Impact of booster vaccination on the control of COVID-19 in the context of waning immunity: Application to France in the autumn-winter 2021-2022

Paolo Bosetti, Cécile Tran Kiem, Alessio Andronico, Juliette Paireau, Daniel Levy-Bruhl, Lise Alter, Arnaud Fontanet, Simon Cauchemez

Impact of booster vaccination on the control of COVID-19 in the context of waning immunity: Application to France in the autumn-winter 2021-2022

Authors: Paolo Bosetti[1*], Cécile Tran Kiem[1,2*], Alessio Andronico[1], Juliette Paireau[1,3], Daniel Levy-Bruhl[3], Lise Alter[4], Arnaud Fontanet[5,6], Simon Cauchemez[1]

Affiliations:

1. Mathematical Modelling of Infectious Diseases Unit, Institut Pasteur, Université de Paris, CNRS UMR2000, Paris, France
2. Collège Doctoral, Sorbonne Université, Paris, France
3. Santé publique France, French National Public Health Agency, Saint-Maurice, France
4. Haute Autorité de Santé, Paris, France
5. Emerging Diseases Epidemiology Unit, Institut Pasteur, Université de Paris, Paris, France
6. PACRI Unit, Conservatoire National des Arts et Métiers, Paris, France

[*] These authors contributed equally to this work

Corresponding author:

Simon Cauchemez

Mathematical Modelling of Infectious Diseases Unit

Institut Pasteur,

28 rue du Dr Roux,

75015, Paris, France

simon.cauchemez@pasteur.fr

Abstract

Europe is confronted with a large COVID-19 wave caused by the Delta variant in autumn-winter 2021-2022. Using a mathematical model applied to Metropolitan France, we find that the hospitalisation peak might be reduced by 25%, 36% and 43% if boosters are administered to those aged 65+, 50+ or 18+, respectively, with a delay of 5 months between the second and third dose. Ten percent reduction in transmission rates might further reduce peak size by 41%, indicating that even small increases in protective behaviours may play a critical role to mitigate the wave.

Most European countries have experienced an important rise in SARS-CoV-2 infections and hospitalisations in the Autumn 2021. In response to this resurgence and to the reported partial decay of immunity, countries have started administering vaccine booster doses, relying on different eligibility criteria. Here, we present modelling analyses assessing different administration strategies for booster doses that informed the recommendations of the French National Immunization Technical Advisory Group (Haute Autorité de Santé) in the context of Metropolitan France.

Modelling immunity and the impact of vaccines

We extended a model presented in detail by Bosetti et al.[1]. We account for age-specific mixing patterns[2] and a lower susceptibility to SARS-CoV-2 infection in children (0-9 y.o. and 10-17 y.o. respectively 50% and 25% less susceptible than 18+)[3,4]. The model considers the epidemic wave due to the Delta variant and does not capture the future impact of the Omicron variant.

Our model explicitly accounts for the decay of vaccine effectiveness[5] (Figure 1). In our baseline scenario, we assume that, after 6 months on average, vaccine effectiveness against infection decreases from 80% to 50% [5] and vaccine effectiveness against hospitalisation decreases from 95% to 85%. In a more pessimistic scenario, vaccine effectiveness against infection decreases to 30% whereas protection against hospitalisation decreases to 80% in those <65 y.o and to 70% in 65+.

We assume that, 7 days after receiving a booster dose, effectiveness against infection and hospitalization is 95%. After 6 months on average, protection against infection drops to 85% (protection against hospitalisation remains constant). We also explore a scenario in which the booster confers 99% protection against hospitalisation. In all scenarios, we assume that vaccinated individuals (with or without a booster dose) and individuals previously infectedare half as infectious as individuals with no prior history of infection or vaccination.

We assume that infected individuals that have not been vaccinated are fully protected against reinfection for 3 months on average. After this, their protection against infection moves to 85% and, after 6 additional months on average, to 60% (protection against hospitalization moves to 90% and 85%).

Administration of vaccine doses

We assume that individuals are eligible for a booster dose i) 4, 5 (baseline) or 6 months after their second dose and ii) if they are aged 65+, 50+ or 18+. Among eligible individuals, we assume that 80% of 50+ and 50% of 18-49 y.o accept the booster dose. We also explore a scenario with an acceptance of 95% for all. We assume that at most 400 000 or 600 000 doses are administered per day. The future roll-out of second doses is captured with an exponential decrease model (see Supplement).

Children aged 5-11 y.o. remain unvaccinated in our baseline scenario. In a sensitivity analysis, this age group is vaccinated from December 15th, 2021 at a pace of 50 000 first doses per day with an acceptance of 70%, regardless of the booster roll-out pace

Epidemiological scenarios during winter

In our baseline scenario, we assume that the reproduction number R_0 (mean number of persons infected by a case with current control measures if there was no population immunity) will remain equal to the one we estimated between November 2nd and November 22nd, 2021 (R_0=4.8 (95%CrI: 4.6-5.0)). In sensitivity analyses, we assume transmission rates decrease by 10% and 20% from December 1st, 2021 as the population compliance to protective behaviours increases and the government strengthens non-pharmaceutical measures in response to the epidemic rise. All scenarios account for seasonal variations (33% amplitude in R_0 between summer and winter)[6]. We assume that the hospitalisation probability for Delta VOC increases by 50% compared to Alpha VOC [7], whereas Alpha VOC is 42% more severe than previously circulating strains [8]. A detailed description of the model and parameters is reported in the Supplement.

Strategies targeting different age groups

In our baseline scenario, we therefore assume i) constant R_0 in the coming weeks; ii) a minimum 5 months delay between the second and third dose; iii) a maximum of 400,000 doses administered per day from December 1st, 2021; iv) an acceptance of 80% and 50% among 50+ and 18-49 y.o., respectively.

If no booster doses are distributed to the population, we anticipate a peak of 4,140 daily hospital admissions and a cumulative number of 380,000 hospitalisations between November 1st, 2021 and May 1st, 2022 (Figure 2A). However, if boosters are distributed to those aged 65+, 50+ or 18+, the hospitalisation peak is reduced by 25%, 36% and 43%, respectively, and the cumulative number of hospitalisations by 23%, 33% and 44%, respectively (Figure 2A).

