

The Chronic Pain Pandemic: How similar is Long Covid Chronic Pain to Fibromyalgia?

Introduction

Chronic pain is described as pain which persists despite adequate time for tissue healing (1). There is no conclusive timeframe, but it is often defined as having been present for more than 12 weeks (2). Chronic pain is a complex condition which has psychological and social implications for a patient, it can be severely debilitating. A systematic review and meta-analysis of the prevalence of chronic pain found that chronic pain affects between ~33-50% of the UK population, corresponding to around 28 million adults (2). With an aging population, and the increase of musculoskeletal problems, chronic pain prevalence is likely to rise further (3). Chronic pain may be caused by a range of identifiable conditions, however, for many patients an identifiable cause is not found. One such condition is fibromyalgia, characterised by widespread pain, fatigue, sleep disturbance and other symptoms (4). Another condition is Long Covid is defined by the National Institute for Health and Care Excellence (NICE) as persistent signs and symptoms of COVID-19 four weeks after contracting COVID-19 illness (5, 6). Musculoskeletal pain is the fourth most common self-reported symptom of Long Covid. Whilst GOV.UK estimate the prevalence of chronic musculoskeletal pain in Long Covid to be ~24% of those with Long Covid (7), a narrative review suggested the actual prevalence is unknown and may be between 0.3 to 65.2% (8). For individuals with pre-existing chronic pain, Long Covid exacerbates their pain symptoms (8). Additionally, there are individuals who were previously unaffected by chronic pain who develop new-onset long-term pain after COVID-19 infection (7). Thus, the number of patients suffering from chronic pain symptoms is rising, increasing the burden on the National Health Care system (9). The nature of chronic pain in Long Covid has been reported as widespread and associated with other symptoms. This essay aims to compare the chronic pain experienced by those with fibromyalgia and Long Covid, aiming to discuss whether the pain is similar in nature, and whether this can direct future management and research.

Prevalence and risk factors for both conditions

The estimated global and UK prevalence of fibromyalgia are 2.7% and 5.4%, respectively (10, 11). Fibromyalgia is the third most common musculoskeletal condition after lumbar pain

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and osteoarthritis (12). By comparison, for Long Covid, an estimated 2.0 million people in the UK (3% of the total population) reported experiencing Long Covid symptoms (7), with approximately 1.3 million (72%) reporting symptoms affected their daily activities.

In both fibromyalgia and Long Covid, women are more commonly affected than men (7, 10, 11), making it the main common risk factor for the two conditions. For fibromyalgia, other risk factors include stressful life events preceding the onset of illness and genetic predisposition (13) and the catechol-O-methyltransferase (*COMT*) gene has been repeatedly associated with the perception and experience of pain (13). Risk factors which are exclusive for Long Covid include pre-existing health conditions: asthma, hypothyroidism, hypertension, obesity, older age and more severe acute illness of COVID-19 infection (14). The usual age of presentation of fibromyalgia is 20 to 50 years, but 35 to 69 years with Long Covid, making those with Long Covid a slightly older cohort (7, 10, 11, 14).

Both fibromyalgia and Long Covid are diagnosed clinically (15). In 2016, there was a revision of the 2010/11 American College of Rheumatology (ACR) diagnostic criteria for Fibromyalgia, **Figure 1** (15). There are no biomarkers and a physical examination is not diagnostically useful because of its poor validity and poor reproducibility (16). A diagnosis of Long Covid is made if a patient has ongoing symptoms of COVID-19 infection after four weeks from the initial illness (5, 6), where no alternative diagnosis can explain symptoms. Long Covid is subdivided into ongoing symptomatic COVID-19, symptoms from four to twelve weeks, and Post-COVID Syndrome (PCS), symptoms after twelve weeks (5, 6).

Feature of chronic pain in both conditions

Importantly, we must examine the type of pain reported by individuals, to determine whether it is similar or different to direct management and research. Symptoms experienced by patients with the two conditions are complex and multifactorial, affected by multiple factors within the individual's life. **Figure 2** is adapted from the International Classification of Functioning, Disability and Health (ICF) framework (17). It demonstrates how an individual's body functions and structures, activities, participation, environmental and personal factors affect fibromyalgia or Long Covid. By comparing the conditions in an

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ICF frameworks we can see how similarly the conditions affect the functioning of an individual. Notably, generalised chronic pain is a feature of both.

