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Clinical outcomes, medical costs, and medication usage patterns of different somatic symptom disorders and functional somatic syndromes: a population-based study in Taiwan

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Abstract

Background. Somatic symptom disorders (SSD) and functional somatic syndromes (FSS) are often regarded as similar diagnostic constructs; however, whether they exhibit similar clinical outcomes, medical costs, and medication usage patterns has not been examined in nationwide data. Therefore, this study focused on analyzing SSD and four types of FSS (fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, functional dyspepsia).

Methods. This population-based matched cohort study utilized Taiwan's National Health Insurance (NHI) claims database to investigate the impact of SSD/FSS. The study included 2 615 477 newly diagnosed patients with SSD/FSS and matched comparisons from the NHI beneficiary registry. Healthcare utilization, mortality, medical expenditure, and medication usage were assessed as outcome measures. Statistical analysis involved Cox regression models for hazard ratios, generalized linear models for comparing differences, and adjustment for covariates.

Results. All SSD/FSS showed significantly higher adjusted hazard ratios for psychiatric hospitalization and all-cause hospitalization compared to the control group. All SSD/FSS exhibited significantly higher adjusted hazard ratios for suicide, and SSD was particularly high. All-cause mortality was significantly higher in all SSD/FSS. Medical costs were significantly higher for all SSD/FSS compared to controls. The usage duration of all psychiatric medications and analgesics was significantly higher in SSD/FSS compared to the control group.

Conclusion. All SSD/FSS shared similar clinical outcomes and medical costs. The high hazard ratio for suicide in SSD deserves clinical attention.

Introduction

Medically unexplained symptoms (MUS) are a common problem in clinical healthcare (Rief & Broadbent, 2007). Various diagnoses are used to describe different types of MUS (Rief & Isaac, 2014). In psychiatry, somatoform disorders were previously the main term used for such diagnoses (Rief & Barsky, 2005). In the DSM-IV and ICD-10, somatoform disorders could be further classified into several diagnoses based on different bodily symptoms, including somatization disorder characterized by multiple symptoms, pain disorder primarily focused on pain, and undifferentiated somatoform disorder manifesting through various other symptoms (Huang, Chen, Chang, & Liao, 2016a). In the contemporary DSM-5 and ICD-11, psychological features have become a more crucial core than medically unexplained nature, as reflected in the diagnostic constructs of somatic symptom disorder (SSD) and bodily distress disorder (Lowe et al., 2022; Rief & Martin, 2014). Despite the criteria changes, there remains a considerable overlap between newer and older diagnostic concepts (Huang et al., 2016a). For the sake of convenience in this context, we used the term 'somatic symptom disorders' (SSD) as a general term for this group of psychiatric concepts (i.e. the meaning of SSD in this article differs slightly from the DSM-5's SSD).

In specialized fields outside of psychiatry, the term 'functional' is often used to describe MUS in contrast to the term 'organic', which implies a clear physiological cause (Henningsen, Zipfel, Sattel, & Creed, 2018). Consequently, some more specific syndromes are referred to as functional somatic syndromes (FSS) (Cheng, Huang, & Huang, 2020).

Diagnoses commonly attributed to FSS include fibromyalgia, characterized primarily by pain, and chronic fatigue syndrome, characterized primarily by fatigue (Cheng et al., 2020). In the field of gastrointestinal disorders, a significant number of functional disorders have been defined, with their own diagnostic system known as the ROME criteria (Schmulson & Drossman, 2017). Among them, irritable bowel syndrome and functional dyspepsia are particularly well-recognized diagnoses (Futagami et al., 2018; Whitehead, Palsson, & Simren, 2017). These diagnoses are primarily defined based on presenting gastrointestinal symptoms. While most diagnoses require the presence of medically unexplained conditions, there are also perspectives suggesting that medically unexplained may not be necessary if other criteria are sufficiently clear (Wolfe et al., 2016).

The relationship between various SSD and FSS poses an intriguing question. There are reports of mutual comorbidity among several FSS (White, 2010). From a statistical perspective, some studies suggest that multiple FSS can be considered as subtypes within the same syndrome (Fink & Schroder, 2010). In essence, a common viewpoint is that despite some differences (e.g. the risk factors) in symptom presentation between various SSD and FSS, they often share many overlapping and similar features, such as psychological aspects like health anxiety (Cheng et al., 2020; Enck et al., 2016; Hauser et al., 2015). The differing complaints and specialized fields of patients seeking treatment may lead to distinct diagnoses for individuals. In fact, many research studies and clinical recommendations advocate for a combined consideration of various SSD and FSS (Cheng et al., 2020; Henningsen et al., 2018).

