Spread of the Delta variant, vaccine effectiveness against PCR-detected infections and within-host viral load dynamics in the community in France

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Abstract
We use a large number of SARS-CoV-2 PCR tests in the community in France from 15th May 2021 to 7th July 2021 and infer 76% vaccine effectiveness against PCR-detected infection, similar effectiveness against Delta and previous variants, a +67% to +217% transmission advantage for Delta depending on the region, and a larger viral load at symptom onset (-2.4 Ct) for Delta variant infections.

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The SARS-CoV-2 variant of concern Delta (clade B.1.617.2), first detected in India, rapidly spread across the world in 2021. Early analyses suggested an estimated transmission advantage of 40-60% over the variant Alpha (clade B.1.1.7) that had become dominant in early 2021 in several European countries (1,2). The Delta variant may be associated with lesser vaccine effectiveness against PCR-detected infection (3) and increased risk of hospitalization after one dose of vaccine (3–5). In France, preliminary results from community testing in the Paris area suggested a prevalence of around 3% in cases on June 1st 2021 and a transmission advantage of +92% with wide confidence intervals compared to the majority Alpha variant (6).

Using data from 132,926 and 51,025 individuals tested by a large private laboratory in the community from 15th May 2021 to 7th July 2021 in two French regions, Provence-Alpes-Côte-d'Azur (PACA) and Ile-de-France (IDF), we investigate the prevalence of Delta, the selective advantage over Alpha, the potential to infect vaccinated individuals, and the viral load of Delta-infected individuals. The Delta variant was identified by PCR targeting the L452R mutation (mostly Delta). The data include self-reported information on whether the individual received two vaccine doses since at least two weeks, or not.

We compared the risk of infection of unvaccinated and vaccinated individuals. In PACA, the positivity rate was 0.0139 in 107,482 unvaccinated and 0.00338 in 25,444 vaccinated individuals, a significant association between infection status and vaccination ($p < 1.e-12$). This amounts to a vaccine effectiveness against PCR-detected infection of 76%, 95% CI [70-80%]. The vaccine effectiveness against PCR-detected Delta infection was 69% [51-81%] and against non-delta infection was 67% [44-80%]. The slightly lower number for variant-specific effectiveness is explained by the smaller number of individuals with variant information, but the confidence intervals largely overlap. We could not calculate the equivalent numbers in IDF as information on vaccination was not consistently reported in this region.

We used a logistic model of confirmed infection by the Delta variant vs others (mainly Alpha; therefore hereafter referred to as Alpha) against time, with vaccination status and age category as covariates. The selection coefficient is the difference in exponential growth rates between Delta and others, and obtained directly from the coefficient of the logistic model. It was estimated at 0.19 per day [0.152-0.232] ($p < 1.e-12$, $N = 475$) in PACA and 0.096 per day [0.0297-0.165] ($p = 0.0044$, $N = 271$) in IDF (Figure 1A-B). We translated these numbers into a transmission advantage using daily cases time series in PACA and IDF, assuming a constant exponential growth rate, a gamma-distributed generation time with mean 6.5 days and s.d. 4 days, and same distribution of generation time in Delta and Alpha. The observed selection

coefficient amounts to a +177% [162-221%] (resp. +126% [115-137%]) transmission advantage for the Delta variant compared to others in PACA and IDF respectively.

In a second linear model, we regressed the cycle threshold (Ct) of the PCR (targeted at gene RdRp) against variant, controlling for time since symptoms and age category in N=158 symptomatic cases in PACA. We could not do the corresponding analysis in IDF for lack of information on time since symptoms. The Ct is the number of PCR cycles needed to detect a target; it is negatively correlated with viral load. It is important to control for symptoms because the age of infection hence the Ct of randomly tested individuals depends on the epidemic growth rate and could thus vary for this reason across variants (7). Indeed, the distribution of Ct value not controlling for the time since symptoms was very distinct in Delta and Alpha, confirming epidemic growth for Delta and decline for Alpha and in line with epidemiological data (Supplementary Figure). We found that the Delta variant has Ct at day of symptoms 2.41 [0.24-4.57] lower than Alpha ($p = 0.032$, $N = 158$), with Ct at symptom onset at 19.7 [16.4-23] for alpha, 17.3 [15-19.7] for delta, and slope of Ct as a function of time of -1.11 [-1.44, -0.79] per day (Figure 1C).

