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Chronic overlapping pain conditions increase the risk of long COVID features, regardless of acute COVID status

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Abstract

Chronic overlapping pain conditions (COPCs) refer to conditions that have similar central nervous system pathophysiologic mechanisms driving widespread pain as well as common comorbid symptoms such as fatigue and problems with sleep, memory, and mood. If COPCs predict the onset of long COVID, this could offer a valuable orientation for long COVID-related research and clinical care. This retrospective cohort study aimed to determine whether having a COPC predicts the onset of long COVID features using US electronic health records and 1:1 propensity score matching without replacement. The study cohorts included (1) people with acute COVID (n = 1,038,402), (2) people with acute influenza (n = 262,092), and (3) a noninfected cohort comprising people with a routine healthcare encounter (n = 1,081,593). Having a COPC increased the risk of long COVID features in all 3 study cohorts. Among those with COVID, having a pre-existing COPC increased the risk by 1.47 (95% CI = 1.46, 1.47). In the influenza cohort, COPCs increased the risk by 1.39 (95% CI = 1.38, 1.40). In the noninfected cohort, COPCs increased the risk by 1.57 (95% CI = 1.56, 1.59). These findings reinforce the likelihood that nociplastic mechanisms play a prominent role in long COVID. Recognizing that this ubiquitous nonspecific syndrome occurs frequently in the population can inform precision medicine therapies that avoid the pitfalls of viewing long COVID exclusively in the framework of postinfectious disease.

Keywords: Post-COVID, Long COVID, Long haulers syndrome, Nociplastic pain, Chronic pain, Pain management, Fatigue, Rheumatology, Musculoskeletal pain, Post-COVID conditions, Pandemic, Electronic medical records, Electronic health records

1. Introduction

As the relationship between the coronavirus disease (COVID) caused by the SARS-CoV-2 virus and the cluster of symptoms described as long COVID is being vigorously debated, chronic overlapping pain conditions (COPCs) may offer a valuable reorientation for long COVID-related research. Chronic overlapping pain conditions reflect the common co-occurrence of chronic pain conditions including fibromyalgia, chronic fatigue syndrome, migraine headache, irritable bowel syndrome, endometriosis, and low back pain to name a few.[1,22] Chronic overlapping pain conditions are also a group of conditions that have the same pathophysiologic mechanism where amplified neural signaling within the central nervous system (CNS) elicits nociplastic pain.[22] Certainly, inflammation and tissue damage because of COVID can result in peripherally mediated, nociceptive pain, but long COVID pain is likely complex, multifactorial, and similar to other chronic pain states, where multiple types of pain are present (ie, mixed-pain states).[8,12]

Despite the overlap of long COVID symptoms and those associated with COPCs, the link between COPCs and long COVID is understudied.[35] Pain in various body locations is among the lingering and emerging symptoms that people began reporting shortly after the start of the COVID pandemic and in the weeks and months after an acute COVID diagnosis.[2,4,9,10,21,25] These long-term health effects are referred to as long COVID, postacute sequelae of SARS-CoV-2 infection (ie, PASC), post-COVID conditions, or long haulers syndrome. In fact, although long COVID includes a comprehensive list of symptoms that vary from person to person, pain is well represented among long COVID's core symptom clusters.[2,25] For example, semantic phenotypic clustering using electronic health records (EHR) revealed 6 long COVID symptom clusters, 4 of which have pain symptoms as defining features and collectively represented 67% of the study sample.[25] In addition, in a study of more than 270,000 COVID survivors, pain was the only long COVID symptom with a higher incidence in the 3- to 6-month period than in the 0- to 3-month period, suggesting that pain is a prominent and relatively persistent element of long COVID.[32] As one would expect if due to nociplastic pain, long COVID pain symptoms can involve any region of the body and include diffuse myalgias, arthralgias, musculoskeletal pain, headaches, chest pain, back pain, abdominal pain, and generalized "body ache."[2,4,9,10,21,25] Yet, widespread pain and COPCs are not

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always considered among the proposed long COVID subtypes[38] or treatment approaches.[13,16]

If COPCs and pre-existing nociplastic pain predict the onset of long COVID, this could inform targeted screening, prognosis, and intervention development. Establishing this relationship would allow clinicians and researchers to leverage the available body of literature on nociplastic pain for the purpose of managing long COVID symptoms and avoid the pitfalls of viewing long COVID symptoms exclusively in the framework of infectious disease. The goal of this retrospective cohort study was to determine whether having a COPC predicts long COVID features using EHR data from healthcare organizations across the United States. Given the importance of a control group when studying long COVID,[3,34,37] we also tested the association of COPCs with the onset of long COVID features within an influenza cohort and a noninfected cohort.