To the best of our knowledge, research investigating the relationship between various SSD and FSS in national databases is currently limited. If the aforementioned view of 'overlap and similarity among the diagnoses' holds true, these patients should exhibit similar characteristics in terms of clinical outcomes, medical costs, and patterns of medication usage. In Taiwan, such information can be examined through the National Health Insurance database (Huang et al., 2022b). Based on this, we have designed a study with the aim of analyzing the clinical outcomes, medical costs, and medication usage patterns of various SSD and FSS, and determining whether there are significant hazard ratios or differences compared to individuals without these diagnoses. The effects of different SSD and FSS diagnoses were examined both together and separately.

Methods

Data source

This study used a population-based matched cohort design, utilizing the claims database obtained from Taiwan's National Health Insurance (NHI) program. The NHI program is a compulsory universal healthcare program encompassing approximately 99% of the Taiwanese population, consisting of 23 million individuals. Individuals will exit the NHI program only if they emigrate. Data from specialized clinical settings and primary care have both been collected in NHI database. In Taiwan, a distinctive feature is the high accessibility of specialized care. People can directly seek treatment from specific specialists without having to go through a general practitioner. Within the claims database, comprehensive information was available regarding patients' demographic attributes, clinical diagnoses, and prescription records. Extensive research has been conducted to establish the reliability and validity of the diagnostic codes within the NHI claims database for both medical and psychiatric disorders (Hsieh et al., 2019; Wu, Kuo, Su, Wang, & Dai, 2020). Ethical approval for this study was obtained from the Research Ethics Committee of the National Health Research Institute (EC1101103-E).

Study population

Using the NHI claims database between 2009 and 2019, we identified a cohort of adult patients (aged ≥ 18 years) with a clinical diagnosis of SSD/FSS, encompassing conditions such as SSD (ICD-9: 300.8; ICD-10: F45), irritable bowel syndrome (ICD-9: 564.1; ICD-10: K58), functional dyspepsia (ICD-9: 536.8; ICD-10: K30), fibromyalgia (ICD-9: 729.1; ICD-10: M79.7), and chronic fatigue syndrome (ICD-9: 780.71, 780.79; ICD-10: R53.82, R53.83). To ensure accuracy, we utilized the principal diagnosis from outpatient claims to identify incident cases, disregarding other additional diagnostic codes. Prevalent cases were excluded by using a one-year observation period, with the date of the first FSS diagnosis considered the cohort entry date. The analysis included a total of 2 615 477 newly diagnosed patients with SSD/FSS. For each individual in the cohort, a matched comparison was randomly selected from the Registry for NHI beneficiaries, ensuring they had no prior diagnosis of SSD/FSS and were matched based on birth year and sex. The cohort entry date for the matched comparison coincided with that of the corresponding case, resulting in an equal number of comparisons being included in the study.

Healthcare utilization and mortality measures

We used various measures to assess the impact of SSD/FSS, including healthcare utilization, mortality, medical expenditure, and medication usage. Healthcare utilization encompassed both all-cause and psychiatric hospitalizations during the follow-up period. To determine mortality, we linked the National Death Registry to ascertain the date of death for each study subject. Suicide was identified using the causes of death codes from Taiwan's National Death Registry (ICD-9-CM external codes: E950–E959 or ICD-10 codes: X60–X84 or X87.0).

Medical expenditure was evaluated by considering the annual medical costs, including outpatient, hospitalization, and emergency department costs. To account for outliers in medical expenditure, we applied a trimming method using the 99th percentile as the high trim point. All costs were exchanged into the US dollar, with an exchange rate of 30.89 New Taiwan dollar against the US dollar in 2019.

Medication usage was classified based on the ATC code into various categories, such as antidepressants (N06A), antipsychotics (N05A excluding lithium [N05AN01]), mood stabilizers (lithium [N05AN01], valproic acid [N03AG01], carbamazepine [N03AF01], and lamotrigine [N03AX09]), anxiolytics and hypnotics (N05B, N05C), paracetamol (N02BE01), NSAIDs (M01A), and opioids (N02A). To determine the average number of days of medication use per year, we calculated the sum of prescription supply days and divided it by the follow-up years.

