Epidemic scenarios of Delta variant in France in the summer 2021

Report #31 [previous reports at: www.epicx-lab.com/covid-19.html]

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RÉSUMÉ

Alors que le variant Delta progresse rapidement en France, avec environ 43,2% des cas détectés attribués à la mutation L452R au cours de la semaine 26, des inquiétudes surgissent quant à la situation épidémique estivale à venir, compte tenu également du ralentissement signalé des vaccinations. Ce bref rapport vise à présenter une gamme de scénarios épidémiques possibles, selon différentes hypothèses sur les scénarios d'administration de vaccins pendant l'été, les conditions de contact, de saisonnalité et de mesures préventives, et en considérant différentes estimations d'avantage de transmissibilité des variantes préoccupantes.

SUMMARY

As the Delta variant rapidly progresses in France, with an estimated 43.2% of detected cases attributed to the L452R mutation in the week 26, concerns arise on the upcoming summer epidemic situation, also given the reported slowdown of vaccinations. This short report aims at presenting a range of possible epidemic scenarios, according to different hypotheses on vaccine administration rollout in the summer, conditions of mixing, seasonality and preventive measures, and considering different estimates for the transmissibility advantages of the circulating variants of concern.

INTRODUCTION

The Delta variant rapidly progresses in France, with an increase in frequency from 5% in week 23 to 43.2% in week 26 of detected cases attributed to the L452R mutation[1]. After several weeks of decreasing viral circulation, week 26 witnessed a marked increase in the case incidence in the 15-44 years old population[2]. Vaccination considerably slowed down in the last month, with first dose injections decreasing from 2.3 millions per week at the end of May to 1.1 million per week at the beginning of July[3], despite the opening of vaccination to adolescents. With a partially vaccinated population, the higher transmissibility of the Delta variant[4–7] poses a serious risk for a substantial resurgence of cases, as already observed in other countries, and a potentially important stress on healthcare[8].

Using a 2-strain age-stratified transmission model[9–11] integrating vaccination and initialized on current Delta frequency, we examine potential epidemic scenarios based on different hypotheses on vaccine administration rollout in the summer, conditions of mixing, seasonality and preventive measures, and considering different estimates for the transmissibility advantages of the variants of concern.

METHODS

Transmission model. We used the model developed by INSERM to respond to the COVID-19 pandemic[9,12,13]. The model was shown to capture the transmission dynamics of the epidemic[9,12], was used to assess the impact of lockdown, exit strategies and reopening of schools[12,13], to evaluate the performance of the test-trace-isolate strategy[9] and of the curfew against the Alpha variant[10]. The model was validated region by region against the estimates of three independent serological studies conducted in France[9]. It is based on a stochastic age-stratified transmission model, integrating demographic, age profile, and social contact data to account for age-specific contact activity and role in COVID-19 transmission. It integrates mobility data to account for control measures and individual response over time. Disease progression is specific to COVID-19 and parameterized to include presymptomatic transmission, asymptomatic and symptomatic infections with different degrees of severity. Four age classes are considered: [0-11), [11-19), [19-65), and 65+ years old (children, adolescents, adults, seniors). The model is fitted to daily hospital admission data through a maximum likelihood approach. Details of the model can be found in Refs.[9–11].

Alpha and Delta variants. The model considers only the circulation of the Alpha and Delta variants – the two strains accounting for 85.6% of the cases sequenced in France in week 23[14] – and neglects the circulation of other lineages. It is initialized on week 26 with 43.2% of Delta variant, the remaining 56.8% assumed to be Alpha. We considered two parameterizations for the transmissibility advantages of the variants compared to the wild type:

i. Alpha is assumed to be +59% more transmissible than the wild type, based on early estimates in France[15], and Delta +60% more transmissible than Alpha, based on available median estimates[4].
ii. Alpha is assumed to be +59% more transmissible than the wild type, as above, and Delta +120% more transmissible than Alpha, to account for the higher range of the spectrum of the available estimations[4,5].

In addition, in Appendix we also explore transmissibility advantages equal to +29% for Alpha (wrt the wildtype) and +53% for Delta (wrt Alpha), according to a recent global analysis of the variants of concern[6]. These estimates also account for the decrease of the transmissibility advantage of Alpha over time measured in several countries, compared to early estimates.

