Association between somatic symptom burden and health-related quality of life in people with chronic low back pain

Tomoko Fujii1*, Hiroyuki Oka1, Junji Katsuhira2, Juichi Tonosu3, Satoshi Kasahara4, Sakae Tanaka5, Ko Matsudaira1

1 Department of Medical Research and Management for Musculoskeletal Pain, 22nd Century Medical & Research Center, Faculty of Medicine, University of Tokyo, Tokyo, Japan, 2 Department of Prosthetics & Orthotics and Assistive Technology, Faculty of Medical Technology, Niigata University of Health and Welfare, Niigata, Japan, 3 Department of Orthopaedic Surgery, Kanto Rosai Hospital, Kanagawa, Japan, 4 Department of Pain and Palliative Medicine, Faculty of Medicine, University of Tokyo, Tokyo, Japan, 5 Department of Orthopaedic Surgery, Faculty of Medicine, University of Tokyo, Tokyo, Japan

* ort4771@gmail.com

Abstract

Depression is a relevant risk factor for low back pain and is associated with the outcomes of low back pain. Depression also often overlaps with somatisation. As previous studies have suggested that somatisation or a higher somatic symptom burden has a role in the outcomes of low back pain, the aim of the present cross-sectional study was to examine whether somatic symptom burden was associated with health-related quality of life in individuals with chronic low back pain independent of depression. We analyzed internet survey data on physical and mental health in Japanese adults aged 20–64 years with chronic low back pain (n = 3,100). Health-related quality of life was assessed using the EuroQol five dimensions (EQ-5D) questionnaire. Somatic symptom burden and depression were assessed using the Somatic Symptom Scale-8 (SSS-8) and the Patient Health Questionnaire-2 (PHQ-2), respectively. SSS-8 score was categorized as no to minimal (0–3), low (4–7), medium (8–11), high (12–15), and very high (16–32). The association between SSS-8 and EQ-5D was examined using linear regression models, adjusting for depression and the number of comorbid diseases. A higher somatic symptom burden was significantly associated with a lower health-related quality of life independent of depression and the number of comorbid diseases (regression coefficient = 0.040 for SSS-8 high vs. very high and 0.218 for non to minimal vs. very high, p trend <0.0001). In conclusion, somatic symptom burden might be important for the health-related quality of life of individuals with chronic low back pain.
Competing interests: All authors declare the following potential conflicts of interest outside the submitted work. KM received the following support: grant support, including an endowed chair from Sumitomo Dainippon Pharma Co., Ltd. and Okamura Corporation; grant support, including an endowed chair and lecture fees from AYUMI Pharmaceutical Corporation, Nippon Zoki Pharmaceutical Co., Ltd., Ono Pharmaceutical Co., Ltd., Eli Lilly Japan K.K., Astellas Pharma Inc., TOTO LTD., and Eisai Co., Ltd.; lecture fees from Pfizer Japan Inc., Hisamitsu Pharmaceutical Co., Inc., Janssen Pharmaceutical K.K., Kaken Pharmaceutical Co., LTD., and Teijin Pharma Limited; and lecture fees and advisory fees from Shionogi & Co., Ltd., outside the submitted work. HO received grants from Teijin Pharma Limited, grants from Pfizer Inc., grants from Fujifilm Medical Co., Ltd., grants and personal fees from AYUMI Pharmaceutical Corporation, grants and personal fees from Nippon Zoki Pharmaceutical Co., Ltd., grants and personal fees from Ono Pharmaceutical Co., LTD., and grants from Eli Lilly Japan K.K. outside the submitted work. ST received personal fees for expert testimony from Amgen Inc., Asahi Kasei Pharma Corporation, Amgen Astellas BioPharma K.K., Ono Pharmaceutical Co., LTD., Kyocera Medical Corporation, Daiichi Sankyo Company, Limited, Teijin Pharma Limited, Eli Lilly Japan K.K., and Pfizer Japan Inc.; endowments from Astellas Pharma Inc., AYUMI Pharmaceutical Corporation, Pfizer Japan Inc., Bristol-Myers Squibb, Daiichi Sankyo Company, Limited, and Chugai Pharmaceutical Co., Ltd.; and grants from the Japan Agency for Medical Research and Development (AMED), the Japan Society for the Promotion of Science (JSPS)/Grant-in-aid for Scientific Research (A), and the Japan Society for the Promotion of Science (JSPS)/Grant-in-aid for Exploratory Research outside the submitted work. This does not alter our adherence to PLOS ONE policies on sharing data and materials. The authors have no other declarations relating to employment, consultancy, patents, products in development, or marketed products for Eli Lilly Japan K.K. TF, JK, JT, and SK have no competing interests to report.

Introduction

Low back pain (LBP) is a common musculoskeletal health problem. Approximately 80% of people experience LBP at some point during their lifetime [1]. Globally, LBP is the leading cause of years lived with a disability [2]. Therefore, LBP is a significant public health issue.