Strengthening protective behaviours

When 18+ individuals are eligible for a booster, reducing R_0 by 10% and 20% from December 1st leads to a reduction in the hospitalisation peak of 41% and 60%, respectively, and a reduction in the cumulative number of hospitalisations of 34% and 59%, respectively, relative to the scenario without reduction in R_0 (Figures 2B-C).

Logistical characteristics of campaign

The reduction in the hospitalisation peak increases from 35% for a delay between the second and third dose of 6 months, to 43% for a delay of 4 or 5 months (Figures 3A). Further impact can be achieved by increasing the number of doses administered daily along with acceptance to the booster. For at most 600 000 doses administered daily and an acceptance of 95% among 18+, the reduction of peak size and of the cumulative number of hospitalisations is 50% and 54%, respectively (Figures 3B; compared to 43% and 44%, respectively, in our baseline scenario).

Vaccine effectiveness

For more pessimistic assumptions about immunity decay, we expect a larger peak size in the absence of boosters, and a larger relative reduction of peak size induced by the booster (61% compared to 43% in the baseline scenario when 18+ are targeted; Figure 3C). A more effective booster (99% reduction against hospitalisation) would also lead to larger reductions (55% when 18+ are targeted; Figures 3D).

Vaccination of children

Vaccinating 5-11 y.o. children from mid-December would have limited impact on the hospitalisation peak of the current wave (1% reduction compared to a scenario where children are not vaccinated ; Figure 3E). It would reduce infections and hospitalisations among 0-9 y.o. by 19% and 20%, respectively, between November 1st 2021 and May 1st 2022. Assumptions regarding the relative infectivity/susceptibility in children (Table S3) can influence our estimates but the impact on the overall peak in hospitalizations remains low in all scenarios.

Discussion

Given the reported immunity decay, we find that the fast administration of booster doses to adults aged 18+ vaccinated at least 5 months ago can substantially mitigate the impact of the current pandemic wave associated with the Delta variant in France. This result is corroborated by the experience of Israel that managed to control a large pandemic wave with such an approach[9].

Administering boosters to all adults has a bigger impact than targeting older adults only because of i) the important decay of protection against infection and ii) the important contribution of young adults to SARS-CoV-2 spread[10]. In this context, increasing their protection reduces community transmission, indirectly protecting frail individuals.

Small reductions in R_0 due to the strengthening of protective behaviours can have an important effect on epidemic dynamics.

While our results may inform recommendations in other European countries, they are sensitive to country-specific features. First, France has achieved high vaccine coverage (about 80% of teenagers and 90% of adults). In countries with lower vaccine coverage, boosting vaccinated individuals should have a more limited impact (since unvaccinated individuals contribute more). Second, the French population was mostly vaccinated with the BNT162b2 vaccine. For vaccines characterized by larger immunity decay, boosting may lead to larger gains. Third, the impact of logistical features (e.g. delay between the second and the third dose, maximum number of doses distributed daily) will depend on the timing of second dose distribution relative to that of the current wave. For example, reducing the delay between doses can provide substantial gains in France because many French people were vaccinated in Summer 2021. Those gains might be more limited if countries achieved high vaccine coverage at a different time.

We find that vaccinating children from mid-December would have little impact on the current hospitalisation wave. This result reflects the late timing of this vaccination with respect to the wave. The impact of vaccinating children could have been substantial if it had started earlier (Figure S4). It is therefore important to anticipate the impact beyond the current Delta wave, particularly with the rise of the Omicron variant[11].

We investigated the impact of boosting on the ongoing Delta-driven pandemic wave. The emergence of the Omicron variant is a cause for concern[11] that will likely add to the burden anticipated for the Delta variant. We will be able to evaluate Omicron impact once its key characteristics (transmissibility, severity, immune escape) have been estimated. In any case, measures available to mitigate the Delta wave (booster doses and strengthening of protective behaviours) will also help delay and mitigate this impact.

Funding: We acknowledge financial support from the Investissement d'Avenir program, the Laboratoire d'Excellence Integrative Biology of Emerging Infectious Diseases program (grant ANR-10-LABX-62-IBEID), HAS, Santé Publique France, the EMERGEN project (ANRS0151), the INCEPTION project (PIA/ANR-16-CONV-0005), the European Union's Horizon 2020 research and innovation program under grant 101003589 (RECOVER) and 874735 (VEO), AXA and Groupama.

