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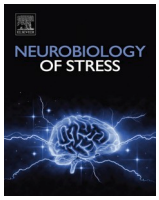

Youth mental health crisis: A translational view of the COVID-19 pandemic

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A B S T R A C T

Mental health problems among children and adolescents have increased over the past two decades, a trend that was further exacerbated by the COVID-19 pandemic. To improve prevention and treatment strategies, developmentally informed and data-driven multidisciplinary approaches are urgently needed to clarify the mechanisms underlying youth vulnerability and resilience. Stress and trauma exposure are among the strongest predictors of youth mental health problems; however, most children and adolescents remain resilient despite such exposures. The widespread and heterogeneous challenges posed by the COVID-19 pandemic offer a unique opportunity to examine, at scale, who develops mental health problems under stress and who remains resilient. Integrating emerging findings on pandemic-related risk and protective factors with evidence from animal models can illuminate sensitive developmental periods of heightened susceptibility to environmental influence and biological embedding. This approach can identify when, how, and through what pathways mental health problems emerge, including gene–environment interactions and epigenetic mechanisms. Such knowledge will inform both behavioral and pharmacological interventions, pinpointing not only specific treatment targets but also the optimal timing for intervention to be the most effective.

Poor mental health is the leading health and social issue affecting the lives and future of children and adolescents (Kieling et al., 2024a; Castelpietra et al., 2022; McGorry et al., 2024). These problems include depressed mood, anxiety, self-harm and suicidal behaviour (Auerbach et al., 2018; James et al., 2018). While a steady decline in the rates of many common diseases has occurred over the past decades, the rates of mental health problems and disorders have remained unchanged (Naghavi, 2019) or even increased in youth (Fig. 1). (Collishaw, 2015; Kassebaum et al., 2017; Morgan et al., 2017; Trivers et al., 2018; Thorisdottir et al., 2017; Ford, 2020; McManus et al., 2019; Bould et al., 2019; Jefferies and Ungar, 2020; Kieling et al., 2024b) Furthermore, a global trend towards earlier onset of mental health disorders has been documented (McGrath et al., 2023), with the peak onset of most mental health disorders occurring during the transition from childhood to adulthood (Solmi et al., 2022).

This is paradoxical given that we know more about mental health now than ever before, and empirically-supported interventions designed to reduce mental health problems exist. (National Institute and for Health and Care Excellence) Due to their rising prevalence and variability in treatment response (Huhn et al., 2014), it is imperative that new, transformative multidisciplinary efforts be made to advance prevention and treatment strategies for mental health problems. This goal can only be achieved through multidisciplinary research, from the societal level to cell level factors, to form an understanding of what causes mental health problems.

Globally, youth today are faced with different types of stressors and trauma exposures than previous generations, which are believed to contribute to this increase in mental health problems (McGorry et al., 2024). These include fear due to climate change, decreased social connectedness, unregulated and unsafe digital world, worsening health behaviors, reduced access to affordable housing, insecurity of employment, and increased intergenerational inequality. Among the most well studied and robust predictors of poor mental health to date include peer relationship problems, bullying, parental divorce, living with someone who is mentally ill, serious accidents, natural disasters, and child abuse and neglect (Bellis et al., 2019). These exposures are also alarmingly common. For instance, in a nationally representative sample of women in Iceland, we found that approximately 80 % of women endorsed experiencing at least one type of stress or trauma exposure (as measured with the Adverse Childhood Experiences scale) prior to age 18 years-old

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(Daníelsdóttir et al., 2022). Similarly high rates for different types of stress and trauma exposures have been reported worldwide (Bellis et al., 2019). Despite the high rates of stress and trauma exposure, not everyone goes on to develop mental health problems.