2. Methods

This study was limited to the analysis of deidentified EHR and did not involve the collection, use, or transmittal of individually identifiable data. Thus, this study was exempted from Institutional Review Board approval. This study was not preregistered.

2.1. Data

We extracted data for this study on April 4 and 5, 2023, from the anonymized EHR for more than 91 million people (insured and uninsured) of 56 US healthcare organizations through TriNetX Analytics. These data included demographics (age, sex, race, and ethnicity) using health level 7 version 3 administrative standards, diagnoses using *International Classification of Diseases, 10th revision* (*ICD-10*) and associated *ICD-9* codes, encounter dates, current procedural terminology (CPT), and laboratory observation identifiers name codes (LOINC) terms. Several studies have used this large network of linked EHR from hospitals, primary care clinics, and specialist providers to study the epidemiology and outcomes associated with COVID and long COVID.[15,19,32,33,36]

TriNetX Analytics complied with the Health Insurance Portability and Accountability Act (HIPAA). The TriNetX Analytics platform displayed data in aggregate form and provided deidentified person-level data sets, consistent with the deidentification standard defined in Section §164.514(a) of the HIPAA Privacy Rule.

For this study, we created 3 primary cohorts: (1) people with COVID, (2) people with influenza, and (3) a noninfected cohort comprising people with a routine healthcare encounter. Within each cohort, all people had to have a visit encounter between January 1, 2018, and January 20, 2020, as well as an encounter at least 6 months after index event. The index event for each cohort was defined by a participant's first instance of the index event (ie, COVID, influenza, or a routine healthcare visit) within the inclusion timeframe. The follow-up period for participants across the 3 cohorts ranged from 180 days to 1165 days, which depended on when an index event occurred between January 20, 2020, and March 30, 2023 (the last encounter date within the data).

The COVID cohort included people who had a confirmed diagnosis (using *ICD-10* and *ICD-9*) or positive laboratory result (using LOINC) indicating a positive COVID infection at age 10 years or older on or after January 20, 2020 (ie, the date of first confirmed COVID infection in the United States) to present (Supplemental Table 1, available at http://links.lww.com/PAIN/B952). The COVID cohort excluded people diagnosed with an influenza virus infection in the month before their index COVID event. The influenza cohort included people who had a confirmed diagnosis or positive laboratory result indicating an influenza virus infection on or after January 20, 2020 (Supplemental Table 2, available at http://links.lww.com/PAIN/B952). The influenza cohort excluded people who had COVID during the inclusion timeframe. The noninfected cohort included people with a routine healthcare visit on or after January 20, 2020, using CPT (Supplemental Table 3, available at http://links.lww.com/PAIN/B952). The noninfected cohort excluded people diagnosed with COVID or influenza within the inclusion timeframe and reflected a random sample of 1,000,000 people ±10% who met cohort inclusion criteria.

2.2. Chronic overlapping pain conditions

Previous work established the *ICD-10* and *ICD-9* code phenotype for COPCs (Supplemental Table 4, available at http://links.lww.com/PAIN/B952).[26] First, Schrepf et al. (2020) consulted with an expert panel to develop a list of codes for 10 common COPCs and then used natural language searchers of EHR to validate the presence of COPCs in association with the proposed codes.

2.3. Long COVID features

Previous work established the *ICD-10* and *ICD-9* code phenotype for long COVID features[32,33] (Supplemental Table 5, available at http://links.lww.com/PAIN/B952). In summary, Taquet et al. (2021) developed a list of codes based on 9 clinical features that are common amongst long COVID definitions (ie, abdominal symptoms, abnormal breathing, anxiety, depression, fatigue/malaise, headache, chest pain, throat pain, other types of pain, and cognitive dysfunction). We identified long COVID features using new diagnosis codes that occurred after the index events. If people had diagnosis codes for long COVID features in their medical record before an index event, it did not count as a long COVID feature.

