DANISH MEDICAL JOURNAL

Brief Research Report

Symptom profiles in long COVID compared to functional somatic disorder and the general population

Jane Agergaard[1, 2], Lisbeth Frostholm[2, 3], Per Fink[2, 3], Thomas Meinertz Dantoft[4], Berit Schiøttz-Christensen[1, 5] & Marie Weinreich Petersen[2, 3]

1) Department of Infectious Diseases, Aarhus University Hospital, 2) Department of Clinical Medicine, Aarhus University, 3) Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, 4) Center for Clinical Research and Prevention, Copenhagen University Hospital – Frederiksberg Hospital, 5) Research Unit of General Practice, University of Southern Denmark, Denmark

Dan Med J 2025;72(10):A09240627. doi: 10.61409/A09240627

ABSTRACT

INTRODUCTION. Long COVID, characterised by persistent symptoms following COVID-19, affects about 10% of individuals recovering from SARS-CoV-2. The overlap of symptoms described in long COVID and functional somatic disorder (FSD) raises questions about shared pathophysiology. This report compares the prevalence and profiles of physical symptoms among patients with long COVID, patients with FSD and the general population.

METHODS. Data from a cohort of patients with long COVID referred for diagnostics, a cohort of patients seen in a regional clinic for FSD and individuals from the general population were used. Questionnaires, including the bodily distress syndrome checklist, were used to assess physical symptoms.

RESULTS. A total of 436 patients with long COVID, 264 patients with FSD and 9,656 individuals from the general population were included. A lower prevalence of symptoms was observed in patients with long COVID than in patients with FSD. However, the prevalence of symptoms in patients with long COVID remained higher than in the general population. In patients with long COVID, dominant symptoms were from the general symptoms (GS) cluster (concentration difficulties, fatigue, headache, memory problems) and muscle pain. Additionally, 11% met the criteria for multi-organ FSD, exhibiting a similar symptom profile to patients with FSD.

CONCLUSIONS. A total of 11% of long COVID patients had a symptom profile similar to that of patients with multi-organ FSD. GS, including fatigue and muscle pain, were common. These findings highlight the need for prospective studies to identify patients with similar symptoms, pathogenesis and treatment options.

FUNDING. None.

TRIAL REGISTRATION. Not relevant.

Long COVID affects millions globally and includes symptoms in the central nervous, cardiopulmonary and musculoskeletal systems [1, 2]. Functional somatic disorder (FSD) is characterised by persisting physical symptoms that cannot be better explained by other physical or mental conditions. The persistence of physical symptoms has been observed after other viral infections besides COVID-19 [3], and prior infections have been reported in patients with FSD [4]. However, research on the possible overlap between FSD and long COVID symptoms is lacking. This comparison is crucial for exploring shared mechanisms and treatments. We

compared symptom prevalence and profiles among three Danish cohorts: patients with long COVID, patients with severe FSD and a general population sample, expecting to find symptom profiles similar to those of FSD in some patients with long COVID.

Methods

Study samples

Patients in the clinical cohorts were ≥ 18 years and referred from their GP to Aarhus University Hospital (AUH), Denmark. All three cohorts completed self-reported questionnaires, including the bodily distress syndrome (BDS) checklist, a diagnostic aid for diagnosing FSD.

The long COVID cohort included patients with complex and prolonged symptoms lasting at least 12 weeks after SARS-CoV-2 infection [5, 6]. If they met long COVID criteria, including attribution to infection with SARS-CoV-2 [5], patients were diagnosed with long COVID (DB948A) and enrolled [6, 7]. During 2021, a total of 436 patients with long COVID were included in the cohort.

The FSD cohort included patients referred to the Research Clinic for Functional Disorders at the AUH, with symptoms present for at least six months and suspected FSD of the multi-organ type. The waiting time was two years. During 2020-2023, a total of 264 patients were included. Data were obtained from the national clinical database, FuncData [8].

The general population cohort came from the Danish Study of Functional Disorders (DanFunD), gathered between 2011 and 2015 [9]. The DanFunD baseline cohort includes a total of 9,656 persons (33.7% of those invited) aged 18-76 years from the western part of Copenhagen.