In available literature, the chronic pain features of fibromyalgia are similar to those in Long Covid. In fibromyalgia, whilst it is considered to be a musculoskeletal condition, literature suggests the chronic pain is often similar to neuropathic pain (18), with descriptions of paraesthesia, or “pins and needles”. Additionally, the chronic pain is described as “tender points”, areas of greater sensitivity to pressure (4). This has been described as central sensitisation, which is defined as hypersensitivity to stimuli (19). In the most recent 20 years, advancing research has demonstrated that patients with fibromyalgia need less pressure stimulus to promote the same pain response in the brain as those without fibromyalgia, suggesting pain processing is altered (20, 21). Alternatively, Some literature considers the chronic pain to be nociplastic pain (19). This describes pain where the central nervous system increases its sensitivity to pain (19), without clear evidence of actual tissue damage. There is a lack of studies which describe the characteristics of chronic pain experienced by those with Long Covid. In available literature, chronic pain is predominantly reported to be musculoskeletal pain and described as “muscle aches” (7). Musculoskeletal pain is defined as arising from structures such as bones, muscles, joints, tendons, and ligaments (22).

For those with fibromyalgia, chronic pain can affect anywhere in the body, from head to toe (4). Patients often have chronic headaches, with or without migraine (4). Many patients have irritable bowel syndrome, causing abdominal pain and discomfort, alongside other symptoms of alternating constipation and diarrhoea. Patients may have pain in their genitals, including valvular vestibulitis or dysmenorrhoea, in females, which may lead to difficulty having sexual intercourse. The location, type, and severity of pain are affected by factors, including comorbidities, such as obesity, variations in temperature, physical and mental stress (4). The other two common symptoms are fatigue, both physical and mental, and sleep disturbances (4). The musculoskeletal pain experienced by individuals who suffer from Long Covid is often described as widespread and generalised (8). Patients commonly experience widespread myalgia; common sites include the lower legs and shoulder girdle (23). Four studies have reported localised pain symptoms in the lower limbs and cervical spine (8). One study has suggested that nociceptive-type pain is significantly more common than neuropathic-type pain (24). The majority of studies have been performed in

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hospitalised patients, rather than non-hospitalised (8). Interestingly, two studies which compared rates of MSK pain (25) and chest pain (26) in hospitalised and non-hospitalised Long Covid patients, found higher rates in non-hospitalised patients. By contrast, higher rates of myalgia pain were found in hospitalised Long Covid patients (26).

The exact pathophysiological mechanism underpinning chronic pain in both fibromyalgia and Long Covid is unknown. For fibromyalgia, hypotheses include the possibility of peripheral and central hyperexcitability, altered pain perception and somatisation (4). For Long Covid, studies have suggested the virus may induce a period of prolonged inflammatory response, with many associated pro-inflammatory cytokines and hyperactivation of immune cells (8, 23).

Prognosis varies for patients with fibromyalgia, with the majority experiencing life-long difficulties managing their pain (4). Long Covid studies have found contrasting findings relating to the prognosis of chronic pain. A review concluded that no consistent pattern of chronic pain can be identified, given the limited studies (8). Additionally, the relatively new nature of the illness makes it impossible to measure the long-term prognosis of Long Covid chronic pain. Fibromyalgia is associated with substantial socioeconomic loss. An estimated 20-50% of those with fibromyalgia report that they are unable to work and of those that do, 36% take an average of two or more absences from work, per month (27, 28). The average number of annual healthcare consultations for patients with fibromyalgia is almost double that of healthy individuals (29), in countries where patients pay for healthcare this is a massive economic burden. Limited data is available about the economic burden of Long Covid, but given it is estimated between 40-70% of individuals are unable to work between 8-12 weeks after hospital admission (30, 31), it is likely they will suffer economically too (27, 28).