Covariates

The demographic characteristics of the patients encompassed variables such as age, sex, the calendar year of cohort entry, monthly income, the Charlson comorbidity index, the number

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of outpatient visits, and the presence of comorbid conditions. These comorbid conditions included hypertension, dyslipidemia, diabetes, chronic liver disease, chronic kidney disease, chronic pulmonary disease, cardiovascular disorder, peptic ulcer disease, cerebrovascular disease, peripheral vascular disease, rheumatoid arthritis, depression, sleep disorders, anxiety disorders, as well as substance and alcohol use disorders.

Statistical analysis

The baseline characteristics of individuals newly diagnosed with SSD/FSS and comparison subjects were described in terms of case numbers and percentages. These demographic and clinical variables might be confounders for comparing the clinical outcomes between SSD/FSS group and control groups. We used propensity score weighting with overlap weights to mitigate the disparity in these variables between the groups (Mlcoch et al., 2019). The propensity scores were generated based on all the variables listed in Table 1 except the specialty. The standardized mean difference was utilized to assess distinctions in characteristics, with a standardized mean difference (SMD) of <0.1 indicating an insignificant distinction between the two groups.

All participants were followed from the cohort entry date until the occurrence of study outcomes, which included death, study outcome occurred, exit from the NHI program, or the end of 2019, whichever came first. Cox regression models were utilized to estimate the hazard ratios for all-cause and psychiatric hospitalization, as well as all-cause mortality and suicide, compared to the control groups. These hazard ratios were adjusted using propensity score weighting.

The distribution of medical expenditure and medication use did not follow a normal distribution. Despite applying a log-transformation, the cost distribution remained skewed and did not align with a normal distribution. Therefore, we used bootstrapping with propensity score weighting (Austin, 2022) to calculate standardized errors for the estimated medical costs and medication usage. For this purpose, we extracted 200 bootstrap samples from the initial random sample. In each of these bootstrap samples, the propensity score was recalculated, and a fresh set of weights was derived based on the updated propensity scores. Using these propensity score weights, medical costs and medication usage were computed for each bootstrap sample. Finally, we obtained the bootstrap-derived estimates for standardized errors and 95% confidence intervals. Additionally, comparisons between individuals with specific diagnoses and controls were also analyzed. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). The statistical significance of relationships was assessed using a 95% confidence interval or a p value below 0.05.

Results

This study identified newly-diagnosed cases from 2009 to 2019. The incidence rates per 100 000 adults were as follows: SSD (27.6), irritable bowel syndrome (210.5), functional dyspepsia (278.2), fibromyalgia (551.1), and chronic fatigue syndrome (131.6).

The demographic characteristics, comorbidities, and specialty of diagnosis for each condition are presented in Table 1. When considering descriptive trends, the following characteristics emerge. Regarding age, SSD, fibromyalgia, and chronic fatigue syndrome exhibited higher proportions among individuals aged 45 or above, while irritable bowel syndrome and functional dyspepsia showed a polarized trend. In terms of sex, all SSD and FSS conditions were more prevalent in females than males. As for the specialty of diagnosis, the primary specialties providing diagnoses for various SSD and FSS were internal medicine and family medicine (both >20%). Additionally, SSD had a relatively higher chance of being diagnosed by the psychiatrists/neurologists, irritable bowel syndrome by the surgeons, and fibromyalgia by the orthopedics and rehabilitation specialists (>5%). Online Supplementary Table S1 shows the demographic and clinical characteristics after propensity score weighting using overlap weights. All the SMD are <0.1.

Table 2 presents the relationship between various diagnoses and clinical outcomes. When considering psychiatric hospitalization, the adjusted hazard ratios for all SSD and FSS were significantly higher than the control group, with SSD showing particularly high ratios. The overall SSD/FSS group also exhibited significantly higher ratios compared to the control group. When considering all-cause hospitalization, the adjusted hazard ratios for all SSD and FSS diagnoses were significantly higher than the control group, both individually and collectively. When considering adjusted hazard ratios for suicide, all SSD and FSS showed significantly higher ratios than the control group, and SSD was particularly high. In terms of all-cause mortality, the adjusted hazard ratios for all SSD and FSS were significantly higher than the control group. The overall SSD/FSS group exhibited a significant increase compared to the control group.

Table 3 presents the healthcare expenditures for each diagnosis. Regardless of overall cost, outpatient expenses, inpatient expenses, and emergency department expenses, SSD, irritable bowel syndrome, functional dyspepsia, chronic fatigue syndrome, fibromyalgia, and the overall SSD/FSS group all exhibited significantly higher costs compared to the control group.