A recent stress or trauma exposure experienced by all at some level was the global COVID-19 pandemic. Worldwide, COVID-19 infections resulted in over 7 million deaths, governmental mandated physical distancing measures resulting in limited (if any) in-person social interactions outside of the home isolation, as well as great uncertainty about the future. For children and adolescents, physical distancing measures resulted in school closures with consequent reductions in social contact, loss of learning, and physical activity. Early during the COVID-19 pandemic, researchers warned of a potential epidemic of mental health problems (Holmes et al., 2020). Consistent with this prediction, research from all over the world – including our team – has shown that the already rising mental health problems among children and adolescents were exacerbated by the pandemic (Thorisdottir et al., 2021; Thorisdottir et al., 2023; Kiviruusu et al., 2024; Ravens-et al.; Shoshani, 2024; Barbieri et al., 2023; van Oers et al., 2023; Park et al., 2024; Haskell et al., 2025).

From a research standpoint, the global COVID-19 pandemic and consequent diverse challenges youth and families were faced with may provide unique opportunities for great insight into who develops mental health problems versus who remains resilient in times of stress. The substantial variation in governmental mandates used to control the spread of the pandemic may provide insight into how diverse environments and social networks impact youth mental health (Fig. 2). In response to anecdotal and survey data (including from our group) on an increase in youth mental health problems, the Icelandic government prioritised keeping preschools and elementary schools open during the pandemic. Other countries were more stringent in their physical distancing mandates, enforcing strict stay-at-home regulations and full school closures. By 2021, as vaccinations became available, social restrictions varied more widely between countries. The aftermath of these differing policies continues to unfold and warrants longitudinal examination to fully understand their impact. At present, studies directly comparing youth mental health outcomes in relation to specific social restrictions remain limited but urgently needed (Solmi et al., 2022).

Several protective and risk factors of youth mental health problems during the pandemic have already been identified. Positive familial relationships, social support, maintaining daily routines, physical exercise, healthy sleep patterns and access to entertainment are among the protective factors most consistently associated with good mental health during the pandemic (Thorisdottir et al., 2021, 2023; Haskell et al., 2025; Samji et al., 2022; Halldorsdottir et al., 2021). The most robust risk factors are female gender and living with neurodiversity and/or chronic physical conditions (Thorisdottir et al., 2021, 2023; Haskell et al., 2025; Samji et al., 2022; Halldorsdottir et al., 2021).

Age at time of stress exposure may also contribute to differential mental health (Thorisdottir et al., 2021). Emerging evidence suggests that there are developmental sensitive periods in which different types of stress and trauma exposures may be the most detrimental (Gerhard et al., 2021; Schaefer et al., 2022). During these periods, environmental exposure can have lasting effects on development and mental health outcomes. The timing matters because the exposure coincides with the period of greatest maturation or plasticity in the brain. Hence, exposure at one point in time may be more potent in shaping mental health than the same exposure occurring earlier or later (Nelson et al., 2020). This may apply to the effect of limited in-person contact with peers on mental health during the COVID-19 pandemic. Specifically, among the most consistent findings is an increase in depressive symptoms during the pandemic has been shown among adolescents (10-24-years-old) (Madigan et al., 2023; Panchal et al., 2023). Indeed, adolescence is a period characterized by dynamic behavioral and neurobiological changes. Coinciding with puberty, adolescence is when the skills and behavioral strategies required for independence from early-life caregivers are developed. Social interactions with peers are key components in developing these skills.

With limited human research on this topic, the rich evidence on the effects of social deprivation from animal models may help us understand the importance of peer contact during adolescence and its connection with mental health. Social contact with peers has been identified as an essential mechanism for healthy social behavior and healthy maturation of the social brain – the network of brain areas involved in social perception and cognition allowing us to understand others (for reviews, see (Burke et al., 2017; Li et al., 2021; Orben et al., 2020)). The social brain regions comprise the prefrontal cortex, temporoparietal junction, hippocampus and amygdala (Mills et al., 2014). Rodent models have shown that even brief complete social isolation (e.g., 24 h) or short-term deprivation of social contact with peers can result in increased anxiety- and depressive-like behaviors and substance use, as well as impaired reward learning and habituation to novel stimuli. Social deprivation during adolescence results in brain-level alterations, including reduced synaptic pruning in the prefrontal cortex in rodents (Burke et al., 2017; Orben et al., 2020). These findings on short-term deprivation of contact with peers are similar among non-human primates. Similarly, recent imaging studies have shown increased volume in the hippocampus among human adolescents during the pandemic, which may indicate accelerated brain maturation due to the pandemic (Cai et al., 2024; Gotlib et al., 2023; Van Drunen et al., 2023).

