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Chronic primary pain in the COVID-19 pandemic: how uncertainty and stress impact on functioning and suffering

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1. Introduction

COVID-19 is a highly infectious disease caused by the severe acute respiratory syndrome (SARS)-CoV-2.⁴⁰ Owing to the virus' rapid spread across the globe, the World Health Organization (WHO) declared it a pandemic in March 2020. As such, COVID-19 has become a major societal concern, not least because of the large number of infections, the potential severity of the disease, and the mounting death toll worldwide. The COVID-19 pandemic has affected many people's lives and health, with potential long-term consequences. Notably, the detrimental impact of this pandemic is not limited to physical health. For some, the *uncertainty and lack of control* imposed by this pandemic may lead to increased stress levels, (health) anxiety, and worry, which may further negatively affect mental health and general well-being of both infected and noninfected people.¹¹⁸ In addition, the restrictions enforced to contain the virus (eg, physical distancing) and to minimize the burden on the healthcare system further disrupt our social lives and prevent people from connecting with each other, causing loneliness, and in turn negatively affecting health and well-being.^{6,53}

People suffering from persistent pain represent a vulnerable group at risk to be disproportionately affected by the COVID-19 pandemic and its measures. First, the reduced access to health care and suspension of routine pain management can exacerbate chronic pain disability.²⁵ Second, uncertainty may prime increased attention to bodily sensations and pain,²⁹ increasing health anxiety, and catastrophic worry, especially in those who are intolerant of uncertainty or those lacking effective coping strategies (eg, seeking support), some of which are unavailable because of the safety measures.⁸⁴ Third, to avoid contamination, physical distancing often boils down to complete self-isolation in individuals with chronic illness; isolation inevitably leads to reduced participation in daily activities and thus increases disability,⁷⁵ as well as it decreases health behaviors and reduces physical activity worsening health outcomes.²⁸ Finally, high-stress situations increase suffering and psychological distress in individuals with chronic pain, eg, in the aftermath of terrorist attacks,⁷² as well as reducing self-rated mental health after the first lockdown.²⁸

In this review, we propose a conceptual framework describing how COVID-19 may affect *modifiable factors* resulting in worsened health outcomes and disability in people with chronic pain. We cautiously suggest strategies targeting these modifiable factors and how these can help to guide treatment and reduce the negative impact of the current pandemic. We present a model (**Fig. 1**) outlining how the impact of known risk factors in the development and maintenance of chronic pain may become more pronounced during a pandemic because of increased uncertainty, perceived uncontrollability, COVID-related stress, and paradoxically by contagion-reducing safety behaviors. Furthermore, other precautions to contain the spread of COVID-19 (eg, physical distancing) may compromise resilience factors (eg, positive affect, optimism, and social support), which may hamper daily functioning and participation of people with chronic pain. Finally, this model aims to inspire future research aimed at a better understanding of how to reduce negative long-term effects of the COVID-19 pandemic in people with chronic pain and prevent patients who are still functioning from becoming severely disabled.^{51,113}

2. COVID-19: an "invisible" and uncertain health threat

Common symptoms of COVID-19 are fever, fatigue, persistent dry cough, and anosmia; more severe symptoms include chest pain and shortness of breath, but it can even result in life-threatening circumstances needing ICU admission, followed by severe speech and motor problems (WHO, <https://www.who.int/health-topics/coronavirus>). Although initially viewed as a respiratory disease,

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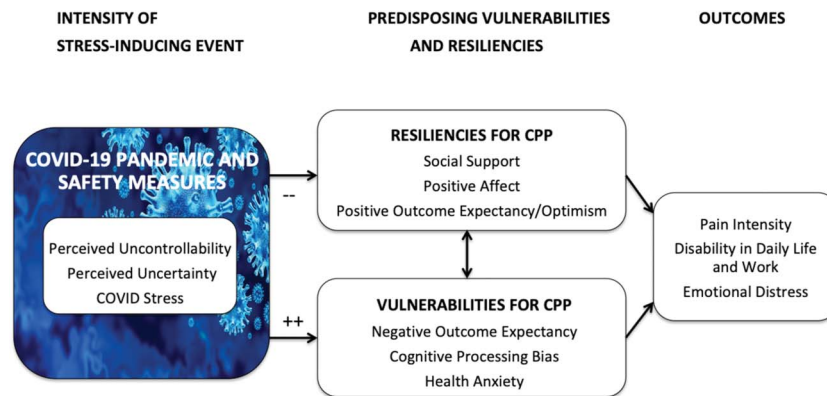


