**Commentary: The impact of Covid-19 on psychopathology in children and**

**young people worldwide- reflections on Newlove-Delgado et al. (2023)**

Samuele Cortese \*1-5, Marco Solmi \*1,6-10, Christoph U. Correll 10-12

1 Centre for Innovation in Mental Health, School of Psychology, University of Southampton

2 Southampton, UK

3 Solent NHS Trust, Southampton, UK

4 Division of Psychiatry and Applied Psychology, School of Medicine, University of Nottingham, Nottingham, UK

5 Hassenfeld Children's Hospital at NYU Langone, New York University Child Study Center, New York City, New York, USA

6 Department of Psychiatry, University of Ottawa, Ottawa, ON, Canada

7 Department of Mental Health, The Ottawa Hospital, Ottawa, ON, Canada

8 School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Canada

9 Ottawa Hospital Research Institute (OHRI) Clinical Epidemiology Program University of Ottawa Ottawa Ontario

10 Department of Child and Adolescent Psychiatry, Charité Universitätsmedizin, Berlin, Germany

11 The Zucker Hillside Hospital, Division of Psychiatry Research, Northwell Health, Glen Oaks, New York, New York, USA

12 Department of Psychiatry and Molecular Medicine, The Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New York, New York, USA

\* equal contribution

**Address correspondence to:**

Prof. Samuele Cortese, School of Psychology, Centre for Innovation in Mental Health (CIMH), Faculty of Environmental and Life Sciences, University of Southampton, Highfield Campus, Building 44, Southampton, SO17 1BJ, UK, Phone: +44 (0) 2380599645, E-mail: samuele.cortese@soton.ac.uk

In the past three years, since the beginning of the Covid-19 pandemic, there has been an impressive flourishing body of publications on the impact of the pandemic and related restrictions on the mental health of children and young people (Dragioti et al., 2022). A scientometric analysis (Cortese, Sabe, & Solmi, 2022) published in this *Journal,* identified 3,692 research outputs on Covid-19 and mental health in children and young people published up to February 2022, even though at least 768 of them (20%) were represented by non empirical studies (i.e., reviews, editorials, case reports). It was about time for a rigorous quantitative evidence synthesis of this large body of research. Newlove-Delgado and colleagues (2023) took on this challenge by completing a systematic review with meta-analysis of epidemiological studies on the impact of Covid-19 on psychopathology in children and adolescents, featured in the 2023 Annual Research Review series of the *Journal*. The authors should be commended for their rigorous and authoritative work, and for addressing a very complex and heterogenous body of research, which entailed a number of methodological choices that are never easy to be made in this type of research.

A rigours evidence synthesis of this literature has indeed the potential of being relevant for patients, clinicians, researchers, resource allocation decision makers and other stakeholders, to inform clinical practice, treatment and prevention strategies, policies and governmental decisions. Such detailed information seems particularly relevant at the time of the writing of the present Commentary (end of December 2022), when concerns are arising about yet again increasing Covid-19 infection cases from China and other countries as well as about possible new mutation variants. These renewed concerns have prompted some governments (e.g., in Italy) to consider reinstating previous stark restrictions amid concerns with regards to surging death rates but also the impact of the restrictions on physical and mental health of the general population and, particularly, vulnerable subgroups, such as children and adolescents.

The Newlove-Delgado et al. study (2023) is certainly not the first meta-analysis focused on the psychopathology in children and young people during the Covid-19 pandemic. A simple search in PubMed using the syntax : “Covid-19 AND (mental or psychopathology) AND (child or children or adolescen\* or youth\* or young)” and the filter *meta-analysis* provided 61 hits (on December 29th, 2022). However, the systematic review and meta-analysis by Newlove-Delgado et al. (2023) stands out for its comprehensive focus, addressing a broad range of mental health outcomes, and the rigour in the selection of the included studies. The authors included longitudinal cohort studies and cross-sectional studies with follow-up, reporting changes from pre-pandemic to intra-pandemic time periods on a validated scale. They also included studies comparing samples from different cohorts or cross-sectional surveys from pre-pandemic to intra-pandemic times, when there was evidence that the populations were comparable. Overall, expectedly, there was a high degree of methodological heterogeneity across the 51 studies retained in the systematic review, owing to variability in terms of study design, setting, timing of the assessment in relation to the pandemic, population characteristics, and length of follow-up, that hampered the statistical pooling of data from many studies. Meta-analyses were run when there was more than one study with the same design, using the same measure, by the same informant (e.g., parent or teacher), and reporting data in a format amenable to statistical pooling. The authors were particularly cautious in decidedly opting against the meta-analysis of outcomes measured with different scales, even when they referred to the same broad construct (e.g., depression). Given these stringent criteria, meta-analysable data were available only from 6 studies for anxiety (11.8% of the total number of studies included in the systematic review, n=51), 5 (9.8% ) studies for depression;  2 (3.9% ) studies for internalizing symptoms; 2 (9.8% studies for externalizing symptoms; 2 (9.8% ) studies for peer relationships; and 0/51 studies for mental health difficulties/global severity, restricting the data and conclusions that could be drawn from them.