Additional symptoms

Some symptoms are common to both fibromyalgia and Long Covid, **Figure 3**. These include, fatigue, anxiety, depression, sleep disturbances, cognitive dysfunction and difficulty concentrating, headache, diarrhoea and autonomic disturbances: dry mouth (xerostomia), dry eyes (xerophthalmia), blurred vision, photophobia, Raynaud phenomenon (4, 7).

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Symptoms which are unique to fibromyalgia include dyspepsia, dysmenorrhoea, vulvar vestibulitis, stiffness, restless leg syndrome, constipation, tender spots, jaw pain (4).

Symptoms which are exclusive to Long Covid include dyspnoea, loss of smell, changes to taste, cough, vertigo or dizziness, chest pain, wheezing, runny nose, sneezing, palpitations and loss of appetite (7).

Management of chronic pain in both conditions

Since scientists have been researching into fibromyalgia for over 50 years, management techniques are evidenced based and have been adapted to holistically support patients (32). Management of fibromyalgia follows the Biopsychosocial Model, incorporating medicinal with psychosocial treatments. NICE issues guidance which focuses on a multidisciplinary team approach which uses a range of healthcare professionals to incorporate holistic treatments (33). Non-pharmacological treatments include self-motivation, aerobic exercise and strength training, aquatic training, relaxation, physiotherapy, and psychological support including cognitive behavioural therapy, which aims to change pain behaviour. Acupuncture is a controversial non-drug treatment; latest studies suggest it appears safe but there is low-to moderate-level evidence that it improves chronic pain symptoms. Pharmacological management options include antiepileptic drugs, benzodiazepines, local anaesthetics, non-steroidal anti-inflammatory drugs, opioids, and paracetamol but these should not be initiated in primary care. NICE recommends limiting or avoiding opioid use where possible. Antidepressants are recommended.

Current Long Covid management guidance suggests referring patients to a COVID assessment clinic (34, 35). The World Health Organisation has created a patient self-management leaflet (35). Guidance is divided to treat the different symptoms of Long Covid. Similarly, to fibromyalgia, non-pharmacological management includes strength and flexibility exercises. Additionally, keeping up general activity, changing position frequently, relaxation techniques, good sleep routine, physiotherapy and avoiding alcohol are recommended (34, 35). Pharmacological treatments include simple analgesics such as paracetamol and ibuprofen (35).

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A group of medications which are controversially increasingly being used for a range of chronic pain conditions are cannabinoids. Recent systematic reviews have found that cannabinoids improve chronic pain symptoms in fibromyalgia, whilst simultaneously reducing rates of depression and anxiety (36, 37); which are known to exacerbate chronic pain further. However, in current studies there is a lack of both internal and external validity and major inconsistency in methodological study design. Studies used different dosages and routes of administration, making comparison of effectiveness difficult (36).

Studies involving the use of cannabis in the management of Long Covid are limited. One case study of an individual with Long Covid chronic pain who used medicinal cannabis reported that her pain score went from 8-9/10 to 3-4/10, using a visual analogue scale, within a week of continuous use (38). At the time this essay is written, there are no randomised control trials which investigate the use of medicinal cannabis for Long Covid pain, this could be assessed in future studies. NICE does not currently recommend cannabis-based medicinal products (33).

Available literature examining the interaction of fibromyalgia and Long Covid

Limited data is available which explores the interaction of the fibromyalgia and Long Covid. A systematic review looked at the relationship between the two conditions (39). It found conflicting evidence about whether the Covid pandemic had positively or adversely effected patients with fibromyalgia (39). The review suggested that the pandemic itself may have affected the lived experience of individuals with fibromyalgia, rather than catching the virus itself. For example, living with such uncertainty in lockdown, with financial insecurity and a reduction in hospital appointments may have made things more difficult (39). Contrarily, the pandemic may have allowed quiet time for patients with fibromyalgia to rest (39). Amital et al., performed a study (n=571) investigating whether infection with Covid had an increased risk of hospitalisation and death (40). Patients with fibromyalgia were not more likely to develop adverse outcomes than those without fibromyalgia. Notably, the study did not evaluate whether the symptoms of fibromyalgia, including pain, were exacerbated by Covid infection. Ursini et al., performed a study which used a questionnaire to ask participants who had experienced Long Covid whether they now had symptoms of Fibromyalgia (41). Importantly, all individuals with pre-existing fibromyaglia were excluded. The survey asked them about the symptoms and duration of acute COVID-19 infection and if they had pre-

