Author's response to reviews

Title: Bodily distress syndrome: A new diagnosis for functional disorders in primary care?

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Author's response to reviews: see over
Dear Editor,

Aarhus, 30 October 2015

RE: Manuscript ID number: (MS) 5115377391750084 (resubmission)

Thank you for the comments on our manuscript entitled ‘Bodily distress syndrome: A new diagnosis for functional disorders in primary care?’

We have revised the manuscript in accordance with most of the recommendations made by the reviewers. Below, you will find our point-by-point response, including details of relevant changes to the manuscript.

We hope that you will consider this revised version for publication. If you have any further questions or comments, please do not hesitate to contact us.

We look forward to hearing from you soon.

Yours sincerely,

Anna Budtz-Lilly
MD, PhD
Comment 1:
We have asked three reviewers to provide comments. As you will see, their reaction is mixed. We are prepared to consider a revised version of your paper with the reviewers' comments taken into account.

Response:
The mixed reactions to this paper indicate that there is a need for a debate paper dealing with the diagnostic classification of functional disorders within a primary care perspective.

Comment 2:
The most important thing will be to convince readers that the diagnostic category you are suggesting is necessary (despite others being available and established) and scientifically justified.

Response:
The currently available diagnoses that unify symptom disorders are located in the psychiatric classifications; these are neither scientifically based nor targeting primary care patients. In contrast to bodily distress syndrome, somatoform disorders, somatization disorder and somatic symptom disorder are all based on consensus and not on evidence. Furthermore, although these diagnoses are established in the international classification systems, evidence has shown that they are rarely applied in primary care.

We have aimed to clarify the necessity of a new diagnostic category in the manuscript, particularly in the introduction.

Reviewer 1:

Comment 1:
Comments reg. the following lines:

a) „symptom counts have been shown to be unreliable in clinical practice because of the poor sensitivity and specificity of this approach [21].“

b) „Box 1: # 3 symptoms from at least one of the following groups: […]
Single-organ BDS (mild-moderate): involves one or two the symptom groups […] Multi-organ BDS (severe): involves three or four of the symptom groups“

c) „The diagnostic category of BDS is based on the symptom clusters pertaining to bodily distress and introduces symptom pattern recognition as a core element of the diagnostic criteria.“

d) „it is the symptom pattern and not each individual symptom which should be assessed as ‘functional’ or not. This differs from the classification of the current somatoform disorders in the ICD-10;“

It is not clear what the difference is between „symptom count“ and pattern recognition with regard to the BDS concept. Box 1 suggests that symptoms are counted, but within different categories. Is this different to existing criteria? What would be helpful in this context:

A. A table in which BDS criteria are compared with existing criteria of various functional
...disorders.

B. A description of the current diagnostic practice of GPs when diagnosing functional disorders. This should be contrasted with the expected diagnostic practice when BDS is applied (i.e. pattern recognition). What change is expected for the GP’s work after implementing BDS?

C. A theoretical background paragraph on diagnostic approaches and criteria like symptom count, pattern recognition and more GP-specific diagnostic approaches (e.g. gut feeling, trigger events in low-prevalence settings, watchful waiting, avoidable serious outcomes etc.) and its implications for the BDS syndrome.

Response:

Add A)
It would be rather difficult in the scope of this paper to add a table that compares BDS with the existing criteria of functional disorders as there are multiple functional somatic syndromes. Furthermore, multiple definitions exist for each functional syndrome. For example, more than 20 definitions exist for CFS/ME; chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME).

Add B)
Like all physicians, GPs are familiar with the pattern recognition approach to diagnostics as this approach is used in most clinical diagnostic work. When a patient presents with complaints/symptoms, you must examine how these fit into a known illness pattern. You must also ask for symptoms that may support or reject the diagnosis you have in mind, including symptoms that support other tentative/differential diagnoses. In case of functional disorders, physicians lack diagnostic criteria (characteristics) for the condition that has led to a diagnosis based on exclusion. The BDS concept provides positive criteria; you can ask whether the patient has the pattern of GI arousal, MS pain, etc.

BDS diagnostic criteria are based on results from comprehensive diagnostic interviews and on statistical analyses of symptom patterns. The GPs can explain to the patients that the knowledge they have on the patients’ disorder or complaint is based on evidence. This will without doubt improve the clinical communication.

Previous research shows that GP diagnostics of somatoform disorders tend to emphasize personal characteristics in the patient rather than to focus on the illness. We know very little about how the GPs will actually apply this diagnosis, and this is an important topic for future research (as stated on page 14).

Add C)
Diagnostic approaches and decision-making processes are of great interest, but these topics are not the focus of this debate paper.