In conclusion, we used community testing data to monitor the spread of the Delta variant in two French regions. We inferred a transmission advantage of 177% and 126 %, much larger than the transmission advantage Alpha had over previous variants. To confirm this large advantage, we used additional public data from Santé Publique France (8), gathering all tests conducted in all French regions. We found across regions a transmission advantage of 67 to 217% and a doubling time of 9.8 to 3.9 days (Figure 1D, Table 1) for Delta, confirming our results. The vaccine effectiveness against PCR-detected infection was at least 76%. We did not detect, contrary to previous results from a population cohort in Scotland (3), a reduced effectiveness of vaccines against PCR-detected infections by Delta. We consider 76% as a lower bound on vaccine effectiveness for two reasons. We use self-reported vaccination status, and errors in the reporting would bias downwards the inferred vaccine effectiveness. Moreover, individuals may be less likely to get tested when they are vaccinated, and may get tested only when they are highly likely to be infected (e.g. have specific symptoms). This would artificially increase the positivity rate among vaccinated individuals and bias downwards our estimate of vaccine effectiveness. Other limitations include the self-reported date of symptom onset, and the fact that the reasons why individuals get tested was unknown (e.g. contact with a case, travel, etc.). Additionally, more intensive contact tracing for infections with Delta could have biased upwards its inferred transmission advantage. The rise of the Delta variant, substantially more transmissible than Alpha which was already more transmissible than historical strains in France (9), threatens epidemic control but increasing the fraction of individuals who are fully vaccinated would limit its spread in the community.

1. Campbell F, Archer B, Laurenson-Schafer H, Jinnai Y, Konings F, Batra N, et al. Increased transmissibility and global spread of SARS-CoV-2 variants of concern as at June 2021. Eurosurveillance. 2021 Jun 17;26(24):2100509.

2. SPI-M-O: Consensus statement on COVID-19, 3 June 2021 [Internet]. GOV.UK. [cited 2021 Jun 28]. Available from: https://www.gov.uk/government/publications/spi-m-o-consensus-statement-on-covid-19-3-june-2021

3. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. The Lancet. 2021 Jun 26;397(10293):2461–2.

4. Public Health England. SARS-CoV-2 variants of concern and variants under investigation in England. Technical Briefing 16 [Internet]. 2021 Jun [cited 2021 Jun 28]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/994997/Variants_of_Concern_VOC_Technical_Briefing_16.pdf

5. European Centre for Disease Prevention and Control. Implications for the EU/EEA on the spread of the SARS-CoV-2 Delta (B.1.617.2) variant of concern [Internet]. Stockholm: ECDC; 2021 Jun [cited 2021 Jun 28]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/Implications-for-the-EU-EEA-on-the-spread-of-SARS-CoV-2-Delta-VOC-23-June-2021_2.pdf

6. Alizon S, Haim-Boukobza S, Foulongne V, Verdurme L, Trombert-Paolantoni S, Lecorche E, et al. Rapid spread of the SARS-CoV-2 δ variant in the area of Paris (France) in June 2021. medRxiv. 2021 Jun 20;2021.06.16.21259052.

7. Hay JA, Kennedy-Shaffer L, Kanjilal S, Lennon NJ, Gabriel SB, Lipsitch M, et al. Estimating epidemiologic dynamics from cross-sectional viral load distributions. Science [Internet]. 2021 Jun 3 [cited 2021 Jun 28]; Available from: https://science.sciencemag.org/content/early/2021/06/02/science.abh0635

8. Santé Publique France. Données de laboratoires pour le dépistage : Indicateurs sur les mutations (SI-DEP) - data.gouv.fr [Internet]. [cited 2021 Jul 16]. Available from: https://www.data.gouv.fr/fr/datasets/donnees-de-laboratoires-pour-le-depistage-indicateurs-sur-les-mutations/

9. 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. Eurosurveillance. 2021 Mar 4;26(9):2100133.