The bodily distress syndrome checklist

The validated 25-item BDS checklist measured physical symptoms of FSD [10]. It categorises symptoms into four clusters: cardiopulmonary, gastrointestinal, musculoskeletal (MS) and general symptoms (GS), and separates patients into three categories: No FSD, single-organ FSD (i.e., symptoms from one or two clusters) and multi-organ FSD (i.e., symptoms from ≥ 3 clusters) [10]. We compared the prevalence of all 25 symptoms as well as profiles in the four symptom clusters, considering profiles alike if the same symptoms in the cluster were most frequent in the compared cohorts.

Cohort characteristics

Health risk factors, including diagnoses before long COVID, were systematically collected in the patients' files. Psychological strains and socioeconomic parameters were included in the patient-reported questionnaire.

Variables were compared using risk ratios with 95% confidence intervals (CI) and χ^2 test for statistical significance, using StataNow/MP 18.5.

Trial registration: not relevant.

Results

Sociodemographic and clinical characteristics

The long COVID cohort showed sociodemographic differences compared to the FSD and the general population cohorts (**Table 1**). Patients with long COVID had diabetes and cardiovascular diseases less often than the general population cohort, whereas symptoms of depression and anxiety were more frequent in the long COVID than in

the general population cohort but less so than in the FSD cohort.

TABLE 1 Characteristics of patients with long COVID compared to those of patients with severe functional somatic disorder and the general population, at the first clinical evaluation and inclusion in the cohort.

	Long COVID cohort[h] (N_{COV} = 436)		FSD cohort (N_{FSD} = 264)		Gen. pop. cohort (N_{GP} = 9,656)		Long COVID compared to, RR (95% CI)[g]	
	% (n)	median (IQR)	% (n)	median (IQR)	% (n)	median (IQR)	FSD	gen. pop.
Sex: males	28 (121)		19 (49)		46 (4,453)		1.50* (1.11-2.00)	0.60* (0.52-0.70)
Age		47 (36-56) yrs		42 (33-52) yrs		54 (44-64) yrs		
Age > 45 yrs	56 (243)		39 (103)		73 (7,017)		1.43* (1.20-1.70)	0.77* (0.70-0.83)
Time from symptom onset to inclusion		6.3 (4.5-10.0) mos.						
Diabetes	2 (7)				5 (439)			0.35* (0.17-0.74)
Asthma	14 (62)				10 (983)			1.40* (1.10-1.77)
COPD	1 (5)				2 (209)			0.53 (0.22-1.28)
Coronary heart disease	1 (3)				2 (162)			0.41 (0.13-1.28)
Cerebrovascular disease	< 1				2 (231)			0.19* (0.05-0.77)
Hypertension	10 (44)				29 (2,754)			0.35* (0.27-0.47)
Previous depression[a]	12 (53)				12 (1,155)			1.01 (0.79-1.32)
Current smoker	7 (29)		17 (46)		13 (1,263)		0.41* (0.26-0.63)	0.54* (0.38-0.77)
BMI > 25, kg/m²	64 (271)		45 (119)		54 (5,224)		1.42* (1.22-1.65)	1.18* (1.10-1.27)
Socioeconomic status								
Higher education:								
0 yrs	22 (98)		19 (51)		10 (995)		1.16 (0.86-1.57)	2.18* (1.81-2.62)
1-4 yrs	67 (293)		66 (175)		58 (5,552)		1.01 (0.91-1.13)	1.17* (1.09-1.25)
> 4 yrs	10 (45)		11 (30)		29 (2,845)		0.91 (0.59-1.40)	0.35* (0.27-0.46)
Employed or self-employed	89 (386)		21 (56)		67 (6,488)[a]		4.17* (3.30-5.28)	1.32* (1.27-1.37)
Not living alone	83 (303)		82 (217)		77 (7,469)		1.01 (0.94-1.09)	1.07* (1.02-1.13)
Mental health and physical symptom load								
Depression score > 8, SCL-13 item 8-13[b]	15 (64)		33 (87)		3 (265)		0.46* (0.35-0.61)	5.54* (4.29-7.15)
Anxiety score > 5, SCL-13, item 1-4[b]	28 (120)		47 (123)		3 (291)		0.61* (0.50-0.74)	9.37* (7.75-11.32)
BDS total sum score		27 (19-38)		48 (36-58)		11 (6-18)		
BDS score > 40[c]	18 (80)		68 (179)		0.23 (223)		0.27* (0.22-0.36)	7.95* (6.27-10.07)
Screening results of functional somatic disorder using the 25 item BDS checklist results								
Overall FSD[d]	65 (284)		88 (233)		16 (1,543)		0.74* (0.68-0.80)	4.08* (3.75-4.43)
Single-organ FSD[e]	55 (238)		47 (124)		15 (1,447)		1.16 (1.00-1.36)	3.64* (3.30-4.02)
Multi-organ FSD[f]	11 (46)		41 (109)		1 (96)		0.25* (0.19-0.35)	10.61* (7.57-14.88)