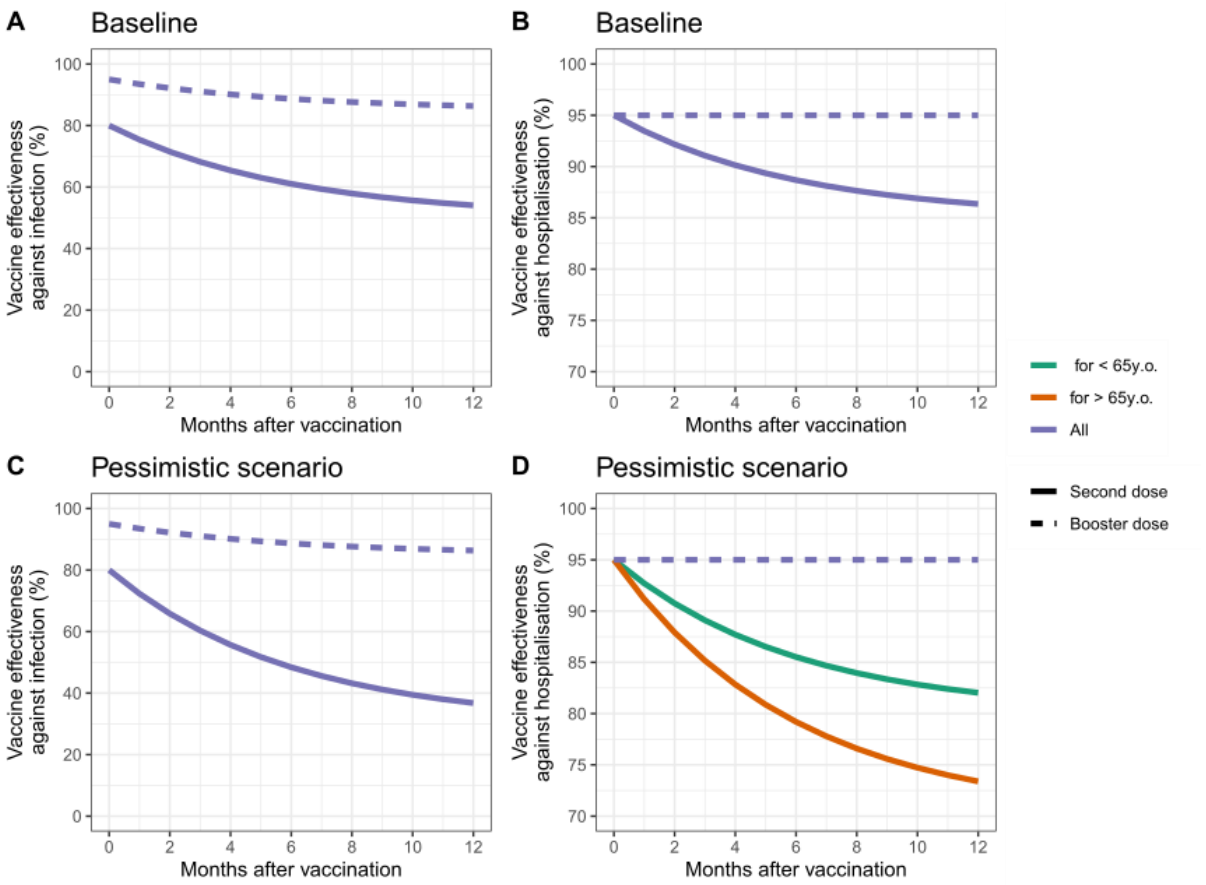

Figure 1: Vaccine effectiveness over time. Vaccine effectiveness after a second dose (plain line) or after a booster (dotted line). **(A)** against infection and **(B)** against hospitalisation in the baseline scenario. **(C)** against infection and **(D)** against hospitalisation in the pessimistic scenario.

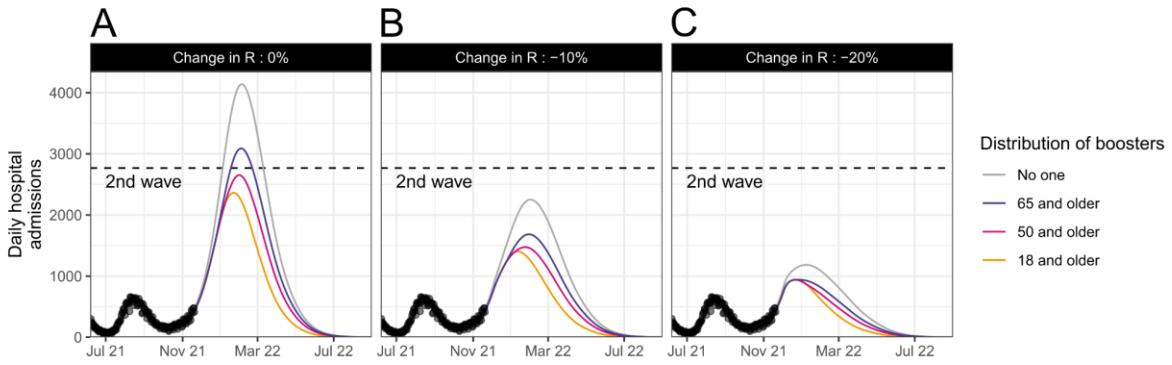

Figure 2: Impact of different boosting strategies on the daily number of hospital admissions. Daily number of hospital admissions assuming transmission rates from December 1st, 2021 **(A)** remain unchanged, **(B)** are reduced by 10% or **(C)** are reduced by 20%. We explore strategies where booster doses are not distributed, distributed in those aged 65 and older only, those aged 50 and older and those aged 18 and older.