The etiology of LBP is multifactorial. Individual, physical, and psychosocial factors such as depression are associated with a risk of developing LBP [3–5]. Notably, depression is also a predictor of chronicity [4, 6]. Quality of life is lower in patients with chronic LBP and depression compared to those without depression [7]. Direct health care costs are higher in LBP patients with depression compared to those without depression [8]. Therefore, assessment of depressive symptoms in patients with LBP may be important for predicting prognosis and choosing treatment options in clinical care settings.

Somatisation, which often coexists with depression [9], is defined by Lipowski as “a tendency to experience and communicate somatic distress in response to psychosocial stress and to seek medical help for it” [10]. A systematic review pointed out that most previous studies of pain have used questionnaires on somatic complaints to assess somatisation, which may not account for the full range of the concept of “somatisation” as defined by Lipowski and recommended to use the term “multiple physical symptoms” rather than “somatisation”[11]. Nevertheless, there is some evidence that a higher somatic symptoms burden or “somatisation” is playing some role in LBP. One study reported that the comorbidity of somatic symptoms predicted the development of persistent LBP in the individuals with mild LBP [12]. Another study found that somatisation at baseline, assessed based on the number of medically unexplained symptoms, predicted treatment outcome in patients with LBP [13]. Although depression has been studied in association with LBP, currently, the role of somatic symptom burden in chronic LBP (CLBP) has not been fully explored.

Several self-reported questionnaires have been used to assess common somatic symptoms. A recent systematic review reported that the Patient Health Questionnaire-15 (PHQ-15) and the 12-item Symptom Checklist-90 somatization scale are the most suitable questionnaires for use in large-scale studies [14]. These questionnaires survey relevant symptoms, are relatively short, and have well-established psychometric properties. The Somatic Symptom Scale-8 (SSS-8) was developed as an abbreviated 8-item version of the PHQ-15 [15]. The aim of the present cross-sectional study was to examine whether somatic symptom burden assessed using the SSS-8 is associated with health-related quality of life (HRQoL) in Japanese individuals with CLBP independent of depressive symptoms. We hypothesized that a higher somatic symptom burden is associated with lower HRQoL for patients with CLBP.

Materials and methods

Participants

Japanese adults aged between 20–64 years with CLBP (n = 3,100) were included in the present study. The data were acquired from a large internet survey on physical and mental health that was conducted in February of 2015. Participants were recruited by an internet research company, United Inc. (Tokyo, Japan), with which more than 1.37 million individuals across Japan have voluntarily registered. The only inclusion criterion for the survey was an age of 20–64 years. Of the approximately 1.25 million eligible individuals, 270,000 were randomly selected and invited by e-mail to complete the online questionnaire on February 6 2015. We expected that the response rate would be approximately 30% and that approximately 50,000 people would respond within 10 days. The survey was closed on February 16 2015. The questionnaire
was configured to automatically reject incomplete responses. All respondents (n = 52,353) gave their consent and were compensated.

A question with an illustration showing the area of pain asked whether a participant had LBP in the past four weeks that may be accompanied with leg pain or numbness, lasted for ≥ one day, and was not related to a menstrual period, pregnancy, or common cold. The following responses were possible: 1) I did not have LBP; 2) I had LBP without difficulty with activities of daily living (ADL); 3) I had LBP with ADL difficulty but without requiring absence from social activities, such as work or school; and 4) I had LBP requiring absence from social activities, such as work or school. Additionally, respondents were asked whether their current LBP lasted for ≥3 months. Individuals with CLBP were defined as those who had LBP with ADL difficulty or sick leave (response 3 or 4 in the first question) which lasted for ≥3 months (affirmative response in the second question), and all respondents with CLBP (n = 3,100) were included in the current analysis. The institutional review board of the University of Tokyo approved this study.

Assessments

**Somatic symptom burden.** Somatic symptom burden was assessed using the Japanese version of the SSS-8, a self-administered questionnaire. The SSS-8 was developed as an abbreviated 8-item version of the PHQ-15 to assess the presence and severity of common somatic symptoms [15]. The PHQ-15 has been used worldwide [16–21]. The SSS-8 assesses how much the respondent has been bothered by the following somatic symptoms during the past 7 days: 1) stomach or bowel problems; 2) back pain; 3) pain in the arms, legs, or joints; 4) headaches; 5) chest pain or shortness of breath; 6) dizziness; 7) feeling tired or having low energy; and 8) having trouble sleeping. Each item is scored 0 (not at all) to 4 (very much) [22]. The SSS-8 was used as a reference measure in the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) (DSM-5) field trials to facilitate the diagnosis of somatic symptom disorder [23]. The German version of the SSS-8 has good reliability and validity for the general German population [22]. We translated the English version of the SSS-8 into Japanese [24]. The Japanese version of the SSS-8 has been linguistically and psychometrically validated [25]. The total SSS-8 score (0–32) was categorized as in Gierk et al. [22] into five groups as follows: no to minimal (0–3); low (4–7); medium (8–11); high (12–15); and very high (16–32).