Figure 1. Theoretical model showing how risk factors for the development and maintenance of chronic pain disability in daily life and work may be triggered or amplified by uncertainty, uncontrollability, and intensity of COVID-related stress, and these COVID-related factors and safety measures may compromise resilience factors affecting long-term health outcomes such as pain intensity, emotional distress (including, but not limited to, fear, anxiety, sleep disturbance or insomnia, depression, and helplessness), and disability in daily life and work (including domains such as family/home responsibilities, recreation, social activity, occupation, sexual behavior, and self-care).

increasing evidence indicates that COVID-19 can affect multiple systems (eg, cardiac, renal, and neurological) and cause multidomain impairment, fatigue, and chronic pain.^{15,55} The variable symptom presentation and the overlap with other conditions impede straightforward diagnosis of COVID-19. Eighty percent of infections are mild or asymptomatic, though still contagious, fueling the spread of the disease.⁹ Furthermore, owing to the long incubation period, people who present themselves without symptoms can be transmitting the virus, thus posing a potential threat for infection. This, in combination with insufficient diagnostic testing and the observation that only 10% of the population produces antibodies,⁹ increases the risk of (re-)infection. To date, uncertainty exists about the newly developed vaccines (in terms of long-term protection, potential side effects, and availability) and the choice to get vaccinated. There is no cure for COVID-19, and except for some risk factors (eg, obesity, age > 60, underlying medical conditions, or compromised immune system), our understanding of for whom the infection will lead to hospitalization or death is limited. This makes COVID-19 an invisible threat to our health, causing *high levels of uncertainty*. This uncertainty is further fueled by nonstop media coverage, often providing conflicting information, as well as contradicting recommendations by public health authorities in different countries, which fosters “uncertainty distress.”¹³ Increased social media exposure brimming with conspiracy theories¹⁰ further triggers COVID-related fear and worry.^{29,52,64,116,117} Finally, uncertainty about the future in general, such as the unknown long-term socioeconomic consequences and unknown duration and likelihood of resurgence of the pandemic, contributes to COVID-related stress and anxiety.

On top of that, the measures taken to slow the spread of the virus impede the *sense of being in control* of our own lives. For example, imposed lockdowns, curfews, and restricting the use of recreational facilities and public spaces may increase helplessness,⁹⁰ anxiety, and stress,⁶⁹ which may further affect negatively on health and well-being.

3. Chronic primary pain: a particularly vulnerable group

Chronic primary pain (CPP) is a prevalent health problem affecting about 20% of the population, leading to personal suffering and putting a huge strain on our healthcare system and society.⁷⁴ Owing to the lacking underlying anatomic cause of their pain, this

group is characterized by diagnostic uncertainty,⁹¹ which may be inflated by the current COVID-related uncertainty, increasing functional impairment and distress. Therefore, we will use CPP as a prototype throughout our review. People suffering from chronic pain may be at risk of disease severity when infected with SARS-CoV-2 because the prevalence of chronic pain in elderly is higher and they also have increased levels of comorbidity,²³ both known risk factors for COVID-19. Chronic pain has also been associated with immunosuppression, often caused or exacerbated by opioid and steroids use⁹²; this implicates that people with chronic pain using opioids or steroids could potentially be more susceptible to COVID-19 and have difficulties to combat the virus. In addition the increased vulnerability for severe COVID-19 illness, individuals with CPP also suffer disproportionately from the measures taken to contain COVID-19, including suspension of routine pain management.²⁵ This is widely recognized by the pain community, reflected, for example, in the European Pain Federation (EFIC) COVID-19 Task Force initiative providing information and advice, as well as the call for continued treatment and e-health alternatives to treat chronic pain during the pandemic.^{16,25,92} In addition, enforced measures potentially compromise resilience factors, such as positive affect, optimism, positive outcome expectancies, and social support,¹⁴ further hampering daily functioning in this vulnerable group. Indeed, research during the first COVID-19 lockdown showed that individuals with chronic pain were more adversely affected compared with pain-free people, showing greater increase in anxiety, depression, loneliness, as well as self-perceived pain.³⁰ Undeniably, individuals with CPP are increasingly prone to suffer severe consequences from both COVID-19 and the taken containment measures, which may culminate into augmented levels of stress.

