Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Risk of hospitalisation and death in children with SARS-CoV-2 delta (B.1.612.2) infection

The SARS-CoV-2 delta (B.1.612.2) variant first emerged in India in December, 2020, and rapidly spread across the globe. At that time, England was facing a second pandemic wave due to the B.1.1.7 (alpha) variant, which led to a national lockdown in January, 2021. The easing of this lockdown started with the return of all children to school from March 8, 2021, which was associated with a small increase in cases, mainly in secondary school-aged children.[1] As England moved into step two easing of the national lockdown on April 8, 2021, and particularly after step three easing from May 17, 2021, cases increased rapidly, especially among unvaccinated age groups (ie, mainly younger adults and teenagers).[1] In early April, 2021, when the alpha variant was the predominant strain circulating, the delta variant was identified in less than 5% of sequenced SARS-CoV-2 strains in England, but reached more than 95% by June, 2021.[2]

In adults, the delta variant is reported to be more transmissible than the alpha variant, with a 2·26-times higher risk of hospitalisation.[3] Children have a significantly lower risk of severe disease, hospitalisation, or death due to COVID-19 than adults.[4] There are, however, little data on disease severity in children infected with different variants. The COVID Symptom Study (Zoe App) reported similar symptom burden (median four symptoms *vs* five symptoms), illness duration (median 5 days for both variants), and hospitalisation (2·0% *vs* 2·2%) in a small cohort of 694 and 706 children aged 5–17 years infected with the alpha and delta variants, respectively.[5] Here, we compared hospitalisation and fatality rates in a national cohort of children (aged ≤15 years) with genotype-confirmed SARS-CoV-2 infection due to the alpha or delta variants over a 9-month period, when the two variants caused sequential pandemic waves in England.

Confirmed cases were linked with national databases for emergency care attendance, hospitalisations, and deaths.[3] Between Nov 1, 2020, and Sept 13, 2021 (before the COVID-19 vaccine was recommended for children aged 12–15 years in the UK), there were 759 307 confirmed childhood SARS-CoV-2 infections; 156 031 were sequenced or genotyped, including 31 182 alpha, 115 795 delta, and the remaining were other variants. Trends in case numbers and hospitalisations for cases with the two variants are given in the appendix (p 1). For both variants, emergency care attendance and hospital admission rates (henceforth referred to as hospitalisations) were higher in the most deprived Index of Multiple Deprivation quintile (appendix p 2). A higher proportion of children infected with the alpha variant were symptomatic at the time of testing than children with the delta variant. There were no deaths within 60 days of a positive test for either variant, consistent with the low overall COVID-19 fatality rates in children.

There were 668 (2·1%) hospitalisations within 14 days of a positive PCR test with the alpha variant, and 3182 (2·7%) with the delta variant. After excluding injury as the primary complaint, the 14-day hospitalisation rate was 1·9% (95% CI 1·7 to 2·0; n=580) for alpha and 2·5% (2·4 to 2·6; n=2892) for delta (risk difference –0·6%, 95% CI –0·8 to –0·5). When restricted to children who were symptomatic at time of testing and after excluding injury attendance, the 14-day hospitalisation rate was 1·5% (1·3 to 1·7) for alpha and 1·6% (1·4 to 1·7) for delta (risk difference –0·1%, 95% CI –0·3 to 0·1).

Our findings provide reassurance of a very low risk of severe or fatal COVID-19 in children infected with SARS-CoV-2, irrespective of variant. In England, COVID-19 hospitalisation rates by age-group are reported weekly,[1] but the strength of this analysis is the large number of sequenced SARS-CoV-2 strains. There are, however, limitations which have also been discussed elsewhere.[3] The delta wave occurred after the alpha wave and, therefore, comparisons are not contemporaneous, which likely explains some of the demographic differences during the two variants, in terms of age, ethnicity, local area deprivation, and region. It is also possible parental thresholds for testing or seeking medical help for their child, as well as clinicians' thresholds for admitting children with COVID-19 might have changed over time. Additionally, hospitalisation rates were estimated using administrative databases that contain limited clinical information. Thus, although we could exclude injury-related hospitalisations, we were unable to distinguish between children seeking medical care for severe COVID-19, because an underlying condition was exacerbated by the infection or for an unrelated condition. For example, when we followed up the first 24 childhood cases confirmed in May, 2021, with their general practitioner, only 11 (46%; six with comorbidities) were hospitalised for COVID-19 (unpublished data).