2.4. Analysis

We used SAS Software (version 9.4) to conduct data analysis after extracting raw data files from the TriNetX Analytics data platform. First, we conducted a 1:1 propensity score match without replacement using the SAS PSMATCHING macro with a 0.1*pooled standard deviation of the propensity score's logit. In the propensity score match, we included a set of established and suspected risk factors for COVID as well as determinants of COVID severity: age, sex, race, ethnicity, diabetes, chronic kidney disease, asthma, chronic lower respiratory diseases, nicotine dependence, substance use disorder, ischemic heart disease and other forms of heart disease, socioeconomic deprivation, cancer (and hematological cancer in particular), chronic liver disease, stroke, dementia, organ transplant, rheumatoid arthritis, lupus, psoriasis, and disorders involving an immune mechanism (Supplemental Table 6, available at http://links.lww.com/PAIN/B952). We split each study cohort (ie, COVID, influenza, noninfected) into 2 matched control cohorts: (1) people with a COPC before their index date and (2) people without a COPC before their index date.

Next, we generated sample descriptions for the 3 study cohorts by COPC status. To estimate the effect of COPC on long COVID features, the risk of receiving a diagnosis for long COVID features was examined 1 to 180 days after index event, comparing COPC to non-COPC in each of the study cohorts. In primary analyses, we defined long COVID as having 1 or more

diagnoses for long COVID features relative to 0 diagnoses for long COVID features.

To provide a qualitative comparison for the effect size of COPC's impact on long COVID features within the COVID cohort, we also calculated risk ratios for sex and acute COVID hospitalization status in our data since they are known risk factors for PASC (ie, females and those with worse acute COVID severity have a higher risk of long COVID onset, more long COVID symptoms, and a longer duration of long COVID).[5,7,11,14,17,18,20,23,24,29–31] In sensitivity analyses, we used 2 additional definitions for long COVID features: (1) 3 or more diagnoses for long COVID features relative to 2 or less diagnoses for long COVID features and (2) 4 or more diagnoses for long COVID features relative to 3 or less diagnoses for long COVID features.

3. Results

Tables 1–3 describe the study cohorts by COPC status before the 1:1 propensity score match. The COVID cohort comprised 1,038,402 people (58.6% of those with a COPC had long COVID features, and 33.6% of those without a COPC had long COVID features), the influenza cohort comprised 262,092 people (68.3% of those with a COPC had long COVID features, and 41.3% of those without a COPC had long COVID features), and the noninfected cohort comprised 1,081,593 people (24.4% of those with a COPC had long COVID features, and 10.8% of those without a COPC had long COVID features). In the COVID and noninfected cohorts, those with a COPC were older and more likely to be women than those without a COPC, whereas there were not large differences by race or ethnicity. In the influenza cohort, these trends were consistent with one exception: Men made up a larger proportion of those with a COPC relative to those without a COPC.

Table 4 presents the association of COPCs with long COVID features in the COVID cohort using a 1:1 propensity score match without replacement (n = 734,722). Among those with COVID, having a pre-existing COPC increased the risk by 1.47 (95% CI = 1.46, 1.47). When looking at individual long COVID features, associations were largest for headache (Risk Ratio [RR] = 2.16; 95% CI = 2.14, 2.19), and pain (RR = 1.69; 95% CI = 1.68, 1.71) and smallest for cognitive symptoms (RR = 1.20; 95% CI = 1.19, 1.22) and abnormal breathing (RR = 1.25; 95% CI = 1.24, 1.26).

Table 1

Baseline characteristics for the COVID cohort.

Baseline characteristics	With COPC		Without COPC	
	n = 411,053		n = 627,349	
	n	%	n	%
Age group at index				
10-17	10,011	2.4%	65,069	10.4%
18-24	21,287	5.2%	56,030	8.9%
25-34	51,465	12.5%	89,456	14.3%
35-44	67,881	16.5%	89,502	14.3%
45-64	156,833	38.2%	196,039	31.2%
65+	103,576	25.2%	131,253	20.9%
Sex				
Male	126,549	30.8%	269,951	43.0%
Female	284,470	69.2%	357,335	57.0%
Unknown	34	0.0%	63	0.0%
Ethnicity				
Hispanic or Latino	38,237	9.3%	63,070	10.1%
Not Hispanic or Latino	300,101	73.0%	421,077	67.1%
Unknown	72,715	17.7%	143,202	22.8%
Race				
Anglo-American	287,209	69.9%	424,019	67.6%
Black or African American	65,062	15.8%	98,590	15.7%
Other (AI/AN, Asian, Native Hawaiian, or other Pacific Islander)	8672	2.1%	18,623	3.0%
Unknown	50,110	12.2%	86,117	13.7%
Long COVID features				
Any	240,870	58.6%	210,578	33.6%
Chest/throat pain	61,866	15.1%	47,363	7.5%
Abnormal breathing	81,035	19.7%	68,528	10.9%
Abdominal symptoms	78,109	19.0%	57,902	9.2%
Fatigue	63,905	15.5%	47,784	7.6%
Anxiety/depression	107,642	26.2%	78,379	12.5%
Anxiety	78,981	19.2%	57,297	9.1%
Depression	66,301	16.1%	42,528	6.8%
Pain	79,199	19.3%	42,817	6.8%
Headache	71,012	17.3%	31,111	5.0%
Cognitive symptoms	30,767	7.5%	25,223	4.0%
Myalgia	24,527	6.0%	13,167	2.1%