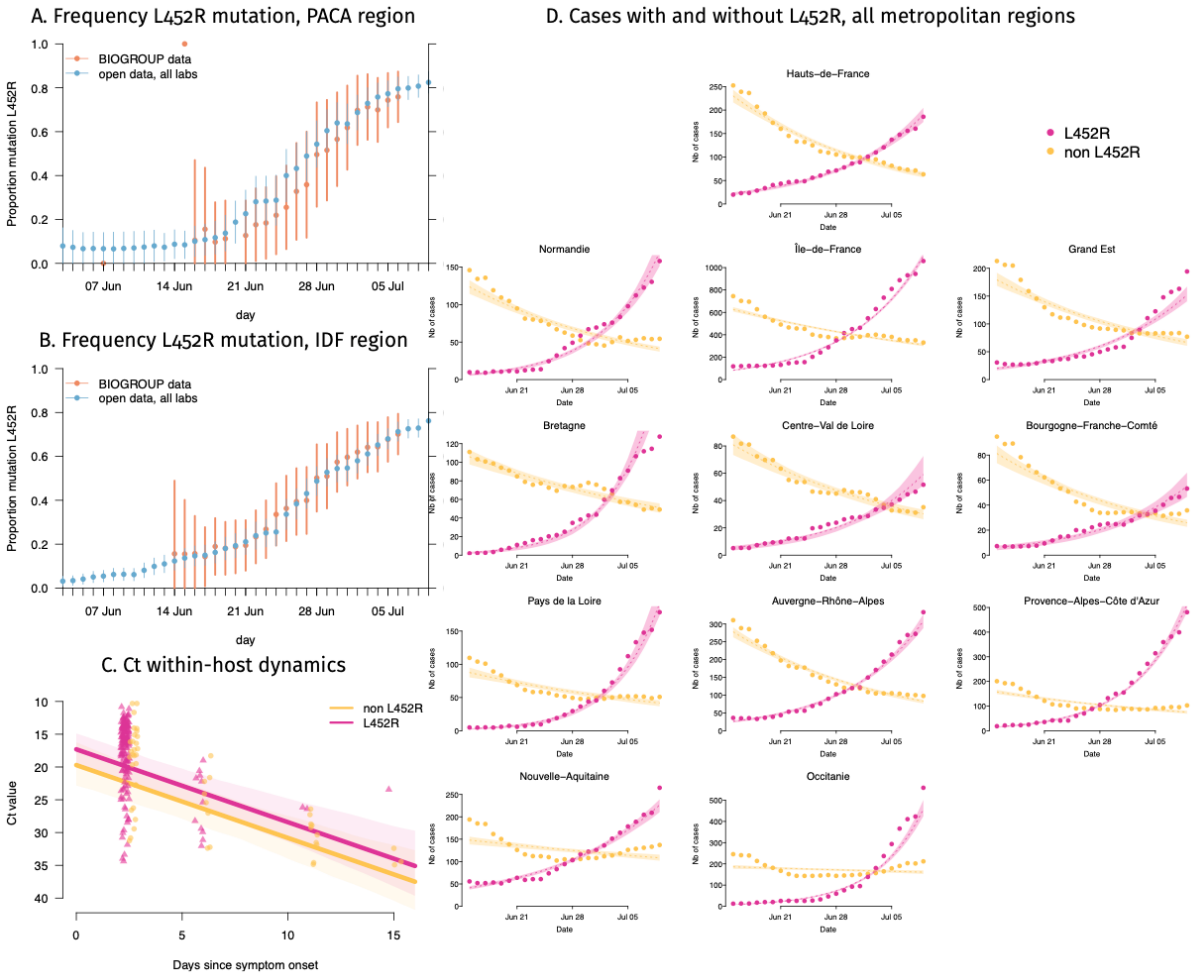
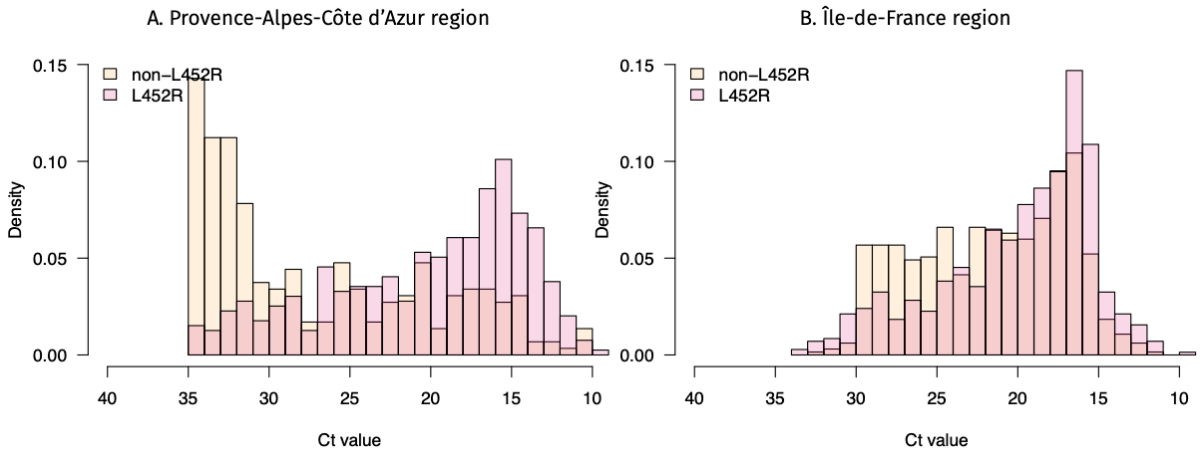