**Depressive symptoms.** Depressive symptoms were assessed using the Patient Health Questionnaire-2 (PHQ-2), an assessment comprising two questions from the original Patient Health Questionnaire-9 [26]. The questions assess whether the respondent has experienced depression and anhedonia within the past 2 weeks. Although each item is rated on a scale of 0–3 in the original PHQ-2, the present study used the National Center of Neurology and Psychiatry version of the Japanese PHQ-2, which gives each item a binary response of yes or no [27]. Thus, the possible scores for PHQ-2 were 0, 1, or 2.

**HRQoL.** HRQoL was assessed using the 3-level version of the EuroQol five dimensions (EQ-5D-3L) questionnaire that measures general health status [28]. The EQ-5D contains five questions assessing mobility, self-care, usual activities, pain/discomfort, and anxiety/depression [28]. Responses are converted into a single index score of general health status ranging from −0.11 to 1.00; a score of 1 indicates perfect health and a score of 0 indicates death. The Japanese version of the EQ-5D contains has been approved by the EuroQol Group and is widely used in research [29]. Because the present study was based on the internet survey, we did not assess the visual analog scale (EQ-VAS).

**Covariates.** Information on age, gender, body weight, height, marital status, education, employment status, and current smoking status were collected through a self-administered
questionnaire. The respondents were asked to choose one response for marital status, education and employment status: current marital status (1. married, 2. never married, 3. divorced and 4. widowed), education background (1. middle school, 2. high school, 3. vocational school, 4. higher professional school, 5. college, 6. undergraduate, 7. graduate, and 8. other), and employment status (1. regular employee, 2. part-time worker, 3. temporary worker, 4. business executives, 5. family business worker, 6. home worker, 7. student, 8. housewife or husband, 9. without an occupation, and 10 other). Smoking status was asked using a single question “Have you ever smoked ≥100 cigarettes or been smoking for ≥6 months and smoked sometimes or every day during the past month?” Participants were asked whether they performed exercises regularly over the past year, such as walking and jogging that lasted for ≥30 minutes. The possible responses were none, 1–2 times per month, once per week, or more than twice per week. Having regular exercise was defined as exercising more than twice per week. Participants were asked to answer whether they were seeking treatment for the following chronic conditions with yes/no response: hypertension, heart disease, dyslipidemia, lung disease, diabetes, gastrointestinal disease, renal disease, liver disease, anemia/hematological disease, thyroid disease, cancer, gynecological disease, urological disease, skin disease, sleep apnea, other otolaryngological disease, eye disease, dental problems, osteoarthritis, headache, rheumatoid arthritis, fibromyalgia, osteoporosis, obesity, and others. Two questions very similar to those about LBP asked whether the respondent had knee pain. Body mass index (BMI) was calculated based on the self-reported body weight and height as weight (kg)/height (m)².

Statistical analysis
Initially, the characteristics of the participants were examined using descriptive statistics such as the mean and percentage and were compared between PHQ-2 groups using Kruskal-Wallis test for continuous variables and chi-square test for categorical variables. To assess the crude correlation between SSS-8 total scores and EQ-5D scores, Spearman correlation coefficient was estimated. To examine the association between somatic symptom burden assessed using SSS-8 and EQ-5D score, linear regression models were used. Because we assumed that relatively high somatic symptom burden would be more problematic rather than one score change in SSS-8, and because of possible non-linear association, we used five categories for SSS-8 scores as the primary independent variable. Model 1 was a crude model which included only SSS-8 as the independent variable. Model 2 included SSS-8 and depression (as measured using the PHQ-2) simultaneously. An interaction between the SSS-8 and PHQ-2 was not statistically significant. Model 3 was further adjusted for age (continuous), sex, and BMI. Model 4 was further adjusted for lifestyle and individual factors: smoking status (yes/no), marital status (married or other), education (≥college degree or other), regular exercise (yes/no), and employment status (regular employee or other). Model 5, the final model, was further adjusted for the number of comorbid diseases (0–25). The p-value for linear trend for the association between SSS-8 and EQ5D was obtained by treating five SSS-8 categories as the ordinal variable. These potential confounders, which would be associated with both somatic symptom burden and EQ5D, were chosen a priori. We did not use methods such as stepwise selection for model building, because these methods could lead to overfitted models and data-driven results. Multicollinearity was not suspected, with all variance inflation factors (VIFs) being < 2. A stratified analysis by sex and age was conducted exploratory. The participants were relatively homogenous in terms of age (20–64). Therefore, we split the participants into two groups: those younger than 50 and those older than 50 years. Significance of interaction by sex, age, or sex-age group was tested. Analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, NC, USA). All analyses were two-sided and an α-level of 0.05 was considered statistically significant.
Results

The characteristics of the participants are shown in Table 1. The mean age of the participants was 44.5 ± 11.2 and 48% were women. The PHQ-2 score was 0 in 1,576 (51%) participants, 1