BDS = bodily distress syndrome; CI = confidence interval; DanFunD = Danish Study of Functional Disorders; FSD = functional somatic disorder; gen. pop. = general population; RR = risk ratio; SCL = Symptom Checklist; SCL-ANX4 = SCL anxiety subscale; SCL-DEP6 = SCL depression subscale.
a) Before SARS-CoV-2 infection/at inclusion in the DanFunD, FSD cohort.
b) Psychological strains were reported by the patients using the SCL-ANX4 and the SCL-DEP6.
c-f) BDS checklist symptoms were rated on a 5-point Likert scale and dichotomised, i.e. symptoms rated to be 'somewhat', 'quite a bit' or 'a lot' bothering were included.
c) We used a cut-off on the total BDS sum score of 40 to represent dichotomised BDS checklist sum score results.
d) ≥ 4 symptoms with a clinically relevant score - somewhat, quite a bit or a lot - in 1-4 organ groups: cardiopulmonary, gastrointestinal, generalised or musculoskeletal symptoms.
e) ≥ 4 symptoms in each of 1-2 organ groups.
f) ≥ 4 symptoms in each of 3-4 organ groups [10].
g) Unadjusted RR.
*) $p < 0.05$, using χ^2 test.

Functional somatic disorder in patients with long COVID

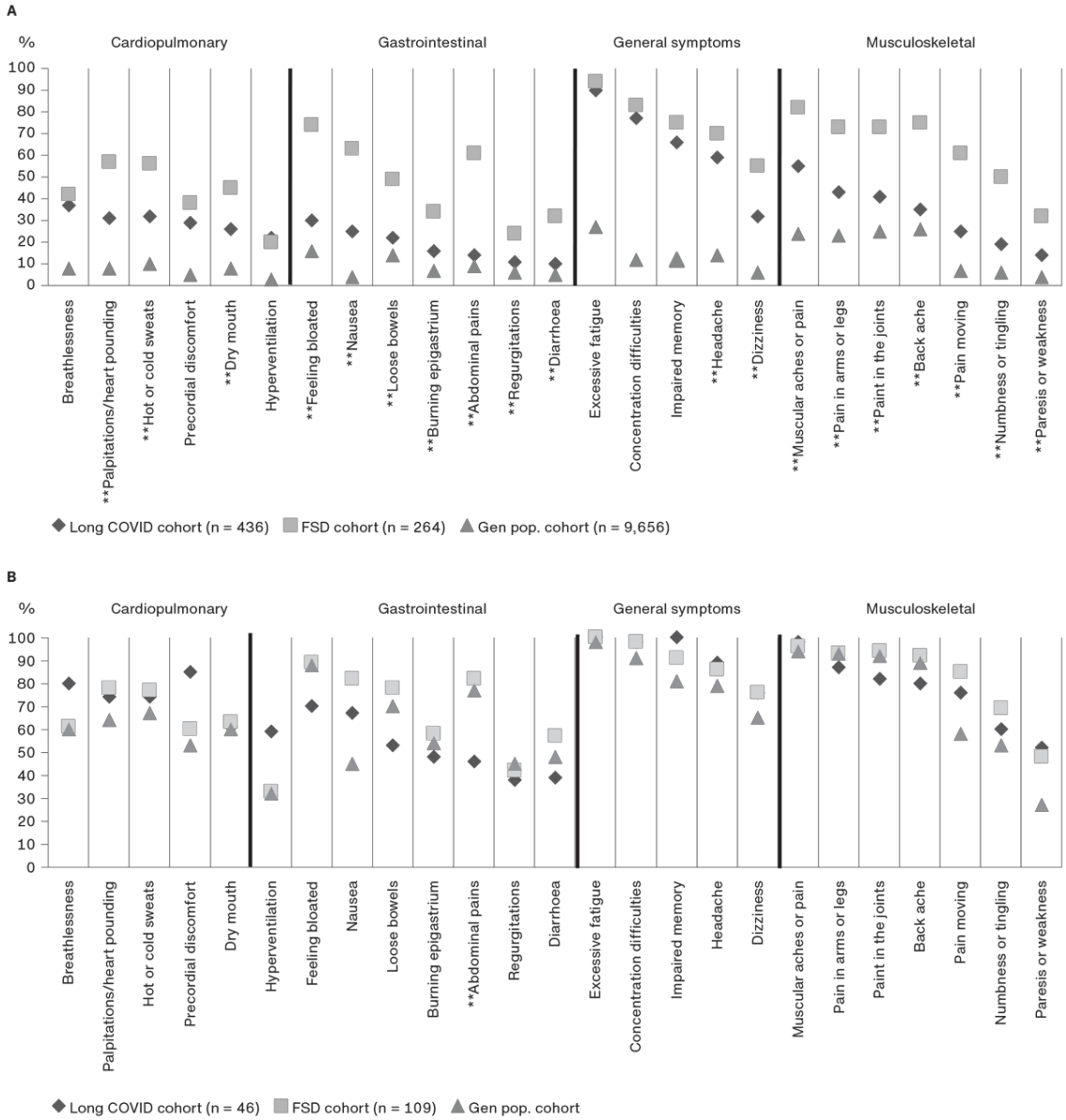
The prevalence of patients meeting criteria for any FSD according to the BDS checklist was 65% in patients with long COVID, 88% in patients with FSD, and 16% among patients in the general population cohort. Among patients with long COVID, 11% met criteria for multi-organ FSD, compared to 41% in patients with FSD and 1% in the general population cohort. Single-organ criteria were met in 55% of patients with long COVID and 47% of patients with FSD (Table 1).

Symptom profiles

Symptom prevalence was lower among patients with long COVID than among patients with FSD and higher than in the general population cohort (**Figure 1** A). GS and, to a lesser degree, MS symptoms predominated in the long COVID cohort. The symptom profiles were visually similar between the long COVID and the FSD cohort, in the GS and MS clusters (Figure 1 A). The subgroup of 11% of patients with long COVID who met the criteria for FSD

of the multi-organ type exhibited symptom prevalence and profiles in all four clusters similar to those of patients with FSD (Figure 1 B).

FIGURE 1 A. Profile of individual symptoms in patients with long COVID, patients with severe functional somatic disorder (FSD) and in the general population (gen. pop.), using the 25-item bodily distress syndrome (BDS) checklist. Frequency (%) shown on the y-axis. In the BDS checklist, symptoms are rated on a five-point Likert scale. Symptoms were dichotomised, i.e. symptoms rated to be 'somewhat', 'quite a bit' or 'a lot' bothering were included. Figures describe the outcome in dichotomised symptom scores. **B**. Multi-organ FSD: having at least four symptoms from three or four of the symptom clusters.



**) Statistically significant difference between long COVID and FSD cohorts (Bonferroni correction, $p < 0.002$. Estimates and confidence intervals not shown).

