Total somatic symptom score as a predictor of health outcome in somatic symptom disorders
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The diagnosis of somatisation disorder in DSM-IV is based on numerous ‘medically unexplained’ symptoms, but this diagnosis has been criticised as the measurement of medically unexplained symptoms is unreliable and the concept is inherently dualistic. These difficulties, together with measurement problems, have meant that many population-based surveys have omitted somatoform disorders, and healthcare planners have tended to ignore these disorders. By contrast, clinical studies have used a checklist of all somatic symptoms and found that total somatic symptom score correlates well with the outcomes of impaired function and medical help-seeking even after adjustment for mental disorders. The current project examined whether these relationships are similar in population-based samples, which are free of any bias related to treatment-seeking. The study aimed to determine whether the associations between somatic symptom score, health status and healthcare use remain after adjustment for important confounders including depression, anxiety and the presence or absence of a medical condition. If so, this would help to determine the value of total somatic symptom score as a clinically useful predictor over and above the presence or absence of depression, anxiety and medical conditions. The present study concerned secondary analysis of data collected in population-based studies and was more comprehensive than previous studies as it included potential key confounders. We hypothesised that total somatic symptom score contributes further to the association with, or prediction of, impairment or healthcare use beyond that of the most important confounders including depression, anxiety and the presence or absence of a medical condition. If this hypothesis is supported this strengthens the validity of syndromes or disorders based on somatic symptom presentations. The study had two secondary aims: (a) to compare total somatic symptom score with medically unexplained symptoms and (b) to examine the effect on outcome of numerous somatic symptoms when this is accompanied by additional health concerns and health anxiety. This combination of burdensome somatic symptoms and other psychological features form part of the diagnostic criteria of DSM-5 ‘somatic symptom disorder’.

Method

Data came from nine population-based studies (total n = 28377). Details are shown in Table 1. The sites were chosen as their samples were all reasonably large, they had used recognised instruments, the investigators were willing and able to send their data to Manchester for analysis (seven sites did so) or they were prepared to analyse their own data in an identical way. The Manchester statistician (B.T.) supplied Oslo and Munich (Early Developmental Stages of Psychopathology (EDSP) study) with SPSS syntax files and excel file templates to this end.

Measurement of somatic symptoms

Five sites used a self-administered questionnaire asking respondents to mark those somatic symptoms that they found bothersome. Two sites each used the Patient Health Questionnaire (PHQ-15) (Marburg and Sri Lanka) and the Zerssen scale (Munich and Dresden); one used the Symptom Checklist-90-Revised (SCL-90-R) somatisation subscale (Bremen) and one site used the Somatic Symptom Inventory (SSI) (Manchester) (Table 1). Four sites used the Composite International Diagnostic Interview (CIDI), which allowed direct comparison between medically unexplained and total number of somatic symptoms (Dresden, Munich (EDSP study), Groningen, Oslo).

We omitted gender-specific (for example painful menstruation) and depression-related items (for example impaired sleep) prior to the creation of a total somatic symptom score. For the self-rated...
questionnaires total somatic symptom score reflected both the number of somatic symptoms and their severity (how bothersome they were). As these symptoms were rated on a three- or four-point scale of severity, their scores ranged as follows: SCL-90-R somatisation items (0–48), PHQ-12 (after removal of gender-specific and depression-related items: 0–24), Zerssen (0–42), SSI (13–52). For the CIDI, after excluding four female-specific items, we agreed a list of 37 somatic symptoms, each of which was rated as present or absent (irrespective of whether they were clinically significant, the effect of drug intake or as a result of a medical condition). Thus, for the CIDI total symptom score was a simple symptom count. For the secondary analysis we examined separately those symptoms that were not fully explainable by a medical condition or have not always been caused by the intake of any substances. These are defined on the CIDI as those symptoms that are 'clinically significant’ (indicated either by seeking help from a medical doctor or other mental health professional, repeated intake of medication or significant distress and interference with daily life because of the symptom) and for which no underlying physical illness had been diagnosed by the doctor and which have not always been the effect of drug intake (such symptoms form the basis of the CIDI diagnostic algorithm for DSM-IV somatoform disorders).