Table 1. Characteristics of the participants with chronic low back pain.

| All | PHQ-2 = 0 | PHQ-2 = 1 | PHQ-2 = 2 | p-value |
|-----|-----------|-----------|-----------|---------|
| (n = 3100) | (n = 1576) | (n = 632) | (n = 892) |         |
| Age, mean (SD) | 44.5 (11.2) | 45.8 (11.0) | 44.5 (11.5) | 42.1 (11.1) | < .0001 |
| Women, n (%) | 1483 (47.8) | 743 (47.1) | 311 (49.2) | 429 (48.1) | 0.669 |
| BMI, n (%) | 2333 (75.3) | 1184 (75.1) | 484 (76.6) | 665 (74.6) | 0.018 |
| Current smoking, n (%) | 1064 (34.3) | 489 (31.0) | 233 (36.9) | 342 (38.3) | 0.0004 |
| Marital status, n (%) | 1327 (42.8) | 544 (34.5) | 299 (47.3) | 484 (54.3) | < .0001 |
| Education, n (%) | 1829 (59.0) | 876 (55.6) | 411 (65) | 542 (60.8) | 0.043 |
| Regular exercise, n (%) | 2487 (80.2) | 1222 (77.5) | 524 (82.9) | 741 (83.1) | 0.001 |
| Employment status, n (%) | 1271 (41.0) | 700 (44.4) | 221 (35) | 350 (39.2) | 0.0001 |
| Number of comorbid disease, mean (SD) | 1.2 (2.0) | 1.0 (1.8) | 1.3 (2.0) | 1.4 (2.3) | < .0001 |
| Chronic knee pain | 639 (20.6) | 239 (15.2) | 148 (23.4) | 252 (28.3) | < .0001 |
| EQ-5D, mean (SD) | 0.78 (0.18) | 0.84 (0.16) | 0.75 (0.17) | 0.70 (0.17) | < .0001 |
| SSS-8 items, n (%)† | 944 (30.5) | 349 (22.1) | 197 (31.2) | 398 (44.6) | < .0001 |
| Stomach or bowel problems | 2192 (70.7) | 1052 (66.8) | 476 (75.3) | 664 (74.4) | < .0001 |
| Back pain | 1336 (43.1) | 573 (36.4) | 301 (47.6) | 462 (51.8) | < .0001 |
| Pain in arms, legs, or joints | 1004 (32.4) | 383 (24.3) | 206 (32.6) | 415 (46.5) | < .0001 |
| Headaches | 570 (18.4) | 161 (10.2) | 133 (21) | 276 (30.9) | < .0001 |
| Chest pain or shortness of breath | 616 (19.9) | 205 (13) | 130 (20.6) | 281 (31.5) | < .0001 |
| Dizziness | 1464 (47.2) | 475 (30.1) | 340 (53.8) | 649 (72.8) | < .0001 |
| Feeling tired or having low energy | 1077 (34.7) | 326 (20.7) | 251 (39.7) | 500 (56.1) | < .0001 |
| Trouble sleeping | 590 (19.0) | 445 (28.2) | 77 (12.2) | 68 (7.6) | < .0001 |
| Low (4–7) | 785 (25.3) | 488 (31.0) | 152 (24.1) | 145 (16.3) | < .0001 |
| Medium (8–11) | 616 (19.9) | 297 (18.9) | 156 (24.7) | 163 (18.3) | < .0001 |
| High (12–15) | 505 (16.3) | 186 (11.8) | 122 (19.3) | 197 (22.1) | < .0001 |
| Very high (16–32) | 604 (19.5) | 160 (10.2) | 125 (19.8) | 319 (35.8) | < .0001 |

*p-value based on a chi-square test or Kruskal-Wallis test.
†Those who were bothered at least somewhat.
Abbreviations: SD, standard deviation; BMI, body mass index; EQ-5D, EuroQol Five Dimension; SSS-8, the Somatic Symptom Scale-8

https://doi.org/10.1371/journal.pone.0193208.t001
in 632 (20%), and 2 in 892 (29%). In these individuals with chronic LBP, 20.6% answered they had chronic knee pain. The mean EQ-5D score was 0.78 ± 0.18, and this score decreased as the PHQ-2 score increased. Mean SSS-8 score was 9.67 ± 6.68. As the PHQ-2 score increased, the proportion of individuals with a very high SSS-8 score increased. SSS-8 total score and EQ5D score were significantly negatively correlated (Spearman correlation coefficient = -0.55, p-value < 0.0001). The results of the regression models are shown in Table 2. In the crude model, SSS-8 categories were significantly associated with EQ-5D. EQ-5D scores were lower in those who had higher SSS-8 scores. With the adjustment for PHQ-2, regression coefficients for SSS-8 were attenuated greater than 10%, but the SSS-8 categories were significantly associated with EQ-5D scores independent of the PHQ-2 score. The PHQ-2 score was also independently associated with EQ-5D. Adjustment for demographic, lifestyle and other individual variables did not change the estimates essentially. In the final multiple model adjusted for the number of the comorbid conditions, the regression coefficients for SSS-8 were further attenuated but the association was still significant. Individuals with CLBP and a higher SSS-8 score had lower EQ-5D scores (regression coefficient $\beta = 0.040$ for SSS-8 high vs. very high, and $\beta = 0.218$ for non to minimal vs. very high, p-trend<0.0001).