Table 4 displays the duration of medication use for each diagnosis. For all psychiatric medications and analgesics, the duration of medication use for each diagnosis was significantly higher than the control group.

Discussion

The main findings of this study are as follows. Firstly, all SSD/FSS exhibited similar patterns in clinical outcomes, healthcare costs, and medication usage. Secondly, among several SSD/FSS, SSD showed a extraordinary high hazard ratio of suicide compared to the control group. These findings warrant further discussion.

Similar clinical outcomes, healthcare costs, and patterns of medication usage suggest that most SSD/FSS may belong to similar populations, and the specific diagnosis received may be related to their chief complaints and specialists of visit. This viewpoint has received some empirical support (Fink & Schroder, 2010; White, 2010), but it is the first time to be examined using the National Health Insurance database in Taiwan. In the literature, comorbidity among chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia is not uncommon (White, 2010). Fink et al.'s concept of bodily distress syndrome is based on the high co-occurrence of multiple FSS, aiming to depict various FSS more comprehensively through a single diagnostic concept (Fink & Schroder, 2010). The transition from somatoform disorders to SSD in the DSM-5 emphasizes psychological features, as even though physiological symptoms may differ, there are similarities in psychological phenomena (Rief & Martin, 2014). Our findings align with the aforementioned information. On the

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Table 1. Demographics, comorbidities and specialty of diagnosis in patients with different SSD and FSS

	Overall SSD and FSS	Somatic symptomdisorders	Irritable bowel syndrome	Functional dyspepsia	Fibromyalgia	Chronic fatigue syndrome	Controls
	2 571 640	59 119	451 595	596 680	1 182 059	282 187	2 571 640
	N (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Age (years)							
18–34	515 469 (20.0)	8201 (13.9)	96 348 (21.3)	149 858 (25.1)	212 595 (18.0)	48 467 (17.2)	515 469 (20.0)
35–44	430 363 (16.7)	9364 (15.8)	75 961 (16.8)	94 622 (15.9)	208 252 (17.6)	42 164 (14.9)	430 363 (16.7)
45–54	546 352 (21.2)	13 498 (22.8)	89 010 (19.7)	109 104 (18.3)	279 934 (23.7)	54 806 (19.4)	546 352 (21.2)
55–64	490 996 (19.1)	12 945 (21.9)	86 277 (19.1)	104 632 (17.5)	232 374 (19.7)	54 768 (19.4)	490 996 (19.1)
≥65	588 460 (22.9)	15 111 (25.6)	103 999 (23.0)	138 464 (23.2)	248 904 (21.1)	81 982 (29.1)	588 460 (22.9)
Sex							
Female	1 432 979 (55.7)	38 452 (65.0)	230 356 (51.0)	350 496 (58.7)	660 841 (55.9)	152 834 (54.2)	1 432 979 (55.7)
Male	1 138 661 (44.3)	20 667 (35.0)	221 239 (49.0)	246 184 (41.3)	521 218 (44.1)	129 353 (45.8)	1 138 661 (44.3)
Monthly income (USD)							
≤674.52 (≤20 000 NTD)	744 767 (29.0)	14 067 (23.8)	95 294 (21.1)	117 455 (19.7)	241 796 (20.5)	64 716 (22.9)	533 328 (20.7)
674.57–1295.05 (20 001–40 000 NTD)	1 211 592 (47.1)	32 705 (55.3)	233 146 (51.6)	333 074 (55.8)	665 657 (56.3)	159 995 (56.7)	1 424 577 (55.4)
>1295.08 (>40 001 NTD)	615 281 (23.9)	12 347 (20.9)	123 155 (27.3)	146 151 (24.5)	274 606 (23.2)	57 476 (20.4)	613 735 (23.9)
Charlson comorbidity index							
0	2 172 856 (84.5)	40 252 (68.1)	313 094 (69.3)	433 030 (72.6)	897 930 (76.0)	194 359 (68.9)	1 878 665 (73.1)
1	248 381 (9.7)	12 051 (20.4)	86 505 (19.2)	99 684 (16.7)	183 727 (15.5)	51 277 (18.2)	433 244 (16.8)
2	91 589 (3.6)	4300 (7.3)	32 049 (7.1)	37 926 (6.4)	64 629 (5.5)	20 659 (7.3)	159 563 (6.2)
≥3	58 814 (2.3)	2516 (4.3)	19 947 (4.4)	26 040 (4.4)	35 773 (3.0)	15 892 (5.6)	100 168 (3.9)
Number of outpatient visits							
0–10	1 700 877 (66.1)	15 879 (26.9)	160 337 (35.5)	210 932 (35.4)	476 618 (40.3)	100 346 (35.6)	964 112 (37.5)
11–20	442 174 (17.2)	13 751 (23.3)	109 444 (24.2)	145 909 (24.5)	288 775 (24.4)	64 995 (23.0)	622 874 (24.2)
≥21	428 589 (16.7)	29 489 (49.9)	181 814 (40.3)	239 839 (40.2)	416 666 (35.3)	116 846 (41.4)	984 654 (38.3)
Comorbidity							
Hypertension	410 804 (16.0)	17 018 (28.8)	108 637 (24.1)	140 666 (23.6)	290 668 (24.6)	83 142 (29.5)	640 131 (24.9)
Dyslipidemia	359 265 (14.0)	9334 (15.8)	67 198 (14.9)	81 054 (13.6)	157 500 (13.3)	44 179 (15.7)	589 352 (11.5)
Diabetes	97 422 (3.8)	2270 (3.8)	19 067 (4.2)	23 715 (4.0)	39 030 (3.3)	13 340 (4.7)	167 020 (3.2)
Chronic liver disease	98 030 (3.8)	4313 (7.3)	32 218 (7.1)	36 976 (6.2)	73 330 (6.2)	25 034 (8.9)	171 871 (6.7)
Chronic kidney disease	33 413 (1.3)	1041 (1.8)	9668 (2.1)	13 582 (2.3)	17 346 (1.5)	6864 (2.4)	48 501 (1.9)
Chronic pulmonary disease	82 066 (3.2)	4180 (7.1)	30 937 (6.9)	37 502 (6.3)	66 826 (5.7)	20 224 (7.2)	159 669 (6.2)