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existing comorbid diseases. The second part of the survey asked about the ACR survey criteria for fibromyalgia. The study found that self-reported clinical features of fibromyalgia are found with an estimated prevalence of 31%. Those that reported they had fibromyalgia symptoms had a more serious form of the initial COVID-19 viral infection, with higher rates of hospitalisation and more needed supplementary oxygen. Ursini et al., also found that obese participants were more likely to self-report fibromyalgia symptoms. This aligns with the already known correlation between obesity and fibromyalgia severity. It also aligns with the correlation between obesity and acute COVID-19 infection severity (42). Ursini et al., stated 60 of 139 (43%) men reported symptoms which met the criteria for a fibromyalgia diagnosis (41). This was statistically significant (OR 9.95, 95% CI 6.02 to 16.43 $P < 0.0001$). This finding was unexpected, given fibromyalgia typically occurs more in females (43). The researchers speculated whether this was because acute COVID disease severity was worse in men than women. However, this does not align with other more reliable sources that find Long Covid to be present more in women (7). There were some study limitations. Probability sampling was not performed, decreasing generalisability of the findings which may increase bias. More women (76.6%) than men were included in the survey, making the sample unrepresentative of the general population. A further criticism of the study is it did not actually measure the severity of COVID-19 using the recommended tool: Disease Severity Classification and COVID-19 Outcomes (44), so relies on surrogate measures. This study could be repeated accounting for disease severity.

Importantly, this study highlights the similarities between Long Covid and fibromyalgia. Given there is such cross over, it asks the question when does one become the other. The article termed this "FibroCOVID". It would also be interesting to see what happens to patients already diagnosed with fibromyalgia.

Other studies have focused on the effect of COVID-19 vaccinations on fibromyalgia. Cherian et al. found adverse effects to COVID-19 vaccines for patients with rheumatic disorders, including fibromyalgia were similar to that in the overall population (45), which is reassuring. Other studies have investigated the uptake of vaccination against COVID-19 in patients with fibromyalgia. Vieira et al., found patients with fibromyalgia have demonstrated vaccine hesitancy (46). Vieira et al., suggested that reasons for this may have high levels of anxiety and felt too stressed to face vaccination. Other reasons included

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that individuals with fibromyalgia already have a reduced quality of life and fear of clinical deterioration after vaccination may have deterred patients (46).

Future research

There are currently no longitudinal follow-up studies of patients with Long Covid, a study is required to understand more about pain symptoms, the disease itself and its progression. Importantly, most studies relating to Long Covid pain have been performed on patients who have been hospitalised (8). If there is a difference in pain patterns in hospitalised versus non-hospitalised patients, this needs to be identified. Especially if one group present more similarly to patients with fibromyalgia, or other chronic pain conditions which we have more available data on, so we will be able to utilize this data to provide the best management for patients. Additionally, whilst some studies are available examining the relationship between fibromyalgia and COVID-19 infection, studies are required which focus on whether pain symptoms are exacerbated by COVID-19 infection.

Conclusion

A comparison has been made between fibromyalgia and Long Covid chronic pain characteristics. Chronic pain is a cardinal feature of fibromyalgia and is the fourth most common symptom of Long Covid. Given we are at such an early stage in our understanding of Long Covid with such limited available data, it is difficult to compare chronic pain features. The global burden of chronic pain is going to increase due to the vast numbers of individuals with Long Covid. This will place additional burden on healthcare resources and economy. Current literature would suggest that the way patients describe the chronic pain experienced in Fibromyalgia is similar to that of Long Covid, but further studies are required to fully understand the clinical characteristics of Long Covid pain. Additionally, whilst there is some crossover in other symptoms, there are stark differences. Patients with Long Covid commonly experience additional symptoms including shortness of breath and loss of smell, which are not experienced by patients with fibromyalgia. Nevertheless, regardless of its cause, chronic pain is severely debilitating, with social and psychological implications for patients. Thus, we need future studies to focus on good holistic management for patients. Since scientists have been researching into Fibromyalgia for over 50 years, perhaps techniques used in the management of fibromyalgia can be adapted to support patients

