The overlap of somatic, anxious and depressive syndromes: A population-based analysis

Sebastian Kohlmann PhD a,⁎,1, Benjamin Gierk MSc a,b,1, Anja Hilbert PhD c, Elmar Brähler PhD c, Bernd Löwe MD a

a Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Hamburg-Eppendorf and Schön Clinic Hamburg Eilbek, Germany
b Department of Psychiatry – Ochsenzoll, Asklepios Clinic Hamburg, Germany
c Integrated Research and Treatment Center Adiposity Diseases & Department of Medical Psychology and Medical Sociology, University of Leipzig, Germany

Abstract

Objective: The comorbidity of somatic, anxious and depressive syndromes occurs in half of all primary care cases. As research on this overlap of syndromes in the general population is scarce, the present study investigated the prevalence of the overlapping syndromes and their association with health care use.

Method: A national general population survey was conducted between June and July 2012. Trained interviewers contacted participants face-to-face, during which, individuals reported their health care use in the previous 12 months. Somatic, anxious and depressive syndromes were assessed using the Somatic Symptom Scale-8 (SSS-8), Generalized Anxiety Disorder-2 (GAD-2) and Patient Health Questionnaire-2 (PHQ-2) respectively.

Results: Out of 2510 participants, 236 (9.4%) reported somatic (5.9%), anxious (3.4%) or depressive (4.7%) syndromes, which were comorbid in 86 (3.4%) cases. The increase in the number of syndromes was associated with increase in health care visits (no syndrome: 3.18 visits vs. mono syndrome: 5.82 visits vs. multi syndromes: 14.16 visits, \( F(2,2507) = 149.10, \( p < 0.00001 \)). Compared to each somatic (semi-partial \( r^2 = 3.4\% \)), anxious (semi-partial \( r^2 = 0.82\% \)) or depressive (semi-partial \( r^2 = 0.002\% \)) syndrome, the syndrome overlap (semi-partial \( r^2 = 6.6\% \)) explained the greatest part of variance of health care use (change in \( R^2 = 11.2\% \), change in \( F(3,2499) = 112.81, p < 0.0001 \)).

Conclusions: The overlap of somatic, anxious and depressive syndromes is frequent in the general population but appears to be less common compared to primary care populations. To estimate health care use in the general population the overlap of somatic, anxious and depressive syndromes should be considered.

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1. Introduction

Somatic, anxiety and depressive disorders are among the most frequently occurring mental disorders in primary care and in the general population [1,2]. Each of these diagnoses is associated with substantial health burdens and increased health care use [3,4]. In primary care settings, however, patients rarely present with a "pure" depressive, anxiety or somatoform disorder. Instead, patients often report a combination of somatic, anxious and depressive syndromes that have been described as the 'Somatization-Anxiety-Depression Triad' [1,5–7]. Thus far, the prevalence of the somatic, anxious and depressive (SAD) syndromes and their overlap has primarily been investigated in patients in primary care and mental health settings [8]. To understand the epidemiology of these highly overlapping mental health syndromes, knowledge of the 'natural' prevalence of the overlap of single SAD syndromes in the general population is vital.

The prevalence of the comorbidity of the SAD syndromes has mainly been investigated in primary care patients: It is estimated that every second patient with one SAD syndrome comorbidly suffers from another of these syndromes [8]. Therefore, it is argued that in primary care patients, "...there is little evidence that depression, anxiety and somatization are separated by natural boundaries" [8]. The data on the overlap of SAD syndromes in the general population are yet not available; studies have investigated the prevalence rates of individual syndromes but have neglected the overlap of single SAD syndromes. These data, however, are crucial for objectively evaluating the overlap of single SAD syndromes at the level of the whole society and using this as the basis of comparison with clinical populations. In addition, knowledge of the overlap of single SAD syndromes is vital to determining whether prevention of the three most common mental health syndromes should focus on each individual syndrome or on all three SAD syndromes [9]. In terms of the comorbidity of psychiatric diagnoses,
one large epidemiological study from Germany concluded that comorbidity is present in 44% of cases with psychiatric diagnoses [2]. The combination of anxiety-affective somatoform disorders occurred in 4.7% of all cases. To design effective prevention programs for psychiatric disorders, it is important to identify risk factors of individuals who are already experiencing mental health syndromes. Regarding the identification of risk factors for the three most common mental health syndromes, it is important to test whether individuals with overlapping SAD syndromes differ in terms of socio-demographic characteristics from individuals with no symptoms, single symptoms or multiple syndromes. Therefore, knowledge of the overlap of SAD syndromes in the general population is of great importance.