Figure 3

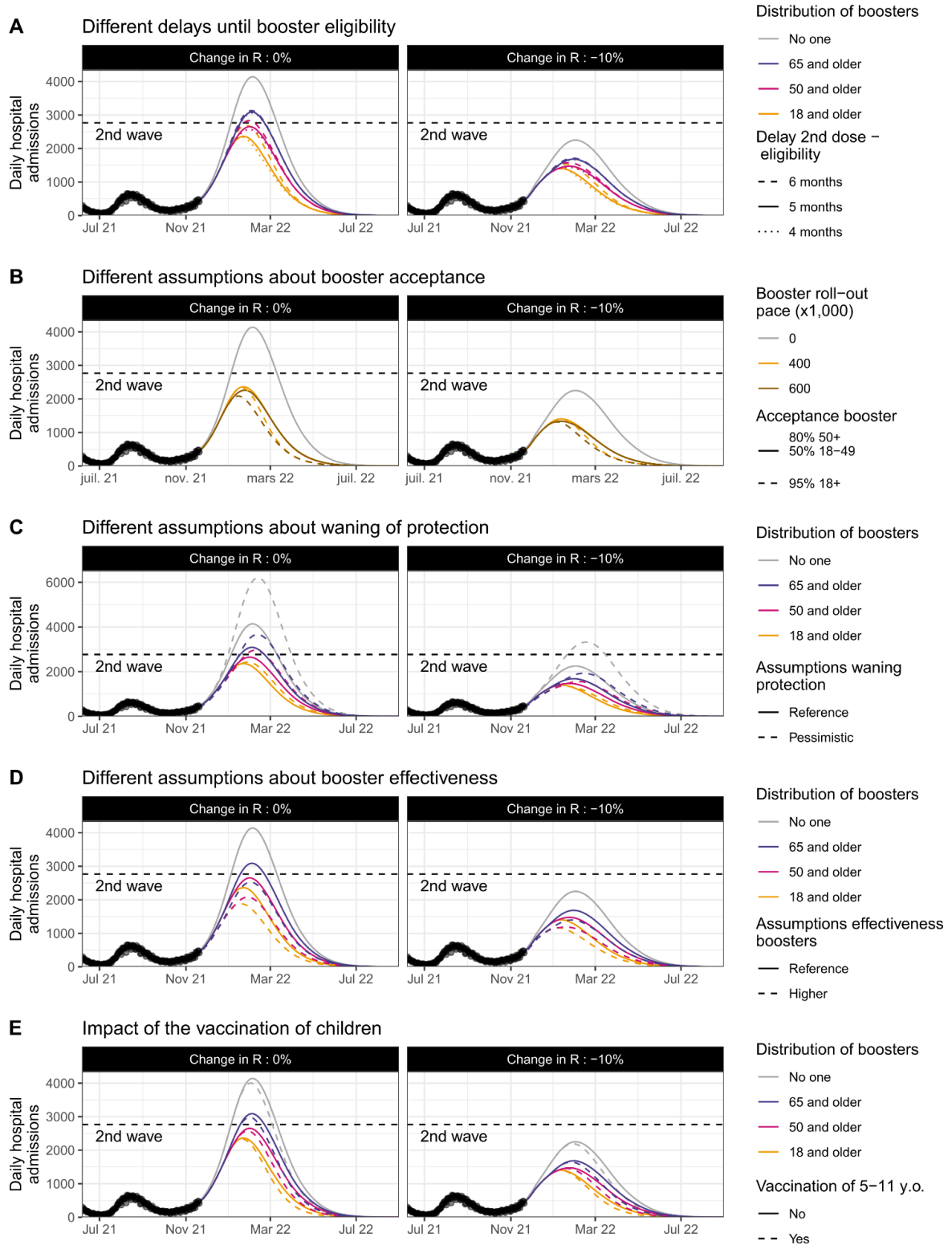

Figure 3: Sensitivity analyses. (A) Impact of changing the delay between receiving a second dose and being eligible for a booster. **(B)** Impact of an increased acceptance of booster doses or a faster roll-out of boosters. **(C)** Impact of more pessimistic assumptions about the waning of protection conferred by vaccination. **(D)** Impact of a higher effectiveness of booster doses.

(E) Impact of the vaccination of children. In (B), the trajectories are presented under the assumption that booster doses are distributed in those aged 18 and older.

References

1 Bosetti P, Tran Kiem C, Andronico A, *et al.* Epidemiology and control of SARS-CoV-2 epidemics in partially vaccinated populations: a modeling study applied to France. 2021; published online Sept 6. https://hal-pasteur.archives-ouvertes.fr/pasteur-03272638/document (accessed Nov 29, 2021).

2 Béraud G, Kazmercziak S, Beutels P, *et al.* The French Connection: The First Large Population-Based Contact Survey in France Relevant for the Spread of Infectious Diseases. *PLoS One* 2015; **10**: e0133203.

3 Viner RM, Mytton OT, Bonell C, *et al.* Susceptibility to SARS-CoV-2 infection amongst children and adolescents compared with adults: a systematic review and meta-analysis. 2020. DOI:10.1001/jamapediatrics.2020.4573 .

4 Davies NG, CMMID COVID-19 working group, Klepac P, *et al.* Age-dependent effects in the transmission and control of COVID-19 epidemics. Nature Medicine. 2020; **26**: 1205–11.

5 Tartof SY, Slezak JM, Fischer H, *et al.* Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study. *Lancet* 2021; **398**: 1407–16.

6 Collin A, Hejblum BP, Vignals C, *et al.* Using Population Based Kalman Estimator to Model COVID-19 Epidemic in France: Estimating the Effects of Non-Pharmaceutical Interventions on the Dynamics of Epidemic. *medRxiv* 2021; : 2021.07.09.21260259.

7 Twohig KA, Nyberg T, Zaidi A, *et al.* Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. *Lancet Infect Dis* 2021; published online Aug 27. DOI:10.1016/S1473-3099(21)00475-8.

8 Bager P, Wohlfahrt J, Fonager J, *et al.* Risk of hospitalisation associated with infection with SARS-CoV-2 lineage B.1.1.7 in Denmark: an observational cohort study. *Lancet Infect Dis* 2021; **21**: 1507–17.

9 Bar-On YM, Goldberg Y, Mandel M, *et al.* Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. *N Engl J Med* 2021; **385**: 1393–400.

10 Tran Kiem C, Bosetti P, Paireau J, *et al.* SARS-CoV-2 transmission across age groups in France and implications for control. *Nat Commun* 2021; **12**: 6895.

11 Pulliam JRC, van Schalkwyk C, Govender N, *et al.* Increased risk of SARS-CoV-2 reinfection associated with emergence of the Omicron variant in South Africa. bioRxiv. 2021; published online Nov 11. DOI:10.1101/2021.11.11.21266068.

Supplementary material of : “Impact of booster vaccination on the control of COVID-19 in the context of waning immunity: Application to France in the autumn-winter 2021-2022”

Model description

We have extended a deterministic age-structured model presented in detail by Bosetti et al. (Bosetti et al. 2021) to account for the progressive waning of protection provided by vaccination (2 doses or booster vaccination) as well as the protection acquired following a SARS-CoV-2 infection. The model accounts for the distribution of SARS-CoV-2 vaccines (distribution of SARS-CoV-2 first and second vaccine doses, i.e. a complete scheme) and the distribution of boosters as well as the impact of climate on the reproduction number.

The flow diagram of the model is depicted in Figure S1.