Results of the meta-analyses of changes in symptom expressions of selected disorders from pre- to intra-pandemic times can be summarised as follows: i) anxiety (self-reported), internalising symptoms (parent-report), and hyperactivity and inattention symptoms (self-reported) did not change significantly; ii) internalising symptoms (self-report) deteriorated slightly); iii) conduct problem symptoms (self-reported) decreased in severity); iv) prosocial behaviors and peer relationships marginally deteriorated (close to non-significance); v) depression symptom changes (self-reported) were mixed, without significant changes when considering some specific self-reported depression measures (questionnaires), and with evidence of deterioration in the severity of symptoms when pooling data using other specific self-reported measures of depression. However, notably, when considering only studies judged by the authors to be of high quality, the findings showed an increase in the severity of the symptoms.

All these meta-analytic findings should be interpreted with caution, as they were based on a limited number of studies, ranging from two to four for any specific outcome scale used to measure symptoms within a disorder category.

Indeed, sometimes, meta-analyses are able to provide a definitive answer to a research question, but more frequently their main value rather lies in pointing to weakness in the available evidence base and areas of future research in the field. The Newlove-Delgado et al. (2023) meta-analysis probably falls in the latter category. A number of aspects, highlighted by the systematic review, are striking, and should prompt serious reflection in the field: 1) less than 8% of the retained studies (7.8%) were deemed of high quality, with the major shortcoming being the lack of representative samples (present in only 5.9% of the studies), despite the fact that, early in the pandemic, a thoughtful paper (Pierce et al., 2020) warned against the bias introduced by the exclusive use of convenience samples; 2) there was a limited focus, in many studies, on the assessment of isolated domains of psychopathology, with an emphasis on internalising behaviors, rather than adopting a broader scope embracing more specific and also general psychopathological dimensions; 3) despite the global pandemic affecting all strata of the populations, in general the studies relied on small samples (e.g., sample sizes ranged for anxiety from 96 to 2099; for depression from 184 to 11,774; for internalizing symptoms from 50 to 1,585; for externalizing symptoms from 59 to 1,585; for mental health difficulties/global severity from 88 to 3,572), reflecting the logistic challenges of recruiting larger samples during the pandemic (due to, among other reasons, time pressures to initiate new research projects at a time of great disruption of the research activities caused by the pandemic, and high competition to obtain funding); 4) samples were restricted to one country/location only in most studies; 5) single time point, cross-sectional studies predominated; 6) in many studies there was a lack of accounting for variation in death rate, severity of the Covid-19 epidemic in specific geographic areas, and restriction measures over time; 7) heterogeneity across studies was high regarding study design, setting, assessment tools and timing of baseline and follow-up assessment as well as time between baseline and follow-up assessments (ranging from 3 months to 3 years, with the bulk of the studies mostly covering <1 year for anxiety), making pooling in meta-analyses highly vulnerable to confounding by time effect of the pandemic and restrictions; 8) vulnerable child *vs*. adolescent samples were seriously underrepresented, e.g. only 2/51 = 3.9% pertaining to anxiety outcomes, with similar trends for depression and internalizing symptoms (3 of 13 studies had mean ages of 12 or below (9.9 and 8.7 years, respectively); 9) potentially very relevant variation in death rate and restriction measures over time were not accounted for; 10) there was a focus on psychopathology rather than resilience and coping strategies; and 11) studies were often characterized by poor reporting, reflecting a possible lowering of the publishing standards, at least in some journals, due to the challenging situation created by the pandemic and time pressures to report results during an evolving pandemic development.