Additionally, when community infection rates are high, such as during the delta wave, incidental infections in hospitalised children will also increase, which probably explains the higher risk difference in overall (symptomatic and asymptomatic) hospitalisation rates between delta versus alpha infections, when compared with the lower risk difference among symptomatic cases only (although we acknowledge that some asymptomatic cases will progress to symptomatic disease after testing). Moreover, we reported hospitalisation within 14 days of a positive PCR test, although some hospitalisations might occur after this period.

Another limitation is potential sampling bias. Only a proportion of SARS-CoV-2 strains were sequenced, and samples from hospitalised cases

Published Online
March 29, 2022
https://doi.org/10.1016/S2352-4642(22)00096-7

See Online for appendix

were more likely to be selected for sequencing. Furthermore, PCR-positive samples with lower cycle thresholds, indicating higher viral load, are more likely to be sequenced successfully. Although these biases might overestimate hospitalisation rates, they should not affect comparisons between the two variants. On the other hand, testing capacity increased over time, so that larger numbers of delta variants were sequenced, which might explain the higher proportion of asymptomatic infections with the delta variant in our cohort.

In conclusion, the low hospitalisation rates in children with alpha and delta variant infections confirmed by genotyping should reassure parents, clinicians, and policy makers of the low risk of severe COVID-19 in children. Delta variant infections have, however, resulted in more childhood hospitalisations than alpha. Further studies are needed to distinguish between incidental infections and hospitalisation for severe COVID-19, especially in children, where the former is common, and the latter is rare. COVID-19 vaccines have been shown to reduce the risk of hospitalisation and severe COVID-19 in adults and adolescents.[6] Similar studies are needed to assess the risk of severe COVID-19 in children infected with more recent and emerging variants.

All authors declare no competing interests.

SNL conceived the study and assisted with writing the Correspondence. ST analysed data and wrote the first draft of the Correspondence. FA collected data. KH validated data. All authors contributed to interpretation of the results and discussion of the findings. This study did not receive any funding. We thank the national collaborative effort undertaken by the institutions participating in the COVID-19 Genomics UK (COG-UK) consortium that enables this national public health response. COG-UK is supported by funding from the Medical Research Council part of UK Research & Innovation, the National Institute of Health Research, and Genome Research Limited, operating as the Wellcome Sanger Institute. The UK Health Security Agency has legal permission, provided by Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002, to process patient confidential information for national surveillance of communicable diseases and as such, individual patient consent is not required to access records.

*Simon Thelwall, Felicity Aiano, Katie Harman, Gavin Dabrera, Shamez N Ladhani
feedback.c19epi@phe.gov.uk

COVID-19 National Epidemiology Cell, UK Health Security Agency, London, NW9 5DF, UK (ST, KH, GD); Immunisation Division, UK Health Security Agency, London, UK (FA, SNL); Paediatric Infectious Diseases Research Group, St George's University of London, London, UK (SNL)

1 UK Health Security Agency. National flu and COVID-19 surveillance reports: 2021 to 2022 season. Public Health England, 2022. https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports-2021-to-2022-season (Feb 28, 2022).

2 UK Health Security Agency. SARS-CoV-2 variants of concern and variants under investigation in England. Report number 17. Public Health England, 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1001354/Variants_of_Concern_VOC_Technical_Briefing_17.pdf (accessed Feb 28, 2022).

3 Twohig KA, Nyberg T, Zaidi A, et al. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. *Lancet Infect Dis* 2022; **22:** 35–42.

4 Viner RM, Mytton OT, Bonell C, et al. Susceptibility to SARS-CoV-2 infection among children and adolescents compared with adults: a systematic review and meta-analysis. *JAMA Pediatr* 2021; **175:** 143–56.

5 Molteni E, Sudre CH, Canas LS, et al. Illness characteristics of COVID-19 in children infected with the SARS-CoV-2 Delta variant. *medRxiv* 2021; published online Oct 7. https://doi.org/10.1101/2021.10.06.21264467 (preprint).

6 Powell AA, Krisebom F, Stowe J,et al. Effectiveness of BNT162b2 against COVID-19 in adolescents. *Lancet Infect Dis* 2022; published online March 21. https://doi.org/10.1016/S1473-3099(22)00177-3.