



## Age- and sex-specific associations between adverse life events and functional bodily symptoms in the general population



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### ABSTRACT

**Objective:** To test age- and sex-specific associations between adverse life events and functional bodily symptoms (FBS) in the general population.

**Methods:** In a population-based cohort, 964 participants (mean age 55 years SD 11, 48% male) completed two measurements waves of the present study. Lifetime exposure to 12 adverse life events was assessed through a modified version of the List of Threatening Experiences. Stress-sensitive personality was assessed with the 12-item neuroticism scale of the Eysenck Personality Questionnaire–Revised. Socio-economic status was retrieved from questionnaires. Participants completed the somatization section of the Composite International Diagnostic Interview to survey the presence of 42 FBS in the previous year.

**Results:** Regression analyses, adjusted for age, revealed that lifetime scores of adverse life events were significantly associated with FBS in the previous year, an association that was nearly identical for females (beta = 0.18,  $t = 4.07$ ,  $p < 0.01$ ) and males (beta = 0.19,  $t = 4.24$ ,  $p < 0.01$ ). This association remained statistically significant when stress-sensitive personality and socio-economic status were added to the model. Associations between adverse life events during childhood and FBS were statistically significant in females (beta = 0.13,  $t = 2.90$ ,  $p = 0.04$ ) but not in males (beta = 0.06,  $t = 1.24$ ,  $p = 0.22$ ), whereas there was a stronger association with adverse life events during adulthood in males (beta = 0.20,  $t = 4.37$ ,  $p < 0.01$ ) compared to females (beta = 0.15,  $t = 3.38$ ,  $p = 0.01$ ). Life events in the previous year were not associated with FBS in the previous year.

**Conclusion:** Adverse life events during lifetime were associated with FBS in the previous year. This association was dependent on age and sex but largely independent of having a stress-sensitive personality or low socio-economic status. Future studies could adopt a life course perspective to study the role of adverse life events in FBS.

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### Introduction

Functional bodily symptoms (FBS) are symptoms that are not explained by conventional somatic pathology. Functional somatic syndromes are characterized by clusters of FBS, such as chronic fatigue syndrome (CFS), fibromyalgia (FM), and irritable bowel syndrome (IBS). When doctors cannot find an organic explanation for somatic symptoms presented by their patients, psychosocial stress is often assumed to contribute to the etiology. Scientific studies have answered the question whether psychosocial stress precedes the onset of FBS or functional somatic syndromes with a “fairly unequivocal yes” [1].

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However, several methodological problems characterize research towards the role of stress in the etiology of FBS and functional somatic syndromes.

With regard to stress and functional somatic syndromes, the field is characterized by case control studies, which have several problems [2]. The presence of a disease label in cases may increase the amount of reported psychosocial life stress through a negative recall bias or by effort after meaning, the latter describing the phenomenon whereby individuals interpret potentially ambiguous events in accord with their implicit theories regarding the causes of their functional somatic syndromes [3]. In addition, selection bias due to the use of patient samples can be problematic, since clinical patient samples may consist of persons with relatively high psychiatric co-morbidity. Thus, the association that has been found between psychosocial stress and functional somatic syndromes in clinical samples may not apply to the development of functional somatic syndromes in general. For etiological research, the association between stress and FBS may be more informative.

When closely appreciating the relationship between psychosocial stress and FBS, however, one observes that straightforward evidence

for a role of recent stress in the etiology of FBS is scarce and characterized by limited generalizability beyond single symptoms, single psychosocial stress variables, or specific populations. For instance, life events in the previous 6 months did precede new onset of chronic widespread pain, but not independent from other psychological factors such as health anxiety and illness behavior [4, 5]. Life events in previous months preceded somatization in the setting of a psychiatric disorder in primary care [5]. In a population-based study among Chinese Americans [6] and a population-based study of adolescents [7], lifetime events were associated with the number of continuously measured somatic symptoms, whereas recent life events within the past year were not a predictor for FBS in the first study [6]. Thus, data are conflicting about the contribution of life events.

Furthermore, meta-analyses showed that childhood trauma is associated with FBS and functional somatic syndromes [8]. Health effects, including FBS, of childhood adversities seem larger in females than in males [9]. A pathway linking psychosocial stress and FBS may be its effects on stress-responsive systems, such as the hypothalamic–pituitary–adrenal axis and the autonomic nervous system [10]. Effects of psychosocial stress on stress-responsive systems may be influenced by timing of exposure during lifespan [11, 12] and may be sex specific [13, 14]. Sex- and age-specific pathways on the association between psychosocial stress and FBS should, therefore, be further investigated.