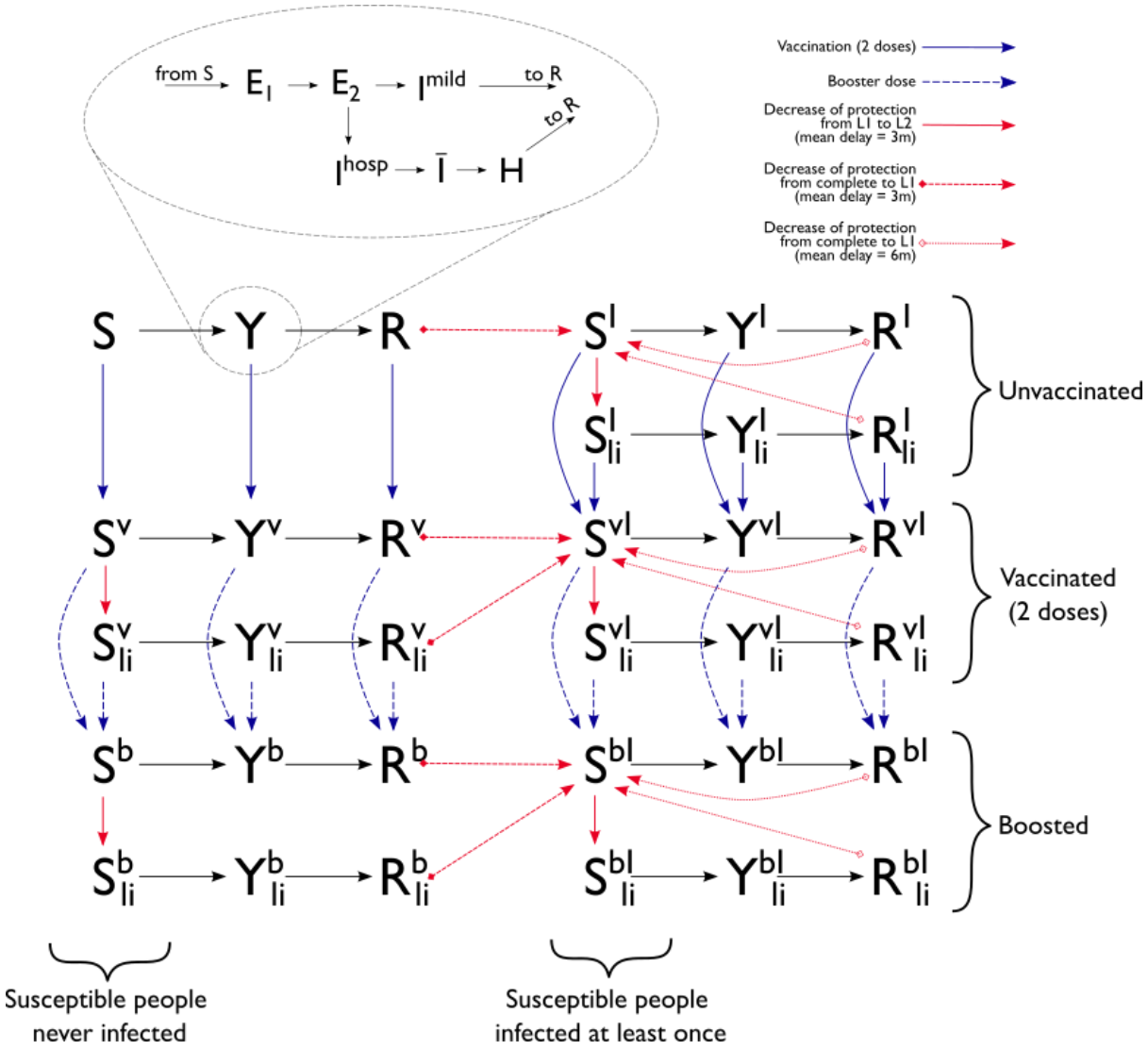

Figure S1. Schematic of the model.

Each path denoted by SYR describes the progression of individuals throughout the different stages of the infection (Salje et al. 2020). Susceptible individuals (S) move to the compartment E_1 upon infection. They remain on average 4.0 days in this compartment before moving to the E_2 compartment, in which they become infectious. In E_2, the average length of stay is 1.0 day. They move to the I compartments (I^{mild} for mild infections or I^{hosp} for infections requiring an hospitalization), where they will stay for an average of 3 days. Individuals in the I^{mild} compartment will eventually move to the recovered compartment (R) while individuals in the I^{hosp} compartment move to the $\bar{I}$ compartment before being admitted in hospital (entry in the compartment H). Finally, Individuals in the H compartment will move to the R compartment after an average delay of 13 days. The average length of stay in the R compartment is 3 months following a primary infection, 6 months following a secondary infection. We account for age-specific probabilities of hospitalization as well as the increased severity associated with the Alpha and Delta VOC. We use probabilities of hospitalization estimated in Lapidus et al. (Lapidus et al. 2021) for the strains circulating in 2020 and assume that Alpha is 42% more severe than historical strains (Bager et al. 2021) and Delta is 50% more severe than Alpha (Twohig et al. 2021).

To account for the different immune status in the population, we consider 11 different SYR paths (starting from ${S^a}_b\ {Y^a}_b\ {R^a}_b$). Individuals without a history of prior vaccination or infection are denoted with the path without a subscript (SYR). The superscripts a in (${S^a}_b\ {Y^a}_b\ {R^a}_b$) indicates the history of prior vaccination, boosting or SARS-CoV-2 infection of the different individuals:

- I indicates compartments where individuals were previously infected but never vaccinated.
- v indicates compartments where individuals were vaccinated (2 doses).
- vI indicates compartments where individuals were previously infected and vaccinated (2 doses).
- b indicates compartments where individuals received a booster dose but were never infected.
- bI indicates compartments where individuals were previously infected and received a booster dose.

The subscript *li* indicates compartments where individuals have partially lost the protection acquired following vaccination, boosting, infection or a combination of these. We assume that the waning of protection occurrs on average 6 months after the acquisition of protection.

Individuals who have been vaccinated/boosted or previously infected who are eventually infected follow the same progression throughout the different disease stages as those without a history of prior infections and vaccination. However, we account for a reduced risk of infection upon contact with an infected individual, a reduced risk of being hospitalized as well a lesser infectivity assuming infection compared to unvaccinated and never-infected individuals (see Table S1, Table S2).

