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time interval for follow-up of 15 days after receiving the second dose was very short. Whether the humoral immune response waned post-vaccination could not be evaluated within such a short period. In February, 2021, Noa and colleagues<sup>8</sup> reported a vaccine efficacy of 46% for BNT162b2 in Israel in a real-world scenario. This waning in vaccine efficacy after 6 months in a fully vaccinated population has been attributed to declining humoral immunity and immune escape due to the delta variant. CVnCoV has been withdrawn from regulatory review by its manufacturer and how it would have performed in the real world will now never be known.

Vaccine efficacy could be improved via a heterologous boost regimen using vaccines based on two different platforms;<sup>9,10</sup> Xinxue Liu and colleagues<sup>10</sup> showed that immunogenicity was higher for heterologous schedules of adenovirus vector-based and mRNA-based vaccines compared with homologous prime-boost schedules. Rather than waiting for higher efficacy vaccines or newer vaccines, existing vaccines could be used in combination with vector-based vaccines in a heterologous boost regimen or as a booster dose to enhance vaccine availability in low-income and middle-income countries to help to end the pandemic.

We declare no competing interests.

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- 1 Kremsner PG, Ahuad Guerrero RA, Arana-Arri E, et al. Efficacy and safety of the CVnCoV SARS-CoV-2 mRNA vaccine candidate in ten countries in Europe and Latin America (HERALD): a randomised, observer-blinded, placebo-controlled, phase 2b/3 trial. *Lancet Infect Dis* 2021; published online Nov 23. [https://doi.org/10.1016/S1473-3099\(21\)00677-0](https://doi.org/10.1016/S1473-3099(21)00677-0).
- 2 Thomas SJ, Moreira ED Jr, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine through 6 months. *N Engl J Med* 2021; published online Sept 15. <https://doi.org/10.1056/NEJMoa2110345>.
- 3 Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384**: 403–16.
- 4 Juthani PV, Gupta A, Borges KA, et al. Hospitalisation among vaccine breakthrough COVID-19 infections. *Lancet Infect Dis* 2021; **21**: 1485–86.
- 5 Pardi N, Hogan MJ, Pelc RS, et al. Zika virus protection by a single low-dose nucleoside-modified mRNA vaccination. *Nature* 2017; **543**: 248–51.
- 6 Richner JM, Himansu S, Dowd KA, et al. Modified mRNA vaccines protect against Zika virus infection. *Cell* 2017; **168**: 1114–25.e10.
- 7 Lutz J, Lazzaro S, Habbedine M, et al. Unmodified mRNA in LNPs constitutes a competitive technology for prophylactic vaccines. *NPJ Vaccines* 2017; **2**: 29.
- 8 Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA COVID-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med* 2021; **384**: 1412–23.
- 9 Kant R, Dwivedi G, Zaman K, et al. Immunogenicity and safety of a heterologous prime-boost COVID-19 vaccine schedule: ChAdOx1 vaccine Covishield followed by BBV152 Covaxin. *J Travel Med* 2021; published online Oct 15. <https://doi.org/10.1093/jtm/taab166>.
- 10 Liu X, Shaw RH, Stuart ASV, et al. Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial. *Lancet* 2021; **398**: 856–69.

## Concerts and COVID: can the beat go on?

Our world has changed. The pleasures that we took for granted before the emergence of SARS-CoV-2 now require risk assessment. The days and long nights of clubs and concerts are tainted with the fear of virus transmission and super spreading events. The so-called new adults, coming of age and emerging from the lockdowns of 2020 and 2021 might never have experienced the raw beat and the emotions of live concerts that were part and parcel of the fabric of social life in the pre-COVID-19 era. But just how risky are such live, large, indoor events in terms of transmission of the SARS-CoV-2 virus? Are precautions such as pre-concert rapid antigen testing, mask-wearing and adequate ventilation sufficient to prevent virus transmission in situations where social distancing is impossible? How adherent are concert goers with mask wearing? What exactly is adequate ventilation and how important is it in mitigating infection risk? How sensitive is rapid antigen testing up to 3 days before concerts as a tool to screen for the infected? In

*The Lancet Infectious Diseases*, Constance Delaugerre and colleagues<sup>1</sup> take on the challenge of addressing these conundrums, by comparing SARS-CoV-2 positivity rates (by means of day 7 post-concert, saliva RT-PCR data) in those who attended a large, live concert on May 29, 2021, in Paris and in non-attendees. They assessed adherence to mask wearing by means of an artificial intelligence tool. It is an ambitious, thoughtful, and well-designed study and the authors tackle important practical questions that have major societal ramifications.