Animal studies can also shed light on potential long-term consequences of the pandemic. For instance, animal studies show that the effects of social isolation may have long-term behavioral and neurobiological consequences (Burke et al., 2017; Orben et al., 2020). Even after being reintroduced to social contact after short-term isolation, there tends to be a reduction in anxiety behaviors but animals continue to

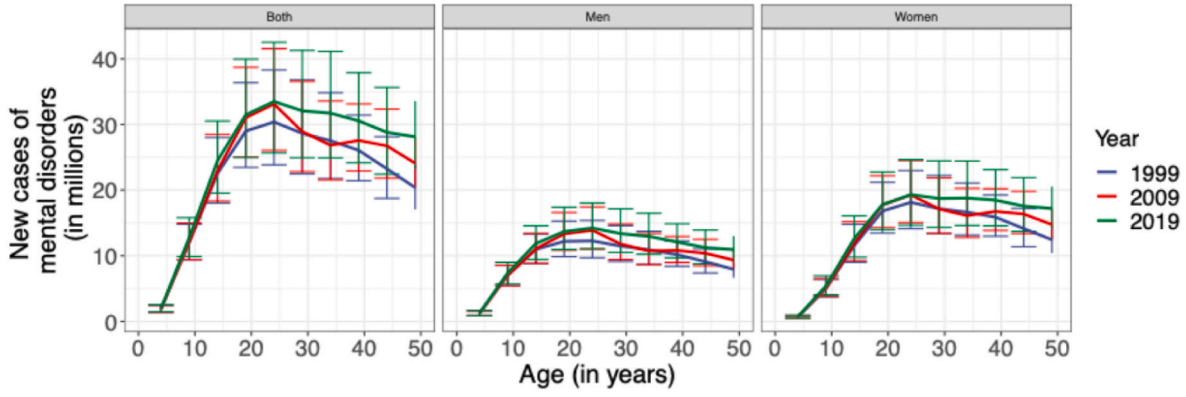

Fig. 1. Incidence rates from the Global Burden of Disease study of mental health disorders by age over a 20-year period across genders and broken down for men and women.

