



HAL
open science

Increased risk of severe COVID-19 in hospitalized patients with SARS-CoV-2 Alpha variant infection: a multicentre matched cohort study

Guillaume Martin-Blondel, François-Xavier Lescure, Lambert Assoumou, Charlotte Charpentier, Jean-Marc Chapplain, Thomas Perpoint, Gaspard Grouteau, Hugues Cordel, Gilles Pialoux, Jérôme Pacanowski, et al.

► To cite this version:

Guillaume Martin-Blondel, François-Xavier Lescure, Lambert Assoumou, Charlotte Charpentier, Jean-Marc Chapplain, et al.. Increased risk of severe COVID-19 in hospitalized patients with SARS-CoV-2 Alpha variant infection: a multicentre matched cohort study. *BMC Infectious Diseases*, 2022, 22, pp.540. 10.1186/s12879-022-07508-x . hal-03727828

HAL Id: hal-03727828

<https://hal.sorbonne-universite.fr/hal-03727828v1>

Submitted on 19 Jul 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

RESEARCH

Open Access



Increased risk of severe COVID-19 in hospitalized patients with SARS-CoV-2 Alpha variant infection: a multicentre matched cohort study

Guillaume Martin-Blondel^{1,2*}, François-Xavier Lescure³, Lambert Assoumou⁴, Charlotte Charpentier⁵, Jean-Marc Chaplain⁶, Thomas Perpoint⁷, Gaspard Grouteau¹, Hugues Cordel⁸, Gilles Pialoux⁹, Jérôme Pacanowski¹⁰, Michael Thy³, Adeline Bauvois¹¹, Didier Laureillard¹², Fadia Hamrouni⁴, Michèle Algarte-Genin⁴, Julien Poissy¹³, Diane Descamps⁵, Dominique Costagliola⁴ for the CoCliCo Study Group

Abstract

Background: The impact of the variant of concern (VOC) Alpha on the severity of COVID-19 has been debated. We report our analysis in France.

Methods: We conducted an exposed/unexposed cohort study with retrospective data collection, comparing patients infected by VOC Alpha to contemporaneous patients infected by historical lineages. Participants were matched on age (± 2.5 years), sex and region of hospitalization. The primary endpoint was the proportion of hospitalized participants with severe COVID-19, defined as a WHO-scale > 5 or by the need of a non-rebreather mask, occurring up to day 29 after admission. We used a logistic regression model stratified on each matched pair and accounting for factors known to be associated with the severity of the disease.

Results: We included 650 pairs of patients hospitalized between Jan 1, 2021, and Feb 28, 2021, in 47 hospitals. Median age was 70 years and 61.3% of participants were male. The proportion of participants with comorbidities was high in both groups (85.0% vs 90%, $p = 0.004$). Infection by VOC Alpha was associated with a higher odds of severe COVID-19 (41.7% vs 38.5%—aOR = 1.33 95% CI [1.03–1.72]).

Conclusion: Infection by the VOC Alpha was associated with a higher odds of severe COVID-19.

Keywords: COVID-19, SARS-CoV-2, Variant of concern Alpha, Severity

Background

Since the end of 2020, the SARS-CoV-2 variant of concern (VOC) Alpha, also known as B.1.1.7 or VOC-202012/01 has rapidly spread across all continents [1, 2]. It has been shown that the VOC Alpha is between 43 and 90% more transmissible than variants from historical lineages (HL) 19A/B and 20A/B/C/D/E/F/G [3–6]. The effect of the VOC Alpha on COVID-19 severity is less clear, although some authors, mostly from the United

[†]Guillaume Martin-Blondel, François-Xavier Lescure, Julien Poissy and Diane Descamps contributed equally to the work

*Correspondence: martin-blondel.g@chu-toulouse.fr

¹Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Toulouse, Toulouse, France

Full list of author information is available at the end of the article



Kingdom, reported an increased risk of hospitalization [7, 8] or of mortality [9–12], while others did not report changes in either symptoms, disease duration [13], or severity [14]. Variation in study designs and settings, particularly when medical infrastructures are strained, may explain these discrepancies.

In France, the VOC Alpha accounted for 3.3% of the viruses sequenced on January 8th, 2021, and reached 83% on April 15th, 2021 [15]. Therefore, while the two first epidemic waves affecting France in 2020 were related to HL, the current epidemic occurring since January 2021 is characterized by a progressive overlapping switch towards VOC Alpha dominance. The aim of this study was to assess the effect of VOC Alpha compared to HL on COVID-19 severity in a multicentre matched exposed and unexposed cohort study with retrospective data collection focusing on patients admitted to the hospital during a time when both the HL and the VOC Alpha coexisted and while there was no limitation in medical resources.

Methods

All adults (age > 18 years) hospitalized for symptomatic acute COVID-19 between Jan 1, 2021, and Feb 28, 2021, with a positive VOC Alpha screening were eligible for the study. Over the same time period, the maximum number of patients concurrently hospitalized for COVID-19 in France was 24,820, including 3492 patients in ICU, which is lower than the maximal bed capacity (108,183 beds in medical wards, including 5433 beds in ICU, and 5954 additional beds in intensive care) [16]. During the time period of the study, COVID-19 diagnosis through PCR on nasopharyngeal sampling was widely and freely available to everyone. VOC Alpha screening was performed using the ThermoFischer kit (TaqPath One-step RT-qPCR, ThermoFischer Scientific, Waltham, MA, USA) with Spike gene target RT-PCR failure or mutations-specific real-time RT-PCR (i.e. deletion 69–70 and N501Y mutation, TIB Molbiol, Berlin, Germany). The combination of spike deletion at residue 69–70 and N501Y mutation was interpreted as a suspicion of VOC Alpha. All eligible participants who objected to the use of their data were excluded from the analyses. Participants with VOC Alpha were matched in a 1:1 ratio to HL on the basis of age (± 2.5 years), sex and administrative region of hospitalization.

Data collection

Data were retrospectively collected from all participating sites of the CoCliCo (Collective of COVID-19 clinicians) network. All sites were asked to identify all adults who met the eligibility criteria and collect the site number, age and sex of these patients for centralized matching. The

list of matched participants was then sent to the sites to fill out the electronic case report form. Data relevant to the study's objectives were extracted from the patients' medical records. Data on COVID-19 vaccination status were not collected in the study at a time where only 2.4% of the eligible population (above 75 years of age or health-care workers) had received a complete vaccine scheme.

Outcomes

The primary outcome was the proportion of participants with a severe form of COVID-19 occurring up to day 29 after the date of hospitalization. Severity was defined by a WHO clinical progression scale > 5 (high flow oxygen therapy (HFOT), non-invasive ventilation (NIV), invasive ventilation, extra-corporeal membrane oxygenation (ECMO) or death) [17] but also by the need of a non-rebreather mask (NRB) in order to consider patients with severe COVID-19 but limitations of life-sustaining treatment. Two participants with missing primary outcome were considered as having a severe form.

The secondary endpoints were: (i) mortality; (ii) WHO clinical progression scale > 5; (iii) admission to an intensive care unit (ICU); (iv) invasive ventilation or ECMO; (v) HFOT, all up to day 29, (vi) time from symptom onset to hospitalization, and (vii) re-admission after discharge up to day 29. Maximal parenchymal lesions extension and pulmonary thrombo-embolism detected on chest CT-scan were collected.

Statistical analyses

For an 80% power, a 5% type I error and an expected severity of 20% in patients infected with HL, 1100 exposed and 1100 unexposed individuals to VOC Alpha were needed to detect a 25% higher risk of severity in participants infected with VOC Alpha compared to HL with 1:1 matching, while the number of matched pairs corresponding to 30%, 40% and 50% higher risk of severity were 769, 444, and 291 respectively.

The analysis population consisted of all individuals exposed to VOC Alpha with a matched unexposed control. The characteristics of exposed and unexposed individuals to VOC Alpha were compared with a Mc Nemar test for categorical variables and Wilcoxon paired test for continuous variables.

Unadjusted and adjusted odds ratios (OR) were calculated using a logistic regression model stratified on each matched pair to assess the association between VOC Alpha infection and the occurrence of a severe form of COVID-19. The following factors associated with COVID-19 severity were accounted for in multivariable models: age, BMI, smoking and comorbidities (cardiovascular disease, chronic lung disease, asthma, chronic kidney disease, chronic liver disease, chronic neurological

disease, active cancer, solid organ or hematopoietic cell transplantation, autoimmune disease, HIV infection, and diabetes). Treatments received during the course of hospitalization could be the result of a worse course of the disease and therefore be on the causal pathway of a more severe disease; therefore, receiving corticosteroids was not included in the main model.

Time-to-event methods, including Kaplan–Meier estimates and Cox proportional-hazards models, were used to analyze all secondary outcomes. Unadjusted and adjusted hazard ratios (HR) were calculated using Cox proportional hazard model stratified on each pair to assess whether VOC Alpha was associated with the outcome. Death was not accounted as a competing risk in the main analysis, and was accounted for in sensitivity analyses for high flow oxygen therapy, ICU admission, and mechanical ventilation or ECMO. Analyses were conducted with SAS software version 9.4 (SAS Statistical Institute, Cary, North Carolina). All statistical tests were 2-tailed, with $\alpha=0.05$.

Results

In this multicentre matched exposed-unexposed cohort study, 882 participants with VOC Alpha infection were eligible and 650 were enrolled and matched on the basis of sex, age and administrative region, to 650 contemporaneous participants infected by HL (Fig. 1).

Characteristics of patients are presented in Table 1 according to SARS-CoV-2 lineage. The median age was 70 years (range 25 to 101) and 61.3% were males. Participants with VOC Alpha infection less often had at least one of the specific comorbidities listed above, and were less often smokers, than their matched participants. The proportion of patients first admitted in the ICU did not differ between groups (16.7% in the VOC Alpha group vs 13.8% in the HL group, $P=0.12$). Median oxygen saturation level before initiation of oxygen therapy was not different (90% (range 32–99) in the VOC Alpha group vs 91% (range 30–99) in the HL group, $P=0.12$), as well as the acme of C-reactive protein level during the first three days of hospitalization (median 93 mg/L (range 1–584) in the VOC Alpha group vs 89 mg/L (range 1–423) in the HL group, $P=0.34$). Proportions of patients who received corticosteroids and other immunomodulatory therapies were higher in the VOC Alpha group (respectively 84.3% and 8.4%) than in the HL group (respectively 76.6%, $P<0.001$ and 5.2%, $P<0.02$). The proportion of participants who received anticoagulant and antibiotic therapy did not differ (93.3% versus 91.3% and 60.3 versus 60.6% respectively). Only 5 participants in each group received monoclonal antibodies or antiviral drugs.

The proportion of severe COVID-19 (defined as a WHO score >5 or the need of a NRB) within 29 days of hospitalization was 41.7% in the VOC Alpha group and 38.5% in the HL group (aOR 1.33 95% confidence

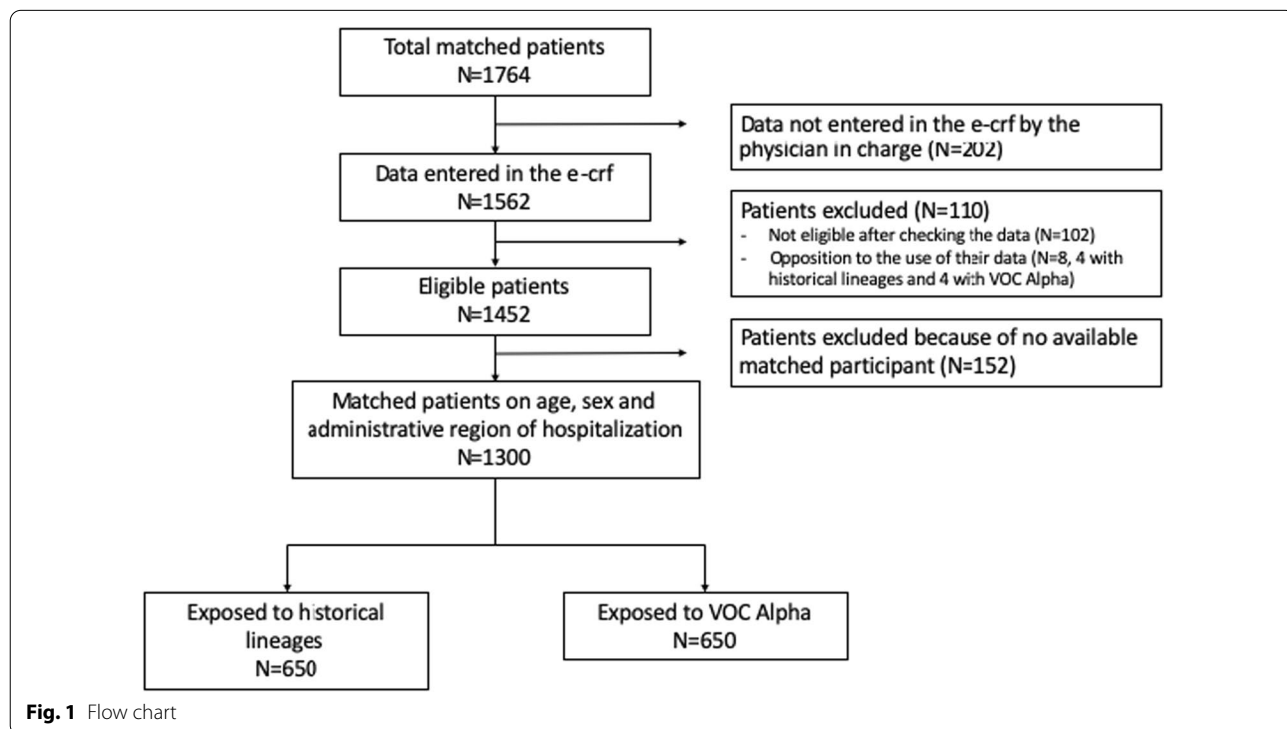


Fig. 1 Flow chart

Table 1 Participants characteristics at hospital admission

	Exposed to historical lineages N = 650	Exposed to VOC Alpha N = 650	P-value
Age (years), median (range)	70 (27–100)	70 (25–101)	
Gender—n (%)			
Male	399 (61.4)	399 (61.4)	
Female	251 (38.6)	251 (38.6)	
Body Mass Index			0.20
N	571	553	
Median (range)	26.8 (13.5–67.2)	27.4 (3.3–76)	
Smoker—n (%)	169 (26.0)	136 (20.9)	0.04
Location of initial care—n (%)			0.12
Conventional hospitalization	560 (86.2)	539 (82.9)	
ICU	90 (13.8)	109 (16.7)	
Comorbidities, n (%)	586 (90.1)	553 (85.0)	0.004
Cardiovascular disease	410 (62.9)	401 (61.6)	0.57
Chronic lung disease	102 (15.6)	74 (11.3)	0.02
Asthma	35 (5.3)	33 (5.0)	1.00
Chronic kidney disease	87 (13.3)	70 (10.7)	0.11
Chronic liver disease	21 (3.2)	12 (1.8)	0.11
Chronic neurological disease	115 (17.6)	88 (13.5)	0.03
Active cancer	80 (12.3)	53 (8.1)	0.01
Solid organ transplant	31 (4.7)	13 (2.0)	<0.001
Autoimmune disease	27 (4.1)	20 (3.0)	0.15
HIV Infection	10 (1.5)	0 (0)	
Obesity	164 (25.2)	176 (27.0)	0.54
Diabetes	197 (30.3)	182 (27.9)	0.29

interval (95% CI): [1.02–1.72] in the multivariable analysis) and similar results were observed for the 2 components of the primary endpoints (Table 2). Regarding secondary outcomes within 29 days after hospitalization, the mortality rate was 24% in the VOC Alpha group and 19% in the HL group (aHR 1.21 [0.93–1.58] in the multivariable analysis), and the proportion of patients reaching a WHO score > 5 was 26.2% in the VOC Alpha group and 20.5% in the HL group (aHR 1.24 [1.00–1.55] in the multivariable analysis). All other secondary endpoints were not significantly associated with infection by the VOC Alpha. The entire multivariable model and Kaplan–Meier curves are provided as Additional file 1.

Acme of parenchymal extent on chest CT-scan was higher in the VOC Alpha group (50%, range 0–95) than in the HL group (40%, range 0–99, univariable analysis $P=0.04$). The proportion of patients diagnosed with pulmonary embolism did not differ (5.3% in the VOC Alpha group, and 6.0% in the HL group, univariable analysis $P=0.29$).

Discussion

In this multicentre matched exposed-unexposed cohort study, we found a 33% (95%CI: 3–72%) higher odds of severe COVID-19 in participants infected by a VOC Alpha, while the increase in the risk of death within 29 days after hospitalization was not significant (21% (95% CI: – 7% to + 58%).

These results are in line with the literature showing an increased severity of VOC Alpha compared to HL. The European Surveillance System analyzed 19,207 cases of VOC Alpha and 3,348 HL cases reported between Sept 14, 2020, and March 14, 2021, from seven European countries [7]. In this study, patients infected with VOC Alpha were found to have a 1.7 times higher risk of being hospitalized for COVID-19. Hospitalized patients were also shown to be younger (by 10 years in median) and to be less comorbid than patients hospitalized for COVID-19 related to HL in this study and others [7, 11, 14]. The latter was also true in our study. Comparison of data concerning the age of infected patients is more complex because of a different epidemiological context and

Table 2 Primary and secondary outcomes

	Exposed to historical lineages N = 650	Exposed to VOC Alpha N = 650	Crude measure of association (95% CI)	Adjusted measure of association (95% CI)
<i>WHO scale > 5 or non-rebreather mask at day 29</i>				
Number of events by Day 29	250	271		
Proportion of participants with an event at Day 29—% (95% CI)	38.5 (34.7–42.3)	41.7 (37.8–45.6)	1.15 (0.91–1.45)	1.33 (1.03–1.72)
<i>Mortality rate at day 29</i>				
Number of deaths by Day 29	112	130		
Kaplan–Meier estimate of mortality by Day 29—% (95% CI)	19.0 (16.3–23.8)	24.0 (20.9–29.4)	1.18 (0.92–1.52)	1.21 (0.93–1.58)
<i>WHO scale > 5 by day 29</i>				
Number of participants with WHO scale > 5 by Day 29	164	179		
Kaplan–Meier estimate of WHO scale > 5 by Day 29—% (95% CI)	20.5 (17.0–24.7)	26.2 (22.2–30.8)	1.19 (0.96–1.48)	1.24 (1.00–1.55)
<i>Non-rebreather mask by day 29</i>				
Number of participants with non-rebreather mask by Day 29	177	208		
Kaplan–Meier estimate of non-rebreather mask by Day 29—% (95% CI)	29.7 (26.0–33.8)	35.2 (31.3–39.5)	1.18 (0.97–1.45)	1.20 (0.98–1.47)
<i>High flow oxygen therapy by day 29*</i>				
Number of high flow oxygen therapy by Day 29	201	240		
Kaplan–Meier estimate of oxygen therapy by Day 29—% (95% CI)	35.4 (31.3–39.9)	42.1 (37.8–46.6)	1.20 (0.99–1.44)	1.18 (0.98–1.40)
<i>ICU admission by day 29*</i>				
Number of ICU admission by Day 29	207	240		
Kaplan–Meier estimate of ICU admission by Day 29—% (95% CI)	36.0 (32.0–40.0)	41.7 (37.6–46.1)	1.15 (0.96–1.39)	1.12 (0.93–1.36)
<i>Mechanical ventilation or ECMO by day 29*</i>				
Number of Mechanical ventilation or ECMO by Day 29	108	107		
Kaplan–Meier estimate of Mechanical ventilation or ECMO by Day 29—% (95% CI)	20.6 (17.0–24.7)	21.5 (17.4–25.7)	0.97 (0.74–1.27)	0.96 (0.73–1.27)
<i>Hospitalization</i>				
Median time from symptoms onset to hospitalization (95% CI)—days	6 (5–6)	7 (6–7)	0.93 (0.83–1.04)	0.96 (0.86–1.08)
Median duration on hospitalization (95% CI)—days	11.5 (10–13)	11.0 (10–12)	1.02 (0.88–1.18)	0.95 (0.81–1.10)
<i>Readmission</i>				
Number of readmissions after previous discharge	28	19		
Kaplan–Meier estimate of re-admission after a discharge—% (95% CI)	5.1 (3.4–7.7)	2.3 (1.2–4.3)	0.68 (0.38–1.23)	(0.42–1.42)

* In an analysis accounting for competing risk of death, the adjusted sHR were estimated as 1.17 (0.97–1.41), 1.09 (0.89–1.35) and 0.96 (0.73–1.25) respectively

vaccine strategies, hence we do not provide additional data on that matter, given that participants were matched on age in our study. We can however underline that the impact of VOC Alpha on the higher occurrence of severe COVID-19 is reinforced by the fact that our patients have less comorbidities than the matched non-exposed patients.

The effect of VOC Alpha on the risk of mortality is still the subject of debate. Both the study from the OpenSAFELY electronic health records [11] and three community-based studies [9, 10, 12] performed

in the United Kingdom from Oct 1, 2020, to Feb 14, 2021, which compared VOC Alpha to HL, showed an increased hazard of death of 1.55 to 1.67. These studies could have been biased by the epidemiological context and overwhelmed hospital capacities, that may have increased the impact of COVID-19 in the most severely ill patients. Of note, although our study may have been underpowered to detect a significant increase in the risk of death, the confidence interval of the mortality hazard in our study is compatible with the reported confidence intervals reported in the United Kingdom

with a higher bound of 1.58. Conversely, rates of ICU admission or death did not differ significantly in any age group in the study from The European Surveillance System [7]. In addition, there was no evidence of an association between severe disease, death and lineage in a hospital-based cohort study of patients acutely admitted to hospitals in London from Nov 9, 2020, to Dec 20, 2020, before the peak of hospital admissions [14], but that study was small and the baseline date was different for participants with symptoms (date of symptoms) and those without (date of hospitalization). These discrepancies between studies underline the need to consider the geographical area, and the potential impact of the epidemiological pressure on healthcare facilities that could have increased morbimortality of COVID-19.

Why VOC Alpha is associated with an increased severity in human beings is unknown. Our study highlights clinically relevant details depicting the course and pathogenesis of COVID-19 related to VOC Alpha. Patients with VOC Alpha infection were not hospitalized sooner after the onset of first symptoms, and were not more frequently admitted to ICU first than patients infected with HL. However, we found a higher maximal parenchymal extent of ground-glass opacities on chest CT-scan. In the meantime, these patients were more likely to reach a WHO score > 5. This suggests that increased pathogenicity of VOC Alpha is not linked with a shortened delay between the first symptoms and the hospital admission. Patients were hospitalized at the beginning of their second week of symptoms, at a time which is considered to be the “inflammatory phase” of the disease. At the same time, high nasopharyngeal viral loads are central to pathogenesis of viral infections and have been shown in SARS to be associated with the onset of symptoms, oxygen desaturation, mechanical ventilation, and death [18]. Recent studies showed that COVID-19 patients infected by VOC Alpha had a viral load 3 to 10 times higher than the HL in nasopharyngeal samples [14, 19, 20]. This higher viral load in SARS-CoV-2 VOC Alpha infection can result from a higher virus binding affinity to the angiotensin-converting enzyme 2 receptor [21], which likely enhances entry to epithelial host cells in the respiratory tract and the lungs and could trigger a stronger immune response causing a more severe disease compared to HL. This might be illustrated by the higher parenchymal extent of ground-glass opacities on chest CT-scan, although the acme of C-reactive protein serum level during the first three days of hospitalization did not differ between groups. In the present study, SARS-CoV-2 nasopharyngeal viral loads, estimated by real-time PCR Ct values, were not recorded due to the

heterogeneity of RT-PCR assays used in this multicentre study, which renders difficult their interpretations due to the inter-assays variations.

In this study we controlled for several potential confounding factors by using a short study period and matching on the basis of administrative region to account for the potential impact of the local burden of the epidemic on the care system which can influence the clinical outcomes. Given the strong effect of age on the severity of the disease we matched participants exposed to the VOC Alpha to participant exposed to HL on age within 2.5 years and we also adjusted the analysis according to age. We also accounted for the presence of comorbidities and smoking, factors known to be associated with a more severe course of the disease. Only 650 of the 882 patients infected with VOC Alpha initially listed as eligible by the clinical sites could finally be enrolled and matched. Although it is unlikely for this drop to be strongly linked with the outcomes, we cannot exclude some selection bias. Socio-economic status and origin were not collected and could not be accounted for, although they are associated with severity of disease. Given the retrospective nature of data collection, we had to restrict data collection to variables available in medical records of most participants. For instance, although obesity was accounted for, we could not collect the exact BMI which would have been more precise. As in any observational studies, the remaining role of additional confounders cannot be ruled out. Finally, we considered the results of SARS-CoV-2 screening test strategies and not of viral genome sequencing, however a very high level of agreement has been described in the literature between the presence of deletion 69–70 and the VOC Alpha [9].

Conclusion

VOC Alpha is associated with an increased severity, and potentially leads to an increased mortality. These considerations have huge implications for vaccine allocation policies. Vaccination should now urgently be made accessible to patients who were not previously prioritized in order to reach herd immunity. These results also point to the importance of limiting the circulation of the virus until a very large proportion of the population is vaccinated.

Abbreviations

VOC: Variant of concern; COVID-19: Coronavirus disease-19; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; WHO: World Health Organization; aOR: Adjusted odds ratios; HR: Hazard ratios; HL: Historical lineages; CoCliCo: Collective of COVID-19 clinicians; HFOT: High flow oxygen therapy; NIV: Non-invasive ventilation; ECMO: Extra-corporeal membrane oxygenation; NRB: Non-rebreather mask.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-022-07508-x>.

Additional file 1: Table S1. Unadjusted and adjusted analysis of factors associated with COVID-19 severity by Day 29 using a stratified logistic regression model on each matched pair. **Table S2.** Multivariable analysis of factors associated with mortality by Day 29 using a stratified Cox regression model on each matched pair. **Table S3.** Multivariable analysis of factors associated with WHO scale >5 by Day 29 using a stratified Cox regression model on each matched pair. **Table S4.** Multivariable analysis of factors associated with non-rebreather mask by Day 29 using a stratified Cox regression model on each matched pair. **Table S5.** Multivariable analysis of factors associated with high flow oxygen therapy by day 29 using a stratified Cox regression model on each matched pair. **Table S6.** Multivariable analysis of factors associated with ICU admission by day 29 using a stratified Cox regression model on each matched pair. **Table S7.** Multivariable analysis of factors associated with Mechanical ventilation or ECMO by day 29 using a stratified Cox regression model on each matched pair. **Table S8.** Multivariable analysis of factors associated with time from symptoms onset to hospitalization using a stratified Cox regression model on each matched pair. **Table S9.** Multivariable analysis of factors associated with duration on hospitalization using a stratified Cox regression model on each matched pair. **Table S10.** Multivariable analysis of factors associated with readmission using a stratified Cox regression model on each matched pair. **Figure S1.** Kaplan–Meir plot for all cause of mortality. **Figure S2.** Kaplan–Meir plot for WHO scale >5. **Figure S3.** Kaplan–Meir plot for non-rebreather mask. **Figure S4.** Kaplan–Meir plot for high flow oxygen therapy. **Figure S5.** Kaplan–Meir plot for intensive care admission. **Figure S6.** Kaplan–Meir plot for Mechanical ventilation or ECMO. **Figure S7.** Kaplan–Meir plot for hospitalization (time from symptoms onset to hospitalization). **Figure S8.** Kaplan–Meir plot for hospital discharge (duration on hospitalization). **Figure S9.** Kaplan–Meir plot for readmission.

Acknowledgements

We wish to thank all the patients and staff from all the units that participated in the study, and the ANRS-MIE (Agence Nationale de Recherches sur le SIDA et les hépatites virales- Maladies Infectieuses Emergentes) for its support. *CoCliCo study group*: Guillaume Martin-Blondel^{1,2}, Pierre Delobel¹, Gaspard Grouteau¹, Jean Roch Le Henaff¹, Vincent Mear¹, Sandra Lagarrigues¹, Alais Frelat¹, Thomas De Nadal¹⁴, Zara Steinmeyer¹⁴, Arnaud Del Bello¹⁵, Stéphanie Ruiz¹⁶, Benjamin Sarton¹⁶, Elise Noel-Savina¹⁷, Jacques Izopet¹⁸, Nathan Peiffer-Smadja³, Michael Thy³, Mathilde Gare³, Diane Le Pluart³, François-Xavier Lescuré³, Christophe Rioux³, Laurène Deconinck³, Yazdan Yazdanpanah³, Benoit Visseaux³, Diane Descamps⁵, Charlotte Charpentier⁵, Jean-Marc Chaplain⁶, Pierre Tattevin⁶, Thomas Perpoint⁷, Maude Bouscambert-Duchamp¹⁹, Hodane Yonis²⁰, Paul Chabert²⁰, Hugues Cordel⁸, Youssouf Mohamed-Kassim⁸, Nolan Hassold⁸, Segolène Brichler²¹, Julien Caliez²², Thomas Rambaud²³, Marilucy Lopez-Sublet²⁴, Frédéric Adnet²⁵, Gilles Pialoux⁹, Christia Palacios⁹, Marwa bachir⁹, Marine Nadal⁹, Mathieu turpin²⁶, Antoine Parrot²⁷, Djeneba Fofana²⁸, Jérôme Pacanowski¹⁰, Karine Lacombe¹⁰, Emmanuelle Gras¹⁰, Laura Levi¹⁰, Laure Surgers¹⁰, Ines Devred¹⁰, Nadia Valin¹⁰, Thibault Chiarabini¹⁰, Jean Luc Meynard¹⁰, Adeline Bauvois¹¹, Clara Duran¹¹, Elyanne Gault¹¹, Jean-Emmanuel Kahn¹¹, Elisabeth Rouveix¹¹, Guillaume Geri²⁹, Didier laureillard¹², Albert Sotto¹², Paul Loubet¹², Claire Roger³⁰, Julien Poissy¹³, Marc Lambert¹³, Ady Assaf³¹, Laurence Bocket³², Firouzé Bani-Sadr³³, Yohan N'Guyen³³, Juliette Romaru³³, Maxime Hentzien³³, Thomas Gabas³⁴, Amélie Chabrol³⁴, Cecilia Billiou³⁵, Philippe Menager³⁶, Christophe Billy³⁷, Jean-Jacques Laurichesse³⁷, Fabrice Ketty N Simba³⁷, Pauline Caraux Paz³⁸, Liliane Tinang³⁹, Agathe Bounhioi³⁹, Catherine Burnat⁴⁰, Sandrine Soriot-Thomas⁴¹, Damien Basille⁴¹, Jean Philippe Lanoix⁴¹, Yoan Zerbib⁴¹, Yoann Zerbib⁴¹, Anne Pouvaret⁴², Fanny Lanterner⁴², Helene Mascitti⁴³, Aurélien Dinh⁴³, Benjamin Davido⁴³, Hôpital Foch, Suresnes, France, Service de Biologie Clinique : Philippe Lesprit⁴⁴, Eric Farfour⁴⁴, Mathilde Neuville⁴⁵, Linda Nait Allaoua⁴⁶, Michèle Lejaillé⁴⁶, Nathalie De Castro⁴⁷, Jean-Michel Molina⁴⁷, Diane Ponscarne⁴⁷, Mariagrazia Tateo⁴⁷, Geoffroy Liegeon⁴⁷, Ines Bousset⁴⁷, Pauline Huriez⁴⁷, André Cabié⁴⁸, Valentine Campana⁴⁸, Isabelle Calmont⁴⁸, Jean-Marie Turmel⁴⁸, Guitteaud Karine⁴⁸, Pierre-François Sandrine⁴⁸, Athéna Marquise⁴⁸, Ornella Cabras⁴⁸, Mélanie Lehoux⁴⁸, Cyrille Chabartier⁴⁹, Vincent Dubeu⁵⁰, Diana

Ndiaye⁵⁰, Caroline Lefevre⁵¹, Achille Kouatchet⁵², Duc Nguyen⁵³, Camille Tumiotto⁵⁴, Pierre Sioniac⁵⁵, Alexandre Boyer⁵⁵, Jean-François Faucher⁵⁶, Edouard Desvaux⁵⁷, Sylvie Rogez⁵⁸, Paul Le Turnier⁵⁹, François Raffi⁵⁹, Emmanuel Canet⁶⁰, Antoine Roquilly⁶⁰, Louise Castain⁶¹, Solène Secher⁶¹, Véronique Mondain⁶², Lionel Piroth⁶³, Christelle Auvray⁶⁴, Pascal Chavanet⁶⁴, Marielle Buisson⁶⁴, Sophie Mahy⁶⁴, François-Xavier Catherine⁶⁴, Clémentine Esteve⁶⁴, Michel Duong⁶⁴, Carole Charles⁶⁴, Sandrine Gohier⁶⁴, Céline Schaffer⁶⁵, Olivier Robineau⁶⁶, Perrine Bortolotti⁶⁶, Maxime Pradier⁶⁶, François Goehring⁶⁷, Alice Corbel⁶⁷, Jeanne Kotzyba⁶⁷, Kévin Alexandre⁶⁸, Gaetan Beduneau⁶⁹, Elodie Alessandri-Gradt⁷⁰, Martin Martinot⁷¹, Simon Gravier⁷¹, Ciprian Ion⁷¹, Victoire de Lastours⁷², Roza Rahlh⁷², Valérie Garrait⁷³, Laurent Richier⁷³, Mounira Smati-lafarge⁷⁴, Guillemette Frémont⁷⁵, Pierre Louis Nivose⁷⁵, Marie Hélène André⁷⁵, Magdalena Gerin⁷⁵, Aicha Hamdi⁷⁶, Naomi Sayre⁷⁷, Stephanie Cossec⁷⁷, Sophie Alviset⁷⁷, Pierre Alain Billy⁷⁷, Marie Gousseff⁷⁸, Emmanuel Forestier⁷⁹, Anne-Laure Destrem⁷⁹, Olivier Rogeaux⁷⁹, Alexie Bosch⁷⁹, Sabrina Bryant⁷⁹, Gaëlle Bourgeois⁷⁹, Ophélie Dos Santos Schaller⁷⁹, Marie-Christine Carret⁷⁹, Nicolas Ettahar⁸⁰, Haciba Moudjahed⁸¹, Nathalie Leone⁸², Mehdi Djennaoui⁸³, Nicolas Lefebvre⁸⁴, Axel Urnsbach⁸⁴, François Danion⁸⁴, Yvon Ruch⁸⁴, Morgane Solis⁸⁵, Hamid Merdji⁸⁶, Loïc Kassègne⁸⁷, Fanny Pommeret⁸⁸, Emeline Colomba Blameble⁸⁸, Merad Manssouria⁸⁹, Annabelle Stoclin⁸⁹, Franck Griscelli⁹⁰, Sophie Deriaz⁹¹, Eric Ozio⁹¹, Laurent Favier⁹¹, Julien Obiols⁹¹, Pascal Gicquel⁹², Christophe Rapp⁹³, Laurence Louve⁹³, Paul Ihout⁹³, Jean-Benoit Zabbé⁹⁴, Laurent Bellec⁹⁵, Tomasz Chroboczek⁹⁶, Sandrine Mégessier⁹⁶, Marie Lacoste⁹⁶, Benjamin Viala⁹⁶, Thibaut Challan-Belval⁹⁶, Chloé Wackenheim⁹⁶, Paule Letertre-Gibert⁹⁶, Olivier Grossi⁹⁷

¹Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; ²Institut Toulousain des Maladies Infectieuses et Inflammatoires (Infinity), INSERM UMR1291—CNRS UMR5051—Université Toulouse III, Toulouse, France; ³Service des Maladies Infectieuses et Tropicales, Hôpital Bichat-Claude-Bernard, APHP, Paris, France; ⁴Sorbonne Université, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (IPLESP), Paris, France; ⁵Service de Virologie, Université de Paris, INSERM, IAME, UMR 1137, AP-HP, Hôpital Bichat-Claude Bernard, F-75018 Paris, France; ⁶Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Rennes, Rennes, France; ⁷Service des Maladies Infectieuses et Tropicales, Hospices Civils de Lyon, Lyon, France; ⁸Service des Maladies Infectieuses et Tropicales, Hôpital Avicenne, AP-HP, Bobigny, France; ⁹Service des Maladies Infectieuses et Tropicales, Hôpital Tenon, APHP, Paris, France; ¹⁰Service des Maladies infectieuses et tropicales, Hôpital Saint-Antoine, APHP, Paris, France; ¹¹Service de Médecine Interne, Hôpital Ambroise Paré, APHP, Boulogne-Billancourt, France; ¹²Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Nîmes, Nîmes, France; ¹³Univ. Lille, Inserm U1285, CHU Lille, Pôle de médecine intensive réanimation, CNRS, UMR 8576—UGSF—Unité de Glycobiologie Structurale et Fonctionnelle, F-59000 Lille, France; ¹⁴Département de Gériatrie, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; ¹⁵Département de Néphrologie, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; ¹⁶Service de Réanimation, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; ¹⁷Service de Pneumologie, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; ¹⁸Laboratoire de Virologie, Centre Hospitalier Universitaire de Toulouse, Toulouse, France; ¹⁹Laboratoire de Virologie, Hospices Civils de Lyon, Lyon, France; ²⁰Service de Réanimation, Hospices Civils de Lyon, Lyon, France; ²¹Laboratoire de Virologie, Hôpital Avicenne, AP-HP, Bobigny, France; ²²Service de Pneumologie, Hôpital Avicenne, AP-HP, Bobigny, France; ²³Service de Réanimation, Hôpital Avicenne, AP-HP, Bobigny, France; ²⁴Service de Médecine Interne, Hôpital Avicenne, AP-HP, Bobigny, France; ²⁵Service des Urgences et SAMU 93, Hôpital Avicenne, AP-HP, Bobigny, France; ²⁶Service de Réanimation, Hôpital Tenon, APHP, Paris, France; ²⁷Service de Pneumologie, Hôpital Tenon, APHP, Paris, France; ²⁸Laboratoire de Virologie, Hôpital Tenon, APHP, Paris, France; ²⁹Service de Réanimation, Hôpital Ambroise Paré, APHP, Boulogne-Billancourt, France; ³⁰Service de Réanimation, Centre Hospitalier Universitaire de Nîmes, Nîmes, France; ³¹Service des Maladies Infectieuses, Centre Hospitalier Universitaire de Lille, Lille, France; ³²Laboratoire de Virologie, Centre Hospitalier Universitaire de Lille, Lille, France; ³³Service des Maladies Infectieuses, CHU de Reims, Reims, France; ³⁴Service de Maladies Infectieuses et Tropicales, Centre Hospitalier Sud Francilien, Corbeil, France; ³⁵Service de Réanimation, Centre Hospitalier Sud Francilien, Corbeil, France; ³⁶Service de Pneumologie, Centre Hospitalier Sud Francilien, Corbeil, France; ³⁷Service de Médecine Interne, CH François Quesnay, Mantes, France; ³⁸Service de Maladies Infectieuses et Tropicales, Hôpital intercommunal, Villeneuve St George, France; ³⁹Centre de Recherche Clinique, Hôpital intercommunal, Villeneuve St

George, France; ⁴⁰Unité d'hygiène, Hôpital intercommunal, Villeneuve St George, France; ⁴¹Centre de Recherches Cliniques CHU Amiens Picardie, Amiens, France; ⁴²Service des Maladies Infectieuses, APHP Hôpital Necker, Paris, France; ⁴³Service de Dermatologie et vénéréologie, APHP Hôpital Raymond Poincaré, Garches, France; ⁴⁴Service de Biologie Clinique, Hôpital Foch, Suresnes, France; ⁴⁵Service de Réanimation, Hôpital Foch, Suresnes, France; ⁴⁶Délégation à la Recherche Clinique et à l'Innovation, Hôpital Foch, Suresnes, France; ⁴⁷Service des Maladies Infectieuses, Hôpital St Louis, Paris, France; ⁴⁸Inserm CIC 1424, CHU de Martinique, Fort de France, France; ⁴⁹Service de Réanimation, CHU de Martinique, Fort de France, France; ⁵⁰Service des Maladies Infectieuses, Hôpital Universitaire, Angers, France; ⁵¹Laboratoire de Virologie, Hôpital Universitaire, Angers, France; ⁵²Service de réanimation, Hôpital Universitaire, Angers, France; ⁵³Service de Maladies Infectieuses et Tropicales, CHU Bordeaux, Bordeaux, France; ⁵⁴Laboratoire de Virologie, CHU Bordeaux, Bordeaux, France; ⁵⁵Service de Réanimation, CHU Bordeaux, Bordeaux, France; ⁵⁶Service de Maladies Infectieuses et Tropicales, CHU Limoges, Limoges, France; ⁵⁷Service de Gériatrie, CHU Limoges, Limoges, France; ⁵⁸Laboratoire de Virologie, CHU Limoges, Limoges, France; ⁵⁹Service de Maladies Infectieuses et Tropicales, Hôpital Hôtel-Dieu, Nantes, France; ⁶⁰Service de Réanimation, Hôpital Hôtel-Dieu, Nantes, France; ⁶¹Laboratoire de virologie, Hôpital Hôtel-Dieu, Nantes, France; ⁶²Service d'Infectiologie, Hôpital de l'Archet, CHU de Nice, Hôpital de l'Archet, Nice, France; ⁶³Département d'infectiologie, CHU Dijon, Bourgogne, Dijon, France; ⁶⁴Laboratoire de Virologie : CHU Dijon, Bourgogne, Dijon, France; ⁶⁵Pole de Biologie, CHU Dijon, Bourgogne, Dijon, France; ⁶⁶Service Universitaire des Maladies Infectieuses, Centre hospitalier de Tourcoing, Tourcoing, France; ⁶⁷Service de Maladies Infectieuses et Tropicales, Centre Hospitalier Régional Universitaire de Nancy, Vandoeuvre lès Nancy, France; ⁶⁸Service des Maladies Infectieuses, CHU Rouen, Rouen, France; ⁶⁹Service de Réanimation, CHU Rouen, Rouen, France; ⁷⁰Laboratoire de Virologie, CHU Rouen, Rouen, France; ⁷¹Service de Maladies Infectieuses et Tropicales Hôpitaux Civils de Colmar, Colmar, France; ⁷²Service de Médecine Interne, APHP, Hôpital Beaujon, Clichy, France; ⁷³Service de Médecine Interne, Centre Hospitalier Intercommunal de Créteil, Créteil, France; ⁷⁴Laboratoire de Microbiologie Centre Hospitalier Intercommunal de Créteil, Créteil, France; ⁷⁵Service de Médecine Interne et Maladies Infectieuses, Centre Hospitalier Intercommunal André Grégoire, Montreuil, France; ⁷⁶Service de Réanimation, Centre Hospitalier Intercommunal André Grégoire, Montreuil, France; ⁷⁷Service de Maladies Infectieuses et Tropicales, CH Saint Denis, St Denis, France; ⁷⁸Service de Médecine Interne, Centre Hospitalier Bretagne Atlantique, Vannes, France; ⁷⁹Service des Maladies Infectieuses, Centre Hospitalier Métropole Savoie, Chambéry, France; ⁸⁰Service de Maladies Infectieuses et Tropicales, Centre Hospitalier de Valenciennes, Valenciennes, France; ⁸¹Laboratoire de biologie médicale, Centre Hospitalier de Valenciennes, Valenciennes, France; ⁸²Unité de recherche clinique, Centre Hospitalier de Valenciennes, Valenciennes, France; ⁸³Département d'information médicale, Centre Hospitalier de Valenciennes, Valenciennes, France; ⁸⁴Service des Maladies infectieuses, Hôpitaux Universitaires de Starsbourg, Strasbourg, France; ⁸⁵Laboratoire de Virologie, Hôpitaux Universitaires de Starsbourg, Strasbourg, France; ⁸⁶Service de Réanimation, Hôpitaux Universitaires de Starsbourg, Strasbourg, France; ⁸⁷Service de Pneumologie, Hôpitaux Universitaires de Starsbourg, Strasbourg, France; ⁸⁸Département d'Oncologie Médicale, Gustave Roussy Cancer Campus, Villejuif, France; ⁸⁹Service de Réanimation, Gustave Roussy Cancer Campus, Villejuif, France; ⁹⁰Laboratoire de Virologie, Gustave Roussy Cancer Campus, Villejuif, France; ⁹¹Service de Médecine Interne, Infectiologie Centre Hospitalier de Béziers, Béziers, France; ⁹²Service de Médecine Polyvalente, Centre Hospitalier de Châteaubriant, France; ⁹³Service de Médecine Interne, Hôpital Américain de Paris, Neuilly sur Seine, France; ⁹⁴Service de Maladies Infectieuses et Tropicales, Centre hospitalier de Périgueux, Périgueux, France; ⁹⁵Service d'Infectiologie, Centre Hospitalier du Centre Bretagne, Pontivy, France; ⁹⁶Service de Maladies Infectieuses et Tropicales, Centre Hospitalier Alpes Leman, Contamine sur Arve, France; ⁹⁷Service de Médecine Interne et Infectiologie, Hôpital Privé du Confluent, Nantes, France

Author contributions

GMB, FXL, LA CC, JMC, TP, JP, DD and DC designed the study. GMB, JMC, TP, GG, HC, GP, JP, MT, AB, DL and members of the CoCliCo study group collected the data. LA, FH, MG and DC analyzed the data. All authors interpreted the data. GMB wrote the first version of the manuscript, with contributions from LA, CC, JP, DD and DC. GMB, LA, FH, MG, JP and DC verified the data. All authors had full access to all the data in the study and had final responsibility for the

decision to submit for publication. All authors read and approved the final manuscript.

Funding

The study was funded by the ANRS Maladies Infectieuses Emergentes who had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data and materials

Data requests should be sent to Prof Dominique Costagliola. Data access must be approved by the French data protection authority, la Commission Nationale de l'Informatique et des Libertés. For further information, please see: <https://www.cnil.fr/>.

Declarations

Ethics approval and consent to participate

The study was approved by the National Institutional Review Board of the SPILF (IRB00011642, reference: COVID 2021–05) and was registered on ClinicalTrials.gov (NCT04863547). All methods were performed in accordance with the guidelines and regulations applicable in France for reuse of medical data. All of the data obtained were de-identified, and need to obtain informed consent was waived by the National Institutional Review Board of the French Society of Infectious Diseases (SPILF) due to the retrospective nature of the data collection. However, all participants were informed about the study and had the ability to object to the use of their data.

Consent for publication

Not applicable.

Competing interests

DC reports HIV grants from Janssen (2017–2018, 2019–2020), personal fees from Janssen (2018) and Gilead (2018, 2020) for lectures on HIV outside the submitted work. CC reports personal fees from Janssen (2018), MSD (2019), Gilead (2018–2020), Theratechnologies (2020) and Viiv Healthcare (2018–2020). HC reports personal fees from MSD (2020) and Viiv Healthcare (2020) for lectures on HIV. GMB reports support for attending meetings and personal fees from BMS, MSD, Janssen, Sanofi, Pfizer and Gilead for lectures outside the submitted work. JP reports support for attending meetings and personal fees from Gilead, Pfizer and Eumedica Gilead for lectures. DD reports personal fees from Gilead, Viiv Healthcare and Janssen for participation on an advisory Board. Other authors declare that they have no competing interest.

Author details

¹Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Toulouse, Toulouse, France. ²Institut Toulousain des Maladies Infectieuses et Inflammatoires (Infinity), INSERM UMR1291, CNRS UMR5051, Université Toulouse III, Toulouse, France. ³Service des Maladies Infectieuses et Tropicales, Hôpital Bichat-Claude-Bernard, APHP, Paris, France. ⁴Sorbonne Université, INSERM, Institut Pierre Louis d'Épidémiologie et de Santé Publique (IPLESP), Paris, France. ⁵Service de Virologie, Université de Paris, INSERM, IAME, UMR 1137, AP-HP, Hôpital Bichat-Claude Bernard, 75018 Paris, France. ⁶Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Rennes, Rennes, France. ⁷Service des Maladies Infectieuses et Tropicales, Hospices Civils de Lyon, Lyon, France. ⁸Service des Maladies Infectieuses et Tropicales, Hôpital Avicenne, AP-HP, Bobigny, France. ⁹Service des Maladies Infectieuses et Tropicales, Hôpital Tenon, APHP, Paris, France. ¹⁰Service des Maladies Infectieuses et Tropicales, Hôpital Saint-Antoine, APHP, Paris, France. ¹¹Service de Médecine Interne, Hôpital Ambroise Paré, APHP, Boulogne-Billancourt, France. ¹²Service des Maladies Infectieuses et Tropicales, Centre Hospitalier Universitaire de Nîmes, Nîmes, France. ¹³University of Lille, Inserm U1285, CHU Lille, Pôle de Médecine Intensive Réanimation, CNRS, UMR 8576, UGSF, Unité de Glycobiologie Structurale et Fonctionnelle, 59000 Lille, France.

Received: 30 August 2021 Accepted: 25 April 2022

Published online: 13 June 2022

References

- Available from: https://cov-lineages.org/global_report_B.1.1.7.html.
- Abdool Karim SS, de Oliveira T. New SARS-CoV-2 variants—clinical, public health, and vaccine implications. *N Engl J Med*. 2021. <https://doi.org/10.1056/NEJMc2100362>.
- Davies NG, Abbott S, Barnard RC, Jarvis CI, Kucharski AJ, Munday JD, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science*. 2021;372:6538.
- Gaymard A, Bosetti P, Feri A, Destras G, Enouf V, Andronico A, et al. Early assessment of diffusion and possible expansion of SARS-CoV-2 Lineage 20I/501Y.V1 (B.1.1.7, variant of concern 202012/01) in France, January to March 2021. *Euro Surveill*. 2021. <https://doi.org/10.2807/1560-7917.ES.2021.26.9.2100133>.
- Leung K, Shum MH, Leung GM, Lam TT, Wu JT. Early transmissibility assessment of the N501Y mutant strains of SARS-CoV-2 in the United Kingdom, October to November 2020. *Euro Surveill*. 2021. <https://doi.org/10.2807/1560-7917.ES.2020.26.1.2002106>.
- Zhao S, Lou J, Cao L, Zheng H, Chong MKC, Chen Z, et al. Quantifying the transmission advantage associated with N501Y substitution of SARS-CoV-2 in the UK: an early data-driven analysis. *J Travel Med*. 2021;28(2). <https://doi.org/10.1093/jtm/taab011>.
- Funk T, Pharris A, Spiteri G, Bundle N, Melidou A, Carr M, et al. Characteristics of SARS-CoV-2 variants of concern B.1.1.7, B.1.351 or P.1: data from seven EU/EEA countries, weeks 38/2020 to 10/2021. *Euro Surveill*. 2021;26(16). <https://doi.org/10.2807/1560-7917.ES.2021.26.16.2100348>.
- Nyberg T, Twohig KA, Harris RJ, Seaman SR, Flannagan J, Allen H, et al. Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis. *BMJ*. 2021;373:n1412.
- Challen R, Brooks-Pollock E, Read JM, Dyson L, Tsaneva-Atanasova K, Danon L. Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study. *BMJ*. 2021;372: n579.
- Davies NG, Jarvis CI, Group CC-W, Edmunds WJ, Jewell NP, Diaz-Ordaz K, et al. Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. *Nature*. 2021;593(7858):270–4. <https://doi.org/10.1038/s41586-021-03426-1>.
- Grint DJ, Wing K, Williamson E, McDonald HI, Bhaskaran K, Evans D, et al. Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England, 16 November to 5 February. *Euro Surveill*. 2021. <https://doi.org/10.2807/1560-7917.ES.2021.26.11.2100256>.
- Patone M, Thomas K, Hatch R, Tan PS, Coupland C, Liao W, et al. Mortality and critical care unit admission associated with the SARS-CoV-2 lineage B.1.1.7 in England: an observational cohort study. *Lancet Infect Dis*. 2021. [https://doi.org/10.1016/S1473-3099\(21\)00318-2](https://doi.org/10.1016/S1473-3099(21)00318-2).
- Graham MS, Sudre CH, May A, Antonelli M, Murray B, Varsavsky T, et al. Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. *Lancet Public Health*. 2021;6(5):e335–45. [https://doi.org/10.1016/S2468-2667\(21\)00055-4](https://doi.org/10.1016/S2468-2667(21)00055-4).
- Frampton D, Rampling T, Cross A, Bailey H, Heaney J, Byott M, et al. Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. *Lancet Infect Dis*. 2021. [https://doi.org/10.1016/S1473-3099\(21\)00170-5](https://doi.org/10.1016/S1473-3099(21)00170-5).
- Available from: <https://www.santepubliquefrance.fr/etudes-et-enquetes/enquetes-flash-evaluation-de-la-circulation-des-variants-du-sars-cov-2-en-france>.
- Available from: https://geodes.santepubliquefrance.fr/#c=indicator&f=0&i=covid_hospit.rea&s=2021-06-08&t=a01&view=map2.
- Characterisation WHO/GotC, Management of C-i. A minimal common outcome measure set for COVID-19 clinical research. *Lancet Infect Dis*. 2020;20(8):e192–e7.
- Hung IF, Cheng VC, Wu AK, Tang BS, Chan KH, Chu CM, et al. Viral loads in clinical specimens and SARS manifestations. *Emerg Infect Dis*. 2004;10(9):1550–7.
- Calistri P, Amato L, Puglia I, Cito F, Di Giuseppe A, Danzetta ML, et al. Infection sustained by lineage B.1.1.7 of SARS-CoV-2 is characterised by longer persistence and higher viral RNA loads in nasopharyngeal swabs. *Int J Infect Dis*. 2021;105:753–5.
- Teyssou E, Soulie C, Visseaux B, Lambert-Niclot S, Ferre V, Marot S, et al. The 501Y.V2 SARS-CoV-2 variant has an intermediate viral load between the 501Y.V1 and the historical variants in nasopharyngeal samples from newly diagnosed COVID-19 patients. *J Infect*. 2021;83(1):119–45. <https://doi.org/10.1016/j.jinf.2021.04.023>.
- Ramanathan M, Ferguson ID, Miao W, Khavari PA. SARS-CoV-2 B.1.1.7 and B.1.351 spike variants bind human ACE2 with increased affinity. *Lancet Infect Dis*. 2021;21(8):1070. [https://doi.org/10.1016/S1473-3099\(21\)00262-0](https://doi.org/10.1016/S1473-3099(21)00262-0).

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

