Omicron Variant in the Critical Care Units of the Paris Metropolitan Area: The Reality Research Group

To the Editor:

A new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant, named Omicron, has recently been reported (1, 2). A reduction in the relative risk of hospitalization for subjects with Omicron infection was shown (3, 4), and subjects with Omicron infection were also less likely to be admitted to ICUs and to receive mechanical ventilation (5). Most of these results were based on administrative databases. The aims of our study were to compare the risk of ICU admission among Delta- and Omicron-infected patients who were admitted to Assistance Publique des Hôpitaux de Paris (APHP) between December 1, 2021, and January 18, 2022, and to compare the characteristics of those patients admitted to its ICUs during the same period.

This study was approved by the ethics and scientific committees of APHP (CSE-21-32). The number of patients admitted to emergency departments, medical wards, and ICUs was collected on a daily basis from the Système d'Information pour le Suivi des Victimes (SI-VIC) database, which provides real-time data on patients with coronavirus disease (COVID-19) hospitalized in France. All consecutive patients with COVID-19 admitted to ICUs of the APHP group have been registered in the Reality clinical database since July 2020.

Some of the results of these studies have been previously reported in preprint form (https://doi.org/10.1101/2022.01.25.22269839).

RT-PCR positivity for SARS-CoV-2 was collected from the APHP laboratory information system. The screening test analyzed the following mutations in the spike protein: L452R (mutation C) and Δ69-70 or N501Y, or K417N (mutation D). In the study period, no α, β, or γ variant was detected by sequencing. Therefore, C1D0 corresponds to a Delta variant, and C0D1 corresponds to an Omicron variant (6, 7).

Only patients who received no doses of vaccine were considered unvaccinated. Causes of immunosuppression were reported as published (8, 9). Patients were treated according to the APHP guidelines.

Only patients hospitalized for COVID-19 were included, as patients with incidental COVID-19 were individualized in the SI-VIC database and not studied and were not included in Reality. The risk of being admitted to the ICU for Omicron and Delta infection was calculated from the SI-VIC administrative database. Characteristics and outcomes of critically ill patients with Omicron and Delta infection were determined from the Reality clinical database. Comparisons were performed using the Wilcoxon test for continuous variables and the chi-square test for percentages. Adjusted analyses were performed using survival analysis in the subgroup of patients hospitalized in ICUs for pneumonia, with in-ICU mortality as the event and ICU discharge alive as the censoring variable. Hazard ratios (HRs) for variables were then reported. Statistical analysis was conducted in R (R Core Team).

We identified 5,140 patients in the hospitals of the APHP group from SI-VIC, of whom 1,379 (26.8%) lacked variant information. Among the 3,761 patients positive for either the Delta ($n = 1,376$) or Omicron ($n = 2,385$) variant, 579 (15.4%) were hospitalized in ICUs, 287 (7.6%) initially and 292 after transfer among the 1,628 patients (17.9%) hospitalized in the ward. The absolute risk of ICU admission with Omicron was 16% less (95% confidence interval [CI], 14.1–19.3%) than with Delta (9.3% vs. 25.8%; $P < 0.001$), with a 64% reduction.

Eight hundred eighty-eight patients were included in Reality (Table 1), 517 of them (58.2%) unvaccinated and 302 (34%) with two or three doses of vaccine. Among the 629 patients with variant information, 400 (63.6%) had Delta variants and 229 (36.4%) had Omicron variants. Compared with Delta-infected patients, those with Omicron infection were more frequently immunocompromised ($P < 0.001$) and more frequently vaccinated ($P < 0.001$) with at least one dose (57.7% vs. 30.1%), two doses (25.8% vs. 14.5%), and even three doses (26.2% vs. 10.8%). BNT162b2 or mRNA-1273 was used in 83.5% of cases, with no difference between the variants. Pneumonia as a cause of hospitalization was less frequent for Omicron than for Delta (67.2% vs. 94.8%; $P < 0.001$). For the Omicron variant, pneumonia was less frequent among vaccinated (62.1%) than unvaccinated patients (80.7%; $P < 0.001$), whereas among the 60 Omicron-infected patients who received three doses of vaccine, 43 (71.7%) were admitted for pneumonia. Subjects with Omicron infection were less frequently invasively ventilated compared with those with Delta infection (41.0% vs. 51%, respectively; $P = 0.02$). Table 2 reports characteristics of both variants in the subgroup of patients admitted for pneumonia. Similar results were observed, even though patients with Omicron were older and more frequently admitted to the ICU in the 5 days after symptom onset ($P = 0.004$). They were still less likely to be invasively ventilated (39% vs. 50.4%; $P = 0.021$).