4. COVID-related stress and vulnerability for chronic primary pain: the perfect storm?

Contemporary pain models assign a key role to psychosocial factors in the development and maintenance of chronic pain and augmented levels of disability and distress.^{18,26,110,112} Among others, *health anxiety*,^{42,43,87} *cognitive-processing biases* for pain and pain-related information, particularly attention²⁷ and interpretation biases,^{56,57,108} and proneness towards *negative outcome expectancies*¹⁰¹ (eg, overgeneralization^{65,66,111} and

catastrophic worry¹⁰³) have often been considered vulnerabilities contributing to pain-related disability in CPP.¹⁰²

Indeed, a wealth of research has shown that negative outcome expectancies are associated with poor pain outcomes. In this context, catastrophic worry has emerged as one of the best psychosocial predictors of pain, distress, and disability.^{27,54,82} Catastrophic worry may exert its detrimental effects through several pathways, such as inducing an aroused, negative emotional state exacerbating pain or prompting helplessness which in turn decreases adaptive pain responding.⁶² Its causal status is further confirmed by studies investigating the processes of change in pain management programs in which reducing catastrophic worry arose as a crucial factor for treatment success.^{5,11–13,93,103} In addition, accumulating evidence suggests that people with chronic pain overgeneralize expectancy of pain outcomes and pain-related fear to technically safe stimuli^{45,46,66,67} and that it takes longer for them to update these expectancies and fear when presented with disconfirming information compared with healthy, pain-free controls.^{68,104} Obviously, protective responses (pain-related fear and avoidance) are adaptive when they prevent further bodily harm, but when they spread to a myriad of safe activities or situations, they may paradoxically compromise daily functioning, leading to disability.

Furthermore, the prevailing biopsychosocial models of chronic pain postulate that interpreting ambiguous bodily sensations as threatening as well as heightened attention (ie, hypervigilance) for pain and pain-related stimuli may drive disability.^{19,99,106} Abundant research demonstrates that people with chronic pain show both a greater tendency to attend to pain and pain-related information (attention bias^{20,100}) and interpret ambiguous stimuli as threatening (interpretation bias⁸⁹), whereby these biases are believed to be underlying poor pain outcomes and maintenance of chronic pain.^{56,81}

Finally, severe and disabling levels of health anxiety have been estimated at 51% for clinic attenders with chronic pain⁸⁷ and have been associated with poor prognosis.⁴² Health anxiety is characterized by catastrophic misinterpretation of bodily sensations, disease conviction, dysfunctional beliefs about health or illness, and maladaptive coping behaviors (eg, reassurance seeking and checking behaviors), which provide relief in the short run but paradoxically perpetuate the dysfunctional beliefs in the long run. Anxiety has been also found to increase nocebo-related effects of negative outcome expectancies in pain.⁹⁸ In particular, high levels of health anxiety also have been reported to increase safety behaviors in people with chronic low back pain,⁹⁶ which can be considered a maintaining factor of erroneous beliefs and disability. In the context of the COVID-19 pandemic, people with increased health anxiety might engage in maladaptive safety behaviors, such as excessive hand washing, social withdrawal, and panic purchasing.³ Although these actions seem harmless, they may paradoxically worsen stress and anxiety¹⁰⁷ and may have a detrimental impact on others in the community (eg, unnecessary hoarding of hand sanitizer, protective gear, and medication).

Crucially, the impact of each of these vulnerabilities is strongly defined by contextual features. Particularly, the presence of heightened stress and uncertainty, typical in times of COVID-19 (see *supra*), may strongly increase the impact of described vulnerabilities on increased disability. In this context, the prevailing *diathesis–stress model* conceptualizes “diatheses” as dormant individual vulnerabilities present that are triggered and worsened by stress²¹ (**Fig. 1**). Undoubtedly, current times of extreme uncertainty induced by the global pandemic qualify as

stressful life events able to awaken or amplify the expression of pre-existing vulnerabilities. Obviously, evidence in the context of COVID-19 to date is largely lacking. Yet, evidence from experimental research suggests that these factors can indeed be increased by uncertainty, lack of control, and stress.

For example, uncontrollability is associated with perceived helplessness and cortisol elevation,^{22,73} confirming that it triggers the human stress response, which may in turn induce cognitive-affective sensitization of pain. Other studies have shown that uncontrollability directly increases suffering, but not necessarily pain intensity.⁶¹ Similarly, uncertainty has been shown to induce hyperalgesic effects in pain perception, and individuals with higher harm vigilance (combined catastrophic worry, trait anxiety, avoidance behavior, and emotional instability) showed stronger spinal facilitation, which in turn contributed more to the observed hyperalgesia.⁹⁷ Furthermore, catastrophic worry has been shown to increase by (experimentally induced) stress^{7,109} and can be conceptualized as an emotion regulation strategy to decrease the negative affect arising from stressful situations.³⁴ In the same vein, stress typically narrows attention to salient environmental cues, consequently enhancing vigilance and attention to potentially threatening stimuli.⁴ Cognitive processing biases thus are expected to be stronger under stressful circumstances.^{70,71,88} Finally, also health anxiety can be amplified by stressful life events such as being ill or suffering from the loss of a significant other.²