We remark that this report is not meant to estimate the transmissibility advantage of the Delta variant from virological surveillance data. However, among the three parameterizations explored, only the one with higher transmissibility of Delta is compatible with the rapid growth of Delta frequency reported in France, under the considered model assumptions.

We considered a 60% increase in hospitalization rates for Alpha compared to the wildtype[16], and 85% for Delta compared to Alpha, according to available evidence[17].

Vaccination. The administration of first and second doses of vaccines by age class was included in the model according to the data[3]. By week 26, 16.5% of adolescents, 59.1% of adults, and 85.6% of seniors were vaccinated with at least one dose (1.7%, 37.0%, 77.4%, respectively, with two doses). In the same week, 4.7% of adolescents, 2.2% of adults, and 0.6% of seniors were administered their first dose; 0.7%, 7.1%, and 3.2%, respectively, received their second dose. Starting week 27, we considered four vaccine rollout scenarios (**Figure 1**):

1. **Pessimistic vaccine rollout scenario, corresponding to no vaccination**, i.e. individuals do not get vaccinated over summer, so that vaccination is virtually interrupted. Even if unrealistic, this is considered here as a worst case scenario, and a benchmark against which other scenarios are evaluated.
2. **Current vaccine rollout, corresponding to recently observed trends**: the total number of vaccines administered per day is at most equal to the value recorded in the last week of data (week 26), and the temporal dynamics of first and second dose vaccinations follows the trends observed in the last three weeks. This scenario does not consider a possible change of attitude of the population towards vaccination, that may occur in light of the current epidemic situation and the recent recommendations of health authorities.
3. **Constant vaccine rollout, assuming it remains constant and equal to last week:** the total number of vaccines administered per day is at most equal to the value recorded in the last week of data (week 26), as above, but the temporal dynamics of first dose vaccinations is constant in time and equal to the value recorded in the last week. This is considered to be optimistic with respect to the recently observed data showing a continuous drop in first doses.
4. **Optimistic vaccine rollout, assuming an increase of 1st doses:** starting from vaccination recorded in week 26, we assume a rebound in vaccination behavior corresponding to a linear increase of 10% of first doses over time. This trend is kept throughout the simulation time. Second doses are administered with a 3-week delay from first doses.

Since 1st-dose administrations have been decreasing in the weeks 23-26 in France (**Figure 1**), the current vaccine rollout scenario (#2) foresees that this rapid decrease continues in time. At the end of the summer, only few additional doses are administered in this scenario compared to the pessimistic vaccine rollout scenario (#1). The constant rollout scenario (#3) assumes instead a constant administration of doses per day from week 27, i.e. the drop is stopped and a change of tendency is considered for the upcoming weeks. The optimistic rollout scenario (#4) assumes a surge in vaccination behavior in the upcoming weeks due for example to health authorities' recommendations, possible novel policies, and increased risk perception induced by the rapid Delta spread.

Maximum coverage by age class is set at 70% for adults and 90% for seniors in the current and the constant vaccine rollout scenarios (#2 and #3), based on most recent survey data on the percentage of individuals being vaccinated or who intend to get vaccinated[18]. The optimistic rollout (#4) considers a higher maximum coverage in adults, set at 80%, assuming that the current epidemic situation with the rapid spread of the Delta variant would not only lead to a surge in vaccinations but also induce a larger portion of the adult population to get vaccinated. We assume that at most 50% of adolescents would get vaccinated in this scenario.

For Alpha, we consider 56% vaccine effectiveness against infection and 95% vaccine effectiveness against symptomatic disease after 2 weeks from the first injection of vaccine Pfizer[19,20], the most common vaccine used in France (>75% as of June 2021). Effectiveness mounts to 92% and 97%, respectively, 2 weeks after the second dose[17,20]. Vaccine effectiveness related to Delta are assumed to be the same as Alpha, except for a 79% effectiveness against infection after 2 doses, estimated to be lower with respect to the vaccine effectiveness against Alpha[17]. We further consider 50% vaccine efficacy against transmission, for both strains.