SAD syndromes contribute to a major health burden as well as to higher health care costs: Studies conclude that each individual syndrome has been found to be associated with increased health care use [3,4,10,11]. Despite the strong associations between SAD syndromes, however, most studies on health care use have not accounted for this overlap of single SAD syndromes. Thus, it is difficult to identify which syndrome contributes the most to health care use. To the best of our knowledge, only one study from primary care adjusted for the syndrome overlap and concluded that the overlap is associated with health care use rather than the individual syndromes alone [8]. Most studies that tested the association between SAD syndromes and health care use were conducted in primary care patients. However, the estimation of health care use may be biased in a selective sample of health care users because some individuals do not utilize the health care system despite experiencing symptoms [12]. To account for these individuals, data from the general population are necessary. However, data from the general population on health care use and SAD syndromes are rare, and the differential associations of the individual SAD syndromes have not yet been considered. Insights as to how the SAD syndromes overlap and are associated with health care use is important — not only to understand the health-related economic consequences of the three most common mental health syndromes but also to estimate and allocate health care resources.

Whereas previous studies have focused on primary care patients, this is the first study to investigate the overlap of single SAD syndromes in the general population. First, we analyzed the distribution of somatic, anxious and depressive syndromes and their overlap. Second, we tested whether there is a relationship between the number of syndromes and health care use. Third, we estimated the relative associations between each syndrome and the overlap of single SAD syndromes with health care use.

2. Material and methods

2.1. Study participants and study design

The study was part of a national, representative general population survey that analyzed individuals aged 14 years or above in Germany. The data were collected between June and July 2012 by professional demographic consultants (company name: Unabhängige Serviceeinrichtung für Umfragen, Methoden und Analysen, http://www.usuma.com, Berlin, Project No. 120402). A random-route sampling procedure with 320 sample points revealed that 4480 households, 4436 were eligible to participate (i.e., n = 19 flats were vacant, n = 25 persons were younger than 14 years). The households were visited by trained face-to-face interviewers who recorded the participants’ demographic information. Other information was collected via paper-and-pencil self-reports. The interviewers made a maximum of 4 contact attempts per household. The individuals who participated gave oral informed consent. The participants did not receive any reimbursement. The study was approved by the medical ethics board at Leipzig University in Germany.

2.2. Study variables

Somatic symptoms were measured with the Somatic Symptom Scale – 8 (SSS-8) [13]. This questionnaire consists of eight items that measure the burden of common somatic symptoms (e.g., back pain, stomach or bowel problems; chest pain or shortness of breath; and fatigue). The SSS-8 is brief, valid and reliable (α = 0.81). In the present study, Cronbach’s α was 0.82. The cut-off scores allowed for the pragmatic classification of the severity of the somatic symptom burden. In accordance with previous studies, we used a cut-off of ≥2 points for a 0–32-point scale to identify individuals with high somatic symptom burdens [14]. In the present study, we use the term ‘somatic burden syndrome’ to refer to these individuals.

Depression was assessed using the Patient Health Questionnaire – 2 (PHQ-2) [15]. This questionnaire consists of two items that measure the fulfillment of the DSM-5 core criteria of major depression (depressed mood and loss of pleasure) and assesses the cognitive-affective aspect of depression. The PHQ-2 is brief, valid and reliable (α = 0.89). In the present study, Cronbach’s α was 0.74. A cut-off score of ≥3 on a 0–6 point scale is recommended for depression screening [16]. We used this cut-off to identify individuals with high levels of depression. In the present study, we use the term ‘depressive syndrome’ to refer to these individuals.

Anxiety was measured with the Generalized Anxiety Disorder – 2 (GAD-2) [15]. This questionnaire consists of two items that assess the DSM-V core criteria of the generalized anxiety disorder (anxiety and worry) and measures the cognitive-affective aspect of anxiety. The GAD-2 is brief, valid and reliable (α = 0.75). In the present study, Cronbach’s α was 0.75. The GAD-2 has good case-finding properties for the most common anxiety disorders: generalized anxiety disorder, panic disorder, social anxiety disorder, and post-traumatic stress disorder. A cut-off score of ≥3 on a 0–6 point scale is recommended for anxiety screening [17]. We applied this cut-off score to identify individuals with high levels of anxiety. In the present study, we use the term ‘anxious syndrome’ to refer to these individuals. A shortened version of the Health Care Utilization Questionnaire was used to assess health care use [18,19]. The questionnaire comprises 5 items that measure the patient-reported retrospective count of contact with health care providers (e.g., GP visits, days in the hospital, daytime clinic visits) during the last 12 months.