Among patients discharged from the ICU on January 18, 2022 (80% of Delta cases and 63.6% of Omicron cases), unadjusted in-ICU mortality between variants did not differ in the overall population (20.0% and 27.9%, respectively; $P = 0.08$; Table 1) and in the subgroup of pneumonia (31.6% vs. 29.7%, respectively; $P = 0.78$; Table 2). After adjustment, variant (Omicron vs. Delta) was not associated with mortality in patients with pneumonia (HR, 1.34; 95% CI, 0.82–2.17; $P = 0.24$). Other variables included in the model were age above the median (HR, 2.31; 95% CI, 1.52–3.5), time from symptom onset to ICU admission (6–8, 9–11, 12–14, and ≥15 d vs. ≤5 d; HRs, 0.44 [95% CI, 0.27–0.71], 0.39 [95% CI, 0.23–0.67], 0.34 [95% CI, 0.16–0.73], and 0.34 [95% CI,

Supported by Assistance Publique des Hôpitaux de Paris. The funder of the study had no role in study design, data analysis, data interpretation, or writing of the report. All authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

Originally Published in Press as DOI: 10.1164/rccm.202202-0411LE on May 10, 2022

Table 1. Characteristics and Outcomes of Critically Ill Patients According to Omicron versus Delta Variant in the 888 Patients Admitted from December 1, 2021, to January 18, 2022 (Reality Clinical Database)

	Delta Cases (*n* = *400* [45%])	Omicron Cases (*n* = *229* [25.8%])	*P* Value (Delta vs. Omicron)	Uninformative Screening Test* (*n* = *98* [11%])	Missing Data† (*n* = *161* [18%])
Age, y	62.0 (51.0–70.0)	63.0 (49.0–71.0)	0.810	59.0 (45.5–64.8)	62.0 (49.0–70.0)
Sex, *n* (%)			0.867		
Female	135 (33.8)	75 (32.8)	—	28 (28.6)	56 (34.8)
Male	265 (66.2)	154 (67.2)	—	70 (71.4)	105 (65.2)
Vaccination, *n* (%)			<0.001		
0 injections	279 (69.8)	83 (36.2)	—	46 (46.9)	109 (67.7)
1 injection	19 (4.8)	13 (5.7)	—	4 (4.08)	5 (3.11)
2 injections	58 (14.5)	59 (25.8)	—	20 (20.4)	25 (15.5)
3 injections	43 (10.8)	60 (26.2)	—	20 (20.4)	17 (10.6)
Unknown	1 (0.3)	14 (6.1)	—	8 (8.2)	5 (3.1)
Immunocompromised, *n* (%)	59 (14.8)	79 (34.5)	<0.001	19 (19.6)	21 (13.2)
Time from symptom onset to ICU admission			0.061		
⩽5 d	69 (17.2)	52 (22.7)	—	15 (15.3)	34 (21.1)
>5 d	316 (79.0)	158 (69.0)	—	78 (79.6)	121 (75.2)
Unknown	15 (3.8)	19 (8.3)	—	5 (5.1)	6 (3.73)
Pneumonia, *n* (%)	379 (94.8)	154 (67.2)	<0.001	69 (70.4)	141 (87.6)
Unvaccinated, $n_{pneumonia}$ (%)	273/279 (97.8)	67/83 (80.7)	—	—	—
Vaccinated, $n_{pneumonia}$ (%)	105/120 (87.5)‡	82/132 (62.1)§	—	—	—
Unknown status, $n_{pneumonia}$ (%)	1/1	5/14	—	—	—
Invasive ventilation, *n* (%)	204 (51.0)	94 (41.0)	0.020	34 (34.7)	71 (44.1)
In-ICU mortality, *n* (%)	90/323 (27.9)	31/155 (20.0)	0.082	11/78 (14.1)	35/139 (25.2)