Comment 2:

Comments reg. the following lines:

“It is not clear to which degree the BDS diagnosis may solve the clinical problems faced by the GP when diagnosing patients with functional disorders.”
“We discuss [...] whether this diagnostic category may be useful and valid in primary care.”

As a reader I look for answers to these questions and cannot find them in the text. What are the problems of GPs? And which hypothesis exists with regard to any changes in GPs’ clinical practice?

Response:
The main problem for the GPs (and their patients) is that they do not have a useful diagnosis for patients presenting with functional symptoms. Without a well-defined concept and general agreement on specific diagnostic criteria, many patients with functional disorders remain undetected, or at least undiagnosed, which implies that they are not offered adequate treatment.

Furthermore, the ailing patient rather than the illness condition is labelled. In this way, primary care treats functional disorders differently from any other medical condition, and patients are thus left without proper care.

Our hypothesis is that presence of valid and useful diagnostic criteria will enable categorization of patients. This will, at least, provide the basis for improved care for patients with functional disorders.

Comment 3:

Comments reg. the following lines:

“evidence points strongly towards an underlying phenomenon of bodily distress. A diagnostic category based on this concept may improve the clinical diagnostics...”

A. Please explain why the diagnosis of an underlying concept is expected to improve clinical diagnostics compared with the diagnosis of various phenotypes of a concept?

“In favour of the validity of BDS is the fact that the clinical description of the BDS symptom profiles originates from cluster analysis based on data from a large study of 978 patients from internal medical and neurological departments and from primary care.”

B. I think a method per se cannot serve as an indicator for validity.

C. To understand your point, more details on this central study on the 978 patients have to be reported, e.g. which diagnoses were included, was BDS developed with a sample of diagnosed functional disorder patients, which type of functional disorders were included, what are the numbers of patients from the diverse settings etc.

Response:

Add A)

BDS is in fact a phenotype. We assume that the reviewer refers to the various functional somatic syndromes when he refers to various phenotypes and concepts. However, to our knowledge, none of these have been tested appropriately to warrant that they are in fact phenotypes. Most studies have been methodologically weak as they have used highly selected patient populations and only included a selected range of symptoms; thus, they have completely missed the poly-symptomatic picture that has been shown in the BDS concept. Furthermore, from the point of view of the GP in clinical practice, it makes little sense to
handle multiple syndrome diagnoses with overlapping symptoms and criteria and consequently diagnose a patient with multiple diagnoses. This problem is solved by the BDS concept.

Add B)
We agree that a statistical method cannot warrant validity when it stands alone. However, a statistical approach and method is necessary in order to assess the two first steps in the validity process according to the Kendall and Guze criteria. Other validators from the template of Kendal/Guze have also been tested in previous studies. As far as we know, most (if not all) diagnoses in this field have not been tested appropriately according to these criteria. In fact, most are consensus-driven without substantial scientific support.

Add C)
A more detailed description of the study on 978 patients has now been included in the manuscript.

Consecutively referred patients were referred to one neurological department (n=120) and one internal medical department (n=157) during a three-month period. From primary care, consecutive patients consulted 38 GPs for a new illness problem (n=701). This means that the sample did not consist of patients diagnosed with a functional disorder. The patients were assessed according to SCAN interviews, and the 76 physical symptoms outlined in the physical health chapter were included.

A later study performed on the same data investigated the overlap between BDS and six functional somatic syndromes (chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, non-cardiac chest pain, hyperventilation syndrome and pain syndrome) and the DSM-IV somatoform disorders characterised by physical symptoms. We have chosen not to include further details on methods, results, etc. from the original works as this would expand this paper considerably and undermine our intention to present a more overviewing approach (helicopter perspective). The answers to the questions posed by the reviewer are found in the original publications, which are listed in the reference list of the paper.

Comment 4:

Comment on line 218/219: “the BDS construct has been confirmed in a primary-care population”

Important point, please report more details on this. How was this done?

Response:

More details on the confirmation study of BDS in primary care have been included in the manuscript.

By use of exploratory factor analyses based on the symptoms included in the BDS diagnosis, the four symptom groups of BDS emerged. By use of confirmatory factor analyses, the model was confirmed. Furthermore, by use of latent class analyses, the three patients groups of the original study (including 978 patients) recurred: no BDS, single-organ BDS and multi-organ BDS. The study was performed as a questionnaire study.
Comment 5:

Comment on the following lines 220-227 “...whether patients with six specific functional somatic syndromes (chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, non-cardiac chest pain, hyperventilation syndrome and pain syndrome) and the DSM-IV somatoform disorders characterised by physical symptoms also met the criteria for BDS. The overall [missing word; e.g. concordance?] between BDS and the investigated diagnoses was 95% (95% CI: 93.1-96.0, kappa 0.86, p<0.0001) [40]. These findings indicate that BDS may capture the different diagnoses that appear across the different chapters of the ICD-10 and the somatoform disorders classified according to the (now outdated) DSM-IV.”