Moreover, objectively measured stressful life events are associated with neuroticism [15, 16]. Yet potential confounding by having a stress-sensitive personality (i.e., trait neuroticism) has usually not been tested in previous studies on the association between psychosocial stress and FBS. When researching the influence of psychosocial stress on physical symptoms, it has been recommended to administer a personality test and examine to what extent and which variance in the stress measure is explained by neuroticism [17]. Likewise, especially in population-based studies, one needs to take into account the distribution of life events according to demographic factors such as socio-economic status. Since it was concluded in a review that adverse life events are more frequent in persons with a low socio-economic status [18] and a low socio-economic status itself is a risk factor for FBS [19], low socio-economic status may act as a confounding factor in the association between life events and FBS. Although life events may also explain part of the increased risk of FBS in low SES populations, SES could act as a confounder given its associations with many other risk factors for FBS such as unhealthy lifestyles and unhealthy living environments [20].

In conclusion, it is unknown to what extent adverse life events are directly associated with FBS, whether there is a critical time frame, whether this association is the same for males and females, and whether this relation exists independently of a stress-sensitive personality or socio-economic status.

This population-based cohort study aims to test whether the generally accepted role of psychosocial stress in the development of FBS is justified and whether there are age- and sex-specific associations. We have the following hypotheses based on previous research. First, the lifetime score of adverse life events increases the risk for FBS in the general population. Second, the effects of adverse life events are stronger in childhood and in females. Third, these associations remain after adjustment for personal (neuroticism) and environmental (socio-economic) factors associated with both psychosocial stress and FBS. Data from a general population of adults, including two measurement waves, were used to examine the hypotheses.

## Methods

### Population

This study has been performed in a cohort derived from PREVENT (Prevention of RENal and Vascular ENd stage Disease), a major Dutch population cohort study investigating risk factors for renal and

cardiovascular disease. The recruitment of participants for PREVENT has been extensively described elsewhere [21]. The PREVENT baseline sample consisted of 8592 subjects randomly selected from the population of the city of Groningen with oversampling for albuminuria (T1). Selection of subjects for the present study was aimed at recruiting a representative sample of the general population of Groningen, while simultaneously rectifying PREVENT's oversampling for albuminuria. Research assistants approached participants in the PREVENT study during their visit to the outpatient clinic during follow-up (2554 participants). Measurements were completed by a total of 1094 participants (43%), forming the present study sample. PREVENT participants who declined to participate in the current study did not significantly differ from those who did participate concerning sex, age, and scores on a 12-item neuroticism scale [22]. Baseline measurements for the present study took place between 2001 and 2002 (T2). Follow-up measurements were made approximately 2 years later, between 2003 and 2004 (T3), and were completed by a total of 976 participants (89%). The study was approved by the University of Groningen medical ethics committee. Written informed consent was obtained from all participants.

### Functional bodily symptoms

FBS were measured by the somatization section of the Composite International Diagnostic Interview (CIDI). The CIDI is a fully structured diagnostic interview developed by the World Health Organization for use in epidemiological studies on mental disorders and provides diagnosis according to *Diagnostic and Statistical Manual, Fourth Edition (DSM-IV)* criteria. A fully computerized version of the CIDI 2.1 was applied, suitable for self-administration. Trained interviewers were present for questions and for participants that needed computer help. In the CIDI somatization section, 43 symptoms are assessed through asking “have you had” this symptom and are considered present when they meet severity criteria, i.e., provoking a health care visit. The symptom sexual indifference was excluded from analysis since it is not surveyed in the CIDI whether this symptom provoked a health care visit. The total number of potential FBS in this study is therefore 42. If the severity criteria are met, the interview assesses in a hierarchical fashion whether a medical doctor diagnosed a symptom as due to physical illness or injury, or whether a symptom was caused by the use of medication, drugs, or alcohol. If these inquiries are negative for medical explanations, the symptom is scored as a FBS. The CIDI has adequate test–retest reliability and validity [23]. Participants first completed the CIDI lifetime version measuring lifetime FBS. A total of 1088 completed CIDs were available at baseline. Two years later, participants were re-interviewed and completed the CIDI 12-months version, in which the occurrence of the 43 symptoms in the previous year is surveyed; 964 completed CIDs were available at follow-up. In the main analyses, we use the sum of all FBS in the previous year, defined as 1-year FBS.

### Adverse life events

The original List of Threatening Experiences (LTE) assesses 12 life events with long-term health consequences [24]. The choice of events on the list was based on earlier work on the social origins of depression [25]. The original LTE was translated in Dutch and applied in a modified version with age categories. Construct reliability was considered acceptable [26]. Participants completed the LTE at home prior to their visit to our research facilities, where a researcher checked with the participant whether the list had been filled out correctly. The original LTE comprises 12 items that were selected for their established long-term consequences [24, 27]. The original LTE asked whether or not these events took place in the previous year. For the purpose of this study, the LTE was extended with the addition of age categories. In addition to the question about the occurrence of adverse life events in the previous

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