Continuous variables are reported as median (interquartile range). Causes of immunosuppression included solid tumors, hematological malignancies, solid organ transplantation, long-term immunosuppressive therapy (i.e., high-dose steroids or any immunosuppressant for >3 mo), and HIV infection (8, 9).
*Variant screening was impossible because the viral load was not sufficient.
†Missing data means that variant screening was not performed.
‡$P < 0.001$ for incidence of pneumonia in vaccinated versus nonvaccinated patients with Delta.
§$P < 0.001$ for incidence of pneumonia in vaccinated versus nonvaccinated patients with Omicron.

Table 2. Characteristics and Outcomes of Critically Ill Patients According to Omicron versus Delta Variant in the Subgroup of 743 Patients Admitted for Pneumonia from December 1, 2021, to January 18, 2022 (Reality Clinical Database)

	Delta Cases (*n* = *379*)	Omicron Cases (*n* = *154*)	*P* Value (Delta vs. Omicron)	Uninformative Screening Test* (*n* = *69*)	Missing Data† (*n* = *141*)
Age, y	62.0 (51.0–70.0)	65.0 (56.0–72.0)	0.033	60.0 (56.0–65.0)	62.0 (50.0–70.0)
Female, *n* (%)	126 (33.2)	56 (36.4)	0.557	20 (29.0)	49 (34.8)
Immunocompromised, *n* (%)	56 (14.8)	61 (39.6)	<0.001	16 (23.2)	17 (12.0)
Vaccination, *n* (%)			<0.001		
Unvaccinated	273 (72)	67 (43.5)	—	—	—
Vaccinated (1, 2 or 3 doses)	105 (27.7)	82 (53.2)	—	—	—
Unknown	1 (0.2)	5 (3.2)	—	—	—
Time from symptom onset to ICU admission, *n* (%)			0.004		
⩽5 d	61 (16.1)	42 (27.3)	—	12 (17.4)	30 (21.3)
>5 d	303 (80.0)	105 (68.2)	—	56 (81.2)	107 (75.9)
Unknown	15 (4.0)	7 (4.5)	—	1 (1.4)	4 (2.8)
Invasive ventilation, *n* (%)	191 (50.4)	60 (39.0)	0.021	23 (33.3)	62 (44.0)
In-ICU mortality, *n* (%)	90/303 (29.7)	31/98 (31.6)	0.780	10/54 (18.5)	35/120 (29.2)

Continuous variables are reported as median (interquartile range). In-ICU mortality was calculated among the 303 patients with Delta (80%) and the 98 patients with Omicron (63.6%) who were already discharged from the ICU.
*Variant screening was impossible because the viral load was not sufficient.
†Missing data means that variant screening was not performed.

0.12–0.97], respectively), vaccination status (at least one dose vs. none; HR, 1.02; 95% CI, 0.64–1.63), and immunosuppression (HR, 1.44; 95% CI, 0.87–2.38). Similar results were found using a Fine and Gray analysis.

