

**Psychology Meets Biology in COVID-19:
What We Know and Why It Matters for Public Health**

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Abstract

Psychosocial factors are related to immune, viral, and vaccination outcomes. Yet, this knowledge has been poorly represented in public health initiatives during the COVID-19 pandemic. This review provides an overview of biopsychosocial links relevant to COVID-19 outcomes by describing seminal evidence about these associations known pre-pandemic as well as contemporary research conducted during the pandemic. This focuses on the negative impact of the pandemic on psychosocial health and how this in turn has likely consequences for critically relevant viral and vaccination outcomes. We end by looking forward, highlighting the potential of psychosocial interventions that could be leveraged to support all people in navigating a post-pandemic world and how a biopsychosocial approach to health could be incorporated into public health responses to future pandemics.

Highlights

- Pre-pandemic evidence links psychosocial factors to viral and vaccination outcomes.
- Early evidence reported during the COVID-19 pandemic is consistent with these prior findings.
- To better support people during future public health crises, we need structural-level policy changes that take a biopsychosocial approach as well as increased access to individual-level psychosocial interventions

Tweet (280 characters)

Could psychology have made the pandemic better? Read here for critical information on how our minds impact COVID-19 outcomes such as viral susceptibility, severity, and effective vaccination responses, and how biopsychosocial interventions might protect our future health.

Psychosocial factors are defined as intersecting social, environmental, and cultural influences on individual thoughts, behaviours and emotions (*APA Dictionary of Psychology*, 2022). Examples include depressive and anxiety symptoms, stress, loneliness, socioeconomic standing, and discrimination. The role that these psychosocial factors play in predicting susceptibility to viral infections and outcomes has been the subject of decades of scientific research (e.g., Cohen, 2021). However, during the COVID-19 pandemic, this evidence was notably absent from public discourse, and was not explicitly drawn upon in the formation of public health policy. Yet, this research has considerable and continued relevance to the COVID-19 pandemic and beyond. These psychosocial factors have been repeatedly shown to influence physiological parameters relevant to infectious disease including inflammation (Muscatell et al., 2020; Rosenblat et al., 2014; Smith et al., 2020; B. Uchino et al., 2018), general immune protection (Avitsur et al., 2009; Segerstrom & Miller, 2004), likelihood of viral infection after virus exposure (Falagas et al., 2010), symptom severity (O'Connor et al., 2021), and vaccine efficacy (Pedersen et al., 2009). The present review highlights the importance of these influences on pandemic outcomes. We argue that our understanding is incomplete if we focus solely on whether or not individuals get exposed to COVID-19. Instead, we must understand the complex interactions between the virus, ourselves, and our social environments to inform policy decisions for future pandemics.

This review serves as a companion article to an Association of Psychological Science task force event held in January 2022, which discussed evidence on biopsychosocial determinants of viral susceptibility, recovery, and vaccine responses relevant to COVID-19 and future pandemics.¹ This review synthesises key evidence and discussions from that event, highlighting what was known prior to the COVID-19 pandemic, evidence that emerged during the pandemic, and recommendations for the future.

Psychosocial factors and COVID-19

Why care about psychosocial factors in the context of the COVID-19 pandemic?

Worldwide psychosocial health was adversely affected by the COVID-19 pandemic. Pre-pandemic estimates placed the worldwide prevalence of anxiety and depressive disorders at 3.6% and 4.4% respectively (World Health Organization, 2017). Although not a perfect comparison, multiple systematic reviews conducted during the pandemic indicated substantial rises in psychological health concerns with estimates suggesting between 14-48% of adults worldwide experienced depressive symptoms, 6-51% experienced anxiety, and 14-50% experienced distress (Chekole & Abate, 2021; Necho et al., 2021; Xiong et al., 2020), with similar increases observed among children (Samji et al., 2022). Meta-analyses have further shown increased prevalence and severity of loneliness (Ernst et al., 2022). Collectively, this evidence demonstrates that the COVID-19 pandemic and resulting stay-at-home orders, changes in routines, and fear and unknowns about contracting the virus placed a significant burden on individuals' psychosocial health (Holman et al., 2020), which may have been exacerbated among people experiencing personal loss or vicarious trauma through media exposures (Thompson et al., 2022). Although worsening psychosocial health is an important outcome itself, what is often overlooked is the concurrent impact psychosocial factors may have on immunity and the possible

¹ The event recording can be viewed here: <https://bit.ly/3fUmAuK>

implications for viral outcomes.