2.3. Statistical analyses

In order to describe the distribution of syndromes, we calculated a cross-table of the following categories: somatic burden syndrome [yes vs. no] × anxious syndrome [yes vs. no] × depressive syndrome [yes vs. no]. Descriptive data are presented as absolute and relative numbers of individuals per cross-table cell. For the analyses investigating health care use, individuals were assigned to three groups based on the degree of burden they reported. The first group included individuals with no syndrome, the second included individuals with one syndrome (i.e., mono anxious syndrome, GAD-2 ≥ 3 points; mono depressive syndrome, PHQ-2 ≥ 3 points; or mono somatic burden syndrome, SSS-8 ≥ 12 points), and the third included individuals with two or three syndromes (i.e., multiple-syndromes). The mean numbers of health care visits were calculated for each group and were compared using an analysis of variance (ANOVA) followed by Tukey post-hoc tests. The group differences in health care use were quantified by using the Cohen’s d effect size measure.

The relative impact of somatic, anxious and depressive symptoms and their overlap in health care use were estimated by using a multiple linear hierarchical regression model. To adjust the analysis for possible covariates, age, gender, living situation, employment status and income were entered ‘block-wise’ as a first step in the hierarchical regression model. As a second step, the continuous scores of the self-report SAD
questionnaires were added. The number of health care visits within the last twelve months was the outcome variable. The total amount of explained variance in health care use was estimated by using the multiple $R^2$ of the regression model. The relative amounts of variance explained by the single predictors were estimated as the squared semi-partial correlations between the predictors and the outcome. The amount of variance in health care use that was explained by the overlap of somatic, anxious and depressive symptoms was calculated as the difference between the multiple $R^2$ of the regression model and the sum of the squared semi-partial correlations of the single predictors.

As a methodological prerequisite, we tested whether the instruments assessed three distinct constructs. Accordingly, we conducted two confirmatory factor analyses: (1) a general factor model with all items loading on one latent dimension and (2) a three-factor model with inter-correlated latent dimensions for somatic, anxious and depressive symptoms. For these analyses, we used mean- and variance-adjusted weighted least square estimations based on a polychoric correlation matrix. Global model fit indices (Tucker-Lewis index [TLI], comparative fit index [CFI], and the root mean square error of approximation [RMSEA]) were compared to determine which model(s) adequately fit(s) the data [20]. The confirmatory factor analyses revealed that a general factor model with all somatic, anxious, and depressive symptoms loading on a single latent dimension did not adequately fit the data (TLI = 0.89, CFI = 0.91, RMSEA [90% CI] = 0.11 [0.11–0.12] [20]). In contrast, a model with three correlated symptom-specific latent dimensions for somatic, anxious, and depressive symptoms achieved acceptable fit parameters (TLI = 0.94, CFI = 0.95, RMSEA [90% CI] = 0.08 [0.08–0.09]). The correlations between the three latent dimensions were very high (r = 0.74 to 0.82) (see Appendix A).

All statistical tests were evaluated using a 0.05 significance level. Missing values were imputed using a hot deck technique [21]. The calculations were performed using SPSS 21 (IBM Corp. SPSS Statistics for Windows, Version 21.0. Armonk, NY.), R 3.0.1 (R Development Core Team (2013) R: A language and environment for statistical computing, Vienna, Austria) and the latent variable analysis R extension package (Lavaan 0.5-14).

### 3. Results

#### 3.1. Sample description

Of the 4436 eligible households, the interviewers had contact with 3736 persons. Of the 3736 individuals, 2538 agreed to participate (67.9% participation rate). However, 23 individuals were excluded due to severe illness that made participation impossible, and 5 individuals were excluded for other reasons. As a result, the data from 2510 individuals were included in the analyses. <1% of the values in the data set were missing. The missing values showed no systematic patterns and were imputed [21]. Table 1 shows the demographic characteristics of the study sample and the samples stratified by number of syndromes.