(*Continued*)

Table 1. (*Continued.*)

	Overall SSD and FSS	Somatic symptomdisorders	Irritable bowel syndrome	Functional dyspepsia	Fibromyalgia	Chronic fatigue syndrome	Controls
	2 571 640	59 119	451 595	596 680	1 182 059	282 187	2 571 640
	N (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Cardiovascular disorder	38 482 (1.5)	1451 (2.5)	10 702 (2.4)	14 721 (2.5)	24 316 (2.1)	9385 (3.3)	60 575 (2.4)
Peptic ulcer disease	100 877 (3.9)	7461 (12.6)	58 498 (13.0)	62 925 (10.6)	92 074 (7.8)	26 364 (9.3)	247 322 (9.6)
Cerebrovascular disease	68 683 (2.7)	2949 (5.0)	18 203 (4.0)	24 047 (4.0)	39 340 (3.3)	16 194 (5.7)	100 733 (3.9)
Peripheral vascular disease	13 986 (0.5)	870 (1.5)	5076 (1.1)	6392 (1.1)	11 534 (1.0)	4404 (1.6)	28 276 (1.1)
Rheumatoid arthritis	18 644 (0.7)	992 (1.7)	5829 (1.3)	6621 (1.1)	13 321 (1.1)	3067 (1.1)	29 830 (1.2)
Depression	42 105 (1.6)	6222 (10.5)	20 721 (4.6)	21 784 (3.7)	37 506 (3.2)	13 142 (4.7)	99 375 (3.9)
Sleep	115 826 (4.5)	15 416 (26.1)	50 916 (11.3)	61 796 (10.4)	111 159 (9.4)	35 921 (12.7)	275 208 (10.7)
Anxiety	25 742 (1.0)	4666 (7.9)	16 763 (3.7)	20 954 (3.5)	16 461 (1.4)	7688 (2.7)	66 532 (2.6)
Substance and alcohol use disorder	3954 (0.2)	477 (0.8)	1369 (0.3)	1652 (0.3)	3893 (0.3)	1682 (0.6)	9073 (0.4)
Specialty							
Internal medicine	945 530 (36.8)	17 903 (30.3)	267 678 (59.3)	284 628 (47.7)	270 781 (22.9)	104 540 (37.0)	
Family medicine	757 855 (29.5)	15 090 (25.5)	76 284 (16.9)	167 173 (28.0)	386 580 (32.7)	112 728 (39.9)	
Otolaryngology	88 094 (3.4)	2382 (4.0)	9906 (2.2)	22 182 (3.7)	47 335 (4.0)	6289 (2.2)	
Rehabilitation	136 030 (5.3)	1880 (3.2)	9685 (2.1)	11 173 (1.9)	108 401 (9.2)	4891 (1.7)	
Surgery	117 782 (4.6)	1939 (3.3)	40 483 (9.0)	17 385 (2.9)	50 000 (4.2)	7975 (2.8)	
Neurology	112 428 (4.4)	5418 (9.2)	9955 (2.2)	12 215 (2.0)	76 072 (6.4)	8768 (3.1)	
Orthopedics	178 964 (7.0)	2780 (4.7)	13 655 (3.0)	18 515 (3.1)	135 566 (11.5)	8448 (3.0)	
Psychiatry	19 495 (0.8)	7162 (12.1)	2762 (0.6)	3015 (0.5)	4803 (0.4)	1753 (0.6)	