We provide for the first time comparison between the Delta and Omicron variants in critically ill patients. Patients with the Omicron variant were more frequently vaccinated than those with the Delta variant, even with three doses, which could suggest a lower efficacy of the vaccine (10). However, they were more frequently immunocompromised and had a reduction in risk of being admitted for pneumonia when they were vaccinated despite the fact that they were older. Hospitalization not due to pneumonia among subjects with Omicron may involve admission to the ICU for severe decompensation of a chronic disease due to symptomatic viral infection or for another disease pattern related to this new variant. Patients with Omicron were also less frequently invasively ventilated, including those with pneumonia, which could be explained by a greater frequency of immunocompromised patients who could have been treated using noninvasive ventilation or high-flow nasal oxygen (8). We observed a relatively low rate of invasive ventilation, probably related to studies that now report the beneficial effect of high-flow nasal oxygen (11, 12) and noninvasive ventilation (13). Unadjusted in-ICU mortality was not different between variants in the overall population, while a trend toward a decrease in Omicron was probably driven by the higher prevalence of severe pneumonia in Delta.

We observed a discrepancy between the numbers of critically ill patients with variant information (Delta or Omicron) in Reality (629 patients) and in the administrative databases (579 patients) because all but one hospital collected patient information in the APHP laboratory information system. Variant screening information was missing in 18% of cases because numerous patients were transferred to ICUs from other non-APHP hospitals where they had already tested positive. We are unable to report information on organ failure or hypoxemia severity, as we favored exhaustive recording of hospitalized patients rather than exhaustive recording of clinical information in Reality. We do not have information on "do-not-intubate" decisions in some immunocompromised patients, and we do not report medications administered while intensivists were following the APHP therapeutic guidelines, which do not recommend adapting treatment according to the type of variant.

In conclusion, Omicron-infected patients are less likely to be admitted to the ICU and, when admitted, are admitted less often for pneumonia. However, vaccination even with three doses was more frequent in subjects with Omicron infection admitted for pneumonia compared with those with Delta infection, but patients were more frequently immunocompromised and older. When hospitalized in the ICU for pneumonia, disease severity appears to be similar to that of Delta, with no difference in the risk of in-ICU mortality. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

Acknowledgment: The authors thank Direction de la Recherche Clinique et de l'Innovation of the APHP group for providing extensive data. The authors thank Guillermo Hayoun from Direction des Systèmes de l'Information for his work in designing and updating the Reality registry as necessary. The authors thank Laure Maillant of the health database of APHP (Entrepôt de Données en Santé) for her help in generating the data. Finally, the authors also thank all the virology laboratories of the APHP group, which performed the RT-PCR screening of their patients.

Antoine Vieillard-Baron, M.D., Ph.D.*
Assistance Publique des Hôpitaux de Paris
Boulogne, France
and
Université de Paris Saclay
Villejuif, France

Rémi Flicoteaux, M.D.
Assistance Publique des Hôpitaux de Paris
Paris, France

Maud Salmona, M.D.
Assistance Publique des Hôpitaux de Paris
Paris, France
and
Université de Paris
Paris, France

Appoline Chariot
Bertrand De Maupeou D'Ableiges
Assistance Publique des Hôpitaux de Paris
Paris, France

Michael Darmon, M.D., Ph.D.
Frédéric Batteux, M.D., Ph.D.
Assistance Publique des Hôpitaux de Paris
Paris, France
and
Université de Paris
Paris, France

For the APHP Reality Research Group

*Corresponding author (e-mail: antoine.vieillard-baron@aphp.fr).

