

# COVID-19 and the amplification of cardiovascular risk by psychological distress

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The COVID-19 pandemic has unleashed a tidal wave of psychological distress. Here we discuss the biobehavioral mechanisms through which psychological distress amplifies the adverse effects of SARS-CoV-2 infection on cardiovascular outcomes. We also examine how the stress of caring for patients with COVID-19 increases cardiovascular risk in healthcare workers.

During the early months of the COVID-19 pandemic, it became clear that patients with underlying cardiometabolic risk factors, including obesity, diabetes and hypertension, were at risk of severe COVID-19 illness. Furthermore, many individuals with COVID-19 developed cardiovascular complications such as acute coronary syndrome (ACS), stroke, myocarditis, arrhythmia and heart failure<sup>1</sup>. We are now learning that many individuals who survive COVID-19 have a long road to recovery, with approximately 30% of patients who have confirmed SARS-CoV-2 infection presenting persistent symptoms such as fatigue, dyspnea and effort intolerance<sup>2</sup>. Cardiovascular injury related to SARS-CoV-2 infection is proposed to underlie some of these persistent symptoms. The SARS-CoV-2 virus is postulated to affect the cardiovascular system through multiple biological pathways, involving both direct and indirect injury from the virus itself, with the extent of injury related to the amount of viral inoculum and host immune response<sup>3</sup>. The virus has been shown to increase inflammation, endothelial cell activation and microvascular thrombosis. However, these models have paid insufficient attention to the potential amplifying effect of psychological distress.

When the first wave of the COVID-19 pandemic swept the globe, many patients were hospitalized with breathing difficulties and kept in isolation owing to social-distancing measures. In some cases, healthcare workers were forced to choose which patients would receive potentially life-saving treatments. Unsurprisingly, for many patients and the healthcare workers who cared for them, COVID-19 induced severe psychological distress. Here we discuss how psychological distress related to COVID-19 illness can heighten the pathways linking SARS-CoV-2 infection with cardiovascular disease. We also consider the effect of COVID-19-related psychological distress on cardiovascular risk factors in healthcare workers.

Multiple studies have documented the high prevalence of psychological distress in those with COVID-19 illness. In cohort studies with systematic assessment of psychological distress, the prevalence of anxiety and depression have generally been high – with 25% experiencing depression and 32% experiencing anxiety in one such study<sup>4</sup>.

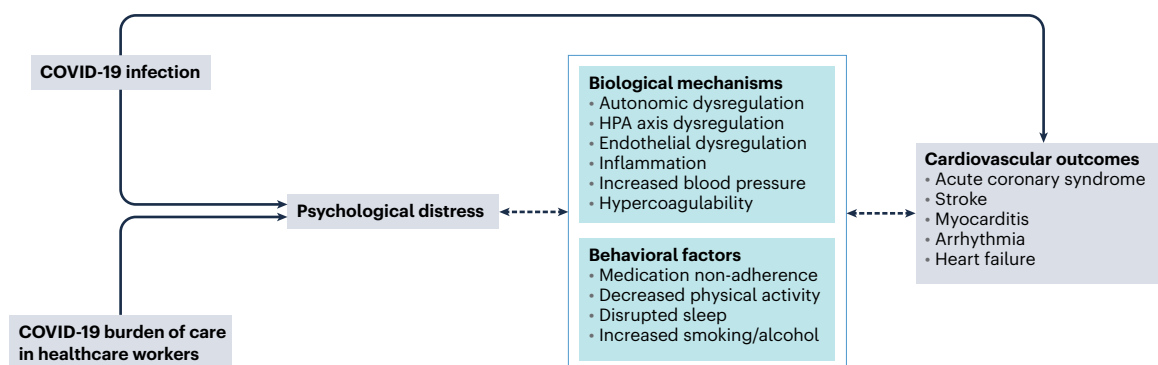
Other studies have demonstrated high rates of post-traumatic stress disorder (PTSD) in patients with severe COVID-19, with around 30% of patients affected<sup>5</sup>.

Decades of mechanistic behavioral medicine research has uncovered how depression, PTSD and other forms of psychological distress increase risk of adverse cardiovascular outcomes through a combination of biological and behavioral pathways (Fig. 1). The association between these psychological factors and cardiovascular risk has remained robust even after adjusting for comorbidities and other potential confounders<sup>6</sup>. Increased inflammation, hypercoagulability, autonomic nervous system and endothelial dysfunction have all been proposed to occur in patients with psychological distress, with varying degrees of supporting evidence. For example, patients with depression have consistently been found to have elevated levels of proinflammatory cytokines, C-reactive protein and markers of cell-mediated immune activation<sup>6</sup>. According to the social signal transduction theory of depression, the neural experience of stress can lead to a proinflammatory state that results in increased depression and comorbid inflammatory conditions such as cardiovascular disease<sup>7</sup>. With respect to PTSD, strong evidence supports sympathetic nervous system hyperreactivity in response to stressors and decreased parasympathetic activity as measured by heart rate variability – both of which have been linked with cardiovascular disease<sup>8</sup>.