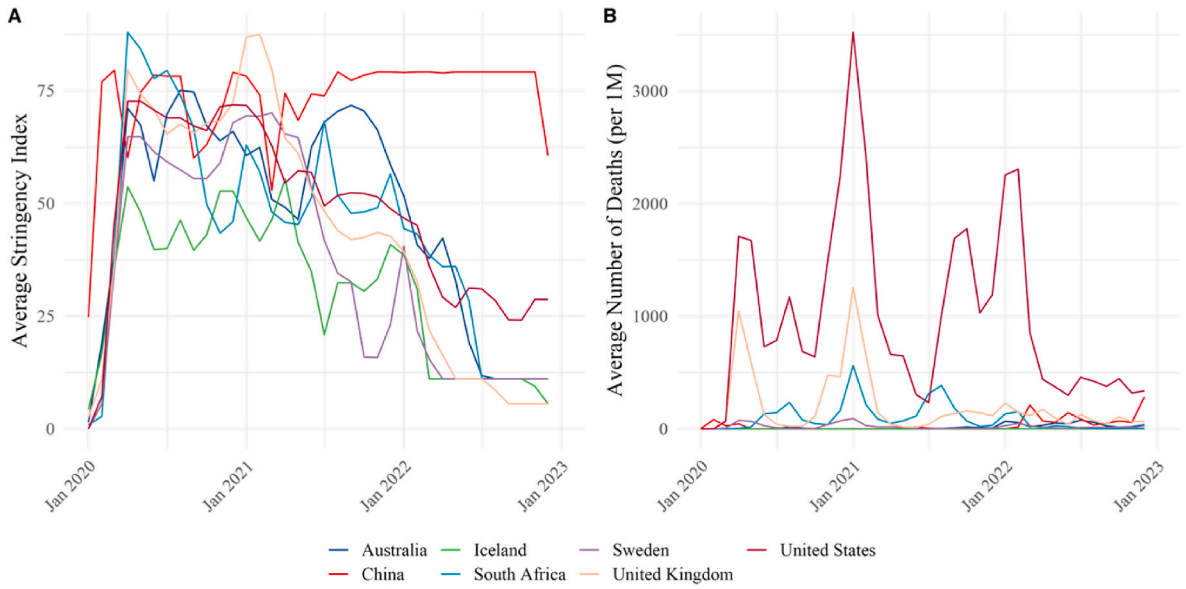

Fig. 2. Comparison of the governmental mandated social restrictions, as measured by the stringency index, implemented in 7 countries (A) and the number of COVID-19-related deaths per 1 million individuals for each country (B). Data to generate the figures was obtained from Our World in Data.
Source: Institute for Health Metrics and Evaluation. Used with permission. All rights reserved.

display some of the negative effects after the acute isolation, such increased ethanol consumption (Burke et al., 2017). Mirroring these animal findings, we found that the elevation in depressive symptoms observed in 2020 among a nationwide sample of 13–18-year-old adolescents in Iceland was maintained in 2022 despite social restrictions being lifted (Thorisdottir et al., 2023). Findings from our most recent measurement conducted on 13-15-year-old in 2023 indicate that depressive symptoms remain higher than pre-pandemic levels, although they are regression towards earlier levels (Haskell et al., 2025). Alcohol intoxication initially decreased in the first year of the pandemic but then increased anew to pre-pandemic levels in 2021, and were even higher than previously among 18-year-old girls, when social restrictions had been lifted (Thorisdottir et al., 2023)

In lieu of in-person interactions, social media became the primary means for many adolescents to socialize during the pandemic (Madigan et al., 2022). Social media has been proposed as a contributor to the global increase in youth mental health problems (McGorry et al., 2024). In our recent population-based study tracking youth mental health throughout the pandemic, we found support for the so-called *Goldilocks* effect of social media use (Haskell et al., 2025). Specifically, 30 min to 1 h of daily social media use was associated with lower mental health problems but higher mental health problems at less or greater time spent on social media platforms. A meta-analysis (Marciano et al., 2022) on studies examining social media during the height of the pandemic showed that one-to-one communication, mutual online friendships, and positive online experiences helped reduce loneliness and stress. Simultaneously, excessive social media use, an overload of negative content and misinformation regarding COVID-19 on social media was found to amplify stress and fear. These findings underscore the relationship between social media use and adolescent mental health is not straight forward but complex and multifaceted. A multilevel approach is essential to disentangle this complexity, as it allows for the examination of specific features of social technology (e.g., platform type, activity type, content exposure) that may contribute to either good or poor youth mental health.

Also pertaining to social networks, evidence suggests that proximity to and awareness of mental health problems can contribute to increased rates of these problems. A recent large-scale study of over 700,000 Finnish adolescents found that having a classmate diagnosed with a mental disorder—particularly anxiety, mood, and eating disorders—increased the likelihood of receiving a similar diagnosis by 10–20 % (Alho et al., 2024). The risk was most pronounced within the first year of a classmate's diagnosis, but a measurable effect persisted for up to five years. The social transmission of mental health problems also extends beyond direct social networks, as media exposure can amplify the prevalence of such problems. For example, media attention and portrayals of mental health struggles have been linked to increased rates of related conditions. This includes rises in mental health problems following social influencers openly discussing their struggles on platforms such as TikTok(Conte et al., 2024), as well as spikes in self-harm and suicide rates following the widespread publicity of celebrity suicides (Niederkrotenthaler et al., 2020) or fictional depictions in TV series (Niederkrotenthaler et al., 2019). These concerning findings highlight the importance of evidence-based guidelines for caregivers, educators, mental health professionals, the media and policymakers on responsible communication about mental health problems. At present, little is known about social transmission and contagion of mental health problems among youth during the pandemic.