Full list of collaborators: Djillali Annane (Service de Médecine intensive et Réanimation, Hôpital Raymond Poincaré, APHP), Soufia Ayed (Service de Médecine intensive et Réanimation, Hôpital Bicêtre, APHP), Elie Azoulay (Service de Médecine intensive et Réanimation, Hôpital Saint-Louis, APHP), Raphael Bellaiche (Département d'anesthésie-réanimation, Hôpital Henri Mondor, APHP), Sadek Beloucif (Département d'anesthésie-réanimation, Hôpital Avicenne, APHP), Enora Berti (Service de Médecine intensive et Réanimation, Hôpital Henri Mondor, APHP), Astrid Bertier (Service de Médecine intensive et Réanimation, Hôpital Henri Mondor, APHP), Sébastien Besset (Service de Médecine intensive et Réanimation, Hôpital Louis Mourier, APHP), Marlène Bret (Service de pneumologie, Hôpital Pitié Salpêtrière, APHP), Alain Cariou (Service de Médecine intensive et Réanimation, Hôpital Cochin), Christophe Carpentier (Service de Médecine intensive et Réanimation, Hôpital Bicêtre, APHP), Oussama Chaouch (Département d'Anesthésie et de Réanimation, Hôpital HEGP, APHP), Cyril Charron (Service de Médecine intensive et Réanimation, Hôpital Ambroise Paré, APHP), Julien Charpentier (Service de Médecine intensive et Réanimation, Hôpital Cochin, APHP), Cherifa Cheurfa (Département d'Anesthésie et de Réanimation, Hôpital Cochin, APHP), Bernard Cholley (Département d'Anesthésie et de Réanimation, Hôpital HEGP, APHP), Benjamin Chousterman (Département d'Anesthésie et de Réanimation, Hôpital Lariboisière, APHP), Sébastien Clerc (Service de Pneumologie et Réanimation Médicale du Département R3S, Hôpital Pitié Salpêtrière, APHP), Yves Cohen (Service de Médecine intensive et Réanimation, Hôpital Avicenne, APHP), Alain Combes (Service de Médecine intensive et Réanimation, Hôpital Pitié Salpêtrière, APHP), Jean-Michel Constantin (Département d'Anesthésie et de Réanimation, Hôpital Pitié Salpêtrière, APHP), Charles Damoisel (Département d'Anesthésie et de Réanimation, Hôpital Antoine Béclère, APHP), Vincent Degos (Département d'Anesthésie et de Réanimation, Hôpital Pitié Salpêtrière,