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recovering from Long Covid chronic pain. Also, given the considerable research in to biomarkers for Long Covid, there may be new interventions developed for Fibromyalgia too.

Appendix

| Diagnostic criteria of fibromyalgia |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1) Widespread pain index (WPI) ≥ 7 and symptom severity scale (SSS) score ≥ 5 OR WPI 4–6 and SSS score ≥ 9 . |
| 2) Generalized pain, defined as pain in at least 4 of 5 regions, is present. |
| 3) Symptoms have been present at a similar level for at least 3 months. |
| 4) A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses. |

Figure 1 The 2010/11 American College of Rheumatology (ACR) diagnostic criteria for Fibromyalgia (15)

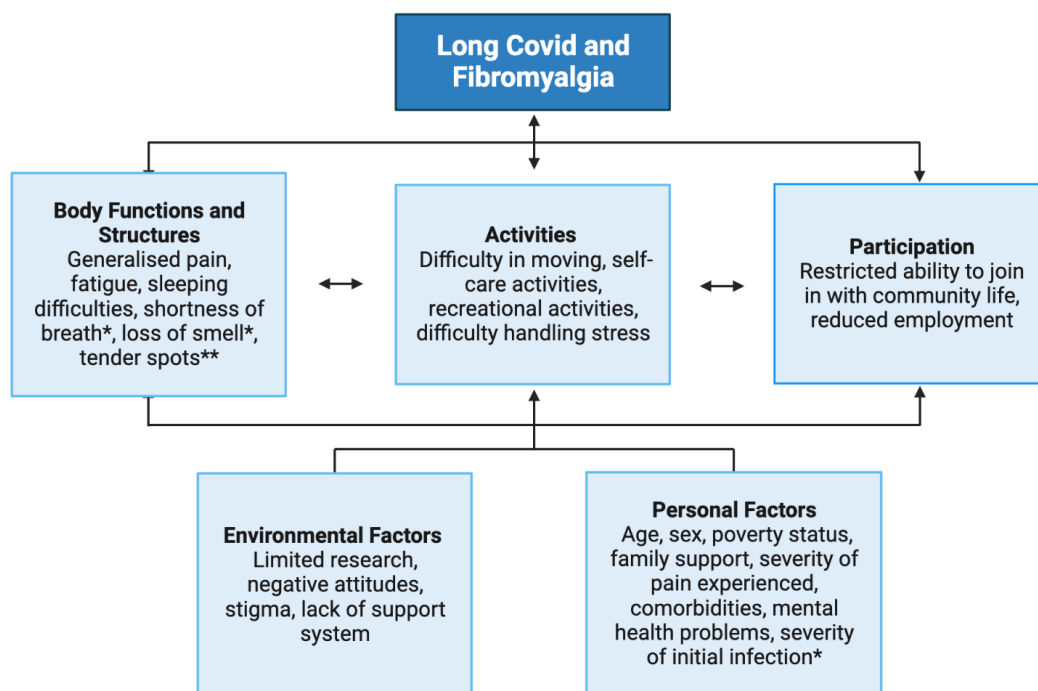


Figure 2 International Classification of Functioning, Disability and Health (ICF) framework, adapted from (17). The ICF framework demonstrates the interaction between components of the individual's life which affect their functioning and disability, in the context of individuals with Long Covid and fibromyalgia. By

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comparing the two ICF frameworks we can see how similarly the two conditions affect the functioning of an individual. Key: *affects Long Covid, **affects fibromyalgia. Image created using Biorender; <https://biorender.com/>