### Covariates

Anxiety and depressive diagnoses or measures of anxiety or depressive symptoms were recorded at all sites (five sites used the CIDI, two used PHQ-9 and PHQ-7 anxiety or ‘GAD-7’20 and by a single question in Sri Lanka.22 At six sites we were able to use a core set of covariates in the multivariate analyses: age, gender, anxiety, depression and general medical illness. At three sites there was no measure of general medical illness (Table 2).

At one site only (Manchester)10 we assessed the proportion of participants who fulfilled the criteria of numerous somatic symptoms, concerns about seriousness of symptoms and marked health anxiety (criteria A and B of DSM-5 somatic symptom disorder). For this purpose we identified those in the top 20% of SSI scores (this corresponds to six somatic symptoms that bothered the respondent quite a bit or worse), and who worried 'quite a bit' or 'a great deal' (a) about there being something seriously wrong with their body and (b) about their health.

### Statistical analysis

In order to demonstrate the distribution of scores in the populations, data are presented in graphical form as a frequency/density plot of total symptom scores (and for medically unexplained symptoms), split by gender, anxiety, depression or physical illnesses.

In order to establish the variables that were correlated with total somatic symptom score at each site we used multiple regression analysis with total somatic symptom score as the dependent variable.
The independent variables were age, gender, anxiety, depression (all sites) and number of general medical illnesses (six sites only). Unstandardised regression coefficients are presented.

In order to test the main hypothesis, we used multivariable analysis to assess the association between somatic symptom score (as an independent variable) and health status and healthcare use (as dependent variables). The following potential confounders were included as independent variables: age, gender, anxiety, depression, general medical disorders (if available) and any other relevant confounders (listed in column 3 in Tables DS1 and DS2). We used multiple regression analysis for continuous dependent variables, logistic regression for dichotomous dependent variables and negative binomial regression when the dependent variable was a number of visits to the doctor. At two sites, no health status or healthcare use data were available. Results presented are standardised regression coefficients for multiple regression analyses, odds ratios per standard deviation for logistic regression or incidence rate ratios per standard deviation for negative binomial regression. This allowed direct comparison of coefficients for total symptom score and medically unexplained symptoms score; the significance of any difference between these was assessed using the stata test command.

To compare total somatic symptom score, number of medically unexplained symptoms and anxiety/depression score as predictors of health status, we used data from Groningen.\textsuperscript{21} We performed receiver operating characteristic (ROC) curve analyses to compare each of these as predictors of five EQ-5D subscales at a 2-year follow-up.

Using data from Manchester\textsuperscript{19} we identified participants with high SSI scores and marked worry about the seriousness of their symptoms and marked health anxiety as defined above. We compared the physical and mental summary scores of SF-12 and the thermometer measure of EQ-5D for this group with the remainder of the participants using ANCOVA to adjust for age, gender, number of general medical illnesses and HADS score. Analyses were carried out in SPSS version 16 or 19, and Stata version 11 on Windows.

### Results

#### Total somatic symptom score in the population

The most common somatic symptoms reported were: back, joint, head and abdominal pains and pain in the extremities. These were reported by 11–77% of respondents on most measures. By contrast, medically unexplained somatic symptoms were reported by 11% or fewer of respondents (online supplements DS1 and DS2).

At all sites the somatic symptom score was distributed as a positively skewed continuous distribution. This was true for total somatic symptom score (Fig. 1) and for medically unexplained symptoms only (Figs 2(c) and 2(d)). The curve is moved to the right in women and for participants who had anxiety or depressive disorder or general medical illnesses (Fig. 1). This effect of anxiety, depressive or general medical disorders is similar for total somatic

