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Letter to the Editor

Early outpatient treatment of SARS-COV-2 infection in non-hospitalised high-risk paediatric patients in London, UK

In the recent review of COVID-19 in children by Powell et al.,[1] we identified a lack of published data on early use of antiviral treatment in high-risk children with confirmed SARS-COV-2 infection.

Compared to adults, children, and young people (CYP) are less likely to develop severe disease leading to hospitalisation or death following SARS-COV-2 infection.[1,2] Certain underlying medical conditions, such as immunosuppression, chronic lung disease, complex neuro-disabilities, are known to increase the risk of severe COVID-19.[3,4] In 2021, a national program was implemented to offer outpatient treatment for high-risk patients with confirmed SARS-CoV-2 infection with the aim of preventing hospitalisation for severe COVID-19. The COVID-19 Medication Delivery Units (CMDUs) in designated hospitals triaged high-risk patients over the telephone and offered outpatient treatment to eligible patients as soon as their infection was confirmed. The programme targeted primarily adults but also included CYP aged 12–18 years and weighing ≥40 kg. The UK Royal College of Paediatrics and Child Health (RCPCH) provided a list of high-risk conditions for CYP based on the best available evidence at the time. The time window for treatment was five days from the start of symptoms.[5] At the time, CYP were eligible for Remdesivir, a nucleotide prodrug of an adenosine analogue that inhibits SARS-CoV-2 viral replication, and Sotrovimab, a neutralising monoclonal antibody which was effective against the alpha and delta variants of SARS-COV-2 which were circulating at the time. Both agents had been proven to be effective in preventing hospital admission and death in high-risk adult patients, but there are no data in their use in CYP.[6,7]

In Southwest London, St. Georges University Hospital triaged all high-risk CYP with confirmed SARS-CoV-2 infection daily, contacted the family and offered outpatient treatment. Between 01 December 2021 and 31 May 2022, 86 CYP were triaged. Most CYP (61/86, 71%) had received ≥1 COVID-19 vaccine prior to infection. Following discussion with the family, 22% (19/86) were identified as ineligible for treatment because their underlying condition did not fulfil the listed criteria. Of the 67 eligible CYP, the most common conditions were immune-mediated inflammatory disorders (22/67, 32%), such as inflammatory bowel disease and rheumatological conditions, followed by Trisomy 21 (15/67, 22%), sickle cell disease (8/67, 12%) and malignancies (8/67,12%).

Of the 67 eligible CYP, 22 (34%) was outside the 5-day treatment window because of delays in confirming the infection by PCR, which was required as part of the national guidelines. A further 19 were either asymptomatic or clinically improving at the time of triage and were not offered treatment. The remaining 26 CYP were offered treatment and after discussion with the family 15 (15/26, 58%) agreed and 11 (11/26, 42%) refused treatment. Altogether, 15 CYP received Sotrovimab (n=14) and Remdesivir (n=1). Both treatments were well-tolerated with no adverse events, except for one CYP experiencing severe bone pain – a known side effect - during Sotrovimab infusion, resulting in treatment interruption.

Two months after their infection, telephone follow-up for all 86 referred cases identified only two hospitalisations, both unrelated to COVID-19. The first case included a CYP with haematological malignancy who presented with febrile neutropenia 2 weeks after Sotrovimab infusion, and the infectious aetiology was not identified. The second case with known chronic kidney disease was also treated with Sotrovimab and was hospitalised for worsening renal function.

In adults, evaluation of the CMDU programme in 4 UK centres found only 17% of 4788 referred patients were eligible, 13% were treated and 1% overall were hospitalised within 2 weeks.[8] Such data are, however, lacking in CYP, especially because very few countries offered outpatient antiviral treatment for high-risk CYP with confirmed SARS-CoV-2 infection on a systematic, national level. Our single-hospital experience found that, like adults, only 17% (15/86) of referred high-risk CYP were eventually treated over the 6-month period. Initial hurdles included the need for PCR-confirmation which resulted in many CYP exceeding the 5-day treatment cut-off. A substantial proportion of referred CYP (19/86 [22%] overall, 15/41 [36%] eligibles) were either asymptomatic or already improving clinically despite being contacted within the 5-day period, which made them ineligible for treatment. 11 of 26 (42%) eligible children declined treatment, mainly because treatment required attendance to hospital, insertion of intravenous cannula and spending several hours in hospital, especially when the child was not particularly ill at the time of triage, despite being high-risk.