Computing the protection acquired following vaccination through time accounting for waning

Let T be a random variable corresponding to the mean duration before waning of immunity. T follows an exponential distribution with mean $1/\lambda$= 6 months. Let VE_1 and VE_2 respectively denote the levels of vaccine effectiveness before and after waning of vaccine induced protection. The average vaccine effectiveness at time t can be derived as:

$$VE(t) = P[T \leq t] \cdot VE_1 + P[T > t] \cdot VE_2 = (VE_1 - VE_2) \cdot e^{-\lambda t} + VE_2$$

Calibration of the model from February 1st 2020 to June 6th 2021 (historical lineage and alpha VOC periods)

We calibrated our model using the two-step technique outlined in Tran Kiem et al. (Tran Kiem et al. 2021) for the period between February 1st 2020 and June 6th 2021, until the emergence of the Delta VOC in France. To do so, we first fit a one-strain model to daily hospital admissions observed in metropolitan France from February 1st 2020 to January 1st 2021. We then fit a two-strains model to

- daily hospital admissions reported between January 1st, 2021 and June 6th, 2021
- the proportion of cases associated with the Alpha variant obtained from a national survey (Flash)(Santé Publique France 2021)

Assumptions regarding the reduction in the probability of being infected upon contact with an infected individual and the risk of being hospitalized are reported with different immune status in Table S1.

Table S1: Protection acquired following infection or vaccination between February 1st 2020 to June 6th 2021 (strains circulating during 2020 and Alpha variant period).

	Protection against infection		**Protection against hospitalization**	
	Level of protection L1 (before the decay)	**Level of protection L2 (after the decay)** (compartments associated with subscript *li*)	**Level of protection L1 (before the decay)**	**Level of protection L2 (after the decay)** (compartments associated with subscript *li*)
Infected* (Compartments associated with the superscript *I*)	100%	90%	95%	
Vaccinated people (2 doses) (Compartments associated with the superscript *v*)	80%	60%	95%	
Infected + Vaccinated people* (Compartments associated with the superscript *vI*)	100%	95%	95%	

**After the first infection you are fully protected for 3 months before going to the level of protection L1. After a secondary infection you are fully protected for 6 months before going to the level of protection L1.*

Calibration of the model from June 6th 2021 to November 20th 2021 (emergence of Delta)

To account for the rapid spread of the Delta variant in the metropolitan French population, we fit a two-strains (Alpha and Delta) model to the daily number of hospital admissions and the percentage of Delta VOC among all case observed in metropolitan France (Santé publique France 2021), as in the previous stage. The initialization of this two-strain model is achieved by populating the Alpha and Delta compartment proportionally based on the estimated proportion of Delta variant among infections by june 6th, 2021.

We explore two scenarios regarding the waning of protection acquired following vaccination (an optimistic - baseline - scenario and a pessimistic scenario). Assumptions regarding the reduction in the probability of being infected upon contact with an infected individual and the risk of being hospitalized are reported with different immune status in Table S2 during this time-period.

Table S2: Protection acquired following infection or vaccination from June 6th 2021 (Delta period).

		Protection against infection		**protection against hospitalization**	
		Level of protection L1 (before the decay)	**Level of protection L2 (after the decay)** (compartments associated with subscript *li*)	**Level of protection L1 (before the decay)**	**Level of protection L2 (after the decay)** (compartments associated with subscript *li*)
Infected* (Compartments associated with the superscript *I*)	**Optimistic and pessimistic**	85%	60%	90%	85%
Vaccinated people (2 doses) (Compartments associated with the superscript *v*)	**Optimistic (Baseline)**	80%	50%	95%	85%
	Pessimistic	80%	30%	95%	80% for < 65y.o 70% for ≥ 65y.o.
Infected + Vaccinated people* (Compartments associated with the superscript *vI*)	**Optimistic and pessimistic**	95%	85%	95%	

*After the first infection you are fully protected for 3 months before going to the level of protection L1. After a secondary infection (or more) you are fully protected for 6 months before going to the level of protection L1.

Distribution of first vaccine doses

We calibrate an exponential decrease model on the curve of primo-vaccinations by age between October 15th and November 5th, 2021. We assume that the daily number of primo-vaccinations by age will continue to steadily decline at this rate. Figure S2 shows the expected dynamics of the proportion of the people that will receive their first dose of vaccine in the different age groups. By December 31st, 2021, we expect 91% of people over 18 y.o. to be vaccinated, and 79% of those aged 12-17. Among those over 18, the projected proportion of people vaccinated by age is relatively homogeneous, with a maximum of 96% for 75-79 y.o. age group. We calculate the number of second-dose vaccinations based on this evolution by assuming a three-week interval between the first and second dose.