Pre-pandemic we knew psychosocial factors impacted immunity and viral outcomes. Systematic reviews and meta-analyses examining associations between a range of psychosocial factors (such as loneliness, positive and negative emotions) and immunity have consistently demonstrated moderate-to-large effects on enumerative and functional immunological measures (Marsland et al., 2007; Segerstrom & Miller, 2004; Zorrilla et al., 2001). For example, a seminal meta-analytic review of over 300 articles concluded that there was robust evidence that psychological stress impacts immunity, with consistent evidence for associations between chronic stressors relevant to the pandemic (e.g., loss of control, bereavement, isolation) and the suppression of both cellular and humoral measures of immunity (Segerstrom & Miller, 2004). Psychosocial factors have been further correlated with viral susceptibility, with one systematic review finding 41 of 44 studies reported at least one statistically significant association between psychosocial variables and risk for acute respiratory tract infections (Falagas et al., 2010).

Considering psychosocial factors through a broader societal lens, socioeconomic disadvantage, which is a chronic and uncontrollable psychosocial stressor, has been associated with increased risk for upper respiratory infections during prior influenza pandemics (Mamelund et al., 2021; Rutter et al., 2012) and higher hospitalisation rates (Levy et al., 2013). Lower socioeconomic status (SES) is thought to confer risk for poorer immune outcomes through a variety of factors, including increased exposure to financial stress, negative affect, and less access to coping resources (Gallo & Matthews, 2003). Relatedly, people of colour from historically marginalised groups have an elevated risk of infections, including higher rates of tuberculosis among Black Americans and immigrants in the US (Stewart et al., 2018) and among indigenous people internationally (Tollefson et al., 2013). Many have argued that structural and interpersonal racial discrimination may underlie such associations (Paradies et al., 2015).

Some of the most rigorous evidence supporting the causal influence of psychosocial factors on viral outcomes comes from experimental viral challenge studies. In these investigations, healthy participants are exposed to standardised doses of viruses, including common cold and seasonal coronaviruses, before being quarantined. Serological and clinical measurements are then taken to determine infection status and symptom severity. A series of such studies have shown that negative emotions, stressful life events, everyday perceived stress, isolation, and conflict measured prior to virus exposure can increase viral susceptibility and symptom severity (see Cohen, 2021). Furthermore, these effects may vary depending on social contextual factors as illustrated by Wiley and colleagues (2022), who found that Black Americans were less likely to benefit from the protective effects of positive psychological factors (e.g., self-esteem) on upper respiratory illness compared to White Americans. This suggests people from marginalised groups of colour may experience diminished benefits from psychological resources that otherwise enhance immunity and protect against infection (Marsland et al., 2007).

Evidence associating psychosocial factors with COVID-19 outcomes. In an early prospective cohort study of over 400,000 people in the United Kingdom (UK), people with a history of psychiatric disorder were around 1.5 times more likely to be diagnosed with COVID-19 or hospitalised and twice as likely to die (Yang et al., 2020). Since then, other large cohort studies have shown similar associations (e.g., Fond et al., 2021; Taquet et al., 2021). Associations between psychological distress and COVID-19 infection and severity have also

been reported in student samples (Vedhara et al., 2022) and the general population (Ayling et al., 2022).

Considering social influences on COVID-19 outcomes, an early review of SES and COVID-19 infections in the UK and US found that lower SES was related to greater risk of infection and severity (Wachtler et al., 2020), which may reflect financial strain, housing insecurity, and poorer air quality that may accompany socioeconomic disadvantage (Rozenfeld et al., 2020). Similarly, two recent reviews reported that Black and Hispanic individuals experienced higher rates of infection, hospitalisation, and COVID-19-related mortality compared to their White peers (Mackey et al., 2021; Mude et al., 2021) and another study found that more racially segregated US counties had higher infection and mortality rates than more integrated counties (Torrats-Espinosa, 2021). Along with racial discrimination and segregation, higher rates of COVID-19 morbidity and mortality among people of colour could be due to greater perseveration regarding finances and contracting (and dying from) the virus (Williams et al., 2022). Although further evidence is needed, early evidence shows that, as with other viral infections, susceptibility to and severity of COVID-19 is associated with psychosocial factors.