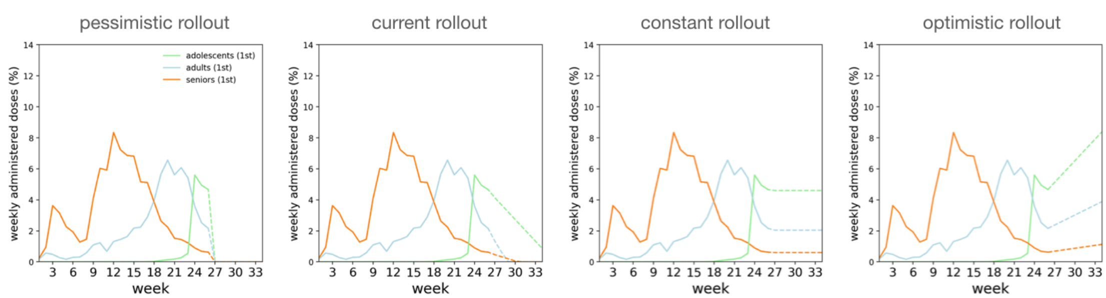

Figure 1. Vaccine rollout scenarios. Weekly first doses administered by age class over time. From left to right, the different vaccination scenarios considered: pessimistic rollout scenario, assuming that vaccination is interrupted during summer; current rollout scenario, assuming that first dose vaccinations continue to decrease as observed in current trends; constant rollout scenario, assuming that administrations remain stable over time; optimistic rollout scenario, assuming a 10% linear increase in vaccinations starting week 27. Continuous lines represent the data, dashed lines indicate the assumed scenarios (curves would stop at different times depending on the assumed maximal coverage in each age class).

Epidemic scenarios. We explore different scenarios of epidemic activity starting week 27, assuming the same conditions estimated during last summer[9] that correspond to a basic reproductive number R_0^w=1.3 for the wild type. This accounts for seasonal effects, the level of mixing and the preventive behaviors in place last summer. We also consider a scenario characterized by social distancing interventions able to reduce transmission to R_0^w=1 (reduction of 23% compared to estimate for last summer), and a scenario with increased overall transmission, corresponding to R_0^w=1.5 (increase of 15%), representing increased relaxation in the adoption of preventive measures and protective behaviors.

The basic reproductive numbers of the Alpha and Delta variants are computed according to the three parameterizations for the transmissibility advantage of the variants compared to the wild type, described previously. The model accounts for the natural immunity built over time since the start of the epidemic and the vaccinations. Immunity is considered to remain constant in time, without waning[21]. Scenarios are shown up to September, but simulations are based on a fixed R_0^w in time, and do not account for the changes in the social contacts due to the school calendar and return to work after the summer break, so simulated trends in September should be interpreted with caution.