APHP), Sophie Demeret (Service de Réanimation neurologique, Hôpital Pitié Salpêtrière, APHP), Etienne De Montmollin (Service de Médecine Intensive et Réanimation infectieuse, Hôpital Bichat, APHP), Alexandre Demoule (Service de Pneumologie et Réanimation Médicale du Département R3S, Hôpital Pitié Salpêtrière, APHP), Francois Depret (Département d'Anesthésie et de Réanimation, Hôpital Saint-Louis, APHP), Jean-Luc Diehl (Service de Médecine Intensive et Réanimation, Hôpital HEGP, APHP), Michel Djibré (Service de Médecine Intensive et Réanimation, Hôpital Tenon, APHP), Chung-Hi Do (Service de Réanimation neurologique, Hôpital Pitié Salpêtrière, APHP), Emmanuel Dudoignon (Département d'Anesthésie et de Réanimation, Hôpital Saint-Louis, APHP), Jacques Duranteau (Département d'Anesthésie et de Réanimation, Hôpital Bicêtre, APHP), Muriel Fartoukh (Service de Médecine Intensive et Réanimation, Hôpital Tenon, APHP), Fabienne Fieux (Département d'Anesthésie et de Réanimation, Hôpital Saint Antoine et Tenon, APHP), Etienne Gayat (Département d'Anesthésie et de Réanimation, Hôpital Lariboisière, APHP), Mael Gennequin (Département d'Anesthésie et de Réanimation, Hôpital Beaujon, APHP), Bertrand Guidet (Service de Médecine Intensive et Réanimation, Hôpital Saint-Antoine, APHP), Christophe Gutton (Département d'Anesthésie et de Réanimation, Hôpital Saint Antoine et Tenon, APHP), Sophie Hamada (Département d'Anesthésie et de Réanimation, Hôpital HEGP, APHP), Nicholas Heming (Service de Médecine intensive et Réanimation, Hôpital Raymond Poincaré, APHP), Romain Jouffroy (Service de Médecine intensive et Réanimation, Hôpital Ambroise Paré, APHP), Hawa Keita-Meyer (Département d'Anesthésie et de Réanimation, Hôpital Necker, APHP), Olivier Langeron (Département d'Anesthésie et de Réanimation, Hôpital Henri Mondor, APHP), Brice Lortat-Jacob (Département d'Anesthésie et de Réanimation, Hôpital Bichat, APHP), Jonathan Marey (Service de Pneumologie, Hôpital Cochin, APHP), Alexandre Mebazaa (Département d'Anesthésie et de Réanimation, Hôpital Lariboisière, APHP), Bruno Megarbane (Service de Médecine intensive et Réanimation, Hôpital Lariboisière, APHP), Armand Mekontso-Dessap (Service de Médecine intensive et Réanimation, Hôpital Henri-Mondor, APHP), Jean-Paul Mira (Service de Médecine intensive et Réanimation, Hôpital Cochin, APHP), Julie Molle (Service de Pneumologie, Département R3S, Hôpital Pitié Salpêtrière, APHP), Nicolas Mongardon (Département d'Anesthésie et de Réanimation, Hôpital Henri Mondor, APHP), Philippe Montravers (Département d'Anesthésie et de Réanimation, Hôpital Bichat, APHP), Capucine Morelot-Panzini (Service de Pneumologie, Département R3S, Hôpital Pitié Salpêtrière, APHP), Safaa Nemlaghi (Service de Pneumologie et Réanimation Médicale du Département R3S, Hôpital Pitié Salpêtrière, APHP), Bao-long Nguyen (Département d'Anesthésie et de Réanimation, Hôpital Pitié Salpêtrière, APHP), Antoine Parrot (Service de Pneumologie, Hôpital Tenon, APHP), Romain Pasqualotto (Département d'Anesthésie et de Réanimation, Hôpital Pitié Salpêtrière, APHP), Nicolas Peron (Service de Médecine Intensive Réanimation, Hôpital HEGP, APHP), Lucile Picard (Département d'Anesthésie et de Réanimation, Hôpital Henri Mondor, APHP), Marc Pineton de Chambrun (Service de Médecine intensive et Réanimation, Hôpital Pitié Salpêtrière, APHP), Benjamin Planquette (Service de Pneumologie, Hôpital HEGP, APHP), Benoit Plaud (Département d'Anesthésie et de Réanimation, Hôpital Saint-Louis, APHP), Stéphanie Pons (Département d'Anesthésie et de Réanimation, Hôpital Pitié Salpêtrière, APHP), Christophe Quesnel (Département d'Anesthésie et de Réanimation, Hôpital Saint Antoine et Tenon, APHP), Jean-Herlé Raphalen (Département d'Anesthésie et de Réanimation, Hôpital Necker, APHP), Keyvan Razazi (Service de Médecine intensive et Réanimation, Hôpital Henri-Mondor, APHP), Jean-Damien Ricard (Service de Médecine intensive et Réanimation, Hôpital Louis Mourier, APHP), Anne Roche (Service de Pneumologie et soins intensifs, Hôpital Bicêtre, APHP), Benjamin Rohaut (Service de Réanimation neurologique, Hôpital Pitié Salpêtrière, APHP), Damien Roux (Service de Médecine intensive et Réanimation, Hôpital Louis Mourier, APHP), Laurent Savale (Service de Pneumologie et soins intensifs, Hôpital Bicêtre, APHP), Jennifer Sobotka (Service des Urgences, Hôpital Saint Antoine, APHP), Jean-Louis Teboul (Service de Médecine intensive et Réanimation, Hôpital Bicêtre, APHP), Jean-François Timsit (Service de Médecine Intensive et Réanimation infectieuse, Hôpital Bichat, APHP), Guillaume Voiriot (Service de Médecine Intensive et Réanimation, Hôpital Tenon, APHP), Emmanuel Weiss (Département d'Anesthésie et de Réanimation, Hôpital Beaujon, APHP), Lucille Wildenberg (Département d'Anesthésie et de Réanimation, Université Paris-Saclay, Hôpital Bicêtre, APHP), Elie Zogheib (Département d'anesthésie-réanimation, Hôpital Avicenne, APHP), Bruno Riou (Service d'Accueil des Urgence, Sorbonne Université, Hôpital Pitié Salpêtrière).

