendix

2 **Recommendations for 2 Numeric Analogue Scale: Non-English examples**

3

4 **German:**

5 * Symptom Stärke: Während der letzten 7 Tage war die Gesamtstärke meiner
6 körperlichen Beschwerden: 0 = überhaupt keine Beschwerden – 10 =

7 schlimmstmögliche Beschwerden

8 * Symptom Beeinträchtigung: Während der letzten 7 Tage haben mich meine
9 körperlichen Beschwerden bei Alltagsaktivitäten beeinträchtigt: 0 = überhaupt nicht –
10 10 = extrem beeinträchtigt

11

12 **Danish**

13 *Symptomernes intensitet: Hvor intense har mine fysiske symptomer været i de
14 sidste 7 dage?: 0 = slet ingen symptomer – 10 = værst mulige symptomer

15 *Symptomernes påvirkning: Hvor meget har mine fysiske symptomer påvirket mine
16 dagligdags aktiviteter i de sidste 7 dage?: 0 = slet ikke påvirket – 10 = påvirket
17 ekstremt meget

18

19 **Dutch**

20 *Intensiteit van symptomen: Gedurende de afgelopen 7 dagen was de globale
21 intensiteit van mijn lichamelijke symptomen: 0 = helemaal geen symptomen – 10 =
22 meest erge symptomen

23

24 *Belemmering door pijn: Gedurende de afgelopen 7 dagen hebben de lichamelijke
25 symptomen mij belemmerd in mijn dagelijkse activiteiten: 0 = helemaal niet – 10 =
26 volledige belemmering

27

28 **French**

29 *Intensité des symptômes: Pendant les 7 derniers jours, l'intensité globale de mes
30 symptômes physiques était: 0 = pas des symptômes du tout – 10 = intensité des
31 symptômes totales

32

33 *Interférence par symptômes: Pendant les 7 derniers jours, mes symptômes
34 physiques interféraient avec mes activités journalières: 0 = pas d'interférence du tout
35 - 10 = interférence totale

36

37 **Lithuanian**

38 *Simptomu intensitāte: Pēdējo 7 dienu laikā manu ķermeņa simptomu intensitāte bija:
39 0 = nebija nekādu simptomu – 10 = vislielākā intensitātē

40 *Simptomu mijiedarbība: Pēdējo 7 dienu laikā mani ķermeņa simptomi traucēja
41 dienas aktivitātēs: 0 = nemaz – 10 = vislielākā mērā

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43 **Norwegian**

44 *Symptomenes intensitet: I løpet av de siste 7 dagene har intensiteten av mine
45 kroppslige symptomer vært: 0 = ingen symptomer i det hele tatt – 10 = verst mulige
46 symptomer

47 *Symptomenes påvirkning: I løpet av de siste 7 dagene har mine kroppslige
48 symptomer påvirket mine daglige aktiviteter: 0 = ikke det det hele tatt – 10 = påvirket
49 disse fullstendig

50

51 **Russian**

- 1 *Интенсивность симптома: В течение последних 7 дней общая интенсивность
- 2 моих телесных симптомов была следующей: 0 = Отсутствие симптомов – 10 =
- 3 Максимальная выраженность симптомов
- 4 *Ограничения вследствие симптома / Вмешательство симптома: Насколько
- 5 сильно в течение последних 7 дней мои телесные симптомы мешали моей
- 6 повседневной жизнедеятельности: 0 = Совсем не мешали – 10 = мешали
- 7 постоянно
- 8
- 9
- 10