RESULTS

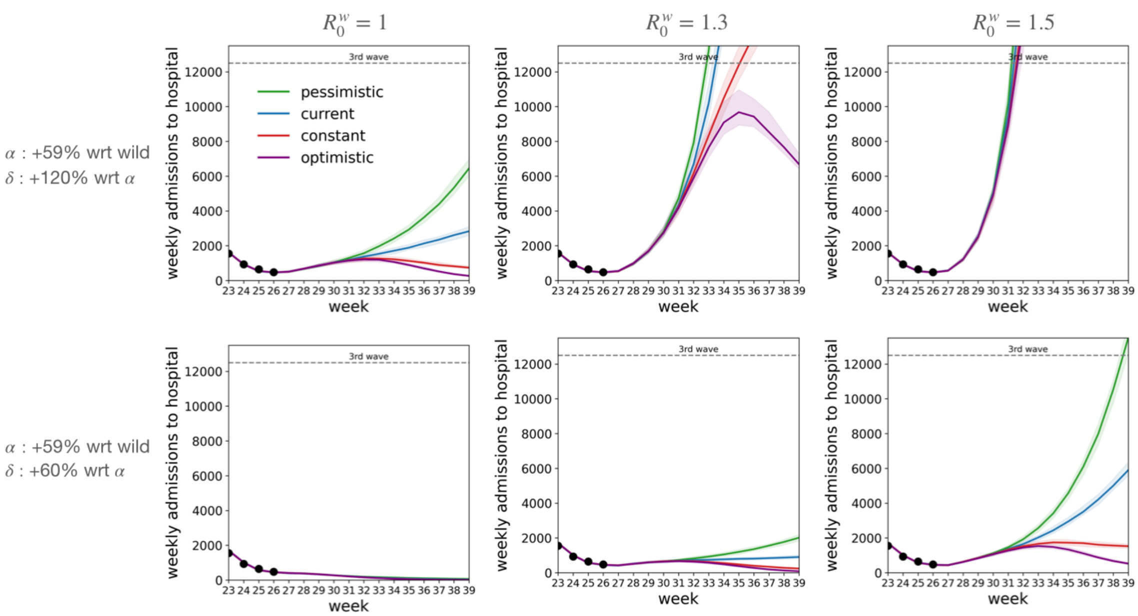

Figure 2. **Projected weekly hospital admissions according to the different scenarios.** From left to right: different epidemic scenarios, characterized by R_0^w=1 (left), R_0^w=1.3 (center), R_0^w=1.5 (right). R_0^w=1.3 corresponds to the value estimated for last summer. From top to bottom: different parameterizations for the transmissibility advantages of the Alpha and Delta variants, i.e. +59% of Alpha wrt to the wildtype and +120% of Delta wrt to Alpha (top), +59% and +60% (bottom). The top parameterization is the only one compatible with the rapid increase of Delta frequency reported in France till w26. Each panel reports the projected number of weekly hospital admissions for each vaccine rollout scenario (pessimistic, current, constant, optimistic). Simulation results are shown up to September, but they are based on a constant R_0^w in time and do not account for changes in contacts due to the start of the school calendar and return to work after the summer break. The horizontal line indicates the value of the peak of the third wave. All plots are shown with the same y axis for comparability.

KEY FINDINGS

- Under the conditions of mixing and transmissibility estimated for last summer (R_0^w=1.3 for the wild type), a rapid resurgence of cases leading to an important rise in hospital admissions is expected during the summer (top row, central plot of **Figure 2**) for the larger transmissibility advantage of the Delta variant examined here, compatible with the rise of variant frequency reported so far. The expected epidemic dynamics with the **current vaccine scenario** (i.e. decreasing trends over time, blue curve) would be minimally different from the one obtained from the **pessimistic rollout scenario** in which vaccination is completely interrupted during the summer (same plot, green curve), because of the strong deceleration of first dose administrations observed in the last period. Continued over time, this deceleration would not allow a substantial gain of vaccinations over the summer in the current rollout scenario to protect at risk individuals from contracting the infection and developing severe forms of the disease requiring hospitalizations. If vaccination trends cease to decrease and remain constant over time (**constant rollout scenario**, same plot, red curve), the rise in hospital admissions would be slightly less rapid. This rollout would only postpone of few weeks the time at which admissions are expected to reach the peak value of the third wave. This is due to the currently low weekly vaccination rates that, despite assumed to be constant over time in this scenario, would mainly provide few additional first doses throughout the summer, while cases surge. As effectiveness of vaccines is not yet complete with one dose only, even such rollout would have a limited impact in contrasting the expected surge of hospitalization under the envisioned conditions. The fourth wave would have a lower impact on the healthcare system than the third wave if vaccination would linearly increase during the summer (10% in a week, **optimistic rollout scenario**, same plot, violet curve). This is achieved through a combination of factors, compared to the constant rollout scenario: a larger coverage in adolescents achieved over the summer, a larger number of first doses over time especially in adults, a higher coverage in adults (assumed to be 80% compared to 70% in the constant scenario). These results overall indicate the need for larger vaccination rates per day than currently observed to manage the fourth wave.

- Social distancing interventions reducing overall transmissibility by 23% compared to last summer (i.e. epidemic conditions corresponding to R_0^w=1, left column of **Figure 2**) would be able to largely limit the rise of cases under all scenarios investigated here (even the worst case of the pessimistic rollout scenario). This would however occur at the expense of reinstating restrictions. An increase in overall transmissibility due for example to further relaxation in the adoption of sanitary protocols and preventive behaviors would not be manageable (here we show the projections for R_0^w=1.5, right column of **Figure 2**).
- Considering lower transmissibility advantages of the circulating variants of concern (bottom row of **Figure 2**, **Figure A1** in the Appendix) would lead to milder epidemic scenarios. The rebound in hospitalizations would be minimal if conditions of mixing and seasonality for summer 2021 were similar to those of summer 2020 (R_0^w=1.3, bottom central panel of **Figure 2**), and manageable with current, constant, or optimistic vaccination rollout if relaxation occurred (R_0^w=1.5, bottom right panel of **Figure 2**). It is important to note that there remain large uncertainties around these estimates, also due to changes in virological surveillance to adapt to the evolving situation, and possible surveillance biases during the initial phase of variant penetration (e.g. due to

strengthened contact tracing around cases carrying the novel variant, possible superspreading events). The rise of Delta frequency reported by virological surveillance data suggests a transmissibility advantage on the higher end of the spectrum of estimates currently available, and compatible with the parameterization chosen for the top panels of Figure 2.