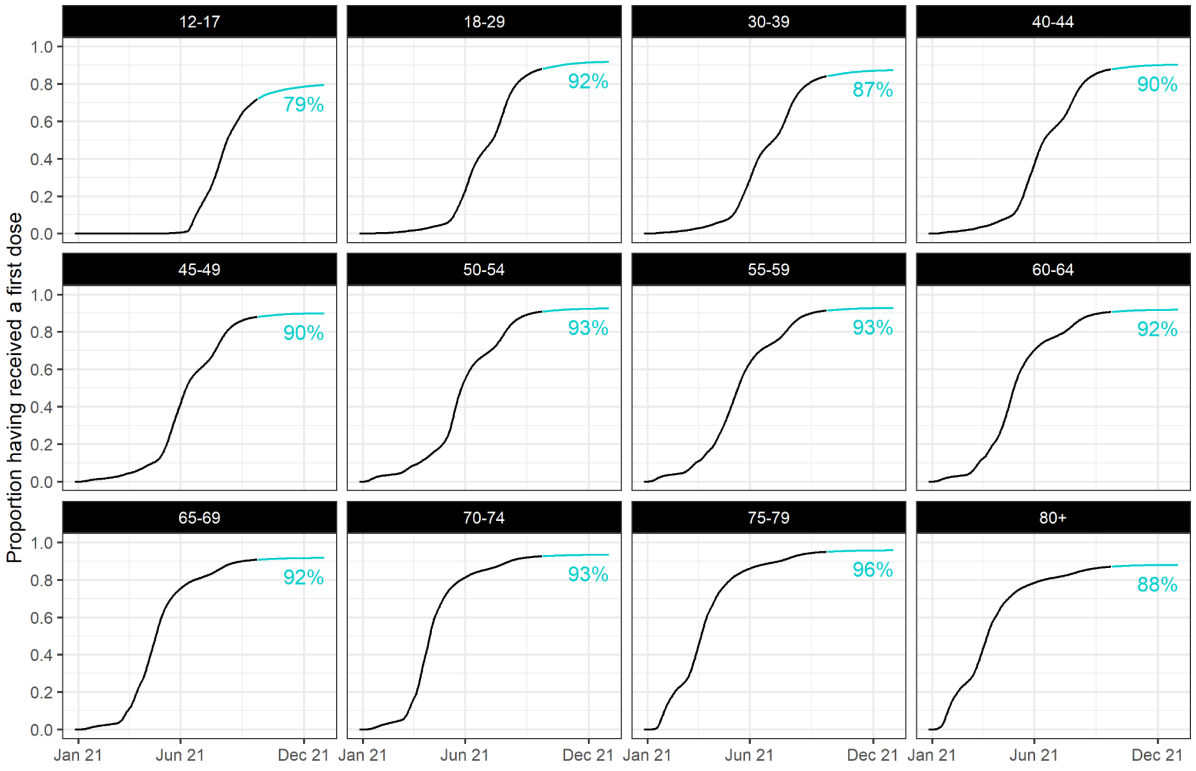

Figure S2: Proportion of the French population having received a first dose in the different age groups by December 31st, 2021. The black lines correspond to the vaccination data and the blue one to the projections using our exponential decrease model. The coverages reported in percent correspond to the predicted proportion having received a first dose in the different age groups by December 31st, 2021.

Eligibility to booster doses

Figure S3 shows the cumulative number of persons that are eligible for a booster dose, under the assumption of a 5-month delay between the second dose and the booster.

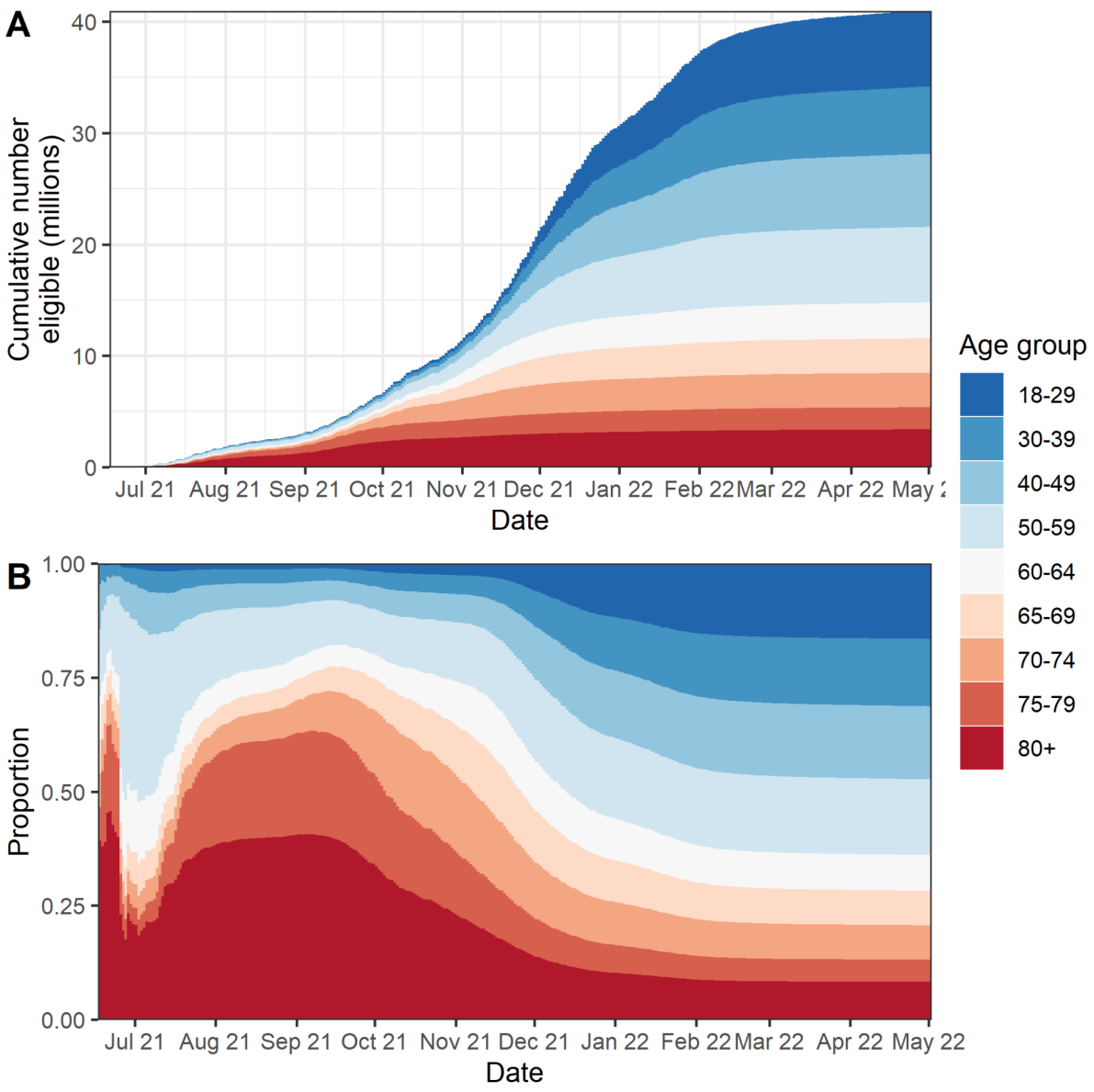

Figure S3: Population eligible to a booster dose assuming a 5 month-delay between second doses and eligibility in metropolitan France. (A) Cumulative number eligible to a booster dose in the different age groups. (B) Proportion of eligible individuals by age group through time.