COPC, chronic overlapping pain condition.

Sex and hospitalization status were also associated with PASC in the COVID cohort (data not shown). The risk of having long COVID features was 1.22 (95% CI = 1.21, 1.23) times higher among females relative to males. Hospitalization because of acute COVID also increased the risk of having long COVID features in these data (RR = 1.39; 95% CI = 1.38, 1.41).

Tables 5 and 6 present the association of COPCs with long COVID features in the influenza and noninfected cohorts using a 1:1 propensity score match without replacement. In the influenza cohort (n = 181,802), COPCs increased the risk of having long COVID features by 1.39 (95% CI = 1.38, 1.40), which is 5% smaller in magnitude relative the association within the COVID cohort. In the noninfected cohort (n = 514,768), COPCs increased the risk of having long COVID features by 1.57 (95% CI = 1.56, 1.59), which is 7% larger in magnitude relative the association within the COVID cohort.

The increased risk of long COVID features because of COPCs was robust in the sensitivity analyses that included more stringent long COVID criteria (Supplemental Tables 7a-c, available at http://links.lww.com/PAIN/B952). For example, when long COVID was defined as having 3 or more diagnoses for long COVID features relative to 2 or fewer diagnoses, having a pre-existing COPC increased the risk of long COVID by 1.68 (95% CI = 1.66, 1.69) among those with COVID. In addition, when the definition of long COVID changed to require $\geq$3 or $\geq$4 diagnoses for long COVID features instead of $\geq$1 diagnoses, the prevalence of long COVID decreased within the study cohorts, as expected.

4. Discussion

We used a national EHR database to demonstrate a relationship between the presence of COPCs and the future development of long COVID features when following participants up to 3 years (1165 days), regardless of whether individuals suffer from acute COVID, influenza, or no infectious exposure at all. In the COVID cohort, the magnitude of COPC effect sizes was comparable with if not larger than the effect sizes for sex and acute COVID hospitalization status, known risk factors for long COVID.[5,7,11,14,17,18,20,23,24,29–31] These findings are consistent with previous research where pre-existing chronic pain conditions including fibromyalgia, back pain, and migraine predict the onset of PASC.[14,30] Our results also contribute to a growing body of evidence that long COVID is due to factors other than acute COVID exposure[27] and at least partly driven by nociplastic, CNS

Table 2

Baseline characteristics for the influenza cohort.

Baseline characteristics	With COPC		Without COPC	
	n = 117,402		n = 144,690	
	n	%	n	%
Age group at index				
10-17	6449	5.5%	33,192	22.9%
18-24	8306	7.1%	16,902	11.7%
25-34	15,304	13.0%	20,553	14.2%
35-44	16,633	14.2%	17,145	11.8%
45-64	37,690	32.1%	31,847	22.0%
65+	33,020	28.1%	25,051	17.3%
Sex				
Male	80,893	68.9%	80,049	55.3%
Female	36,502	31.1%	64,619	44.7%
Unknown	7	0.0%	22	0.0%
Ethnicity				
Hispanic or Latino	12,329	10.5%	18,155	12.5%
Not Hispanic or Latino	97,717	83.2%	110,168	76.1%
Unknown	7356	6.3%	16,367	11.3%
Race				
Anglo-American	88,901	75.7%	103,699	71.7%
Black or African American	16,953	14.4%	19,861	13.7%
Other (AI/AN, Asian, Native Hawaiian, or other Pacific Islander)	2897	2.5%	5766	4.0%
Unknown	8651	7.4%	15,364	10.6%
Long COVID features				
Any	80,196	68.3%	59,745	41.3%
Chest/throat pain	41,338	35.2%	27,213	18.8%
Abnormal breathing	48,035	40.9%	32,921	22.8%
Abdominal symptoms	45,901	39.1%	30,763	21.3%
Fatigue	38,857	33.1%	24,673	17.1%
Anxiety/depression	44,627	38.0%	26,269	18.2%
Anxiety	33,979	28.9%	18,980	13.1%
Depression	30,623	26.1%	16,405	11.3%
Pain	51,306	43.7%	31,776	22.0%
Headache	40,373	34.4%	22,135	15.3%
Cognitive symptoms	22,483	19.2%	13,001	9.0%
Myalgia	23,838	20.3%	12,734	8.8%