This high concordance is not surprising assuming that BDS and its symptom clusters were derived from a sample with exactly these diagnoses in reference 2. (As said before, more details on this central study are necessary to report.) Readers may not understand why this concordance justifies a new diagnostic concept.

Response:

Please see response to comment 3.

Comment 6:

There is some confusion about the statistical methods used: Line 168: “cluster analysis” Line 172/173: “principal component analysis” Line 173: “symptom clusters”

A cluster analysis reveals clusters (mostly done on patient level), a PCA reveals factors/components (mostly done on item/symptom level). It is not clear, what was done in this study and on what output (clusters or factors/factor loadings) the symptoms in Box 1 are based. Furthermore, it is not clear why these „clusters“are an indicator of validity for the new BDS and not only a confirmation of the several kinds of existing functional disorder diagnoses? If several clusters can be derived from a heterogeneous simple, I would intuitively conclude that there are different illness entities and not an underlying concept.

It would be helpful to describe the difference between the diagnostic entity BDS described in box 1 and the already existing various diagnostic entities associated with the four symptom clusters from box 1 (e.g. irritable bowel syndrome). It seems like BDS is a new umbrella term which subordinates all functional disorders and renames them as multi-organ or single-organ BDS, but by counting the same symptoms as before.

Response:

PCA was used in the original study on which BDS is based. The terminology has now been corrected in the manuscript in line with this.

The BDS concept displayed in Box 1 is based on latent class analysis (LCA), which is the state-of-the-art analytical method for classification. Results from LCA show that patients constitute three groups: one group consists of patients with symptoms from multiple organ systems, a second group consists of patients with symptoms mainly from one group, and a third group consists of healthy individuals. The single-organ BDS group includes 4 subtypes, which could resemble fibromyalgia, IBS, CFS/ME, and a cardiac type. The BDS concept is thus not and either-or concept. You can still work with subcategories, like IBS (which in this terminology may be called BDS GI
type). But as regards patients with multi-organ BDS, it would not make much sense to classify the symptom patterns as IBS, CFS/ME, fibromyalgia and other syndromes for which they do fulfill criteria simultaneously.

Comment 7:

Ideas for future research should be outlined in more detail. In particular, it would be instructive to present a design idea for a trial which compares clinical patient outcomes when GPs apply BDS criteria vs. the existing ICD or DSM criteria for functional disorders. Furthermore, a research design would be interesting, which examines how the BDS concept (vs. traditional concepts) fits to the specific decision making process in general practice.

Response:

We agree that the utility of BDS should be investigated in future studies, and patient outcome is of course a main criterion that should be assessed. However, as the current diagnoses for functional disorders are rarely used in primary care, it would make little sense to use them as a gold standard.

As regards the decision-making process in clinical practice, please see response to Comment 1.

Comment 8:

Page 9, lines 161-164: References are not correct or not in concordance with the reference list.

Response:

Thanks for drawing our attention to this. The references have been corrected.

Reviewer 2:

Comment 1:

I am not sure what type of manuscript is this submission. It is not a comprehensive review, it does not seem to be an editorial or an opinion. It introduces a new term to "replace" some others. Usually the introduction of a new term if it is not encompassing (with justification) many others in order to replace them is adding to the confusion and I think this paper does just that.

Response:

As a debate paper, the objective of this paper was to discuss whether BDS may be a useful diagnosis for functional disorders in a primary care setting. This was done in the context of diagnostic validity and diagnostic utility.

Comment 2:

The review of the literature is very poor and misses important papers on the subject.

Response:

The paper is NOT a systematic review. However, we have tried to include the most relevant and recent literature throughout the manuscript.
Comment 3:
*The aim as stated in the paper is not achieved.*

Response:
As described on page 6, the aim of the manuscript was to present a brief overview of the underlying concept of functional disorders, followed by an exploration of BDS as a probable, valid and useful alternative to the current diagnostic categories. Furthermore, the paper discusses whether BDS fits the clinical phenomenon behind functional disorders and whether this diagnostic category may be useful and valid in primary care.

We do believe that the paper has presented the overview and discussed the utility and validity of BDS.

Comment 4:
*The paper makes assumptions like on line 76 that are not substantiated.*

Response:
In the context of this debate paper, the objective was to discuss and debate the diagnostic classification of functional disorders.

Reviewer 3:

Overall

The authors have provided a manuscript that reads well and contains important concepts that will be relevant to the practicing primary care physician. The concept of functional syndromes, somatoform disorders, somatic symptom disorders and BDS is often difficult for healthcare practitioners to understand and the authors are to be commended for attempts to reduce such confusion and also overcome disease labelling relevant to that specific specialty a patient presents to. The changes and comments mentioned below correspond to minor essential revisions.