Discussion

In this comparative study, we found that patients with long COVID reported more physical symptoms than the general population and fewer symptoms than patients referred to an FSD clinic. At diagnosis (median seven months after SARS-CoV-2 infection), 11% of patients with long COVID met the criteria for multi-organ FSD, and these patients had similar symptom prevalence and profiles to those in the FSD cohort.

Long COVID symptoms have been widely documented [1, 11]. More than 200 symptoms have been attributed to long COVID [12]. The higher symptom prevalence than in the general population cohort was therefore not surprising. The lower symptom prevalence in long COVID than in patients with FSD aligns with referral criteria based on suspected FSD.

General symptoms such as headaches, concentration and memory problems, fatigue and muscle pain predominated in patients with long COVID. The frequent occurrence of fatigue (Figure 1 A) – a common feature of post-viral conditions – raises the question of whether it represents a physiological post-viral reaction or bodily and mental stress following infection that may trigger the development of FSD, and whether there is an overlap in disease mechanisms [3, 13].

Persistent symptoms have been observed following infections such as Epstein-Barr virus (EBV) infection [14], dengue, chikungunya [15], viral meningitis [16] and human herpesvirus 6 infection [17]. Fatigue following EBV and cognitive issues after viral meningitis have been documented, but comparisons of symptom profiles are limited [14, 16]. Similarities suggest common pathogenesis, with inflammatory mechanisms and potential neuromuscular damage [18] along with mitochondrial defects noted in patients with long COVID and in patients with chronic fatigue [19, 20]. Some patients with FSD may have developed FSD triggered by infection, and it is important to explore whether predominant GS symptoms or other characteristics are descriptive of such patients.

The BDS checklist was used for research purposes without diagnostic verification. Bias may arise from differences in study design, age, sex, symptom duration, comorbidities, calendar effects, geographic variations and questionnaire presentation. Patient selection was influenced by disease severity, health literacy and healthcare structure. The graphical similarities of profiles were not statistically tested and should be interpreted with caution. Despite these limitations, this study is the first to compare symptom prevalence and profiles among patients with long COVID, patients with FSD, and the general population. This study cannot determine shared disease mechanisms, and similarities may be due to selection bias.

CONCLUSIONS

Patients meeting the criteria for multi-organ FSD exhibited similar symptom profiles. GS, including fatigue and muscle pain, were common in both the long COVID and FSD cohorts, suggesting a potential overlap in pathogenesis. Prospective studies on various infections are needed to further investigate shared symptom profiles, underlying mechanisms and treatment options.

Correspondence *Jane Agergaard*. E-mail: janeager@rm.dk

Accepted 20 June 2025

Published 9 September 2025

Conflicts of interest none. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. These are available together with the article at ugeskriftet.dk/dmj

Acknowledgements We acknowledge all members of the MULTICOV consortium for sharing their ideas and for productive interaction