The results of the stratified analysis by sex, age and sex-age group are shown in Table 3. The results were consistent with those in the overall sample. Although the p-values for high SSS-8 in men aged ≥50 year and women aged ≥50 years were >0.05, this could be due to the small sample size in these groups. No significant interaction by age, sex or age-sex categories was found.

**Discussion**

We found that a higher somatic symptom burden was associated with lower EQ-5D scores independent of depressive symptoms and the number of comorbid diseases in Japanese
individuals with CLBP. The results were consistent across sex and age. The difference in EQ-5D between SSS-8 high vs. very high was 0.04 and was 0.22 for SSS-8 non to minimal vs. very high among all participants. Yoshizawa et al. reported that the minimal clinically important change (MCIC) of EQ-5D in Japanese with chronic noncancer pain was 0.10 [30]. Soer et al. reported a MCIC of EQ-5D as 0.03 in patients with chronic LBP in Netherland [31]. According to these studies, the differences in EQ-5D between SSS-8 groups would be clinically meaningful. Our result suggests that somatic symptom burden is important for the quality of life of individuals with CLBP.

Somatisation is defined by Lipowski as “a tendency to experience and communicate somatic distress in response to psychosocial stress and to seek medical help for it” [10]. Somatisation, depression, and anxiety are frequent mental disorders in primary health care, and often overlap in patients [9]. Depression has been studied extensively, and it is established that depression is a predictor of the chronicity of LBP [4, 6]. Somatisation has also been studied for LBP and other pain research. Nonetheless, the assessment of “somatisation” is problematic. Crombez et al. noted in their systematic review that most previous studies of pain have used questionnaires on somatic complaints to assess somatisation, which may not account for the

| Parameters | Men | Women | Total |
|------------|-----|-------|-------|
| Intercept  | β   | SE    | p-value |
| Age <50 years | 0.799 | 0.031 | <.0001 |
| SSS-8†     | 0.229 | 0.018 | <.0001 |
| No to minimal | 0.200 | 0.016 | <.0001 |
| Low        | 0.156 | 0.016 | <.0001 |
| Medium     | 0.107 | 0.017 | <.0001 |
| High       | 0.052 | 0.017 | 0.003 |
| Very high  | reference | reference | reference |
| n = 996    |     |       |       |
| Age ≥50 years | 0.917 | 0.087 | <.0001 |
| SSS-8†     | 0.229 | 0.023 | <.0001 |
| No to minimal | 0.207 | 0.021 | <.0001 |
| Low        | 0.147 | 0.022 | <.0001 |
| Medium     | 0.106 | 0.022 | <.0001 |
| High       | 0.038 | 0.025 | 0.123 |
| Very high  | reference | reference | reference |
| n = 621    |     |       |       |
| Total      | 0.782 | 0.021 | <.0001 |
| SSS-8†     | 0.229 | 0.014 | <.0001 |
| No to minimal | 0.205 | 0.012 | <.0001 |
| Low        | 0.153 | 0.013 | <.0001 |
| Medium     | 0.108 | 0.013 | <.0001 |
| High       | 0.047 | 0.014 | 0.001 |
| Very high  | reference | reference | reference |
| n = 1617   |     |       |       |

SSS-8†: no to minimal (0–3); low (4–7); medium (8–11); high (12–15); very high (16–32)

Adjusted for PHQ-2, continuous age, sex (when not be stratified), body mass index, smoking, marital status, education, regular exercise, employment status, and the number of chronic diseases

β, coefficient; SE, standard errors; SSS-8, the Somatic Symptom Scale-8; PHQ-2, Patient Health Questionnaire-2

https://doi.org/10.1371/journal.pone.0193208.t003
full range of the concept of “somatisation” as defined by Lipowski, such as whether symptoms were not explained by pathological findings and whether the individual was attributing the symptom to physical illness and seeking medical help for it. The authors recommended using the term “multiple physical symptoms” rather than “somatisation”[11]. The authors also warn that somatisation scores could be elevated artificially by the somatic symptom that is the primary complaint, such as LBP.

Nevertheless, there is some evidence that somatic symptoms burden or “somatisation” is associated with HRQoL. Somatisation, depression, and anxiety can coexist, but each of them may have an independent role in HRQoL. Lowe et al. reported that depression, anxiety, and somatisation were each independently associated with Short-Form General Health Survey (SF-20) scores in primary clinic patients, although the effect size of each was only small to moderate [9]. In this study, somatisation was defined as a PHQ-15 score of $\geq$ 15. The authors discussed that using this high threshold would reflect somatisation and not just somatic symptom severity. A review of nine population-based studies found that total somatic symptom scores were associated with healthcare use and predicted health status independent of depression, anxiety, and a number of general medical illnesses [32]. We adjusted for the counts of chronic conditions as in this review study to try to consider the comorbid disease and to reflect how much individuals were bothered by somatic symptoms, which is one nature of somatisation. Our study results were consistent with these previous studies, showing that somatic symptom burden is associated with HRQoL independent of depression and the number of comorbid diseases in a group of individuals with CLBP.