LIMITATIONS

- It is hard to anticipate the vaccine rollout expected for the summer, as this will depend on individual behaviors and attitudes, risk perceptions, recommendations and possible changes in policies (regarding e.g. the access to certain events or locations on the basis of the vaccination status). This report examined four vaccination rollout scenarios to provide a large spectrum of possibilities, and anticipate the resulting epidemic dynamics and healthcare impact.
- Estimates for the transmissibility advantage of the Delta variant still suffer from a large uncertainty. This report did not aim to estimate this advantage but rather to anticipate the expected impact on healthcare on the basis of available estimates. We note that a large transmissibility advantage of the Delta variant compared to Alpha is needed to capture the rapid increase of its frequency reported in France. We also note that, as observed with the Alpha variant, this advantage may reduce over time – studies are still ongoing to investigate the mechanisms responsible for this. This aspect is however not considered in this report.
- Simulations are shown till September, however they do not account for the change of mixing expected after the summer period due to the start of the school calendar and the return to work. These aspects may further accelerate viral diffusion in that period.
- This report does not take into account the other lineages currently circulating beyond Alpha and Delta, as they represent <15% of the total detected viruses.
- The model is applied to the population of mainland France through an age-stratified approach and thus it neglects the spatial heterogeneity in incidence, trends, and variant frequency. Missing elements of spatial structure, model projections may be overall more pessimistic compared to results from region-specific models that capture more precisely the local context. See the Report #32 for a risk assessment at the department level.

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APPENDIX

Additional parameterization of transmissibility advantages of variants of concern from a global analysis

Here we show model projections considering transmissibility advantages equal to +29% for Alpha (wrt the wildtype) and +53% for Delta (wrt Alpha), according to a recent analysis of the variants of concern worldwide[6]. These estimates also account for the decrease of the transmissibility advantage of Alpha over time measured in several countries.

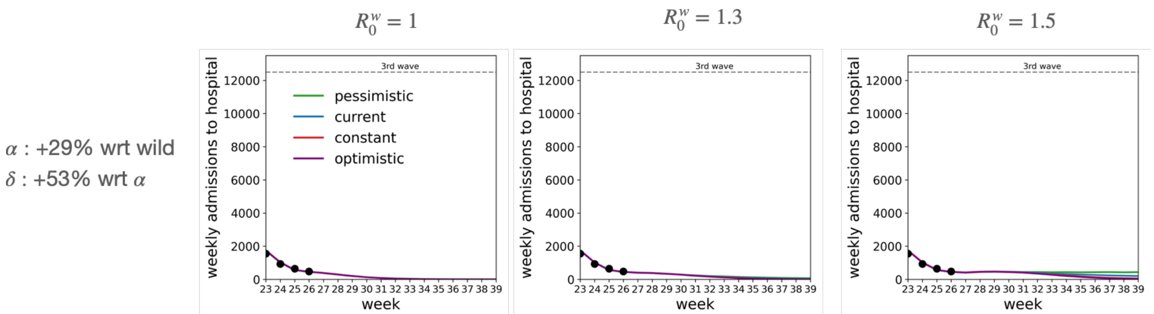

Figure S1. Projected weekly hospital admissions according to the different scenarios assuming that Alpha is +29% more transmissible than the wildtype and Delta is +53% more transmissible than Alpha. From left to right: different epidemic scenarios, characterized by R_0^w=1 (left), R_0^w=1.3 (center), R_0^w=1.5 (right). R_0^w=1.3 corresponds to the value estimated for last summer. Each panel reports the projected number of weekly hospital admissions for each vaccine rollout scenario (pessimistic, current, constant, optimistic). Simulation results are shown up to September, but they are based on a constant R_0^w in time and do not account for changes in contacts due to the start of the school calendar and return to work after the summer break. The horizontal line indicates the value of the peak of the third wave.