Importantly, despite the widespread impact of the pandemic, as with most stress and trauma exposures, most youth remained resilient when it comes to their mental health, and some even thrived during the pandemic (Halldorsdottir et al., 2021; Bruining et al., 2020). In line with Rutter's conceptualization of resilience as a **dynamic process** shaped by individual–context interactions over time, rather than a fixed trait (Rutter, 2012), many young people adapted positively despite significant disruptions.

For instance, over a third of 16-year-olds reported that the increased time spent sleeping, with family or relaxing and decreased stress due to school and schoolwork had a positive effect on their mental health (Halldorsdottir et al., 2021). These findings highlight that for some adolescents, the altered routines and social demands during the pandemic created **protective conditions,** enabling emotional recovery or even growth. This is consistent with previous research suggesting that schools may, under some conditions, act as a significant source of stress contributing to adolescent mental health problems (Davico et al., 2024). This perspective not only broadens our understanding of adolescent adaptation during collective stressors like the pandemic, but also presents **unique opportunities for future research and application**. Identifying the specific contextual factors—such as reduced academic pressure or increased family time—that promote resilience may inform

targeted interventions or **policy shifts** aimed at strengthening youth mental health under both normal and crisis conditions.

To explain the varying outcomes following stress exposure, the most influential mental health theories (Belsky, 2016; Belsky et al., 2021; Belsky and Pluess, 2009; McEwen and Stellar, 1993; Halldorsdottir and Binder, 2017) posit that mental health results from an interplay between environmental factors and genetic predisposition. Genome-wide association studies (GWAS), which assesses the association between millions of common variants with a complex trait, have successfully identified numerous common genetic variants and biological pathways linked to increased risk of mental health disorders and traits associated with mental health (Smoller, 2019; Akingbuwa et al., 2022). Derived from GWAS findings, polygenic risk scores are the weighted sum of an individual's genetic risk for a particular trait. These scores have been found to predict risk for mental health problems within different contexts. For example, we have found that the polygenic risk score for major depression (MD PRS) was associated with depressive symptoms and a clinical diagnosis of major depression in children and adolescents (Halldorsdottir et al., 2019a). Interestingly, the MD PRS did not interact with exposure to childhood trauma to predict depressive symptoms or MDD in youth.

According to the differential-suspectibility theory(Belsky, 2016; Belsky et al., 2021; Belsky and Pluess, 2009)¯(Belsky, 2016; Belsky et al., 2021; Belsky and Pluess, 2009), certain genotypes may respond very differently in supportive versus adverse environments. In support of this theory, we found that children with two copies of the risk *FKBP5* haplotype who were exposed to intimate partner violence prior to 2 years of age were more likely to have a developmental trajectory characterized by high and prolonged stress-induced cortisol reactivity and emotional reactivity in toddlerhood, followed by low executive function at school entry and high emotional and behavioral problems and low reading ability in the primary school grades (Halldorsdottir et al., 2019b). Conversely, children with two copies of the risk *FKBP5* haplotype who were not exposed to intimate partner violence at an early age tended to have the best self-regulation outcomes.

Within the context of the COVID-19 pandemic, there is limited research on whether polygenic risk scores are associated with mental health during the COVID-19 pandemic (Ahrens et al., 2022; Schowe et al., 2024; Taylor et al., 2022; Warmerdam et al., 2022). The few available studies in children and adolescents have yielded mixed results. For instance, in a study of 700 10-year-olds, those with higher polygenic risk for attention-deficit/hyperactivity disorder (ADHD) displayed worse neuropsychiatric symptomatology during the peak of social restrictions, while those with lower ADHD polygenic risk scores showed no change (Hernández-Lorca et al., 2023). In contrast, a smaller study of 263 children aged 7-10 years-old found no association between polygenic risk scores for depression, schizophrenia and loneliness and emotional well-being during the pandemic (Nguyen et al., 2023). Among older adolescents, a population-based study of 7787 16–17-year-olds in Norway reported that lower PRS for depression were paradoxically associated with greater mental distress following repeated quarantines. However, PRS for anxiety, anorexia nervosa, and neuroticism showed no association with mental health outcomes (Pettersen et al., 2024). These findings reflect the complexity of gene-by-environment interactions and methodological challenges, including small sample sizes, this relatively novel field has been faced with (Smoller, 2019). Yet, with the rapid advances within this field, the insights gained from genetic research, including polygenic risk scores, may eventually inform personalized and precision-based interventions, complementing environmental and psychological strategies. Thus, the inconsistencies in genetic findings should be seen as an opportunity to refine methodologies, foster interdisciplinary collaboration, and integrate findings from diverse approaches.