#### 3.2. Distribution of syndrome overlap

Table 2 shows the distribution of syndromes of the general population. Of the individuals experiencing high levels of symptoms (236 of 2510 individuals; 9.4%), the cut-off score for depression (n = 148; 5.9%) was most often exceeded, followed by somatic symptom burdens (n = 118; 4.7%) and anxiety (n = 84; 3.4%).

Fig. 2 depicts the syndrome overlap of individuals who exceeded at least one cut-off score for a somatic, anxious or depressive syndrome. Whereas 36.4% (86 individuals) experienced burdens in multiple domains, 63.6% (150 individuals) experienced burdens in a single-syndrome domain (i.e., one somatic, anxious, or depressive syndrome).

The distribution in reference to each individual syndrome was as follows: Of the 148 individuals who exceeded the cut-off score for the depressive syndrome, 49.3% (73 individuals) also reported anxious or somatic burden syndrome or both. Of the 84 individuals who exceeded the cut-off score for the anxious syndrome, 71.1% (60 individuals) also reported depressive or somatic syndromes or both. Of the 118 individuals who experienced somatic burden syndrome, 56.8% (67 individuals) also experienced depressive or anxious syndromes or both.

#### 3.3. Health care use

The mean number of health care visits in the last twelve months significantly differed between individuals with no syndrome, one

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**Table 1**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Complete sample</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Differences *</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>2510 (100%)</td>
<td>2274 (90.6%)</td>
<td>150 (6.0%)</td>
<td>86 (3.4%)</td>
<td>None</td>
</tr>
</tbody>
</table>

| Sex (female), N (%) | 1340 (53) | 1212 (53.3) | 83 (55.3) | 45 (52.3) | None |
| Age, Mean (SD) | 49.38 (18.00) | 48.89 (17.86) | 52.65 (19.19) | 56.44 (17.81) | A, B < C |
| Age group, N (%) | 14–24 | 275 (11.0) | 254 (11.2) | 17 (11.3) | 4 (4.7) |
| | 25–34 | 349 (13.9) | 324 (14.2) | 18 (12.0) | 7 (8.1) |
| | 35–44 | 361 (14.4) | 332 (14.6) | 18 (12.0) | 11 (12.8) |
| | 45–54 | 463 (18.4) | 419 (18.4) | 24 (16.0) | 20 (23.3) |
| | 55–64 | 467 (18.6) | 432 (19.0) | 21 (14.0) | 14 (16.3) |
| | 65–74 | 405 (16.1) | 363 (16.0) | 31 (20.7) | 11 (12.8) |
| | ≥75 | 190 (7.6) | 150 (6.6) | 21 (14.0) | 19 (22.1) |
| Living with a partner, n (%) | 1461 (58.2) | 1342 (59.0) | 76 (50.7) | 43 (50.0) | None |
| Years of education, n (%) | 1044 (41.6) | 919 (40.4) | 78 (52.0) | 47 (54.7) | None |
| | <10 | 1039 (41.4) | 968 (42.6) | 47 (31.3) | 24 (27.9) |
| | 10–12 | 427 (17.0) | 387 (17.0) | 25 (16.7) | 15 (17.4) |
| | ≥12 | 1567 (62.4) | 1478 (65.0) | 65 (43.3) | 24 (27.9) |
| Net household income per month, € ≥2500, n (%) | 828 (33.0) | 786 (34.6) | 30 (20.0) | 12 (14.0) |
| | A > B > C | A > B > C |

Note: * Differences between groups tested with ANOVA using Bonferroni-adjustment, significant if p < 0.0167.

Group A: Individuals exceeding no cut-off score.

Group B: Individuals exceeding one cut-off score.

Group C: Individuals exceeding two or more cut-off scores.
syndrome and multiple-syndromes \( (F_{2,2507} = 149.10, p < 0.00001) \). Tukey post-hoc tests revealed that individuals with one syndrome had significantly more health care visits than individuals with no syndrome \((5.82 \text{ vs. } 3.18 \text{ visits, } p < 0.001, \text{ effect size } d = 0.44)\). Similarly, individuals with multiple-syndromes had significantly more health care visits than individuals with no syndrome \((14.16 \text{ vs. } 3.18 \text{ visits, } p < 0.001, \text{ effect size } d = 1.84)\). Finally, individuals with multiple-syndromes had significantly more health care visits than individuals with one syndrome \((14.16 \text{ vs. } 5.82 \text{ visits, } p < 0.001, \text{ effect size } d = 1.40)\). Fig. 1 illustrates this finding.