Pre-pandemic we knew psychosocial factors were related to vaccination responses.

Given that psychosocial factors can influence immunity, and vaccination relies on the body mounting an appropriate immune response, there has been a long-standing interest in the association between psychosocial factors and vaccination outcomes.

Pre-pandemic, many observational studies demonstrated an association between negative emotional states (including stress, depressive symptoms, and negative affect) and reduced antibody responses to a range of vaccinations including influenza (Pedersen et al., 2009) and Hepatitis B (Marsland et al., 2006). Psychological stress has been the most widely investigated psychosocial factor in this context, with meta-analytic evidence demonstrating a small-to-moderate negative association between stress and vaccine specific antibody responses, particularly among older adults (Pedersen et al., 2009) and caregivers (Kiecolt-Glaser et al., 1996; Vedhara et al., 1999). Furthermore, evidence from studies measuring positive mood find significant associations in the opposite direction (Ayling et al., 2018; Marsland et al., 2006).

Studies have also examined the impact of loneliness on vaccine responses with Pressman and colleagues (2005) finding that loneliness and small social network size were associated with poor antibody responses to influenza vaccination among first-year college students. Other work has focused on contextual social features such as race and SES. For example, children of lower SES had poorer antibody responses to several childhood vaccines (Hoes et al., 2018). Stetler and colleagues (2006) also found lower influenza vaccine antibody responses among Black adults randomised to recall experiences of racial discrimination prior to vaccination as compared to participants in a control condition who were not primed to recall such experiences. Results from meta-analyses support these findings with evidence of small, but significant positive associations of social integration and perceptions of social support with magnitude of antibody response to vaccination (Uchino et al., 2020).

This observational evidence is supported by a small number of experimental studies that have attempted to enhance vaccine outcomes by employing psychological interventions, so-called psychological adjuvants. In a recent systematic review, Vedhara and colleagues (2019) concluded there was early evidence to suggest that psychological interventions may enhance antibody responses to vaccination but larger and more rigorous trials are needed.

Evidence associating psychological factors and SARS-CoV2 vaccination responses.

Although evidence supports the influence of psychosocial factors on antibody responses to vaccination, to date limited research has examined this in the context of SARS-CoV-2 vaccines, although we are aware of several studies that are underway. One of the few published studies in this area is of 676 adults from an ongoing UK-based longitudinal study who had antibodies measured following a single dose of COVID-19 vaccine. The authors report less social cohesion was associated with lower antibody responses, and this was in part mediated by feelings of loneliness (Gallagher et al., 2022). However, they did not examine whether effects differed by vaccine type. Nonetheless, this mirrors pre-pandemic work that found greater loneliness and small social network size to predict poorer antibody response to influenza vaccination among first-year college students (Pressman et al., 2005).

In summary, decades of research have shown that psychosocial factors influence viral susceptibility and vaccine efficacy, with early COVID-19 research following a similar pattern. These psychosocial factors are thought to impact COVID-19 viral susceptibility and vaccine efficacy through a variety of interacting biobehavioral pathways. This includes systemic inflammation, autonomic and neuroendocrine functioning, and health behaviours that may have been disrupted by public health policies to mitigate the spread of the virus. These pathways are illustrated in Figure 1 and described in the Supplemental File.²

Moving forward, what could be done differently?

Many public health initiatives created to mitigate the spread of COVID-19 were well-intentioned and dramatically reduced the spread of COVID-19 and excess deaths. Nevertheless, along with losing loved ones and fears about the virus, these mitigation efforts may have had unintended consequences for psychosocial well-being and in turn, viral and vaccine outcomes. Unfortunately, as can be seen from the above, many of these consequences were entirely predictable, with ample pre-pandemic evidence demonstrating that psychosocial factors influence viral and vaccine outcomes. Yet, prior findings relating to biopsychosocial relationships in this context appear to have been largely overlooked when formulating public health policy responses. While we cannot change the past, in the following sections we look forward, considering what steps could be taken to address similar oversights in the future.