Figure 1: Panels A and B, the frequency of the L452R mutation (characteristic of the Delta variant) as a function of time, in PACA (A) and IDF (B). The frequency obtained from Santé Publique France data, which gathers PCR screening data from several large laboratories, is shown in blue for comparison. Panel C, the within-host dynamics of Ct for L452R and non-L452R infections controlling for time since symptom onset. Points show the data, lines show the linear regression. Panel D, the dynamics of L452R and non-L452R cases over time by French region. The points show the data, the lines an exponential growth model fit with 95% CI.

Region	s (CI)	R advantage (CI)	L452R doubling time (CI)
Auvergne-Rhône-Alpes	0.15 (0.14-0.16)	1.57 (1.45-1.71)	6.8 (6.3-7.2)
Hauts-de-France	0.14 (0.13-0.15)	1.45 (1.33-1.59)	7.8 (7-8.4)
Provence-Alpes-Côte d'Azur	0.17 (0.16-0.18)	1.77 (1.65-1.96)	4.7 (4.4-5)
Grand Est	0.13 (0.12-0.14)	1.18 (1.06-1.33)	8.2 (7.4-8.9)
Occitanie	0.17 (0.16-0.19)	1.57 (1.46-1.72)	4.2 (3.9-4.4)
Normandie	0.17 (0.15-0.19)	1.92 (1.77-2.21)	5.2 (4.6-5.5)
Nouvelle-Aquitaine	0.082 (0.072-0.092)	0.666 (0.599-0.735)	9.8 (9.1-11)
Centre-Val de Loire	0.13 (0.11-0.16)	1.34 (1.18-1.74)	7.1 (5.6-8)
Bourgogne-Franche-Comté	0.13 (0.11-0.15)	1.37 (1.18-1.71)	7.6 (6-8.8)
Bretagne	0.18 (0.16-0.21)	2.17 (1.98-2.74)	3.9 (3.3-4.3)
Pays de la Loire	0.2 (0.18-0.22)	2.15 (1.95-2.63)	4 (3.4-4.3)
Île-de-France	0.14 (0.13-0.14)	1.26 (1.21-1.31)	6.4 (6.3-6.6)

Table 1: For each French region, the inferred selection coefficient s per day, transmission advantage ("R advantage") and doubling time in days of L452R mutations (Delta variant) against others. Data from Santé Publique France.



Supplementary Figure: The distribution of Ct values in L452R and non-L452R PCR-detected infections, without control for time since symptom onset. The large number of high viral loads (low Ct value) partly reflects epidemic growth.