<table>
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<th>Table 2</th>
<th>Correlates of somatic symptom scores using multiple regression\textsuperscript{a}</th>
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<tr>
<td><strong>Studies that assessed MUS and total somatic symptom score using CIDI</strong></td>
<td></td>
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<tr>
<td>Lieb et al, Wittchen et al\textsuperscript{13–15} (EDSP study)</td>
<td>Adolescent</td>
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<tr>
<td>Munich, Germany</td>
<td>Adult</td>
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<tr>
<td>Leiknes et al\textsuperscript{16}</td>
<td>Adult</td>
</tr>
<tr>
<td>Rosmalen et al\textsuperscript{17}</td>
<td>Adult</td>
</tr>
<tr>
<td>Groningen, The Netherlands</td>
<td>Adult</td>
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<tr>
<td>Dresden, Germany</td>
<td>Adult</td>
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<td><strong>Studies that assessed total somatic symptom score using questionnaires</strong></td>
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<tr>
<td>Essau\textsuperscript{12}</td>
<td>Adolescent</td>
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<tr>
<td>Bremen, Germany</td>
<td>Adult</td>
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<td>Rief et al, Mewes et al\textsuperscript{17}</td>
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<tr>
<td>Marburg, Germany</td>
<td>Adult</td>
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<tr>
<td>Jacobi et al\textsuperscript{18}</td>
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<td>Dresden, Germany</td>
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<td>Ludwig et al\textsuperscript{19}</td>
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<tr>
<td>Munich, Germany</td>
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<tr>
<td>Creed et al\textsuperscript{20}</td>
<td>Adult</td>
</tr>
<tr>
<td>Manchester, UK</td>
<td>Adult</td>
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<tr>
<td>Sumathipala\textsuperscript{21}</td>
<td>Adult</td>
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</table>

MUS, medically unexplained symptoms; EDSP, Early Developmental Stages of Psychopathology Study; M-CIDI, Munich version of Composite International Diagnostic Interview; CIDI, Composite International Diagnostic Interview; SCL-90-R, Symptom Checklist-90 Revised; PHQ, Patient Health Questionnaire; SSI, Somatic Symptom Inventory; HADS, Hospital Anxiety and Depression scale.

a. The dependent variable was the relevant measure of somatic symptoms used at each site. The independent variables were age, gender, anxiety, depression and general medical illness, where available. Figures are the unstandardised regression coefficient, b, for each correlate.

b. Only included adolescents aged 12–17 years. No measure of physical illness was available. Only depression was entered as a psychiatric diagnosis, since anxiety was only reported by one participant, who also had depression.

c. The PHQ-15 excluding two depression items and one female-only item.
Correlates of total somatic symptom score
The correlates of total somatic symptom score for each site are shown in Table 2. At all sites female gender, anxiety, depression and general medical illnesses (where measured) were significantly correlated with a higher somatic symptom score. Older age was associated with increased number of somatic symptoms at five sites.

Total somatic symptom score and health status
After adjustment for age, gender, anxiety/depression, general medical illness (where available), and other relevant covariates, total somatic symptom score was a correlate of health status at all seven sites where this was assessed (Table DS1). Five of these analyses were cross-sectional, but at the two sites with prospective data (Groningen21 and Manchester10) baseline total somatic symptom score predicted subsequent health status (1–2 years later) after adjustment for confounders.

Total somatic symptom score and healthcare use
In all five cross-sectional analyses, where relevant data were available, total somatic symptom score was significantly correlated with (retrospectively reported) healthcare use after adjustment for confounders (Table DS2). In one prospective study (Manchester10), baseline total somatic symptom score (SSI) was correlated with retrospective, but not prospective, healthcare use.

Comparison of total somatic symptom score and medically unexplained symptoms
At the four sites where we could analyse both, the correlates of number of medically unexplained symptoms were similar to those shown for total somatic symptom score (Table 2, further details available from the authors on request).

For the four sites where data were available (Table DS1) the association with health status, after adjustment for confounders, was stronger for total somatic symptom score than for number of medically unexplained symptoms. This difference was significant for Munich (EDSP study)13–15 ($P = 0.006$); Oslo18 ($P < 0.001$); and Dresden19 ($P < 0.001$ for SF-36 physical but not SF-36 mental component score) and Groningen21 (mobility ($P = 0.044$), self-care ($P = 0.002$), usual activities ($P < 0.001$) and pain/discomfort ($P = 0.007$)).

The prospective data from Groningen21 indicated also that total somatic symptom score was a more accurate predictor of follow-up EQ-5D scores than the number of medically unexplained symptoms (Table 3). For the four EQ-5D subscales except anxiety/depression, the area under the curve (AUC) was significantly greater for total symptom score (AUC = 0.76–0.84) than for medically unexplained symptoms (AUC = 0.61–0.69).