### 3.4. Relative associations with health care use

Increases in health care use were associated with higher scores on somatic \((\beta = 0.27, p < 0.001)\) and anxious \((\beta = 0.12, p < 0.001)\) symptom questionnaires. In contrast, the depressive symptom score \((\beta = 0.02, p = 0.49)\) was not significantly associated with health care use. The following covariates also showed associations with increased health care use: higher age \((\beta = 0.06, p = 0.013)\), female gender \((\beta = 0.04, p = 0.04)\) and not currently working \((\beta = 0.07, p = 0.008)\). The complete hierarchical regression model explained 16.5% of the variance in health care use \((F_{11,2499} = 55.95, p < 0.001}\). In a first step, covariates were entered in the regression model and accounted for 5.3% of the variance \((\text{change in } F_{2,2507} = 24.29, p < 0.001)\). Compared to the first step of the regression model, the second step — where SAD syndrome questionnaires were entered — explained the larger part of variance in health care use \((\text{change in } F_{3,2499} = 112.81, p < 0.001)\). Of the 11.2% variance explained by SAD symptoms, 0.002% can be attributed to depressive symptoms, 0.82% to anxious symptoms, 3.4% to somatic symptoms and 6.6% to the overlap of somatic, anxious and depressive symptoms.

![Diagram of symptom overlap](image)

**Fig. 1.** The overlap of somatic burden, anxious and depressive syndromes \((N = 236)\). Note: The term ‘syndrome’ refers to the following cut-off scores: Somatic Symptoms Scale-8 ≥ 12 points, Patient Heath Questionnaire-2 ≥ 3 points, Generalized Anxiety Disorder-2 ≥ 3 points. Values indicate the number of individuals and percentages are given in parenthesis.

### 4. Discussion

The present study investigated the overlap of somatic, anxious and depressive syndromes in the general population and tested the differential associations between different syndromes and health care use. The results indicate that 9.4% of the general population experience somatic, anxious or depressive syndromes, which are comorbid in one-third of the cases. The association between the number of syndromes and health care use is linear, and the results suggest that the syndrome overlap, rather than the individual syndromes, shows the strongest association with health care use.

#### 4.1. Distribution and characteristics of SAD syndromes

The theoretical concepts and diagnostic criteria of depressive disorders and most anxiety disorders include somatic symptoms (e.g., having low energy, feeling your heart race, shortness of breath). Thus, on a theoretical level the overlap of single SAD syndromes is already defined.
Data from clinical populations support these theories [22]. Results from this study also support these diagnostic concepts on a population level. In line with previous epidemiological studies, our results suggest that every tenth individual in the general population is affected by a somatic, anxious or depressive syndrome [1]. Our study extends these findings to show that somatic, anxious and depressive syndromes are not separated but occur comorbidly in the general population: While nearly two-thirds of individuals with the syndromes experience only one syndrome, one-third are affected by two or more syndromes. From a clinical perspective, this finding illustrates that each syndrome is more likely to be experienced separately rather than comorbidly in the general population. Thus, it can be assumed that somatic, anxious and depressive syndromes represent distinct categories of mental health burden in the general population [23]. This result partially contrasts with data from primary care patients, where every second patient presents comorbid SAD syndromes [8]. Thus, it may be that individuals from the general population only seek medical help in primary care settings when syndromes occur comorbidly. Interestingly, more than half of the individuals in the current study who experienced a somatic burden syndrome also experienced a comorbid depressive syndrome, anxious syndrome, or both. The assumption that the somatic burden syndrome appears to play a key role in the manifestation of other anxious or depressive syndromes should be investigated longitudinally. In addition, this pattern of SAD syndromes has been repeatedly found in patients with chronic physical conditions [24,25]. Thus, our results raise the question of whether the overlap of single SAD syndromes may play an important role in both the development and adjustment of chronic physical conditions in the general population [3,26].