References

1. Karim SSA, Karim QA. Omicron SARS-CoV-2 variant: a new chapter in the COVID-19 pandemic. *Lancet* 2021;398:2126–2128.
2. World Health Organization. What you need to know about the new Omicron COVID-19 variant. Geneva, Switzerland: World Health Organization; 2021 [updated 2021 Mar 12; accessed 2021 Dec 9]. Available from: https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2021/12/what-you-need-to-know-about-the-new-omicron-covid-19-variant.
3. Ferguson N, Ghani A, Hinsley W, Volz E; Imperial College COVID-19 Response Team. Report 50: hospitalisation and risk for Omicron cases in England. London, United Kingdom: Imperial College London; 2021 [updated 2021 Dec 22; accessed XXX]. Available from: https://spiral.imperial.ac.uk/bitstream/10044/1/93035/10/2021-12-22%20COVID19%20Report%2050.pdf.
4. Wolter N, Jassat W, Walaza S, Welch R, Moultrie H, Groome M, *et al.* Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study. *Lancet* 2022;399:437–446.
5. Maslo C, Friedland R, Toubkin M, Laubscher A, Akaloo T, Kama B. Characteristics and outcomes of hospitalized patients in South Africa during the COVID-19 Omicron wave compared with previous waves. *JAMA* 2022;327:583–584.
6. Viana R, Moyo S, Amoako DG, Tegally H, Scheepers C, Althaus CL, *et al.* Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. *Nature* 2022;603:679–686.
7. Auvigne V, Vaux S, Le Strat Y, Schaeffer J, Fournier L, Montagnat C, *et al.* Serious hospital events following symptomatic infection with SARS-CoV-2 Omicron and Delta variants in France, December 2021 – January 2022: a retrospective, population-based, matched cohort study [preprint]. medRxiv; 2022 [accessed XXX]. Available from: https://doi.org/10.1101/2022.02.02.22269952.
8. Azoulay E, Mokart D, Kouatchet A, Demoule A, Lemiale V. Acute respiratory failure in immunocompromised adults. *Lancet Respir Med* 2019;7:173–186.
9. Azoulay E, Fartoukh M, Darmon M, Géri G, Voiriot G, Dupont T, *et al.* Increased mortality in patients with severe SARS-CoV-2 infection admitted within seven days of disease onset. *Intensive Care Med* 2020; 46:1714–1722.
10. Tenforde MW, Self WH, Adams K, Gaglani M, Ginde AA, McNeal T, *et al.*; Influenza and Other Viruses in the Acutely Ill (IVY) Network. Association between mRNA vaccination and COVID-19 hospitalization and disease severity. *JAMA* 2021;326:2043–2054.
11. Ospina-Tascón GA, Calderón-Tapia LE, García AF, Zarama V, Gómez-Álvarez F, Álvarez-Saa T, *et al.*; HiFLo-Covid Investigators. Effect of high-flow oxygen therapy vs conventional oxygen therapy on invasive mechanical ventilation and clinical recovery in patients with severe COVID-19: a randomized clinical trial. *JAMA* 2021;326:2161–2171.
12. Demoule A, Vieillard Baron A, Darmon M, Beurton A, Géri G, Voiriot G, *et al.* High-flow nasal cannula in critically ill patients with severe COVID-19. *Am J Respir Crit Care Med* 2020;202:1039–1042.
13. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, *et al.*; RECOVERY-RS Collaborators. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS randomized clinical trial. *JAMA* 2022;327:546–558.