SSD, somatic symptom disorders; FSS, functional somatic syndromes; NTD, New Taiwan dollar.

Table 2. Clinical outcomes in patients with different SSD and FSS

	Crude HR (95% CI)	Adjusted HR[a] (95% CI)
Psychiatric hospitalization		
Overall SSD and FSS	2.00 (1.93–2.08)	1.37 (1.32–1.42)
Somatic symptom disorders	4.68 (4.68–4.34)	2.39 (2.21–2.58)
Irritable bowel syndrome	1.91 (1.91–1.80)	1.20 (1.14–1.27)
Functional dyspepsia	1.60 (1.60–1.51)	1.17 (1.11–1.23)
Fibromyalgia	1.65 (1.65–1.58)	1.24 (1.19–1.28)
Chronic fatigue syndrome	3.51 (3.51–3.32)	1.92 (1.82–2.03)
All-cause hospitalization		
Overall SSD and FSS	1.94 (1.93–1.95)	1.43 (1.43–1.44)
Somatic symptom disorders	1.89 (1.89–1.86)	1.20 (1.18–1.22)
Irritable bowel syndrome	1.92 (1.92–1.90)	1.30 (1.29–1.31)
Functional dyspepsia	2.11 (2.11–2.09)	1.40 (1.39–1.41)
Fibromyalgia	1.75 (1.75–1.74)	1.23 (1.22–1.23)
Chronic fatigue syndrome	2.45 (2.45–2.43)	1.45 (1.44–1.47)
Suicide		
Overall SSD and FSS	1.79 (1.71–1.87)	1.36 (1.30–1.42)
Somatic symptom disorders	4.29 (4.29–3.90)	2.42 (2.20–2.67)
Irritable bowel syndrome	1.73 (1.73–1.60)	1.28 (1.20–1.37)
Functional dyspepsia	1.40 (1.40–1.30)	1.18 (1.11–1.25)
Fibromyalgia	1.69 (1.69–1.60)	1.20 (1.15–1.26)
Chronic fatigue syndrome	2.20 (2.20–2.03)	1.41 (1.31–1.52)
All-cause mortality		
Overall SSD and FSS	1.46 (1.45–1.47)	1.20 (1.19–1.21)
Somatic symptom disorders	1.57 (1.57–1.54)	1.11 (1.09–1.14)
Irritable bowel syndrome	1.26 (1.26–1.25)	1.04 (1.03–1.05)
Functional dyspepsia	1.33 (1.33–1.32)	1.20 (1.19–1.21)
Fibromyalgia	1.40 (1.40–1.39)	1.05 (1.04–1.05)
Chronic fatigue syndrome	2.27 (2.27–2.24)	1.41 (1.40–1.43)

SSD, somatic symptom disorders; FSS, functional somatic syndromes; HR, hazard ratio.
[a]Adjusted HR were calculated using propensity score weighting.

other hand, some studies indicate that beyond the mentioned similarities, there may still be subtle differences in the psychological characteristics of different FSS (Huang, Chang, & Liao, 2022a). Therefore, it is possible that it is not solely a matter of 'the same group of cases receiving different diagnoses from different specialties', and distinguishing between several FSS constructs may still have clinical significance.

