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Long covid in children and adolescents

Risk appears low, but many questions remain

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Symptoms involving almost every organ system have been reported after SARS-CoV-2 infection.[1-3] Estimates of the prevalence of long covid (also called post-covid-19 condition, post-acute sequelae of covid-19, or chronic covid syndrome) vary considerably, partly because of confusion around the definition. The term long covid encompasses a broad range of symptoms, including objective complications of covid-19 (pulmonary fibrosis, myocardial dysfunction), mental health conditions, and more subjective, non-specific symptoms resembling those seen in post-viral chronic fatigue syndrome (myalgic encephalomyelitis). Most studies to date have substantial limitations, including small cohorts, absence of control groups, non-standardised capture of symptoms, lack of correction for pre-existing medical conditions, participant reported infection, and variation in follow-up, as well as selection, non-response, misclassification, and recall biases.[4]

In children and adolescents, acute covid-19 is less severe than in adults.[5,6] Concern among many parents has therefore focused more on the potential long term effects of SARS-CoV-2 infection. Unfortunately, fewer data are available on long covid in young people compared with adults.[7] The widely quoted one in seven frequency in children is based on a study with a 13% response rate.[7,8]

The linked study by Magnusson and colleagues (doi:10.1136/bmj-2021-066809) used nationwide register data from Norway to estimate the impact of covid-19 on long term healthcare use among 1.3 million children and adolescents.[9] The authors identified a short term increase in primary (but not specialist) care use after covid-19 in all the studied age groups. This increase was related to respiratory and general or non-specific conditions, mostly in the four weeks after infection. The increase in primary care use persisted for up to six months among children aged 1-5 years. Notably, covid-19 in children had limited overall impact on healthcare services.

The study's strengths include its population based design, the inclusion of SARS-CoV-2 negative and non-tested control groups, and comparison with pre-pandemic healthcare use. An unavoidable limitation is that asymptomatic children or those with mild symptoms might not have been tested. Also, changes in testing patterns could have occurred in different age groups and over time, and children testing positive for SARS-CoV-2 might also have had greater exposure to other respiratory viruses. Finally, the anxiety surrounding this previously unknown infection in children might have caused primary care providers and parents to schedule unnecessary follow-up visits after a positive test result.

Magnusson and colleagues' study highlights the difficulty of accurately determining risk of long covid in children and adolescents, and the urgent need for further rigorous studies. Reports suggest that more than half of children who did not have covid-19 experienced symptoms such as headaches, fatigue, sleep disturbance, and concentration difficulties during the pandemic.[7] Distinguishing long term symptoms caused by SARS-CoV-2 infection from pandemic related symptoms remains a challenge. One large study in the UK found that nearly all symptoms reported by children who tested positive for SARS-CoV-2 were also reported by those who tested negative.[7] Moreover, no difference was reported between the two groups in mental health, overall wellbeing, or impairment of activities. Other studies with control groups have also reported minimal differences in persisting symptoms between children with SARS-CoV-2 infection and those without.[4] This underlines the importance of appropriate control groups, including children with other infections and those admitted to hospital for other reasons.

In addition to the uncertainty around the true prevalence of long covid, several other important questions remain unanswered. Firstly, what are the risk factors for developing long covid? Although some studies in adults have suggested that severity of the initial infection, hospital admission, female sex, white ethnicity, middle age, and asthma are risk factors for persistent symptoms,[1,2,10,11] the most recent and comprehensive meta-analysis concluded that data were insufficient to determine the influence of these factors.[3] Secondly, what are the molecular, immunological, and psychological mechanisms underlying long covid? Suggested mechanisms include direct effects of the virus (including viral latency, persistent activation of the immune system,[12] and neuronal apoptosis) and indirect effects related to mental health problems such as post-traumatic stress and social isolation.[13] Thirdly, are the long term effects of covid-19 specific to SARS-CoV-2 infection or are they similar to post-viral syndromes seen after other viral infections? Fourthly, can long covid be prevented? Recent studies in adults suggest that covid-19 vaccination is associated with a lower risk of several, but not all, sequelae in those with breakthrough SARS-CoV-2 infections.[14,15] Finally, what is the optimal treatment? Even if risk of long covid is low, the high incidence of SARS-CoV-2 infections, especially with the omicron variant, means that large numbers of children might require treatment.

Currently a third of all children and adolescents reports negative emotions, such as sadness or anxiety, highlighting the toll from the pandemic in

this age group.[7] Vaccinating young people might help reduce some of the indirect harms caused by repeat testing and isolation, lockdowns, school closures, and reduced social activities. As SARS-CoV-2 remains predominantly a mild infection in the paediatric population, the incidence of long covid is a critical factor in the risk-benefit equation for policy and parental decisions on covid-19 vaccines for children.[16]

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