## Comment

## Tracing and vaccinating: how to REACT to COVID-19 pandemic 🕡 💭

COVID-19, the disease caused by SARS-CoV-2 infection, is one of the most complex health-related challenges of the past century. Since March 11, 2020, when WHO declared COVID-19 a pandemic,<sup>1</sup> extraordinary progress has been made in understanding the disease's clinical features, pathogenetic mechanisms, and identifying effective containment measures. However, almost 2 years into the pandemic, several questions remain, and SARS-CoV-2 infections and COVID-19 fatality rates remain high worldwide, with the disease incidence peaking in subsequent waves of infections.

All the COVID-19 vaccines approved by the European Medicines Agency and US Food and Drug Administration have effectively reduced the SARS-CoV-2 infection rate and clinical severity of COVID-19 illness, although to different extents. However, the emergence of viral variants, especially delta (B.1.617.2) and, more recently, omicron (B.1.1.529), has resulted in an international effort to understand the efficacy of vaccines (and other developed drugs) on these variants.<sup>2,3</sup>

In this context, efficiently tracing and sequencing SARS-CoV-2 infections is an essential approach to understanding COVID-19 epidemiology, thus applying the most appropriate containment measures.

The **REal-time** Assessment of Community Transmission-1 (REACT-1) study has been developed in England, a country with one of the highest rates of confirmed COVID-19-associated mortality globally.<sup>4</sup> Since May, 2020, the REACT-1 study has conducted a series of random cross-sectional surveys in the general population in England (aged  $\geq 5$  years) with the aim of epidemiologically characterising the evolution of the COVID-19 pandemic. In particular, the study has estimated the changing community-based prevalence of SARS-CoV-2, transmission dynamics, and, more recently, vaccine effectiveness against infection.<sup>5</sup> In The Lancet Respiratory Medicine, Marc Chadeau-Hyam and colleagues<sup>6</sup> report the results of round 14 of REACT-1 (run from Sept 9 to 27, 2021) and provide some crucial findings. Notably, to fully understand the study results, it is essential to know that the vaccination programme in England was expanded since April, 2021, to include adults younger than 50 years, and that a single vaccine dose was offered to children aged

16-17 years from August, 2021, and to children aged 12-15 years from mid-September, 2021.

Chadeau-Hyam and colleagues found an increasing prevalence of SARS-CoV-2 infections among schoolaged children (ie, aged 5-17 years) in England in September, 2021, coinciding with the increased social interactions for the autumn school term. These findings contrast with what has been observed in adults, for whom a decreasing prevalence was reported in the same period,<sup>6</sup> probably reflecting the effects of previous natural infections and vaccines. The increase in paediatric cases, a group in which vaccination rates are low, needs to be taken into serious consideration. Although paediatric COVID-19 is usually mild,<sup>7</sup> severe cases have been reported. Additionally, multisystem inflammatory syndrome in children (MIS-C) is a rare but severe concern for children with SARS-CoV-2 infection.8 Nonetheless, the intense circulation of SARS-CoV-2 among children will continue to promote substantial spreading of the virus in the community, representing a risk for susceptible individuals who might not respond to COVID-19 vaccines-eq, immunocompromised individuals.

Another crucial finding reported here regards vaccine effectiveness. Combining data from the study rounds 13 (run from June to July, 2021) and 14, the estimate of vaccine effectiveness against infection was 63% in adults after two doses compared with those who were unvaccinated. Notably, breakthrough infections in vaccinated adults occurred more frequently after 3 months following two vaccine doses. Moreover, all the sequenced swabs taken during testing were positive for the delta variant, confirming that this variant had almost completely replaced all other variants in England at this time.

Overall, these results are highly informative and should guide decisions to tackle the COVID-19 pandemic. First, a third booster vaccination is recommended after two doses of vaccine to restore protection against SARS-CoV-2 infection. Second, children need to be vaccinated to protect them from severe COVID-19 and MIS-C,<sup>9</sup> and to control the spread of COVID-19 in the community. Third, the REACT-1 study clearly shows the importance of tracing infections to understand the epidemiological evolution of the pandemic,



Lancet Respir Med 2022 Published Online

January 24, 2022 https://doi.org/10.1016/ S2213-2600(22)00016-9

See Online/Articles https://doi.org/10.1016/ S2213-2600(21)00542-7 which is even more important now that we are facing the challenge of the omicron variant.<sup>4</sup> Although encouraging results have been reported on the effective in-vitro neutralisation of SARS-CoV-2 omicron infection with serum samples from people who have received a booster vaccination,<sup>10</sup> real-world data are urgently needed. Indeed, the future rounds of the REACT-1 study will be highly informative to answer the unanswered questions and fully understand the effect of the omicron variant and guide appropriate health policies.

We declare no competing interests.

## Riccardo Castagnoli, \*Gian Luigi Marseglia gl.marseglia@smatteo.pv.it

Pediatric Clinic, Fondazione IRCCS Policlinico San Matteo, University of Pavia, 27100 Pavia, Italy; Department of Clinical, Surgical, Diagnostic and Pediatric Sciences, University of Pavia, Pavia, Italy

- 1 Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed 2020; **91:** 157–60.
- 2 Barda N, Dagan N, Cohen C, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. *Lancet* 2021; **398**: 2093–100.

- 3 Burki TK. Omicron variant and booster COVID-19 vaccines. Lancet Respir Med 2022; 10: e17.
- 4 Riley S, Atchison C, Ashby D, et al. REal-time Assessment of Community Transmission (REACT) of SARS-CoV-2 virus: study protocol. *Wellcome Open Res* 2021; **5:** 200.
- 5 Elliott P, Haw D, Wang H, et al. Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant. *Science* 2021; **374**: eabl9551.
- 6 Chadeau-Hyam M, Wang H, Eales O, et al. SARS-CoV-2 infection and vaccine effectiveness in England (REACT-1): a series of cross-sectional random community surveys. *Lancet Respir Med* 2022; published online Jan 24. https://doi.org/S2213-2600(21)00542-7.
- 7 Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr 2020; 174: 882–89.
- 8 Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet* 2020; **395:** 1771–78.
- 9 Zambrano LD, Newhams MM, Olson SM, et al. Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA vaccination against multisystem inflammatory syndrome in children among persons aged 12–18 years—United States, July–December 2021. MMWR Morb Mortal Wkly Rep 2022; published online Jan 7. https://doi.org/10.15585/mmwr.mm7102e1.
- Nemet I, Kliker L, Lustig Y, et al. Third BNT162b2 vaccination neutralization of SARS-CoV-2 Omicron infection. N Engl J Med 2021; published online Dec 29. https://doi.org/10.1056/NEJMc2119358.