Outcome when both numerous somatic symptoms and additional health concerns and anxiety are present
The data from Manchester10 showed that the participants who had a high total somatic symptom score (SSI score of 26 or more) and who also expressed concerns about the seriousness of their bodily symptoms and marked health anxiety ($n = 23$, 2.5% of the sample) had more impaired health status than participants who had a low...
Discussion

Main findings
This study has two new important findings. First, whichever somatic symptom measure was used, total somatic symptom score was associated with female gender, anxiety, depression and general medical illness at all sites where these were measured. Second, and most importantly, after adjustment for these confounders, total somatic symptom score was associated with health status and healthcare use in cross-sectional analyses and predicted health status in the two prospective studies. Furthermore, our results suggest strongly that the association with (physical) health status and healthcare use was somewhat stronger for total somatic symptom score than for number of medically unexplained symptoms alone. We were able to test, at one site only, whether outcome is impaired most markedly when a high total somatic symptom score was accompanied by high health anxiety and marked concern about the seriousness of bodily symptoms, and found this to be the case.

Strengths and limitations
The study has strengths and limitations that must be recognised. One of the main limitations of this study is the variety of instruments used at the different sites, which meant that we were not able to combine the results from different sites or make exact comparisons between sites. Another limitation was that, at most sites, we had only a checklist of medical illnesses completed by the respondent and we did not have a measure of severity of general medical illnesses. Only at two sites were the medical diagnoses verified by a doctor. We found that general medical illness was an important confounder of the association between

Table 3

<table>
<thead>
<tr>
<th>EQ-SD scores</th>
<th>Mobility</th>
<th>Self-care</th>
<th>Usual activities</th>
<th>Pain/discomfort</th>
<th>Anxiety/depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total somatic symptom score, AUC (95% CI)</td>
<td>0.76 (0.73–0.80)</td>
<td>0.84 (0.78–0.89)</td>
<td>0.77 (0.73–0.81)</td>
<td>0.77 (0.74–0.80)</td>
<td>0.68 (0.63–0.72)</td>
</tr>
<tr>
<td>Number of MUS, AUC (95% CI)</td>
<td>0.62 (0.57–0.67)</td>
<td>0.61 (0.49–0.73)</td>
<td>0.67 (0.62–0.72)</td>
<td>0.69 (0.65–0.72)</td>
<td>0.67 (0.62–0.71)</td>
</tr>
<tr>
<td>Difference between AUC for total somatic symptom score and AUC for MUS, P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.002</td>
<td>&lt;0.001</td>
<td>0.76</td>
</tr>
<tr>
<td>Symptom Checklist (SCL-8) score, AUC (95% CI)</td>
<td>0.60 (0.55–0.65)</td>
<td>0.73 (0.65–0.82)</td>
<td>0.71 (0.67–0.75)</td>
<td>0.64 (0.61–0.68)</td>
<td>0.82 (0.78–0.85)</td>
</tr>
</tbody>
</table>

AUC, area under the curve derived from receiver operating characteristic curve analysis; SCL, Symptom Checklist; MUS, medically unexplained symptoms.

* Comparison of Composite International Diagnostic Interview (CIDI) symptoms over previous year using total somatic symptom score and medically unexplained symptoms only as predictors of EQ-SD scores at 2-year follow-up. Data for five EQ-SD scores (mobility, self care, etc.) scored as any problem in each domain vs. no problem.
number of somatic symptoms and outcome, accounting for a proportion of the variance similar to that of depression or anxiety. It is possible that severity of general medical illness might have accounted for a greater proportion of the variance; this has been inadequately considered in most previous studies. The inclusion of a single site from a different culture (Sri Lanka)\(^22\) is also a limitation; a greater number of sites from different cultures would be necessary before making any observation about the relationship between variables across different cultures.

