



A step towards a new delimitation of functional somatic syndromes: A latent class analysis of symptoms in a population-based cohort study

Marie Eliassen^{a,b,*}, Andreas Schröder^c, Per Fink^c, Svend Kreiner^d, Thomas Meinertz Dantoft^{a,b},
Chalotte Heinsvig Poulsen^{a,b,e}, Marie Weinreich Petersen^c, Lene Falgaard Eplov^e, Sine Skovbjerg^b,
Torben Jørgensen^{a,b,d,f}

^a Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark

^b Research Centre for Prevention and Health, The Capital Region of Denmark, Glostrup, Denmark

^c Research Clinic for Functional Disorders and Psychoomatics, Aarhus University Hospital, Aarhus, Denmark

^d Department of Public Health, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark

^e Mental Health Centre Copenhagen, The Capital Region of Denmark, Hellerup, Denmark

^f Faculty of Medicine, Aalborg University, Aalborg, Denmark

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ABSTRACT

Objectives: The current delimitation of functional somatic syndromes (FSS) is inconsistent. We aimed to investigate somatic symptom profiles in the general adult population to contribute to a new, data-driven delimitation of FSS.

Methods: Information on 31 self-reported somatic symptoms used in the delimitation of various FSS and bodily distress syndrome (BDS) was obtained from the DanFunD study—a population-based cohort study on 9656 adults (participation 33.6%) from Greater Copenhagen, Denmark. Latent class analysis was used to identify symptom profiles. The profiles were described by their relation with sex, age, chronic disease, self-perceived health, symptom impact, self-reported FSS, and BDS case-status.

Results: Eight symptom profiles were identified. The largest profile had no symptoms (49% of the population). Three profiles were characterized by a few, specific symptoms: muscle and joint pain (17%), gastrointestinal symptoms (6%), and general symptoms (13%). Three profiles had multiple symptoms in specific combinations: musculoskeletal and general symptoms (7%); fatigue, musculoskeletal and gastrointestinal symptoms (3%); and cardiopulmonary, gastrointestinal and general symptoms (3%). Lastly, one profile (2%) had high probability of all symptoms. The last four profiles (15%) were strongly associated with BDS case-status, poor self-perceived health and high impact of symptoms. Analyses excluding persons with multi-symptomatic chronic disease showed similar results.

Conclusions: We identified eight symptom profiles characterized by specific combinations of symptoms. Four of these had multiple symptoms from several bodily systems showing large overlap with BDS, possibly indicating subtypes of FSS. The profiles contribute to a new delimitation of FSS by illustrating the importance of specific symptom combinations.

1. Introduction

Functional somatic syndromes (FSS) such as fibromyalgia (FM), chronic fatigue syndrome (CFS) and irritable bowel syndrome (IBS) are associated with poor health status, increased health care use and high economic costs for the society [1,2]. FSS are common in the general population [3]; however, little is known of the etiology, risk factors and

prognosis. One reason for this knowledge gap is inconsistencies and uncertainties in the diagnosis of FSS, limiting the quality of research in the field. Traditionally, FSS had been defined as conditions of exclusion, i.e. syndromes that cannot be explained by conventional medical or psychiatric conditions [4]. However, the exact delimitation of FSS is questionable [4–6]. Most formal diagnoses are based on consensus criteria, which decreases the validity substantially [6]. Further

Abbreviations: FSS, Functional Somatic Syndromes; FM, Fibromyalgia; CFS, Chronic Fatigue Syndrome; IBS, Irritable Bowel Syndrome; BDS, Bodily Distress Syndrome; LCA, Latent Class Analysis; DanFunD, Danish Study of Functional Disorders; MS, Musculoskeletal; GI, Gastrointestinal; CP, Cardiopulmonary; COPD, chronic obstructive pulmonary disease; OR, Odds ratio; CI, Confidence Interval

* Corresponding author at: Center for Clinical Research and Prevention, Frederiksberg Hospital, Hovedvejen, Entrance 5, Nordre Fasanvej 57, DK-2000 Frederiksberg, Denmark.

E-mail address: marie.holm.eliasen@regionh.dk (M. Eliassen).

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complicating the delimitation is the considerable overlap of the different FSS [4,7,8], leading some to propose that they are manifestations of the same disorder or a group of closely related conditions [7]. The overlap and the commonalities of FSS should therefore be considered when studying FSS [5,9]. However, the differences between the syndromes should not be ignored either [9]. Hence, valid delimitations of FSS are warranted based on appropriate statistical analyses which encompass the symptoms of different FSS.

The construct of Bodily Distress Syndrome (BDS) is a result of a previous attempt on delimitating FSS based on statistical analyses. BDS comprises various FSS into one diagnosis with four subtypes according to affected bodily system [10–13]. It was developed based on factor and latent class analysis (LCA) on patient samples [12] and confirmed in a sample of primary care patients [14]. While the factor analysis explored the clustering of symptoms, the LCA explored the segmentation of individuals based on their symptom pattern. The latter is especially relevant to explore boundaries between groups, which is necessary for diagnostic purposes [6,15,16]. In the BDS studies, three groups were identified based on number of affected bodily systems: one without symptoms, one with symptoms from primarily one bodily system, and one with symptoms from several bodily systems [12]. Two other studies exploring the delimitation of FSS using similar methods identified only two groups described by number of symptoms [17,18], while three other studies identified five [19], seven [20] and eleven [21] groups described by specific symptom combinations. Divergent materials and methods may explain these conflicting results. For example, only two of the studies were based on the general population [17,19], while the others, including the BDS studies, were based on more selected populations e.g. patients [12,14,18,20,21]. This may have resulted in considerable selection bias including higher symptom prevalence in the study population. Furthermore, analyses on a few symptoms [19] or groups of symptoms [12,14,21] may have limited the identifiable nuances of the symptom profiles. Relatively small study samples had potentially similar consequences [15,17,18]. In a previous study, we looked at various somatic symptoms in a large population-based study and identified 10 person groups characterized by specific symptom combinations [22]. Even though some groups were described by symptom patterns similar to FSS, the included symptoms were highly general and were indicated for a relatively short period. Additionally, we could not investigate the impact of symptoms on daily activities or the influence of well-defined diseases, generally required in the diagnosis of FSS. Thus, the groups were too general to identify persons with FSS.