Previous studies suggest that somatisation has a role in the outcomes of LBP [6]. Matsudaira et al. reported that the comorbidity of somatic symptoms, as assessed using the brief job stress questionnaire (BJSQ), was associated with the development of persistent LBP in urban Japanese workers with mild LBP [12]. In patients with LBP that were treated by chiropractors, somatisation at baseline that was assessed using the Four Dimensional Symptom Questionnaire was associated with pain intensity, functional status, and perceived recovery [33]. In hospital patients with LBP, baseline somatisation based on the number of symptoms for which physicians could find no clear cause assessed using the Screening for Somatoform Disorders Questionnaire, was correlated with HRQoL (MOS 36-Item Short-Form Health Survey (SF-36) scores) at follow-up, and was inversely associated with $\geq$ 50% reduction in pain one-year after surgical or conservative treatment [13]. These studies suggest the possibility that somatic symptom burden would lead to a worse LBP outcome and result in a lower HRQoL. However, these studies do not always adjust for depression. Depression is a risk factor for the onset and chronicity of LBP [4, 6], and somatisation often coexists with depression. Therefore, it might be difficult to determine whether somatic symptom burden predicts LBP outcomes independent of depression.

There is another possible explanation for our study results. Individuals with LBP often suffer from multisite pain or other musculoskeletal disorders [34–36], which could result in higher somatic symptom assessment scores. Previous studies show that as the number of pain sites increase, functional ability or HRQoL decreased [35, 36]. Although we did not assess pain in another body site other than LBP or knee pain, 43% of the participants answered that they were bothered at least somewhat by “pain in arms, legs, or joints” in the SSS-8. In addition, studies have showed that chronic conditions such as fibromyalgia, chronic LBP, irritable bowel syndrome, temporomandibular joint disorder, interstitial cystitis, chronic fatigue syndrome, and headache are linked by central sensitization and called functional somatic syndromes (FSS) [37–39]. The FSS conditions may overlap in one patient [39]; therefore, it is possible that individuals with more disabling chronic LBP suffered from other musculoskeletal disorders and/or FSS symptoms that decreased HRQoL in these individuals.
A strength of the present study is its large sample size with information on relevant covari-
ables. The participants were not recruited in clinical settings; therefore, the possibility of selec-
tion bias due to seeking treatment should be low. The independent variable and the outcome
were assessed using the validated tools, which would reduce the risk of classification bias.
However, there are a few limitations of the present investigation. First, depression was assessed
using only two questions; thus, misclassification is possible, which would be non-differential.
Second, measures of anxiety were not available. Anxiety also often overlaps with somatisation
and is associated with HRQoL [9]; thus, residual depression and anxiety may have confounded
the results. This could have contributed to the overestimation, but the magnitude is unknown.
Third, we did not collect the information on the pain in other sites than LBP and knee pain.
Finally, the participants of the present study were recruited online and thus our results are not
necessarily representative of the Japanese population.

In conclusion, somatic symptom burden might be an important factor for HRQoL in indi-
viduals with CLBP independent of depressive symptoms and the number of chronic
conditions.

Supporting information
S1 File. Data set. Data set for this analysis. (CSV)
S2 File. STROBE check list. STROBE checklist for cross-sectional studies. (DOC)

Author Contributions
Conceptualization: Ko Matsudaira.
Data curation: Hiroyuki Oka.
Formal analysis: Tomoko Fujii.
Funding acquisition: Ko Matsudaira.
Supervision: Ko Matsudaira.
Writing – original draft: Tomoko Fujii.
Writing – review & editing: Hiroyuki Oka, Junji Katsuhira, Juichi Tonosu, Satoshi Kasahara,
Sakae Tanaka, Ko Matsudaira.

References
1. Walker BF, Muller R, Grant WD. Low back pain in Australian adults: prevalence and associated disabil-
ity. J Manipulative Physiol Ther. 2004; 27(4):238–244. https://doi.org/10.1016/j.jmpt.2004.02.002
PMID: 15148462
2. Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, preva-
lence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries,
1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015; 386
(9995):743–800. https://doi.org/10.1016/S0140-6736(15)60692-4 PMID: 26063472
3. Heneweer H, Staes F, Aufdemkampe G, van Rijn M, Vanhees L. Physical activity and low back pain: a
systematic review of recent literature. Eur Spine J. 2011; 20(6):826–845. https://doi.org/10.1007/
s00586-010-1660-7 PMID: 21221663
4. Pinheiro MB, Ferreira ML, Refshauge K, Ordonana JR, Machado GC, Prado LR, et al. Symptoms of
Depression and Risk of New Episodes of Low Back Pain: A Systematic Review and Meta-Analysis.
Arthritis Care Res. 2015; 67(11):1591–1603.
Somatic symptom burden and health-related quality of life in chronic low back pain