COPC, chronic overlapping pain condition.

Table 3

Baseline characteristics for the noninfected cohort.

Baseline characteristics	With COPC		Without COPC	
	n = 257,752		n = 823,841	
	N	%	n	%
Age group at index				
10-17	12,314	4.8%	185,019	22.5%
18-24	14,703	5.7%	70,730	8.6%
25-34	29,931	11.6%	94,641	11.5%
35-44	44,995	17.5%	114,469	13.9%
45-64	124,237	48.2%	292,342	35.5%
65+	31,572	12.2%	66,640	8.1%
Sex				
Male	80,527	31.2%	318,491	38.7%
Female	177,203	68.7%	505,243	61.3%
Unknown	22	0.0%	107	0.0%
Ethnicity				
Hispanic or Latino	15,981	6.2%	64,553	7.8%
Not Hispanic or Latino	204,818	79.5%	627,941	76.2%
Unknown	36,953	14.3%	131,347	15.9%
Race				
Anglo-American	190,369	73.9%	571,574	69.4%
Black or African American	31,740	12.3%	107,047	13.0%
Other (AI/AN, Asian, Native Hawaiian, or other Pacific Islander)	8734	3.4%	40,153	4.9%
Unknown	26,909	10.4%	105,067	12.8%
Long COVID features				
Any	62,911	24.4%	89,039	10.8%
Chest/throat pain	6098	2.4%	8617	1.0%
Abnormal breathing	5538	2.1%	8078	1.0%
Abdominal symptoms	13,887	5.4%	20,209	2.5%
Fatigue	7373	2.9%	9753	1.2%
Anxiety/depression	26,167	10.2%	42,298	5.1%
Anxiety	19,416	7.5%	32,217	3.9%
Depression	13,846	5.4%	20,084	2.4%
Pain	14,102	5.5%	12,408	1.5%
Headache	14,960	5.8%	8140	1.0%
Cognitive symptoms	2896	1.1%	4611	0.6%
Myalgia	3233	1.3%	2217	0.3%

COPC, chronic overlapping pain condition.

symptoms that are consistent with COPCs. The development of long COVID treatment and interventions should draw from the rich literature concerning COPCs and nociplastic pain, such as multicomponent approaches that include patient education, care coordination, and nonpharmaceutical therapies.[28]

Our findings emphasize the need to articulate long COVID diagnostic criteria within the context of COVID and challenge whether it is distinct from long COVID features after other infectious episodes or in the absence of acute illness. For example, defining long COVID as one or more diagnostic features, as in past work by Taquet et al.,[32,33] likely lacks specificity. In addition, the National Institutes of Health RECOVER Initiative recently proposed a long COVID definition based on having 12 or more patient-reported symptoms.[34] Using this criterion, Thaweethai et al. (2023) reported a 20% prevalence of long COVID among those infected with COVID and a 4% prevalence of long COVID among those uninfected. These results are comparable with our findings when requiring 3 or more diagnoses to define long COVID in sensitivity analyses; the prevalence of those with long COVID features was 20.4% among those with COPCs in the COVID cohort and 3.3% among those with COPCs in the noninfected cohort (after the 1:1 propensity score match). However, we also included an influenza cohort as a control group, and the prevalence of those with long COVID features was higher in the influenza cohort relative to the COVID

Table 4

The risk ratios for chronic overlapping pain condition on long COVID features in the COVID cohort.*

	Risk ratio	95% CI
All PASC	1.47	1.46, 1.47
Chest/throat pain	1.36	1.35, 1.37
Abnormal breathing	1.25	1.24, 1.26
Abdominal symptoms	1.42	1.41, 1.43
Fatigue	1.33	1.32, 1.34
Anxiety/depression	1.42	1.41, 1.43
Anxiety	1.41	1.40, 1.42
Depression	1.46	1.45, 1.47
Pain	1.69	1.68, 1.71
Headache	2.16	2.14, 2.19
Cognitive symptoms	1.20	1.19, 1.22
Myalgia	1.66	1.63, 1.69

* n = 734,722 people.