Whilst acknowledging the relatively small CYP cohort in our single-centre experience, our experience highlights several important findings for future consideration. Most importantly, none of the 86 referred high-risk CYP went on to develop severe COVID-19. This is consistent with published studies reporting a very low risk of hospitalisation or death, even among high-risk CYP.[1] Consequently, future recommendations need to consider carefully the risk benefits as well as the costs and resource implications of providing such a service during peak periods of the pandemic, especially for an age-group with a very low risk of severe disease. At the same time, the recommended intervention involved attendance to the hospital, as well as insertion of intravenous lines and administration of intravenous infusions which was often not agreeable to the families, especially when their child was not very ill even during the peak of their illness. This is particularly the case now, in 2025, that most CYP have already developed immunity against SARS-CoV-2 through multiple exposures and vaccination.

Because none of the children were eventually hospitalised for severe COVID-19, we are unable to comment on the effectiveness of either treatment in preventing hospitalisations in our small cohort of

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patients. As such, we recommend that any such future programmes should include national pathways for systematic information collection to evaluate the intervention in near real-time and allow informed decisions to be made on continuing, modifying or halting the programme based on robust data. The availability of oral formulations such as Paxlovid (Nirmatrelvir/ritonavir) which has been used with good results in at-risk adult patients is now available for CYP from 12 years of age, could help circumvent many of the hurdles encountered.[9,10] However, such an intervention should demonstrate clinical and cost-effectiveness in high-risk CYP before recommending wider implementation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Powell AA, Dowell AC, Moss P, Ladhani SN, sKIDs Investigation T. *Current state of COVID-19 in children: 4 years on. J Infect* 2024;**88**(5):106134. 106134.
2. Nikolopoulou GB, Maltezou HC. *COVID-19 in children: where do we stand? Arch Med Res* 2022 Jan;**53**(1):1–8.
3. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. *Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr* 2020;**174**(9):882–9.
4. Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, et al. *Risk factors for severe COVID-19 in children. Pediatrics* 2022;**149**(1):e2021053418.
5. COVID-19 – guidance for management of children admitted to hospital and for treatment of non-hospitalised children at risk of severe disease. *RCPCH Guidance*; 2022. www.rcpch.ac.uk/resources/guidance-management-children-viral-respiratory-tract-infections.
6. Gupta A, Gonzalez-Rojas Y, Juarez E, Crespo Casal M, Moya J, Falci DR, et al. *Early treatment for Covid-19 with SARS-CoV-2 neutralizing antibody sotrovimab. N Engl J Med* 2021;**385**(21):1941–50.
7. Gottlieb RL, Vaca CE, Paredes R, Mera J, Webb BJ, Perez G, et al. *Early remdesivir to prevent progression to severe Covid-19 in outpatients. N Engl J Med* 2022;**386**(4):305–15.
8. Brown M, Saund J, Qureshi A, Plowright M, Drury K, Gahir J, et al. *Demographics and outcomes of initial phase of COVID-19 medicines delivery units across 4 UK centers during peak B1.1.529 Omicron epidemic: a service evaluation. Open Forum Infect Dis* 2022;**9**(10):ofac527. 6.
9. Najjar-Debbiny R, Gronich N, Weber G, Khoury J, Amar M, Stein N, et al. *Effectiveness of paxlovid in reducing severe coronavirus disease 2019 and mortality in high-risk patients. Clin Infect Dis* 2023;**76**(3):e342–9.
10. Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. *Oral nirmatrelvir for high-risk, nonhospitalized adults with Covid-19. N Engl J Med* 2022;**386**(15):1397–408.

Borbala Zsigmond *
Department of Paediatric Infectious Diseases, St. George's Hospital, Blackshaw Road, London SW17 0QT, UK

Nadia Trecchi
Department of Infection, St George's University Hospitals NHS Foundation Trust, London, UK

Shamez N. Ladhani, Katja Doerholt
Department of Paediatric Infectious Diseases, St. George's Hospital, Blackshaw Road, London SW17 0QT, UK
Immunisation Division, UK Health Security Agency, 61 Colindale Avenue, London, UK

*Corresponding author.
E-mail address: borbala.zsigmond@stgeorges.nhs.uk (B. Zsigmond).