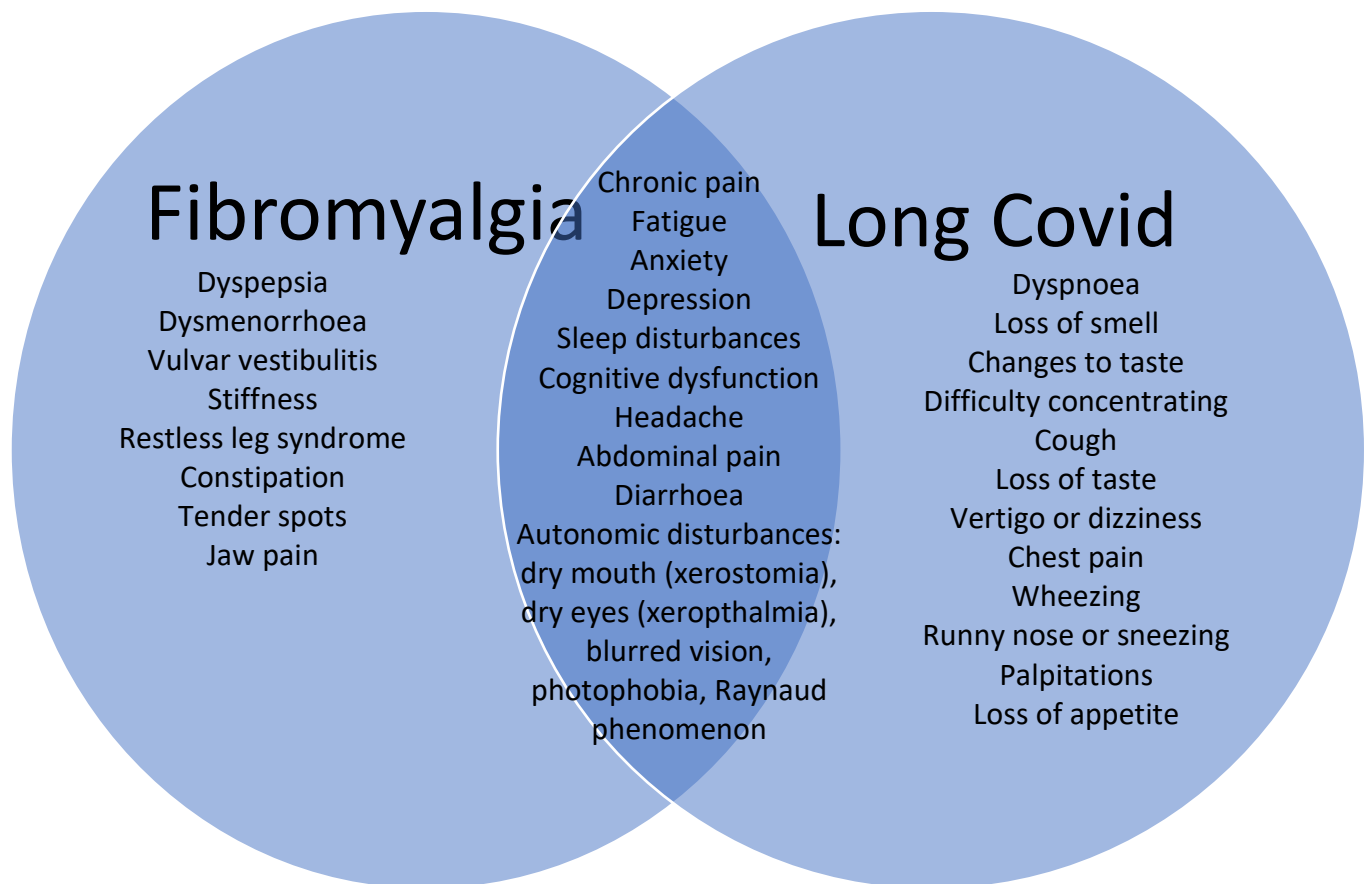


Figure 3 Venn diagram to demonstrate the signs and symptoms of Fibromyalgia and Long Covid, including where there is overlap in presentation.

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