On the other hand, the similarity of the results across sites, even though different measures were used, might be regarded as a strength as well as a limitation, as it suggests greater generalisability of the findings. This variation also applies to the measures of covariates (anxiety, depressive and general medical disorders), which differed at the different sites. More prospective studies are required as somatic symptoms have been excluded from many large-scale epidemiological studies, in spite of the high frequency of somatiform disorders in population studies.\(^4,6,32,33\)

The total number of participants in this study (total \(n = 28\,377\)) makes this the largest study of its kind and the samples were all population based, thus removing the possibility of bias from treatment-seeking and weighting towards patients with mental health concerns, which is a limitation of primary care studies in the area.\(^34\)

**Explanation for our findings**

There is a very close relationship between number of somatic symptoms, anxiety/depression and general medical illness. The number of somatic symptoms in chronic general medical illness increases with anxiety and depression\(^35\) but we have shown in this study that somatic symptoms, number of reported general medical illnesses and anxiety/depression are all independent correlates of health status. It is known that numerous somatic symptoms predict a poor outcome of depressive disorder\(^36\) and a poor outcome of medical disorders.\(^37\) In this study we have shown that this negative impact of numerous somatic symptoms on outcome is a general one found in studies at several different sites, even after adjustment for confounders.

The association between total somatic symptom score and health status may have been stronger than that for medically unexplained symptoms because total somatic symptom score includes a measure of how bothersome each symptom is regarded to be by the respondent. This leads to a larger spread of scores and, in addition, includes a dimension of emotional response associated with the somatic symptom, which may add to the predictive value of the measure. This explanation cannot explain the difference between CIDI total symptom score and CIDI medically unexplained symptoms (Table DS1), as both were simple symptom scores.

There has been one previous large study of primary care attenders that demonstrated that the association between numerous somatic symptoms and impaired health status occurred with both medically explained and medically unexplained somatic symptoms; the association was strongest for people with both types of somatic symptoms.\(^6,38\) One clinic study has shown that the pattern of association between number of somatic symptoms and health status and healthcare costs was very similar whether the presenting symptoms were medically explained or unexplained.\(^37,39\) This association has been demonstrated recently in cancer and sickle cell disease, where it may be impossible to distinguish explained and unexplained somatic symptoms.\(^40,41\)

Our study demonstrated that even medically unexplained symptoms are associated with general medical illness. Such findings suggest that the adverse effect on outcome of multiple bothersome somatic symptoms may affect all patients whether or not they have general medical illnesses. This moves away from the view that patients with medically unexplained symptoms are a separate group; a fact that has been recognised in the DSM-5 somatic symptom disorder diagnostic category.\(^1\)

**Implications**

Diagnostic concepts in mental health disciplines may not be separated by natural boundaries but many have high clinical utility as they provide useful information concerning outcome, aetiology and treatment response.\(^42\) Within this framework, our findings are important in identifying total somatic symptom score as a predictor or correlate of outcome (health status and healthcare use), independent of anxiety, depression and general medical illnesses. Thus, somatic symptoms cannot be regarded as primarily a reflection of concurrent anxiety and depression.\(^43\) Indeed, there is some evidence that the number of somatic symptoms is a predictor of treatment response in depression as well as other conditions.\(^44-46\) Our findings support the validity of a separate dimension based on numerous bothersome somatic symptoms that could be a useful measure in clinical or epidemiological studies aimed at predicting health status. A diagnostic category, such as that in DSM-5, that includes distressing somatic symptoms as one criterion, should have greater clinical utility than one based on medically unexplained somatic symptoms.

Further prospective studies are needed to replicate the results presented here that total somatic symptom score is a predictor of subsequent health status and to determine whether this does indeed predict subsequent healthcare use. From the data presented...
here it seems likely that a short questionnaire measuring bothersome somatic symptoms might be used in large-scale population-based studies to clarify the true importance of somatic symptoms as a predictor of outcome.\(^1\)

The analysis of data from a single site in this study suggests that the presence of certain psychological features (criteria B of the new DSM-5 diagnosis) as well as numerous bothersome symptoms describes a group with greater impairment of health status. However, this result is limited by small numbers.

In sum, these findings are important in view of the changes to the diagnostic criteria for DSM-5 somatic symptom disorder, which move away from ‘medically unexplained symptoms’ as the core diagnostic feature to ‘any severely distressing somatic symptoms’.\(^3\)

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**References**