5. Taylor JB, Goode AP, George SZ, Cook CE. Incidence and risk factors for first-time incident low back pain: a systematic review and meta-analysis. Spine J. 2014;14(10):2299–2319. https://doi.org/10.1016/j.spinee.2014.01.026 PMID: 24462537

6. Pincus T, Burton AK, Vogel S, Field AP. A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. Spine. 2002;27(5):E109–120. PMID: 11880847

7. Herr KA, Mobily PR, Smith C. Depression and the experience of chronic back pain: a study of related variables and age differences. Clin J Pain. 1993; 9(2):104–114. PMID: 8358133

8. Baumeister H, Knecht A, Hutter N. Direct and indirect costs in persons with chronic back pain and comorbid mental disorders—a systematic review. J Psychosom Res. 2012; 73(2):79–85. https://doi.org/10.1016/j.jpsychores.2012.05.008 PMID: 22789408

9. Lowe B, Spitzer RL, Williams JB, Mussell M, Schellberg D, Kroenke K. Depression, anxiety and somatisation in primary care: syndrome overlap and functional impairment. Gen Hosp Psychiatry. 2008; 30(3):191–199. https://doi.org/10.1016/j.genhospsy.2008.01.001 PMID: 18433651

10. Lipowski ZJ. Somatization: the concept and its clinical application. The American journal of psychiatry. 1986; 145(1):1358–1368. https://doi.org/10.1176/ajp.145.1.1358 PMID: 3056044

11. Crombez G, Beirens K, Van Damme S, Eccleston C, Fontaine J. The unbearable lightness of somatization. J Psychosom Res. 2009; 145(1–2):31–35. https://doi.org/10.1016/j.jpain.2009.04.006 PMID: 19427734

12. Matsudaira K, Konishi H, Miyoshi K, Isomura T, Inuzuka K. Potential risk factors of persistent low back pain developing from mild low back pain in urban Japanese workers. PloS one. 2014; 9(4):e93924. https://doi.org/10.1371/journal.pone.0093924 PMID: 24714616

13. Nickel R, Egle UT, Romej J, Eysel P, Hoffmann SO. Somatisation predicts the outcome of treatment in patients with low back pain. J Bone Joint Surg Br. 2002; 84(2):189–195. PMID: 11922359

14. Zijlma WL, Stolk RP, Lowe B, Riel W, White PD, Rosmalen JG. How to assess common somatic symptoms in large-scale studies: a systematic review of questionnaires. J Psychosom Res. 2013; 74(6):459–468. https://doi.org/10.1016/j.jpsychores.2013.03.093 PMID: 23731742

15. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. Psychosom Med. 2002; 64(2):256–266. PMID: 11914441

16. Han C, Pae CU, Parkar AA, Masand PS, Kim KW, Joe SH, et al. Psychometric properties of the Patient Health Questionnaire-15 (PHQ-15) for measuring the somatic symptoms of psychiatric outpatients. Psychosomatics. 2009; 50(6):580–585. https://doi.org/10.1176/appi.ps.50.6.580 PMID: 19996228

17. Karekla M, Pilipenko N, Feldman J. Patient Health Questionnaire: Greek language validation and subscale factor structure. Compr Psychiatry. 2012; 53(8):1217–1226. https://doi.org/10.1016/j.comppsych.2012.05.008 PMID: 22901833

18. Lee S, Ma YL, Tsang A. Psychometric properties of the Chinese 15-item patient health questionnaire in the general population of Hong Kong. J Psychosom Res. 2011; 71(2):69–73. https://doi.org/10.1016/j.jpsychores.2011.01.016 PMID: 21767685

19. Nordin S, Palmquist E, Nordin M. Psychometric evaluation and normative data for a Swedish version of the Patient Health Questionnaire 15-Item Somatic Symptom Severity Scale. Scan J Psychol. 2013; 54(2):112–117.

20. Ros Montalban S, Comas Vives A, Garcia-Garcia M. Validation of the Spanish version of the PHQ-15 questionnaire for the evaluation of physical symptoms in patients with depression and/or anxiety disorders: DEPRE-SOMA study. Actas Esp Psiquiatr. 2010; 38(6):345–357. PMID: 21188674

21. Yazici Gulec M, Gulec H, Simsek G, Turhan M, Aydin Sunbul E. Psychometric properties of the Turkish version of the Patient Health Questionnaire-Somatic, Anxiety, and Depressive Symptoms. Compr Psychiatry. 2012; 53(5):623–629. https://doi.org/10.1016/j.comppsych.2011.08.002 PMID: 22000476