Inclusion of psychosocial risk factors in public health models

The evidence outlined above illustrates that a range of psychosocial factors should be considered as risk factors for viral complications in the same way that other risk factors (e.g., chronic health conditions, age) are routinely considered in formulating public health policy and interventions. Importantly, these psychosocial risk factors need to be recognised not as static risks but as bi-directional and dynamic contextual factors that may influence public health policies. In the context of COVID-19, different groups of people experienced varying levels of exposure to the virus itself and susceptibility to the negative psychosocial consequences associated with mitigation efforts. This was evident among people with past or current mental health difficulties, from lower SES backgrounds, or from marginalised racial and ethnic groups. Moving forward, it is essential we acknowledge these differences and properly address these vulnerabilities. Below we discuss the potential benefits that could be achieved through

² The supplemental file can be found here: https://osf.io/7yjmz/?view_only=8fd04f409d8344af8b0ad1677349794f

psychosocial interventions implemented in tandem with (versus in place of) public policies to address structural and environmental determinants of health inequalities (e.g., paid sick and parental leave, liveable wages) to achieve health equity.

Promoting psychosocial interventions and tools

Interventions that reduce loneliness and manage distress while enhancing connection, positive affect, and coping could be used in tandem with established pandemic regulations (e.g., social distancing) to buffer the negative health consequences of mitigation efforts. For example, Fischer et al. (2020) synthesised over 30 meta-analyses examining interventions individuals could use during the pandemic to manage anxiety, depressive symptoms, stress, and promote well-being. Self-guided therapeutic approaches (e.g., mindfulness, cognitive-behavioural therapy), multi-component and activity-based interventions (e.g., music, physical activity), and certain positive psychological interventions (e.g., gratitude, compassion-based) were the most effective for improving psychological health, but dose effects of these interventions were inconsistent.

Loneliness has also been identified as a useful point of intervention due to widespread disruption of social networks caused by pandemic restrictions. Parks and Boucher (2020) conducted an 8-week randomised control trial of a digital positive psychological intervention platform on loneliness among US adults. Among participants who completed more activities, those in the intervention reported significantly greater improvements in loneliness compared to those in the placebo control. Similarly, meta-analytic findings from Bertuzzi and colleagues (2021) found that psychological support interventions reduced distress and burnout among health care workers and informal caregivers while increasing their self-efficacy and well-being regardless of the type of intervention (e.g., music therapy, psychoeducation).

As the above demonstrates, numerous psychosocial interventions could be drawn upon to potentially decrease distress and improve social connectedness during future public health crises. Their use could potentially leverage the relationship between psychosocial factors with viral and vaccination outcomes to reduce individual and societal burden from infection. However, many of these interventions have not been considered in a pandemic context or in relation to viral and vaccine outcomes. We also note the considerable potential of behavioural interventions, given behavioural factors are often closely entwined with psychosocial factors. A full discussion of behavioural interventions goes beyond the scope of the present article but we provide some brief discussion of their potential benefit in the Supplemental File.³

Considering implementation, it is critical to target and co-design interventions with populations that are especially susceptible to negative health outcomes during the pandemic, including healthcare workers, individuals experiencing psychological distress due to pandemic restrictions or infection in themselves or a loved one, and individuals with existing mental health conditions that may be exacerbated by mitigation efforts or infection (Inchausti et al., 2020). Further research has identified groups at greater risk for isolation and loneliness, including those with poorer health, lower income, and who live alone (O'sullivan et al., 2021), who may benefit from intervention. As such, policymakers could follow a proportionate universalism approach

³ The supplemental file can be found here: https://osf.io/7yjmx/?view_only=8fd04f409d8344af8b0ad1677349794f

whereby psychosocial interventions are delivered universally to all people during future health crises but modified in terms of intensity depending on people's needs.

Promoting change in public health

There is also a pressing need to move towards a greater recognition of a biopsychosocial model of health to prepare for future health crises. This includes medical training acknowledging how the body and mind are intimately connected, that these associations are dynamic and unfold across time and development, and must be considered in the context of socioeconomic and racial inequalities in health. Simplistic models of disease that separate mind and body or that overlook the psychosocial environment are incomplete and will continue to dominate public health policies if we do not make a paradigm shift. Thus, as a research community we need to better convey our science in a way that reaches experts in other disciplines in order to establish collaborations. This includes holding cross-disciplinary conferences, implementing interdisciplinary coursework into our training programs, and building connections with policymakers and stakeholders in government.