4.2. SAD syndromes and health care use

Based on previous research from primary care and the general population, we expected to see a positive association between the number of SAD syndromes and health care use [8,12]. Indeed, individuals with only one syndrome had more than twice as much contact with the health care system than individuals with no SAD syndromes. Furthermore, individuals with two or more syndromes had nearly three times as many health care visits than individuals who reported no syndromes. As follows, individuals with SAD syndromes may be a group at risk of using additional health care resources. This assumption is supported by our finding that somatic, anxious and depressive symptoms and their overlap had differential associations with health care use. Whereas the somatic symptom and SAD symptom overlap was substantially related to the number of health care visits, symptoms of anxiety showed only marginal associations with health care use. Accordingly, the number of health care visits in the general population should be estimated on the basis of the SAD overlap rather than each syndrome individually. Interestingly, the symptoms of depression do not appear to be associated with health care use in the general population. In contrast, somatic symptoms appear to be a key motivation to seek medical help. This supports the notion that health care resources may be primarily utilized by individuals presenting with somatic symptoms but not anxious or depressive symptoms [10,27]. Thus, the results also raise the question of whether the mental health stigma prevents individuals with anxious or depressive syndromes to seek medical help. It may be that individuals with severe depressive or anxious symptoms first become aware that they have a problem when somatic symptoms occur comorbidly. To design effective prevention programs, the research should investigate whether treatment needs differ between individuals with different syndromes. As this study is of a cross-sectional nature, future studies should also longitudinally investigate the mechanism underlying the associations between SAD syndromes and increased health care use. Analyses that investigate methods of referral, medical overuse and underuse in individuals with SAD syndromes could offer further insights to improve mental health care services [28].

4.3. Implications

Because somatic, anxious and depressive syndromes are not only frequent but also occur comorbidly in one-third of these cases, a diagnostic screening strategy that assesses all three syndromes should be clearly favored in the general population. The psychometrically well-validated PHQ-2, GAD-2, and SSS-8 comprise only 12 items that reliably assess the three most common mental health syndromes. We want to introduce a combination of these tools, which we call the Patient Health Questionnaire – Somatic-Anxious-Depressive Symptom Screener (PHQ-SADSS; see Appendix B). The simple and efficient PHQ-SADSS instrument is open-source and can be easily implemented in different health care settings. Its use facilitates the early detection of high symptom burdens and therefore may prevent the development and aggravation of single SAD syndromes. As the PHQ-SADSS is short and simple to understand, it can be administered online or in a health app for smartphones. Due to its brevity, the PHQ-SADSS can also facilitate epidemiological research and ecological momentary assessment studies that investigate the interplay of the SAD symptoms with respect to well-being, health care use and the development of severe disorders.

4.4. Limitations

Although the present study is based on a large representative sample of the general population, there are some limitations: First, the data were assessed in Germany and may not be applicable to other countries. However, the German demographic structure is comparable to other Western European countries and the United States. Second, our data were cross-sectional and does not allow cause–effect interpretations to be drawn. The results showing that the overlap of single SAD syndromes is strongly associated with health care use may stimulate longitudinal research. Third, the data on health care use were based on self-reports and may be biased due to memory lapses. Fourth, our assessment did not include a standardized psychiatric interview, and we cannot infer psychiatric diagnoses. However, the assessment was performed in person, missing values were rare, and the questionnaires were psychometrically well validated. Fifth, we were not able to adjust the analysis of health care use for the presence of psychological disorders, somatic diseases, or medication intake. Due to the general population approach, a valid medical assessment was not feasible. However, we assume that the link between somatic symptoms and health care use was not inflated by medical diagnoses because previous studies have demonstrated that the presence of SSS-8 somatic symptoms are unrelated to medical disorders in most cases [29,30]. Sixth, the SSS-8 includes two items (i.e., feeling tired or having low energy, trouble sleeping) that are symptoms of the diagnostic depressive disorder. This may have inflated the number of the overlap of single SAD syndromes. The PHQ-2 was used to account for this possible bias because the PHQ-2 does not include these two items. In addition, our analyses support the factorial independence of the questionnaires (see Appendix A).

5. Conclusions

Every tenth individual in the general population reports SAD syndromes. The syndrome overlap is frequent in the general population but appears to be less common compared to primary care populations. In light of this frequent syndrome overlap and the strong association between the overlap of single SAD syndromes and increased health care use, somatic, anxious and depressive symptoms should be assessed simultaneously. The results of this study raise the question of whether somatic symptoms — rather than depressive or anxious symptoms — appear to be the key motivation to seek medical help. Future studies should longitudinally investigate the underlying mechanisms that link different syndromes with potential medical over- and underuse. To establish effective prevention programs, referral strategies and innovative
References