PASC, postacute sequelae of SARS-CoV-2 infection.

Table 5

The risk ratios for chronic overlapping pain condition on long COVID features in the influenza cohort.*

	Risk ratio	95% CI
All PASC	1.39	1.38, 1.40
Chest/throat pain	1.25	1.23, 1.26
Abnormal breathing	1.22	1.21, 1.23
Abdominal symptoms	1.28	1.27, 1.29
Fatigue	1.26	1.24, 1.27
Anxiety/depression	1.37	1.36, 1.39
Anxiety	1.38	1.37, 1.40
Depression	1.38	1.36, 1.40
Pain	1.34	1.32, 1.35
Headache	1.49	1.47, 1.51
Cognitive symptoms	1.22	1.20, 1.24
Myalgia	1.33	1.30, 1.35

* n = 181,802 people.
PASC, postacute sequelae of SARS-CoV-2 infection.

cohort no matter how we defined long COVID. This suggests that particular attention is required to determine whether long COVID features after COVID infection can be distinguished from clinical features that develop after other viral infections such as influenza. A lack of specificity regarding long COVID diagnostic criteria can have implications for clinical care and treatment development. For example, long-term health problems after an acute illness or hospitalization are not unique to acute COVID.[17,24] This was demonstrated in a recent study that followed participants who sought care for symptoms suggestive of acute COVID and compared outcomes for those who received a positive COVID test with those who received a negative COVID test.[37] In these data, a higher proportion of those in the COVID-negative group reported persistently poor physical, mental, or social well-being at 3-month follow-up relative to the COVID-positive group (54% vs 40%, respectively). In addition, those in the COVID-positive group experienced greater improvements across these well-being domains than the COVID-negative group.

4.1. Strengths and limitations

This study provides evidence that having a pre-existing COPC increases the risk of being diagnosed with long COVID features within a large, nationwide database of EHR. However, our results should be considered alongside its limitations. For one, although EHR are an efficient means to analyze data from a large study sample, they can be vulnerable to measurement error and misclassification.[6] In addition, those with a diagnosed COPC may be more likely to seek treatment for future symptoms relative to those without a COPC, and these findings may not be generalizable to those who obtain care outside of healthcare organizations.

Table 6

The risk ratios for chronic overlapping pain condition on long COVID features in the noninfected cohort.*

	Risk ratio	95% CI
All PASC	1.57	1.56, 1.59
Chest/throat pain	1.45	1.41, 1.49
Abnormal breathing	1.36	1.32, 1.40
Abdominal symptoms	1.45	1.43, 1.48
Fatigue	1.47	1.43, 1.51
Anxiety/depression	1.40	1.38, 1.42
Anxiety	1.38	1.36, 1.40
Depression	1.49	1.46, 1.52
Pain	1.94	1.90, 1.99
Headache	3.36	3.24, 3.48
Cognitive symptoms	1.34	1.30, 1.40
Myalgia	2.34	2.21, 2.48

* n = 514,758 people.
PASC, postacute sequelae of SARS-CoV-2 infection.

5. Conclusions

The onset of long COVID features was relatively common regardless of acute COVID exposure. In addition, those with pre-existing COPCs had an increased risk of being diagnosed with long COVID features. These findings reinforce the likelihood that nociplastic pain is a key mechanism in long COVID and can inform precision medicine therapies that avoid the pitfalls of viewing long COVID exclusively in the framework of infectious disease. Specifically, our findings indicate that individuals with COPCs are at risk of developing long COVID features either spontaneously or associated with an infection. More research is needed to determine whether there is an etiologic difference between long COVID and COPCs. For clinicians who treat people with long COVID, it may be helpful to review the medical record and see whether someone had a pre-existing COPC diagnosis before long COVID onset.

Conflict of interest statement

Drs. Bergmans and Clauw report consulting fees from Tonix Pharmaceuticals Inc. Drs. Harris and Lederman and Ms. Flint report employment by Tonix Pharmaceuticals Inc.

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