The hazard ratio of suicide in SSD was particularly high, as indicated by both the crude hazard ratio and the adjusted hazard ratio. There are two possible explanations for this. Firstly, individuals who meet the diagnostic criteria for SSD may have a more pronounced risk of suicide. Secondly, these cases may initially seek treatment in the psychiatric department due to the presence of comorbid conditions such as depression and anxiety, which are associated with a higher risk of suicide. To the best of our knowledge, there have been no comparative studies on the suicide risk between SSD and other FSS. However, the comorbidity of SSD with depression and anxiety is a widely reported cross-cultural finding. Research in Taiwan has shown that individuals with somatoform disorders experience levels of depression and anxiety comparable to panic disorder, which are considered to be highly distressing (Huang et al., 2016b). The proportion of SSD cases with comorbid depression and anxiety, as reported in the literature, ranges from 20% to 66.7%, with variations likely arising from the inclusion of depressive/anxiety symptoms or diagnoses (Grover et al., 2015; Leiknes, Finset, Moum, & Sandanger, 2007). A nationwide study in Taiwan revealed that 33.58% of SSD cases had clinically significant depression or anxiety issues warranting attention (Huang, Chang, Wu, & Liao, 2023). Table 1 also indicates that compared to other FSS, SSD has a higher proportion of comorbid depression and anxiety. Therefore, among the two explanations mentioned earlier, the latter may account for the particularly high crude hazard ratio of SSD. However, even after adjusting for comorbid depression

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Table 3. Annual medical costs in patients with different SSD and FSS

	Overall SSD and FSS	Somatic symptom disorders	Irritable bowel syndrome	Functional dyspepsia	Fibromyalgia	Chronic fatigue syndrome	Controls
Overall cost (USD)	1998 (1985, 2010)	1944 (1912, 1976)	2234 (2195, 2274)	2005 (1982, 2029)	1849 (1831, 1867)	2234 (2195, 2274)	1697 (1691, 1703)
Outpatient cost (USD)	1045 (1040, 1051)	1090 (1076, 1105)	1093 (1082, 1103)	1039 (1028, 1049)	1025 (1015, 1036)	1058 (1045, 1070)	890 (888, 893)
Hospitalization cost (USD)	833 (825, 842)	774 (751, 798)	821 (805, 838)	889 (872, 907)	755 (741, 768)	1074 (1043, 1105)	741 (736, 745)
Emergency department cost (USD)	75 (75, 76)	80 (78, 82)	72 (71, 73)	77 (76, 79)	69 (68, 70)	103 (101, 104)	66 (66, 66)

SSD, somatic symptom disorders; FSS, functional somatic syndromes.
Average annual cost = total cost/follow-up period years.
1 USD = 30.8869 New Taiwan Dollar.
The medical costs of the case groups were higher than those of the control group, and the 95% confidence intervals did not overlap with the controls, except for the hospitalization costs in the case of fibromyalgia.

Table 4. Medication using patterns in patients with different SSD and FSS

	Overall SD and FSS	Somatic symptom disorders	Irritable bowel syndrome	Functional dyspepsia	Fibromyalgia	Chronic fatigue syndrome	Controls
Average days, mean (95% CI)							
Antidepressants	38.9 (38.7–39.1)	75.0 (74.1–75.8)	41.8 (41.4–42.2)	38.0 (37.6–38.4)	35.4 (35.1–35.7)	42.9 (42.6–43.3)	28.0 (27.9–28.1)
Antipsychotics	15.1 (15.0–15.2)	26.3 (25.8–26.8)	16.7 (16.5–16.9)	16.0 (15.8–16.3)	12.9 (12.7–13.1)	17.7 (17.4–18.0)	11.2 (11.1–11.2)
Mood stabilizers	3.7 (3.7–3.8)	4.9 (4.7–5.1)	3.9 (3.7–4.0)	3.6 (3.5–3.7)	3.5 (3.4–3.6)	4.5 (4.4–4.7)	2.8 (2.7–2.8)
Benzodiazepines	87.3 (87.1–87.6)	158.1 (157.0–159.1)	93.5 (93.0–94.1)	85.5 (84.9–86.0)	81.6 (81.2–82.1)	90.3 (89.8–90.9)	65.8 (65.6–65.9)
Acetaminophen	32.1 (32.0–32.3)	39.4 (39.0–39.8)	32.1 (31.9–32.3)	34.5 (34.2–34.7)	30.3 (30.1–30.5)	33.8 (33.5–34.0)	27.1 (27.0–27.1)
NSAID	60.3 (60.1–60.5)	67.3 (66.7–68.0)	56.3 (55.9–56.6)	56.7 (56.4–57.0)	63.5 (63.2–63.9)	59.7 (59.3–60.2)	50.6 (50.5–50.7)
Opioids	8.4 (8.3–8.5)	8.6 (7.0–10.3)	7.5 (7.4–7.6)	7.5 (7.4–7.7)	9.1 (8.9–9.3)	8.4 (8.2–8.6)	6.3 (6.3–6.3)