22. Gierk B, Kohlmann S, Kroenke K, Spangenberg L, Zenger M, Brahler E, et al. The somatic symptom scale-8 (SSS-8): a brief measure of somatic symptom burden. JAMA Intern Med. 2014; 174(3):399–407. https://doi.org/10.1001/jamainternmed.2013.12179 PMID: 24276929

23. Narrow WE, Clarke DE, Kuramoto SJ, Kraemer HC, Kupfer DJ, Greiner L, et al. DSM-5 field trials in the United States and Canada, Part III: development and reliability testing of a cross-cutting symptom assessment for DSM-5. Am J Psychiatry. 2013; 170(1):71–82. https://doi.org/10.1176/appi.ajp.2012.12071000 PMID: 23111499

24. Matsudaira K, Kawaguchi M, Murakami M, Fukudo S, Hashizume M, Oka H, et al. Development of a Linguistically Validated Japanese Version of the Somatic Symptom Scale-8 (SSS-8). Jpn J Psychosom Med. 2016; 56(9):931–937.

25. Matsudaira K, Oka H, Kawaguchi M, Murakami M, Fukudo S, Hashizume M, et al. Development of a Japanese version of the Somatic Symptom Scale-8: Psychometric validity and internal consistency.
Gen Hosp Psychiatry. 2017; 45:7–11. https://doi.org/10.1016/j.genhospsych.2016.12.002 PMID: 28274342

26. Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. Med Care. 2003; 41(11):1284–1292. https://doi.org/10.1097/01.MLR.0000093487.78664.3C PMID: 14583691

27. Muramatsu K, Miyaoaka H, Kamijima K, Muramatsu Y, Yoshida M, Otsubo T, et al. The patient health questionnaire, Japanese version: validity according to the mini-international neuropsychiatric interview-plus. Psychol Rep. 2007; 101(3 Pt 1):952–960.

28. EuroQol Group. EuroQol—a new facility for the measurement of health-related quality of life. Health policy. 1990; 16(3):199–208. PMID: 10109801

29. The Japanese EuroQol Translation Team. The development of the Japanese EuroQol Instrument. J Health Care Soc. 1998(8):109–123.

30. Yoshizawa K, Kobayashi H, Fujie M, Ogawa Y, Yajima T, Kawai K. Estimation of minimal clinically important change of the Japanese version of EQ-5D in patients with chronic noncancer pain: a retrospective research using real-world data. Health Qual Life Outcomes. 2016; 14:35. https://doi.org/10.1186/s12955-016-0438-2 PMID: 26931101

31. Soer R, Reneman MF, Speijer BL, Coppes MH, Vroomen PC. Clinimetric properties of the EuroQol-5D in patients with chronic low back pain. Spine J. 2012; 12(11):1035–1039. https://doi.org/10.1016/j.spinee.2012.10.030 PMID: 23199409

32. Tomenson B, Essau C, Jacobi F, Ladwig KH, Leiknes KA, Lieb R, et al. Total somatic symptom score as a predictor of health outcome in somatic symptom disorders. Br J Psychiatry. 2013; 203(5):373–380. https://doi.org/10.1192/bjp.bp.112.114405 PMID: 24072756

33. Alliet L, Rubinstein SM, Knol D, van Tulder MW, de Vet HC. Somatization is associated with worse outcome in a chiropractic patient population with neck pain and low back pain. Man Ther. 2016; 21:170–176. https://doi.org/10.1016/j.math.2015.07.007 PMID: 26254262

34. Natvig B, Bruusgaard D, Erikson W. Localized low back pain and low back pain as part of widespread musculoskeletal pain: two different disorders? A cross-sectional population study. J Rehabil Med. 2001; 33(1):21–25. PMID: 11480465

35. Kamaleri Y, Natvig B, Ihlebaek CM, Bruusgaard D. Localized or widespread musculoskeletal pain: does it matter? Pain. 2008; 138(1):41–46. https://doi.org/10.1016/j.pain.2007.11.002 PMID: 18077092

36. Yamada K, Matsudaira K, Takeshita K, Oka H, Hara N, Takagi Y. Prevalence of low back pain as the primary pain site and factors associated with low health-related quality of life in a large Japanese population: a pain-associated cross-sectional epidemiological survey. Mod Rheumatol. 2014; 24(2):343–348. https://doi.org/10.3109/14397595.2013.854067 PMID: 24593211

37. Kindler LL, Bennett RM, Jones KD. Central sensitivity syndromes: mounting pathophysiologic evidence to link fibromyalgia with other common chronic pain disorders. Pain Manag Nurs. 2011; 12(1):15–24. https://doi.org/10.1016/j.pmn.2009.10.003 PMID: 21349445

38. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011; 152(3 Suppl):S2–15. https://doi.org/10.1016/j.pain.2010.09.030 PMID: 20961885

39. Bourke JH, Langford RM, White PD. The common link between functional somatic syndromes may be central sensitisation. J Psychosom Res. 2015; 78(3):228–236. https://doi.org/10.1016/j.jpsychores.2015.01.003 PMID: 25598410