Psychological distress is also associated with lower adherence to cardioprotective health behaviors, including recommendations for physical activity, diet, smoking cessation, medication adherence and sleep (Fig. 1). For example, in the first three months after hospitalization for suspected ACS, patients with elevated PTSD symptoms were half as likely to take their cardiac medication each day than those without<sup>9</sup>. Patients with depression and stable coronary artery disease were similarly less likely to engage in cardiovascular-risk-reducing health behaviors<sup>10</sup>. Among patients assessed six months after SARS-CoV-2 infection, poor sleep quality was among the most commonly reported symptoms<sup>11</sup>. These behavioral factors could predispose patients with COVID-19 to cardiovascular events. The extent to which COVID-19-related psychological distress affects health behaviors that are important to cardiovascular recovery, including participation in rehabilitation or other forms of physical activity, needs to be incorporated into research on long COVID.

The psychological context in which patients with COVID-19 receive care must also be considered. For example, a previous study showed that patients with ACS were more likely to develop persistent PTSD symptoms if they presented to the hospital when the emergency department was more crowded<sup>12</sup>. The adverse impact of crowding was likely magnified during surges in the COVID-19 pandemic when hospital systems were stretched beyond their limits.

We would be remiss if we did not consider the physical and mental health impact of COVID-19 on healthcare workers. Frontline healthcare workers were exposed to environmental stressors, such as overcrowded



**Fig. 1 | Mechanisms by which psychological distress may amplify cardiovascular risk in patients with COVID-19 and in the healthcare workers who care for them.** Note that the distress and burnout experienced by healthcare workers might further exacerbate cardiovascular outcomes

in patients with COVID-19 by negatively impacting the quality of care that healthcare workers provide (not shown in the figure). HPA axis, hypothalamic–pituitary–adrenal axis.

emergency departments, for sustained periods throughout the pandemic. Unique challenges such as perceived lack of control, difficult triage or rationing decisions, being redeployed outside of their specialty, and potentially transmitting SARS-CoV-2 to family members were identified as considerable sources of healthcare worker distress<sup>13</sup>. Together, this has resulted in alarmingly high rates of anxiety, depression and PTSD in healthcare workers. Similar to patients, the psychological distress experienced by healthcare workers might increase cardiovascular risk (Fig. 1). For example, previous work has shown that nurses with PTSD symptoms had increased risk of incident cardiovascular events<sup>14</sup>. Chronic insomnia, observed in up to one in four healthcare workers during the pandemic, is another known measure of psychological distress that is associated with increased cardiovascular risk<sup>15</sup>.

Given what we know about the adverse impact of psychological distress on cardiovascular outcomes, what can be done to mitigate these factors? Although not exhaustive, we propose some possible solutions.

First, increased detection of psychological distress in patients with COVID-19 should be a starting point. Although the health benefits of systematic screening for depression or other forms of psychological distress in patients with COVID-19 remain uncertain, increased awareness of the high potential for psychological distress is needed among those caring for patients with COVID-19. Patients with severe COVID-19 and family members could benefit from psychoeducation during or soon after hospitalization so that they know to be on the lookout for these symptoms and are active in seeking treatment when symptoms arise. However, increased detection will not be helpful if not linked with access to affordable evidence-based mental health treatment. Unfortunately, few healthcare settings have integrated behavioral medicine into cardiovascular or COVID-19 treatment.

We should also determine whether our existing psychological interventions need to be tailored for patients with COVID-19 and healthcare workers. Without the benefit of psychoeducation, there might be lower engagement in psychological treatments among patients recovering from COVID-19 because these individuals might be more pre-occupied by their physical health problems. Patients with PTSD symptoms related to COVID-19 might avoid healthcare settings so that they are not reminded of their underlying disease. Telehealth-, internet- or app-delivered behavioral interventions may need to be expanded for these patients. More research on mind–body

interventions including mindfulness meditation and sleep- and mood-focused chronotherapies such as light therapy should be conducted to provide additional evidence-based options for patients with COVID-19 and healthcare workers.

Finally, we need to improve the environment in which patients receive care. Systems engineers have been experimenting with staffing models that reduce overcrowding. These interventions might have the collateral benefit of reducing burnout in healthcare workers. We should examine which psychosocial factors or modifiable behaviors might be protective against the development of psychological symptoms in healthcare workers facing stressful working conditions. Approaches at individual (for example, resilience training and promoting healthy sleep) and organizational levels (for example, leadership support, team structures and reduced clerical task burden) should be tested to inform policies that promote well-being and reduce burnout in healthcare workers.

With increased population-level immunity achieved through vaccination and previous infections, many parts of the world are learning to live with COVID-19. The most severe impact of the pandemic on psychological distress and cardiovascular outcomes might be receding. However, concerns remain that with greater globalization and climate change, COVID-19-like pandemics are likely to occur more frequently in the years ahead. Now is the time to better understand how to mitigate the adverse effect of psychological distress on cardiovascular risk in patients with COVID-19 and in the healthcare workers who treat them. In doing so, we will be better prepared to address the psychological and cardiovascular impacts of future pandemics.

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### Competing interests

The authors declare no competing interests.