Moreover, it is critical for researchers to conduct methodologically rigorous research using probability-based representative samples of individuals to reinforce that psychological research should, and can be, better integrated into public health initiatives in response to future pandemics. To this end, funding lines should be created to fund studies that examine **1)** efficiently delivering biopsychosocial interventions tailored toward vulnerable groups, especially during health crises, **2)** keeping communities properly informed regarding pandemic regulations and illness rates by working with media outlets to improve accuracy, and **3)** developing theoretical models that address emerging health crises (as opposed to relying on old models that may generalise to pandemic circumstances). Such funding could integrate different health psychology experts into teams that make major decisions during epidemics and pandemics. Having a diverse set of health knowledge and viewing health from a biopsychosocial lens will help prepare us for future threats by being proactive versus reactive in the face of future crises. Finally, and perhaps most importantly, researchers need to make our science more accessible to the public and use community-led research to inform the development and adaptation of biopsychosocial interventions. Our research is less effective if we cannot reach the populations that our interventions are intended to benefit or if we leave out the voices of the people for whom our interventions are developed.

Ultimately, the best response to health events such as the COVID-19 pandemic is one that is equally spearheaded by the public, policymakers, and scientific community. Organisations such as the World Health Organization, National Health Services, Centers for Disease Control (CDC), National Institutes of Health, and major psychological organisations (e.g., Association for Psychological Science, International Society for Behavioral Medicine, Academy of Behavioral Medicine Research) must work in tandem with state- and community-level entities to foster collaborations and develop holistic, multi-level approaches to addressing psychosocial risk factors for viral and vaccine outcomes so that we are better prepared for future health crises.

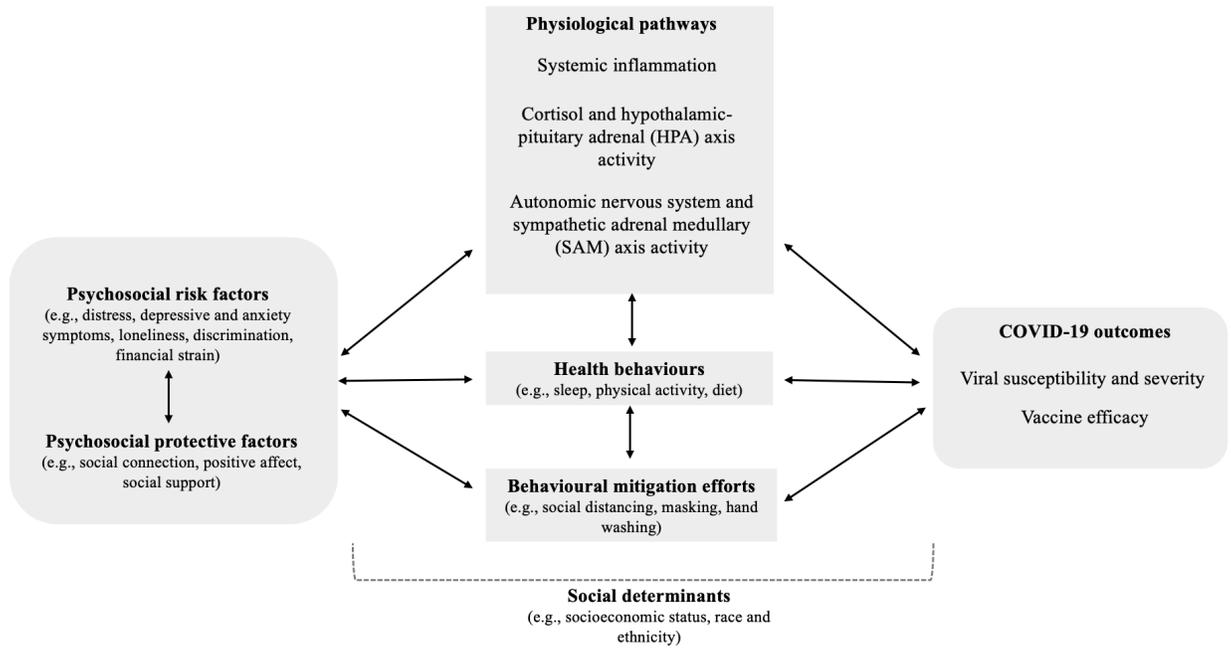


Figure 1. Psychosocial factors may relate to COVID-19 through interacting physiological, health behaviour, and behavioural mitigation pathways that may differ depending on socioeconomic status, race, and ethnicity.

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