Counterfactual analysis assuming the vaccination of children started on September 1st, 2021

We present in Figure S4 the retrospective impact the vaccination of children could have had assuming the roll-out of first doses started in children aged 5-11 y.o. on September 1st, 2021 with a vaccine acceptance of 70% in this group and assuming first doses are being administered at a pace of 50,000 per day. In this scenario, the vaccination of children might have reduced hospitalisation peak by 32% and the number of infections and hospitalisations among 0-9 y.o. children by 55% and 61%, respectively. Table S3 shows how these results would be modified under the assumption that children aged 0-9 y.o. are 50% less infectious than adults.

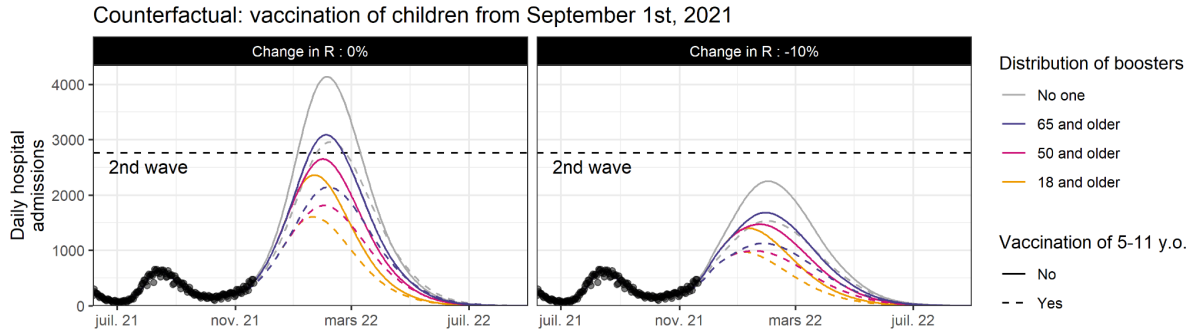

Figure S4: Counterfactual analysis of the impact of initiating the vaccination of children aged 5-11 y.o. on September 1st, 2021. Daily hospital admissions for different groups targeted for the roll-out of boosters (colors) and assuming children are vaccinated are not starting from September 1st, 2021 (dashed/plain lines). We explore scenarios where transmission rates remain unchanged after December 1st, 2021 and where they are reduced by 10%.

Table S3: Sensitivity analysis for the baseline and counterfactual scenario, assuming children aged 0-9 are as infectious, 50% less infectious than adults or only 25% less susceptible than adults compared to 50% in our baseline scenario.

	Reduction of the peak in daily hospital admissions		Reduction of the cumulative number of infections in children aged 0 - 9 y.o.		Reduction of the cumulative number of hospitalizations in children aged 0 - 9 y.o.	
Start of the vaccination in 5-11 y.o.	**Dec 15th (reference)**	**Sep 1st (counterfactual)**	**Dec 15th**	**Sep 1st**	**Dec 15th**	**Sep 1st**
Children as infectious as adults and 50% less susceptible than adults (reference)	1%	32%	19%	56%	20%	61%
Children 50% less infectious than adults and 50% less susceptible than adults	2%	11%	14%	39%	16%	45%
Children as infectious as adults and 25% less susceptible than adults	<1%	46%	7%	51%	7%	56%

References

Bager, Peter, Jan Wohlfahrt, Jannik Fonager, Morten Rasmussen, Mads Albertsen, Thomas Yssing Michaelsen, Camilla Holten Møller, et al. 2021. “Risk of Hospitalisation Associated with Infection with SARS-CoV-2 Lineage B.1.1.7 in Denmark: An Observational Cohort Study.” *The Lancet Infectious Diseases* 21 (11): 1507–17.

Bosetti, Paolo, Cécile Tran Kiem, Alessio Andronico, Vittoria Colizza, Yazdan Yazdanpanah, Arnaud Fontanet, Daniel Benamouzig, and Simon Cauchemez. 2021. “Epidemiology and Control of SARS-CoV-2 Epidemics in Partially Vaccinated Populations: A Modeling Study Applied to France,” September. https://hal-pasteur.archives-ouvertes.fr/pasteur-03272638/document.

Lapidus, Nathanael, Juliette Paireau, Daniel Levy-Bruhl, Xavier de Lamballerie, Gianluca Severi, Mathilde Touvier, Marie Zins, Simon Cauchemez, Fabrice Carrat, and SAPRIS-SERO study group. 2021. “Do Not Neglect SARS-CoV-2 Hospitalization and Fatality Risks in the Middle-Aged Adult Population.” *Infectious Diseases Now* 51 (4): 380–82.

Salje, Henrik, Cécile Tran Kiem, Noémie Lefrancq, Noémie Courtejoie, Paolo Bosetti, Juliette Paireau, Alessio Andronico, et al. 2020. “Estimating the Burden of SARS-CoV-2 in France.” *Science* 369 (6500): 208–11.

Santé Publique France. 2021. “Enquêtes Flash : évaluation de La Circulation Des Variants Du SARS-CoV-2 En France.” 2021. https://www.santepubliquefrance.fr/etudes-et-enquetes/enquetes-flash-evaluation-de-la-circulation-des-variants-du-sars-cov-2-en-france.

Santé publique France. 2021. “Données de Laboratoires Pour Le Dépistage : Indicateurs Sur Les Mutations.” https://www.data.gouv.fr/fr/datasets/donnees-de-laboratoires-pour-le-depistage-indicateurs-sur-les-mutations/.

Tran Kiem, Cécile, Clément R. Massonnaud, Daniel Levy-Bruhl, Chiara Poletto, Vittoria Colizza, Paolo Bosetti, Arnaud Fontanet, et al. 2021. “A Modelling Study Investigating Short and Medium-Term Challenges for COVID-19 Vaccination: From Prioritisation to the Relaxation of Measures.” *EClinicalMedicine* 38 (August): 101001.

Twohig, Katherine A., Tommy Nyberg, Asad Zaidi, Simon Thelwall, Mary A. Sinnathamby, Shirin Aliabadi, Shaun R. Seaman, et al. 2021. “Hospital Admission and Emergency Care Attendance Risk for SARS-CoV-2 Delta (B.1.617.2) Compared with Alpha (B.1.1.7) Variants of Concern: A Cohort Study.” *The Lancet Infectious Diseases*, August. https://doi.org/10.1016/S1473-3099(21)00475-8.