The results showed no significantly increased SARS-CoV-2 transmission risk in attendees compared with non-attendees. The day 7 RT-PCR was positive for eight of the 3917 attendees (0.20%: 95% CI, 0.09–0.40) and three of 1947 non-attendees (0.15%: 0.03–0.45). Global mask adherence among concert goers was estimated at 91.4%.

It is still unclear whether herd immunity against SARS-CoV-2 can be achieved, but high immunisation



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rates reduce the transmission rate, the probability of infection, and the viral load amongst infected individuals. One-fifth of the young adults participating in the SPRING trial had had previous symptomatic COVID-19 and thus almost certainly developed a robust immunological response.<sup>2</sup> Although less than 10% of the participants had received two vaccine doses at the time of the concert, more than half had received at least one vaccine dose. Seroprevalence of virus-neutralising antibodies was not assessed during this trial, but a certain degree of herd-protection can certainly be postulated since more than half of the study population had received at least one vaccination dose and one-fifth had previously suffered from COVID-19.

Infected cases were detected, pre-concert, by means of rapid-antigen testing and not PCR. Since rapid antigen testing has a lower sensitivity (and specificity) than PCR, asymptotically infected individuals are certainly under-reported in this study, especially given the very low overall rate of infected individuals,<sup>3</sup> and a bias towards asymptomatic infections with low viral loads in the exposed group cannot be excluded because of the prevalent immunity and supposedly low viral load that they were exposed to during the concert.

Masks work; they prevent direct person-to-person transmission that is associated with high infectious doses. They reduce the aerosolisation of the SARS-CoV-2 virus and onward transmission to others. They protect even during the viral shedding period 2–3 days before onset of symptoms. Even in a crowded, indoor event and in smaller closed settings,<sup>4</sup> universal mask use has been shown to be effective. At the Paris concert, mask use was mandatory and monitored and adherence of greater than 90% was confirmed. The use of an artificial intelligence tool to monitor adherence to masking has been effectively used at airports,<sup>5</sup> and was also successful at the Paris concert and might be applicable to other indoor events. What if alcohol and other drugs are in play? Alcohol is a strong entactogen and consumption of alcohol might also lead to a reduced adherence to mask mandates. Since alcoholic beverages were banned during the SPRING concert, the high degree of mask use there cannot be generalised to concerts serving alcoholic beverages.

The role of aerosol transmission in indoor spaces is important. Wearing masks and keeping your distance will impede the inhalation of aerosols but at events such as indoor concerts, social distancing is impossible and

this is when ventilation systems are of key importance. In the SPRING study in Paris, optimal ventilation was available. Ventilation was provided by eight air-handling units working with 100% outside air and no re-circulated air. All areas accessible to the concert attendees were similarly ventilated and ventilation was started 3 h before the public entered. This powerful system was designed for a full capacity concert of some 20 000 attendees, more than four times higher than the number actually present. The positive effect of such ventilation,<sup>6</sup> and air quality cannot be underestimated particularly in the context of indoor concerts. Air replacement systems are vital to remove virus-laden, exhaled particles. Further research is needed in aerosol science and in the creation of better ventilation systems, and application of that research in the context of concerts and indoor settings will be a game changer for such events.

In May, 2021, most SARS-CoV-2 infections in France were caused by the alpha variant. The delta variant is more transmissible and associated with higher viral densities. Would the results of the SPRING study be different now with delta dominance and circulation of highly transmissible SARS-CoV-2 variants? Hopefully not, as transmission barriers such as masks and ventilation will also protect against variants, and it augurs well that concerts will be able to continue. This study kindles hope but caution is also indicated. The SPRING concert represents an epidemiologically near-optimal setting, involving mask mandates, banning of alcoholic beverages, universal testing before the event, and a study population of young healthy adults not prone to severe COVID-19, as well as circulation of a less transmissible virus variant—all factors in favour of a low transmission rate.