5. COVID-19 pandemic and safety measures compromise resilience factors

By contrast, social support,^{41,63} optimism³⁹ and positive outcome expectancies,¹⁷ and positive affect^{31,77} protect against the negative impact of chronic pain on disability and distress.⁹⁴ Positive affect and optimism execute their bolstering effect⁴⁴ through broadening attention towards positive stimuli and revoking cognitive processing biases,^{35,114} undoing the detrimental effect of negative emotions,³⁶ reducing overgeneralization of fear and pain outcome expectancy,³⁷ and tackling catastrophic worry.⁷⁶ On the other hand, isolation, loneliness, and lacking social support may worsen stress⁷⁸ and increase disability,⁷⁵ whereas social support is associated with better adaptation to chronic pain and increased well-being. Owing to the COVID-related uncertainty and stress, the situation of people with CPP may worsen or propel the transition from a manageable situation into a crippling condition when protective factors are removed and the buffering effect against the existing vulnerabilities is withdrawn.

6. Targets for clinical practice and prevention

The provided theoretical framework has important consequences for the treatment of people with CPP during a pandemic. Indeed, based on this framework, we argue that healthcare providers should be attentive for increased levels of stress, perceived uncertainty, and uncontrollability in CPP because they may boost the expression of vulnerability factors, resulting in increased pain, distress, and disability. Nowadays, a plethora of interventions are available to do so, ranging from simple, such as clear communication and providing unambiguous information,^{33,83} full-fetched add-on uncertainty and stress management interventions³⁸ to cognitive-behavioral therapy, whereby reduced uncertainty is established by promoting beneficial use of emotion regulation, self-management skills, and psychoeducation. In addition, protocols targeting intolerance of uncertainty that have mainly been developed and proven efficacious in the context of

psychopathology (eg, generalized anxiety disorders)^{8,24,60,86,105,115} may be translated to and implemented in the context of the pandemic. Finally, acceptance-based and mindfulness-based techniques may be used to reduce the negative impact of uncertainty by increasing tolerance of uncertainty⁵⁰ and increasing psychological flexibility. These strategies may not only affect uncertainty, health anxiety, and perceived COVID-related stress by altering the appraisal of uncertainty from danger to opportunity or acceptance⁸⁵ but also downregulate pain⁵⁸ and stress-related biomarkers.⁴⁹

Our framework additionally urges to strengthen resilience, which may be compromised by not only enforced measures to contain the spread of COVID-19 but also COVID-related stress and perceived uncertainty. A broad range of possibilities is available varying from very simple, eg, increasing social connectedness online to combat loneliness,⁵³ to more extensive techniques, such as full-blown positive psychology interventions focusing on increasing positive affect or optimism.⁸⁰ In addition, increased positive affect broadens attention towards positive stimuli^{35,36,114} and thereby tackling hypervigilance for bodily symptoms and sensations.⁴⁴ Finally, increased psychological resilience through boosting positive emotions predicts decreases in catastrophic worry.⁷⁶ Further research is needed to validate our theoretical model because there is an urgent need to develop (and evaluate) specific interventions in the context of the current pandemic.

7. Future research directions and conclusion

The current COVID-19 pandemic and the enforced measures to contain the virus brings along great uncertainty, lack of control, and COVID-related stress. People with CPP may be especially at risk to suffer disproportionately under these circumstances. We used CPP as a prototypic pain diagnosis, but this model may be extended or applied to other chronic pain diagnoses (eg, arthritis, cancer, and diabetes) and even to subacute or new-onset pain. In our conceptual framework, perceived uncertainty, uncontrollability, and elevated stress levels may awaken or amplify known vulnerabilities for chronic pain disability (such as, but not limited to, negative outcome expectancies, cognitive processing biases, and health anxiety) and compromise resilience factors (eg, positive affect, positive outcome expectancies, optimism, and social support) leading to worsened mental health outcomes and increased disability. We have argued that healthcare professionals should consider targeting these factors in treatment and foster strategies to prevent pandemic-induced worsened outcomes in CPP. Our model is not exhaustive and other factors may be worth investigating, such as the differential impact in different stages or waves of the pandemic; individual differences such as trait intolerance of uncertainty and social anxiety; and more distal factors such as sex,⁴⁷ economic stress,⁵⁹ education, and race, which may moderate the outcomes in our model. Furthermore, the provided framework does not specify how the pandemic may affect factors evolving across the lifespan (eg, social roles) and how this affects pain outcomes. Exhaustive research from a developmental perspective, spanning from pediatrics to geriatrics, is warranted to answer these questions. These future findings could then complement the current framework. Finally, the COVID-19 pandemic may impede physical activity and exercise which is associated with reduced mental health^{1,28,79} and sleep which affect described mental health outcomes as well as pain and interference directly.^{32,48,95} Therefore interventions aiming to restore sleep and physical exercise may also be considered as treatment options.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplemental video content

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