In this study, we aimed to identify and describe groups of persons with similar symptom patterns, denoted symptom profiles, to contribute to a new data-driven delimitation of FSS. Additionally, this could create basis for further epidemiological studies in FSS. To overcome limitations of the previous studies, we used a large population-based cohort with main focus on FSS assessing several symptoms characteristic for FSS. This limited the potential selection bias and increased the possibilities of identifying nuanced profiles in contrast to previous studies. Moreover, we included information on symptoms' impact on daily activities, chronic diseases, self-reported FSS and BDS case-status.

2. Materials and methods

2.1. Population

The study was based on data from the Danish Study of Functional Disorders (DanFunD) conducted in 2011–15; described in detail elsewhere [3]. In brief, the cohort was initiated to investigate FSS in the general population and includes information from questionnaires and from a general health examination. It consists of two sub-samples: a five-year follow-up study of an existing cohort (Health2006 [23]) including 2308 persons (participation rate 67.8%) and a population-

Table 1
Prevalence of somatic symptoms. Sorted by prevalence. N = 9603.

Symptom	N	%	(95% CI)
Fatigue ^a	2572	26.8	(25.9–27.7)
Back ache ^a	2497	26.2	(25.3–27.1)
Joint pain ^a	2459	25.9	(25.0–26.8)
Muscle pain ^a	2319	24.3	(23.5–25.2)
Pain in arm ^b	1935	20.6	(19.8–21.4)
Pain in leg ^b	1642	17.5	(16.7–18.2)
Altering stool ^c	1625	17.1	(16.4–17.9)
Headache ^a	1339	14.0	(13.3–14.7)
Neck pain ^d	1219	12.9	(12.2–13.6)
Distention ^c	1218	12.8	(12.2–13.5)
Concentration problems ^a	1135	11.8	(11.2–12.5)
Memory impairment ^a	1134	11.8	(11.1–12.5)
Hot or cold sweats ^a	960	10.1	(9.5–10.7)
Palpitations ^a	810	8.5	(7.9–9.0)
Dry mouth ^a	759	8.0	(7.4–8.5)
Breathlessness ^a	738	7.7	(7.2–8.3)
Abdominal pain ^c	703	7.4	(6.9–8.0)
Rumble ^c	656	6.9	(6.4–7.4)
Moving pain ^a	653	6.9	(6.4–7.4)
Flushing ^a	647	6.8	(6.3–7.3)
Dizziness ^a	592	6.2	(5.7–6.7)
Numbness ^a	570	6.0	(5.5–6.5)
Precordial discomfort ^a	473	5.0	(4.5–5.4)
Heartburn ^c	423	4.5	(4.1–4.9)
Pain in upper stomach ^c	417	4.4	(4.0–4.8)
Paresis ^a	370	3.9	(3.5–4.3)
Trembling ^a	369	3.9	(3.5–4.3)
Respiratory distress ^a	283	3.0	(2.6–3.3)
Acid regurgitation ^c	251	2.7	(2.3–3.0)
Nausea ^c	182	1.9	(1.6–2.2)
Vomit ^c	28	0.3	(0.2–0.4)

^a Somewhat/quite a bit/considerably bothered.

^b Frequently/constantly bothered.

^c Frequent/constant experience.

^d Average severity ≥ 5 out of 10.

based random sample of 7493 persons (29.5%). Both subsamples were sampled from the general adult population in the western part of Greater Copenhagen. Totally, 9656 persons (33.6%) aged 18–76 years participated in the DanFunD study (145 persons participated in both subsamples, but only data from the new sample were included).

All participants gave written informed consent before participating. The study was approved by the Ethical Committee of Copenhagen County (Ethics Committee: KA-2006-0011; H-3-2011-081; H-3-2012-0015) and the Danish Data Protection Agency.

2.2. Somatic symptoms

The participants filled in a questionnaire on the experiences of various somatic symptoms within the last year. For this study, we included 31 essential symptoms required for the diagnosis of FM, IBS and dyspepsia, CFS, and BDS. The symptoms included nine musculoskeletal (MS) symptoms, nine gastrointestinal (GI) symptoms, eight cardio-pulmonary (CP) symptoms and five general symptoms (Table 1). For this study, all symptoms were dichotomized using cut points that secured clinical relevance. Thus, depending on the exact symptom question, scoring positive on a symptom was defined as one of the following: 1) being somewhat/quite a bit/considerably bothered, 2) being frequently/constantly bothered, 3) experiencing the symptom frequently/constantly, or 4) rating the average severity to ≥ 5 out of 10 (Appendix A, Table A.1).

2.3. Covariates

Characteristics of the symptom profiles were described according to sex, age and chronic disease. Information on sex and age was extracted from the Civil Registration System. Chronic disease was assessed in the

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