Abstract

The abstract reads well

Background

The literature review is sound and the concept of BDS, though reported in the literature previously, is currently presented to a wider readership in primary care.

One consideration of such a catch-all category which captures a spectrum of disorders is how to
classify severity, duration and level of associated disability – currently it is unclear the duration required for a diagnosis of BDS.

Comment 1:
The literature would also indicate that the longer someone has a disorder (somatoform/functional/etc.), the increased likelihood for intractability. The current model does not comment on this and if patients were tracked longitudinally, this could lead to varying findings given that cohorts of people with BDS may not exactly correspond e.g. one group of BDS may have a median illness duration for 1 year versus another cohort with mean illness duration for 8 years.

Response:
We agree with the reviewer that time is an issue, especially with regard to prognosis. However, this is no different from the current diagnoses for functional disorders.

Comment 2:
There are numerous cultures that have a tendency to somatise and the construct of BDS has been validated in predominantly Western contexts, how this translates to other settings is yet to be seen.

Response:
We agree that this point is highly important. Under the auspices of WHO, field trial studies are currently being performed worldwide; this also includes primary care populations in Brazil, Mexico, Spain, Pakistan and Hong Kong. Results have not yet been published, and rigorous trials in other cultures are called for.

Discussion
Comment 3:
Page 11 (line 224) – there appears to be a missing word/concept

Response:
The sentence has been corrected.

Comment 4:
While there is acceptability of the term BDS for patients – what is their understanding of aetiology or contributors to the disorder?

Response:
This is a very interesting question. Patients mostly have multiple explanations for MUS [1]. We also know from earlier studies that patients with functional disorders often have negative illness beliefs. See the generic disease model provided in Figure 1.
But specifically with regard to BDS, patient beliefs and patient understanding have not been explored. However, as described in the manuscript on page 14, two clinical studies on BDS reported very low dropout rates. This is likely to imply that the diagnosis and the explanations of contributors and aetiology of the disorder have appeared acceptable to the patients in these studies.

Comment 5:
Box 1 –
Minor tweak under severity to state: Single-organ BDS (mild-moderate): involves one or two “of” the symptom groups.

Response:
The sentence has been corrected.

Comment 6:
Where are non-epileptic seizures included? Where would non-cardiac chest pain be found?

Response:
If standing alone without other physical symptoms, non-epileptic seizures will not necessarily be covered by the BDS concept. The same is true for other dissociative/functional neurological disorders (cf. reference 65). A limitation like this is an important drawback, which is discussed on page 15, lines 324-326.

Non-cardiac chest pain is included in the cardio pulmonary symptom group.

Comment 7:
Would pain be a separate useful category (regardless of organ/system affected?)

Response:
Almost all primary pain syndromes are captured by BDS (see reference 40, where this has been tested). This regards particularly fibromyalgia and chronic widespread pain. However, patients with only one pain site may not captured by the concept (see discussion on page 15).

Comment 8:
In primary care, it might be difficult to rule out differential diagnoses unless a service had access to appropriate investigations – when referring to their hospital-based colleagues, would people with BDS be viewed as potential or possible BDS rather than arrive with this diagnosis?

Response:
This depends on the situation. In some cases, additional investigations may be necessary to establish a definite diagnosis. In other cases, the patient may be referred to a specialized unit for confirmation of the diagnosis. However, a tentative referral diagnosis of ‘potential BDS’ would be a huge step forward in the communication between primary care and medical specialists.
Comment 9:

As severity can change longitudinally i.e. someone can start off as mild, how does the classification take into account illness progression?

Response:

Impairment and illness duration are correlated in epidemiological research, but an individual illness course may also fluctuate. One advantage of the BDS diagnosis is that it is not conceptualized as a ‘chronic’ condition per se (such as somatization disorder). A more advanced classification may further specify illness course (episodic, chronic with increasing impairment, chronic with stable impairment, etc.). However, our knowledge regarding illness course in functional disorders is currently scarce.

Comment 10:

There are people with intractable chest-pain or non-epileptic seizures who might fall under the mild category given the symptom count but in reality be disabled with intractable symptoms and therefore on the severe end of clinical categorisation, how does that match up with the severity indicators currently proposed?

Response:

We fully agree with this point. For the individual patients, the severity is specified by a combination of BDS type and clinical impairment. While illness severity and BDS type (single vs. multi-organ) may correlate highly in epidemiological research, a clinical diagnosis needs specific attention regarding impairment.

Criterion 2 in Box 1 is now described more specifically.

Reference: