Detecting Rapid Spread of SARS-CoV-2 Variants, France, January 26–February 16, 2021
Stéphanie Haim-Boukobza, Bénédicte Roquebert, Sabine Trombert-Paolantoni, Emmanuel Lecorche, Laura Verdurme, Vincent Fouloungne, Christian Selinger, Yannis Michalakis, Mircea Sofonea, Samuel Alizon

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Since the end of 2020, at least 3 strains, or “variants,” of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) bearing a high number of mutations have been associated with rapid epidemic spread in the United Kingdom (lineage B.1.1.7) (1), South Africa (lineage B.1.351) (2), and Brazil (lineage P.1) (3). Because of their increased transmissibility (4; E. Volz et al., unpub. data, https://www.medrxiv.org/content/10.1101/2020.12.30.20249034v2; A.S. Walker et al., unpub. data, https://www.medrxiv.org/content/10.1101/2021.01.13.21249721v1) and potential ability to evade host immunity (5; S. Cele et al., unpub. data, https://www.medrxiv.org/content/10.1101/2021.01.26.21250224v1), monitoring these variants is crucial in the context of mass vaccination.

In France, beginning February 5, 2021, every sample that tested SARS-CoV-2–positive by reverse transcription PCR (RT-PCR) underwent an additional variant-specific RT-PCR with probes targeting the Δ69–70 deletion and the N501Y mutation, both in the spike glycoprotein. Both targets are present in lineage B.1.1.7. For lineages B.1.351 and P.1, only the N501Y mutation is present. If only the Δ69–70 deletion is detected, the infection might be caused by another variant or by a wild-type strain with a deletion. Finally, if neither target is detected, the infection is considered to be caused by a wild-type strain. These tests are cheaper and easier to implement than full-genome sequencing, which enables their rapid deployment on a wide scale. We report the results of this testing program.

The Study
RT-PCR testing for SARS-CoV-2 strains was conducted using 2 assays, VirSNiP SARS-CoV-2 Spike del+501 (TIB Molbiol, https://www.tib-molbiol.de) and ID SARS-CoV-2/UK/SA Variant Triplex (ID Solutions, https://www.id-solutions.fr), which target the Δ69–70 deletion and N501Y mutation. We performed tests on 42,229 positive samples collected during January 26–February 16, 2021, from 40,777 persons from 12 regions in France. Most samples came from the general population, and 3,323 (7.9%) samples came from hospitals. For the 1,397 patients for whom multiple tests were performed, only the first test was considered. We only included data from persons 5–80 years of age to minimize the weight of preschool children and persons living in aged-care facilities in our analysis. Finally, we removed persons whose age or testing region was unknown. This study was approved by the Institutional Review Board of the CHU of Montpellier and is registered at ClinicalTrials.gov (identifier NCT04738331).

Overall, we analyzed 35,208 SARS-CoV-2–positive samples from the same number of persons (Appendix 1 Table 1, https://wwwnc.cdc.gov/EID/article/27/5/21-0397-App1.xlsx). Results of 6,702 (19%) variant-specific RT-PCR tests were uninterpretable, mainly because of an insufficient amplification of the control, which targets the SARS-CoV-2 Δ69–70 deletion.
lineages B.1.1.7, B.351, and P.1 in regions in France during January 25–February 16, 2021. We did not find any significant difference between the 2 specific RT-PCR kits used, suggesting that similar data collected in France could be pooled. Our results have several practical implications.

In general, we found that many infections screened were caused by variants, especially B.1.1.7, and the trend increased over time. On the basis of our estimates, by February 16, 2021, more than half of SARS-CoV-2 infections in France could have been caused by variants, although with pronounced spatial heterogeneity. In a conservative scenario, where all uninterpretable tests were assumed to be caused by the wild type, most infections would have been caused by variants by the end of week 7 of 2021, and the estimated variants transmission advantage was 36% (95% CI 26%–48%) (Appendix 2, Figure 4).

Variant-positive samples originated from significantly younger patients, which is consistent with an earlier report (E. Volz et al., unpub. data) but contrasts with Davies et al. (4). Our analysis did not enable us to discriminate between epidemiologic effects (e.g., if variants’ transmission chains were seeded in different populations than the wild types), sampling biases, or biologic effects. Additional data might help clarify the biological impact of many of the variants identified in France.

**Table 1. Risk for variant detection estimated using the general linear model in study of rapid spread of severe acute respiratory syndrome coronavirus 2 variants, France, January 26–February 16, 2021**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>OR</th>
<th>2.5% CI</th>
<th>97.5% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date, per day</td>
<td>1.07</td>
<td>1.03</td>
<td>1.11</td>
</tr>
<tr>
<td>Age, per year</td>
<td>0.993</td>
<td>0.992</td>
<td>0.995</td>
</tr>
<tr>
<td>Kit 2</td>
<td>0.94</td>
<td>0.93</td>
<td>1.16</td>
</tr>
<tr>
<td>Nonhospital location</td>
<td>1.25</td>
<td>1.13</td>
<td>1.39</td>
</tr>
</tbody>
</table>

*For categorical variables, reference values are the other kit (1) and the hospital setting. Bold indicates statistical significance. OR, odds ratio.

**Conclusions**

We used 2 variant-specific RT-PCR tests to detect the fraction of infections caused by SARS-CoV-2 lineages B.1.1.7, B.351, and P.1 in regions in France during January 25–February 16, 2021. We did not find any significant difference between the 2 specific RT-PCR kits used, suggesting that similar data collected in France could be pooled. Our results have several practical implications.

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We used 2 variant-specific RT-PCR tests to detect the fraction of infections caused by SARS-CoV-2

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**Figure 1. Estimated variants frequency kinetics in study of rapid spread of severe acute respiratory syndrome coronavirus 2 spread, France, January 26–February 16, 2021.** Triangles indicate the general linear model–fitted values, line indicates output of the logistic growth model estimation, and shading indicates 95% CIs. Overall estimated transmission advantage of the variants (with respect to the wild-type reproduction number) is 50 (95% CI 38%–64%) (Appendix 2, https://wwwnc.cdc.gov/EID/article/27/5/21-0397-App2.pdf). VOC, variant of concern.
from RT-PCR amplification cycles could provide useful insights. Finally, earlier reports have found variant proportion to be associated with higher basic reproduction number (4; E. Volz et al., unpub. data). We found such a trend among regions in France, but it is not statistically significant.

A limitation of this study is that, in spite of its intensity, the sampling was performed retrospectively, which could generate biases if, for instance, transmission chains associated with variants were increasingly sampled. However, we found that samples that originated in hospitals were associated with a lower variant detection. Because testing in the general population is usually performed a week after infection and hospital admissions occur ≈2 weeks after infection (M.T. Sofonea et al., unpub. data, https://www.medrxiv.org/content/10.1101/2020.05.22.20110593v1), we expect hospital data would reflect an older state of the epidemic than screening data. RT-PCR does not have the resolution of full-genome sequencing, and other variants of concern could be underestimated or missed with this approach. However, the time scale considered and the relatively slow evolutionary rate of SARS-CoV-2 make this approach appropriate to monitor variant spread. Furthermore, next-generation sequencing performed on 48 samples showed a strong consistency with the specific RT-PCR tests (Cohen κ of 1 for the TIB Molbiol test and 0.87 or 0.88 for the ID Solutions test depending on the variant; data not shown).

These results illustrate that variant-specific RT-PCRs are an option for SARS-CoV-2 epidemic monitoring because of their affordability and rapid deployment. They also demonstrate that SARS-CoV-2 variants spread in France was faster than anticipated (L.D. Domenico et al., unpub. data, https://www.medrxiv.org/content/10.1101/2021.02.14.21251708v1), which stresses the importance of swift public health responses.

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**About the Author**

Dr. Haim-Boukobza is a virologist and head of the Department of Infectious Disease at Cerba Laboratory, Saint Ouen L’Aumône, France. Her primary research interests are viral hepatitis, human papillomaviruses, and HIV, with additional interests in gut and vaginal microbiomes.

**References**


Rapid Spread of SARS-CoV-2 Variants, France


Address for correspondence: Samuel Alizon, MIVEGEC, CNRS, IRD, Université de Montpellier, 911 av. Agropolis, 34394 Montpellier CEDEX 5, France; email: samuel.alizon@cnrs.fr

December 2020

Zoonotic Infections

- Outbreak of Anthrax Associated with Handling and Eating Meat from a Cow, Uganda, 2018
- Mycoplasma bovis Infections in Free-Ranging Pronghorn, Wyoming, USA
- Control and Prevention of Anthrax, Texas, 2019
- Animal Rabies Surveillance, China, 2004–2018
- Small Particle Aerosol Exposure of African Green Monkeys to MERS-CoV as a Model for Highly Pathogenic Coronavirus Infection
- Coronavirus Disease Model to Inform Transmission-Reducing Measures and Health System Preparedness, Australia
- Genomic Epidemiology of Severe Acute Respiratory Syndrome Coronavirus 2, Colombia
- Flight-Associated Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 Corroborated by Whole-Genome Sequencing
- Risk for Hepatitis E Virus Transmission by Solvent/Detergent–Treated Plasma
- Game Animal Density, Climate, and Tick-Borne Encephalitis in Finland, 2007–2017
- Trends in Population Dynamics of Escherichia coli Sequence Type 131, Calgary, Alberta, Canada 2006–2016 G. Peirano et al. 2907
- Outbreak of Haff Disease along the Yangtze River, Anhui Province, China, 2016
- Equine-Like H3 Avian Influenza Viruses in Wild Birds, Chile
- Clinical and Multimodal Imaging Findings and Risk Factors for Ocular Involvement in a Presumed Waterborne Toxoplasmosis Outbreak, Brazil
- Tuberculosis among Children and Adolescents at HIV Treatment Centers in Sub-Saharan Africa
- Human-Pathogenic Kasokero Virus in Field-Collected Ticks
- Characterization and Source Investigation of Multidrug-Resistant Salmonella Anatum from a Sustained Outbreak, Taiwan
- Human Monocytic Ehrlichiosis, Mexico City, Mexico
- Hantavirus Cardiopulmonary Syndrome in Canada
- Outbreaks of H5N6 Highly Pathogenic Avian Influenza (H5N6) Virus Subclade 2.3.4.4h in Swans, Xinjiang, Western China, 2020
- Differential Tropism of SARS-CoV and SARS-CoV-2 in Bat Cells
- Highly Pathogenic Avian Influenza A(H7N3) Virus in Poultry, United States, 2020
- Sensitive Detection of SARS-CoV-2–Specific Antibodies in Dried Blood Spot Samples
- Antibody Profiles According to Mild or Severe SARS-CoV-2 Infection, Atlanta, Georgia, USA, 2020
- Experimental Infection of Cattle with SARS-CoV-2
- Susceptibility of Raccoon Dogs for Experimental SARS-CoV-2 Infection
- Coyotes as Reservoirs for Onchocerca lupi, United States, 2015–2018
- Direct Transmission of Severe Fever with Thrombocytopenia Syndrome Virus from Domestic Cat to Veterinary Personnel
- Endovascular Infection with Kingella kingae Complicated by Septic Arthritis in Immunocompromised Adult Patient
- Lymphocytic Choriomeningitis Virus Infections and Seroprevalence, Southern Iraq
- Range Expansion of Bombali Virus in Mops condylurus Bats, Kenya
- Novel Rickettsia Species Infecting Dogs, United States
- Detection and Characterization of Bat Sarbecovirus Phylogenetically Related to SARS-CoV-2, Japan

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