SSD, somatic symptom disorders; FSS, functional somatic syndromes; NSAID, non-steroidal anti-inflammatory drugs.
Medication usage within the case groups was higher than that of the control group, with non-overlapping 95% confidence intervals.

and anxiety, SSD still exhibits a higher hazard ratio compared to other diagnoses, which aligns better with the former explanation. One possibility is that in the Eastern world, some SSD cases may involve bodily symptoms that are a manifestation of depression (i.e. masked depression) (Kleinman, 2004). This would result in a stronger association between SSD and suicide, given its closer relationship with depression.

A recent systematic review examined the possible connection between somatic symptom and related disorders and suicide outcomes (Torres et al., 2021). Somatic symptom and related disorders were found to be associated with increased risks of both suicidal ideation and attempts. The risk of these suicide outcomes seemed independent to comorbid mental disorders. This trend is similar to our finding. Suicide deaths in patients with somatic symptom and related disorders were not adequately examined in previous studies. Our result further indicates that suicide death is also a notable issue in this population.

To examine whether the findings of hospitalization and mortality are characteristic in SSD/FSS, we considered three other diagnoses not belonging to SSD/FSS: multiple sclerosis, rheumatoid arthritis, and inflammatory bowel disease. The analysis results are shown in online Supplementary Tables S2–S4. Adjusted hazard ratios of all-cause hospitalization and all-cause mortality for these three diagnoses were significantly increased, but somewhat higher than SSD/FSS (all-cause hospitalization: 3.45–5.18; all-cause mortality: 1.89–2.07). The adjusted hazard ratio for multiple sclerosis was higher than the crude hazard ratio. In terms of psychiatric hospitalization, the adjusted hazard ratio for multiple sclerosis was similar to SSD/FSS (1.39), whereas for rheumatoid arthritis and inflammatory bowel disease, it was slightly higher than SSD/FSS (2.79–3.06). These results indicate that the similarity among various SSD/FSS is higher than the similarity between SSD/FSS and these three diagnoses.

Several limitations of this study should be interpreted cautiously. Firstly, the diagnoses in the Taiwan National Health Insurance database are entered by physicians, and the accuracy of these diagnoses is hence limited. The diagnoses were not obtained according to structured interview or other more reliable standard. Therefore, the results reflected their patterns in clinical practice more than their real features. Even when using the same ICD-9 or ICD-10 codes, different physicians may have varying interpretations of the same diagnostic name. For example, in the case of fibromyalgia, physicians may apply different criteria for diagnosis (Hauser et al., 2015). More rigorous studies would consider both diagnostic codes and prescribed medications to ensure diagnostic reliability (Huang et al., 2022b). However, SSD/FSS lacks sufficiently consistent medications to enable such analyses. Secondly, the cost and medication analyses we conducted are based on data accessible through the national health insurance system. Some cases of SSD/FSS may seek treatment through private payment methods, and this information cannot be included in the estimation. Thirdly, although we used SSD as the term for this group of cases seen in psychiatric departments, psychiatric diagnoses of this nature also exhibit heterogeneity. For instance, the psychological mechanisms of functional neurological disorder and SSD may be different (O'Neal & Baslet, 2018). However, these diagnoses may not always be applied precisely in clinical practice, and therefore, we consider further subdividing the diagnostic codes to be of limited significance. Fourthly, in our study sample, there were individuals with multiple SSD/FSS diagnostic codes; however, due to their low number, we do not believe the information in the database is sufficient to accurately determine the extent of comorbidity in real-world cases. To obtain more reliable answers regarding the coexistence of various SSD/FSS, prospective studies are needed. Fifthly, the incident rates could potentially be underestimated due to two primary factors: the identification of cases is limited to those who have sought treatment because we conducted this study based on claims database; our analysis only considered cases where the respective condition was the primary diagnosis, omitting those with concurrent comorbidities.

This study is the first to examine the relationship among several SSD/FSS based on nationwide data in Taiwan. We found that all SSD/FSS exhibit similar characteristics in terms of clinical outcomes, healthcare costs, and medication usage patterns. SSD defined by psychiatric criteria showed an extraordinary high hazard ratio of suicide that warrants attention. These findings may provide clinicians with better expectations regarding the healthcare prognosis and utilization patterns of patients with these conditions and highlight the importance of considering potential comorbid physiological and psychological issues.

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