In addition to environmental factors and genetic predisposition, biological embedding is an important mechanism in the development of mental health problems (Aristizabal et al., 2019; Halldorsdottir et al., 2022). Biological embedding occurs when experiences get under the skin and alter ongoing developmental processes, with consequences for behaviour and mental health over the lifecourse (Hertzman and Boyce, 2010). Epigenetic mechanisms, such as DNA methylation, are considered a likely candidate underlying the biological embedding of experiences (Aristizabal et al., 2019). Epigenetic alterations induced by stress, such as social isolation, have been shown to have long-lasting consequences. Recent evidence suggests that biological embedding may be dependent on the developmental timing, as well as the type of stress or trauma exposure (Halldorsdottir et al., 2022). In relation to the COVID-19 pandemic, a study of 263 newborns during the COVID-19 pandemic found that the timing of lockdowns during pregnancy was associated with DNA methylation in stress-related genes, specifically the glucocorticoid receptor gene (*NR3C1*) and the serotonin transporter gene (*SLC6A4*) (Nazzari et al., 2022). Specifically, newborns of mothers who experienced the first lockdown in Northern Italy during the second and third trimesters exhibited higher *NR3C1* and *SLC6A4* methylation levels compared to those exposed during the first trimester. In the same cohort, prenatal exposure to high levels of maternal pandemic-related stress during the third trimester was linked to higher *SLC6A4* methylation levels in newborns, which in turn was associated with the infants' temperament at 3 months of age (Provenzi et al., 2021). These preliminary findings may suggest that epigenetic mechanisms may mediate the embedding of pandemic-related stress exposure occurring during pregnancy on the infant's development. At present, the role of biological embedding as mechanism linking stress exposure during the pandemic with in mental health problems in children and adolescents remains unexplored. However, the identification of sensitive periods with increased susceptibility to environmental influences and biological embedding will provide important insights into when and through what pathways and mechanisms mental health problems emerge.

Given the complexity and multilevel nature of mental health development, future research must integrate biological, psychological, and environmental data using both hypothesis-driven and data-driven approaches. While prior studies have typically examined risk factors in isolation, machine learning and artificial intelligence now enable the simultaneous modeling of interactions among genetic risk (e.g., polygenic scores), environmental exposures (e.g., social deprivation), and developmental timing. These tools can be used not only to improve prediction accuracy but also to uncover novel patterns or subgroups that traditional analyses may overlook. Importantly, this should not replace theory-guided research but rather complement it, particularly in exploring sensitive periods when exposures may have heightened effects. Integrative models that combine longitudinal, multilevel data with rigorous analytic frameworks hold significant promise in informing precision-targeted prevention and intervention strategies for youth mental health.

To summarize, the broad scope of factors contributing to the rise in mental health problems among youth, the limitations of current prevention and treatment efforts, underscores the urgent need to prioritise a multidisciplinary approach to address this large-scale societal concern. Just as significant progress has been made in reducing the burden of medical disorders like cardiovascular disease and cancer, similar advancements in youth mental health require bridging the gap between basic science and real-world applications. The intricate interplay of biological, psychological, and social factors shaping mental health demands that we leverage every available tool to enhance our understanding of mental health problems. This collective, comprehensive and developmentally grounded knowledge will directly advance evidence-based pharmacological, behavioral, and policy strategies, ultimately improving mental health outcomes for youth.

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Declaration of competing interest

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