We look forward to future studies addressing these important issues, highlighted by the meta-analysis by Newlove-Delgado et al. (2023). The Collaborative Outcomes study on Health and Functioning during Infection Times (COH-FIT) (Solmi et al., 2022a) (Solmi et al., 2022b), whose results related to the first two years of the pandemic should be available soon, is one such example. COH-FIT, which is addressed to adults as well as children and young people in the general population, is an anonymous on-line survey, ongoing since 26/04/2020, targeting the general population, involving over 220 researchers from 49 different countries, and available in 30 languages. Notably, COH-FIT is being disseminated via both snowball and representative sample recruitment. Rather than focusing on a limited number of specific outcomes, COH-FIT targets a broad range of psychopathological measures. This approach was made possible by using abbreviated portions of established questionnaires to allow for broad-based questioning within a still feasible questionnaire completion time. The COH-FIT questionnaire was validated and contributed to a 7-dimension psychopathology P-factor (Solmi et al., 2023). COH-FIT also measures quality of life, wellbeing and copying strategies in addition to potentially relevant moderators and mediators (Arango et al., 2021) (Solmi et al., 2021) of change in psychopathology and wellbeing (Solmi et al., 2022a) (Solmi et al., 2022b). Although COH-FIT is a cross-sectional study, individuals are asked to retrospectively rate their state pre-pandemic and currently intra-pandemic, allowing for the analysis of changes at the population level. Designing a study that captures the effects of an evolving pandemic stressor in the general population and potentially vulnerable subgroups requires some compromise between what is ideal and what is feasible. Although building a large, international, prospective cohort study would have been ideal, pandemic-related challenges in organizing and securing funding for such a study were insurmountable. Instead, COH-FIT relies on continuous snowball recruitment with intermittent representative sampling. Despite the inevitable shortcomings associated with this design, COH-FIT addresses at least many of the caveats highlighted by Newlove-Delgado and colleagues (2003) and should make a valuable contribution to the literature.

Additionally, a formal analysis of moderators, or subgroup analyses by age, gender, ethnicity or other factors, such as socio-economic status, was beyond the scope of the Newlove-Delgado et al. (2003) review. As such, its results should be considered alongside those of a recently published systematic review and Bayesian nonlinear dose–response meta-analysis (Salanti et al., 2022). This meta-analysis included 43 studies from 13 countries with participants (adults or children/adolescents) from the general population, reporting data on any mental health condition for at least two time points, with at least one time point during the pandemic, and relying on a validated rating scale. Overall, results showed an average worsening of anxiety and depressive symptoms from pre- to intra-pandemic time periods, albeit with considerable between-study heterogeneity. Of note, in meta-regression analyses, none of the explored factors (age and sex of participants, study design, country, risk of bias, and type of data collection) accounted for this heterogeneity. Interestingly, a dose-response meta-analysis exploring the severity of anxiety and depression as a function of days since the first recorded case of Covid-19 showed a U shape relationship, with anxiety and depressive symptoms worsening during the first 60 days, and then a flatter slope after two months. Furthermore, there was a linear association between severity of depression and anxiety symptoms and stringency index, a composite measure indicating the stringency of policy-related containment restrictions. The association between number of cases (log-cumulative cases) and worsening of depression/anxiety symptoms was also nearly linear, whilst the association between cumulative deaths and worsening of depression/anxiety symptoms was uncertain. Overall, these findings add significantly to the Newlove-Delgado et al. (2003) meta-analysis, although we look forward to similar analyses in future larger samples of studies, specifically in children and adolescents

To conclude, in our view there are two main and related take-home messages from the Newlove-Delgado et al. (2023) meta-analysis. First, the meta-analysis shows that the relationship between mental health and covid-19 pandemic in children and adolescents (similarly to the one in adults) is complex and, as such, it ought to be addressed by studies using rigorous methods and advanced analytic strategies. Second, collectively, as a field, we should and could do better with regards to the scope and quality of the studies in this area. These are two main message that researchers, but also patients co-designing and co-contributing to research, as well as funders, need to consider as a priority in order to generate research that can rigorously inform practice and policies during the current and, potentially, future pandemics.

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