References can be found with the article at ugeskriftet.dk/dmj

Cite this as Dan Med J 2025;72(10):A09240627

doi 10.61409/A09240627

REFERENCES

1. Ballering AV, van Zon SKR, Hartman TCO, et al. Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study. Lancet. 2022;400(10350):452-461. https://doi.org/10.1016/S0140-6736(22)01214-4
2. Davis HE, McCorkell L, Vogel JM, et al. Long COVID: major findings, mechanisms and recommendations. Nat Rev Microbiol. 2023;21(3):133-146. https://doi.org/10.1038/s41579-022-00846-2
3. Choutka J, Jansari V, Hornig M, et al. Unexplained post-acute infection syndromes. Nat Med. 2022;28(5):911-923. https://doi.org/10.1038/s41591-022-01810-6
4. Donnachie E, Schneider A, Enck P. Comorbidities of patients with functional somatic syndromes before, during and after first diagnosis: a population-based study using Bavarian routine data. Sci Rep. 2020;10(1):9810. https://doi.org/10.1038/s41598-020-66685-4
5. Danish Health Authority. Senfølger ved COVID-19. Anbefalinger til organisering af indsatsen for patienter med langvarige symptomer ved COVID-19. Danish Health Authority, 2021. www.sst.dk/da/udgivelser/2020/Senfoelger-ved-covid-19 (Jul 2025)
6. Agergaard J, Ullahammer WM, Gunst JD, et al. Characteristics of a Danish post-COVID cohort referred for examination due to persistent symptoms six months after mild acute COVID-19. J Clin Med. 2022;11(24):7338. https://doi.org/10.3390/jcm11247338
7. Agergaard J, Gunst JD, Schiøttz-Christensen B, et al. Long-term prognosis at 1.5 years after infection with wild-type strain of SARS-CoV-2 and Alpha, Delta, as well as Omicron variants. Int J Infect Dis. 2023;137:126-133. https://doi.org/10.1016/j.ijid.2023.10.022
8. Eefsen AM, Petersen MW, Vaegter HB, et al. FuncData - a national database for functional somatic disorders in Denmark. J Psychosom Res. 2023;164:111092. https://doi.org/10.1016/j.jpsychores.2022.111092
9. Dantoft TM, Ebstrup JF, Linneberg A, et al. Cohort description: the Danish study of functional disorders. Clin Epidemiol. 2017;9:127-139. https://doi.org/10.2147/CLEP.S129335
10. Budtz-Lilly A, Fink P, Ørnbøl E, et al. A new questionnaire to identify bodily distress in primary care: the 'BDS checklist'. J Psychosom Res. 2015;78(6):536-545. https://doi.org/10.1016/j.jpsychores.2015.03.006
11. Whitaker M, Elliott J, Chadeau-Hyam M, et al. Persistent COVID-19 symptoms in a community study of 606,434 people in England. Nat Commun. 2022;13(1):1957. https://doi.org/10.1038/s41467-022-29521-z
12. Thaweethai T, Jolley SE, Karlson EW, et al. Development of a definition of postacute sequelae of SARS-CoV-2 infection. JAMA. 2023;329(22):1934-1946. https://doi.org/10.1001/jama.2023.8823
13. Sukocheva OA, Maksoud R, Beeraka NM, et al. Analysis of post COVID-19 condition and its overlap with myalgic encephalomyelitis/chronic fatigue syndrome. J Adv Res. 2022;40:179-196. https://doi.org/10.1016/j.jare.2021.11.013
14. Jason LA, Cotler J, Islam MF, et al. Risks for developing myalgic encephalomyelitis/chronic fatigue syndrome in college students following infectious mononucleosis: a prospective cohort study. Clin Infect Dis. 2021;73(11):e3740-e3746. https://doi.org/10.1093/cid/ciaa1886
15. Kuna A, Gajewski M. Chronic symptoms persisting after travel-related infections. Int Marit Health. 2018;69(3):207-212. https://doi.org/10.5603/IMH.2018.0033
16. Damsgaard J, Hjerrild S, Andersen H, et al. Long-term neuropsychiatric consequences of aseptic meningitis in adult patients. Infect Dis (Lond). 2015;47(6):357-363. https://doi.org/10.3109/23744235.2015.1018838
17. Kleinstäuber M, Schröder A, Daehler S, et al. Aetiological understanding of fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome and classificatory analogues: a systematic umbrella review. Clin Psychol Eur. 2023;5(3):11179. https://doi.org/10.32872/cpe.11179
18. Agergaard J, Khan BYA, Engell-Sørensen T, et al. Myopathy as a cause of long COVID fatigue: evidence from quantitative and single fiber EMG and muscle histopathology. Clin Neurophysiol. 2023;148:65-75. https://doi.org/10.1016/j.clinph.2023.01.010

19. Appelman B, Charlton BT, Goulding RP, et al. Muscle abnormalities worsen after post-exertional malaise in long COVID. Nat Commun. 2024;15(1):17. https://doi.org/10.1038/s41467-023-44432-3

20. Tomas C, Brown A, Strassheim V, et al. Cellular bioenergetics is impaired in patients with chronic fatigue syndrome. PLoS One. 2017;12(10):e0186802. https://doi.org/10.1371/journal.pone.0186802