Further studies are needed to gauge the effect of the more transmissible, emerging variants at large gatherings and conditions in real-life settings. Event managers and the policy makers must appreciate the power of ventilation in creating safe, indoor environments to mitigate SARS-CoV-2 transmission and also the transmission of other respiratory infections be they emerging variants or influenza. Increasing vaccination rates in younger age groups, use of proven mitigation measures including masks and ventilation systems, and agile adaptation to the results of evidence-based studies are paramount if indoor concerts are to safely resume. And the beat goes on....<sup>7</sup>

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- 1 Delaugerre C, Foissac F, Abdoul H, et al. Prevention of SARS-CoV-2 transmission during a large, live, indoor gathering (SPRING): a non-inferiority, randomised, controlled trial. *Lancet Infect Dis* 2021; published online Nov 26. [https://doi.org/10.1016/S1473-3099\(21\)00673-3](https://doi.org/10.1016/S1473-3099(21)00673-3).
- 2 Jonsdottir HR, Bielecki M, Siegrist D, Buehrer TW, Züst R, Deuel JW. Titers of neutralizing antibodies against SARS-CoV-2 are independent of symptoms of non-severe COVID-19 in young adults. *Viruses* 2021; **13**: 284.

- 3 Dinnes J, Deeks JJ, Berhane S, et al. Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection. *Cochrane Database Syst Rev* 2021; **3**: CD013705.
- 4 Hendrix MJ, Walde C, Findley K, Trotman R. Absence of apparent transmission of SARS-CoV-2 from two stylists after exposure at a hair salon with a universal face covering policy—Springfield, Missouri, May 2020. *MMWR Morb Mortal Wkly Rep* 2020; published online July 14. [https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e2.htm?s\\_cid=mm6928e2](https://www.cdc.gov/mmwr/volumes/69/wr/mm6928e2.htm?s_cid=mm6928e2).
- 5 Elachola H, Ebrahim SH, Gozzer E. COVID-19: Facemask use prevalence in international airports in Asia, Europe and the Americas, March 2020. *Travel Med Infect Dis* 2020; **35**: 101637.
- 6 Tang JW, Marr LC, Li Y, Dancer SJ. Covid-19 has redefined airborne transmission. *BMJ* 2021; **373**: n913.
- 7 The Whispers (1979). And the beat goes on. Los Angeles, CA: Sound of Los Angeles Records.

## SARS-CoV-2 delta variant: a persistent threat to the effectiveness of vaccines

Vaccine effectiveness studies are important tools to assess the usefulness of vaccines during the post-approval period in the real-world context. Global experience in evaluating many previous vaccines has enabled formulation of best practices and guidelines for conducting such observational epidemiological studies in a short time frame,<sup>1</sup> to guide immunisation policies. These studies are of particular importance during the COVID-19 pandemic, where the roll-out of vaccines has been much faster than usual.

In *The Lancet Infectious Diseases*, Devashish Desai and colleagues<sup>2</sup> report the findings from their test-negative, case-control, vaccine effectiveness study of a whole-virion inactivated SARS-CoV-2 vaccine, BBV152, during the peak of the second wave of the COVID-19 pandemic in New Delhi, India, which was presumably driven by the delta (B.1.617.2) variant. The adjusted vaccine effectiveness against symptomatic COVID-19 after two doses of BBV152, with the second dose administered at least 14 days before RT-PCR testing, was 50% (95% CI 33–62). This is, to our knowledge, a first independent report on the vaccine effectiveness of BBV152, which is being administered to millions of people in India and other low-income and middle-income countries.<sup>3</sup> The key message of the study is the reduced effectiveness of BBV152, even with two doses of vaccine, against SARS-CoV-2 infections attributed to the delta variant compared with the effectiveness

against the wild type (77.8% [95% CI 65.2–86.4]) that was reported in the phase 3 trial.<sup>4</sup> It is important to note that the vaccine effectiveness estimated was not against delta variant infections only, but against infections that occurred during the surge in SARS-CoV-2 cases dominated by the delta variant.<sup>5</sup>

A strength of the study by Desai and colleagues is the test-negative, case-control design in an organised study population—employees of a tertiary-level health-care institution—who were offered unbiased vaccination and testing services. The study has some methodological limitations, such as absence of comorbidity data and no objective assessment of previous infection, as discussed by the authors. The decline in vaccine effectiveness against SARS-CoV-2 infection during a delta-driven surge in cases is neither surprising nor exclusive to inactivated SARS-CoV-2 vaccines including BBV152. The delta variant has high transmissibility, infectivity, and virulence, which causes severe disease.<sup>5,6</sup> These attributes might have contributed to a reduced vaccine effectiveness against symptomatic infections, which has been reported to be as low as 56% for other vaccines in multiple studies worldwide.<sup>7,8</sup> Furthermore, this study was conducted in a high-risk population with a high exposure to SARS-CoV-2 in a tertiary care hospital caring for patients with COVID-19, in the context of a massive surge in infections, with high test-positivity rates of up to 34%, which could have been



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