Assessment of the Omicron BA.2 sub-lineage presence and growth rate in regions of France

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RESUME

En utilisant les données de surveillance génomique des enquêtes Flash du 3 au 30 janvier 2022 (consolidées le 9 février), nous estimons un taux de croissance quotidien de la sous-lignée Omicron BA.2 par rapport à la BA.1 au niveau national dans l'interval 0,20 - 0,24 /jour, confirmant la croissance rapide déjà observée dans d'autres pays. On prévoit que la sous-lignée Omicron BA.2 deviendra la souche dominante en France autour de la mi-février. Les données Flash rapportent une prévalence plus élevée du nouveau variant dans les régions Nouvelle-Aquitaine (NAQ), Occitanie (OCC), Grand-Est (GES) et Île-de-France (IDF) par rapport au reste du pays. Seules ces quatre régions ont rapporté des fréquences Omicron BA.2 exploitables pour évaluer la dynamique des sous-lignées dans le temps à l'échelle régionale, montrant une croissance rapide compatible avec l'estimation nationale. Des données supplémentaires seront nécessaires pour fournir des estimations pour les autres régions. Nous estimons un avantage de taux de propagation de la sous-lignée BA.2 sur BA.1 de 1,61 (95%CrI 1,52-1,69) au niveau national, et en moyenne de 1,46 parmi les 4 régions avec des données exploitables, en accord avec les estimations du Royaume-Uni. Malgré la courbe épidémique décroissante, les cas de BA.2 augmentent avec le temps, avec un nombre de reproduction estimé à 1,30 (1,22-1,39) dans la semaine du 31 janvier au niveau national.

SUMMARY

Using genomic surveillance data from Flash surveys from January 3 to January 30, 2022 (consolidated on February 9), we estimate a daily growth rate of Omicron sub-lineage BA.2 over BA.1 at the national level in the range 0.20 - 0.24 /day, confirming the rapid growth that was already observed in other countries. Omicron BA.2 sub-lineage is predicted to become the dominant strain in France around mid-February. Flash data report a higher prevalence of the new variant in Nouvelle-Aquitaine (NAQ), Occitanie (OCC), Grand-Est (GES) and Île-de-France (IDF) regions compared to the rest of the country. Only these four

regions reported exploitable Omicron BA.2 frequencies to assess the sub-lineage dynamics in time at regional scale, showing a fast growth compatible with the national estimate. Additional data will be needed to provide estimates for the other regions. We estimate a spreading rate advantage of sub-lineage BA.2 over BA.1 of 1.61 (95%CrI 1.52-1.69) at national level, and on average of 1.46 among the 4 regions with exploitable data, in agreement with UK estimates. Despite an overall decreasing epidemic curve, BA.2 cases increase over time, with an estimated reproductive number of 1.30 (1.22-1.39) in the week of January 31 at national level.

INTRODUCTION

Omicron sub-lineage BA.1 rapidly expanded in Europe during December and is now dominant in most of the European countries[1,2]. BA.2 sub-lineage became dominant in Denmark during January, and it is rapidly growing in frequency in other countries like Germany, Sweden and England[3,4]. The aim of this report is to assess the current situation in France, based on available genomic surveillance data.

METHODS

We estimate the share of Omicron BA.2 sub-lineage cases in France based on data from genomic surveillance. We use sequence data from the EMERGEN Consortium[5].

The EMERGEN database includes the number of sequences classified by variant and analyzed by participating laboratories, provided by department and by date of collection. For each sequence, additional information on whether it belongs to a Flash survey and/or it is linked to a cluster or travel history is provided. Flash surveys weekly sequence a random sample of RT-PCR positive cases[6].

Based on the available data, we compute the Omicron BA.2 sub-lineage frequency as the ratio of BA.2 sequences among all interpretable sequences:

$$Omicron\ BA.2\ frequency = \frac{Omicron\ BA.2}{interpretable\ sequences} \quad ,$$

considering only samples sequenced as part of Flash surveys, and further excluding those belonging to clusters or linked to travel. We consider data from week 1 (starting January 3, 2022) to week 4 (ending January 30, 2022) at regional and national scale. Data are consolidated on February 9. Some regions show no Omicron BA.2 confirmed cases in the study period. Sequence data in the week starting on January 31 are not yet consolidated as they include a limited number of samples; being partial, these data are not used to fit the growth rate.

We estimated the growth rates and the corresponding doubling times of the Omicron BA.2 sub-lineage by region and at national level with an exponential growth model[7]. We inform the effective reproductive number for the Omicron BA.1 sub-lineage in each area according to the corresponding estimates of the week starting on January 3. For both Omicron sub-lineages we assume a generation time of 4.1 days, i.e

0.5 days shorter[8] than the one estimated for Delta (mean 4.6 days)[9]. We use an MCMC approach maximizing the following likelihood function independently in each region and at national level:

$$L = \prod_{t} Binomial\,(O(t);\ N(t), p(t))$$

with p(t) defined as:

$$p(t) = 1 \,/\, \left(1 + \frac{1-p_0}{p_0}\, e^{(r_1 - r_2)t}\right)$$

where t is the weekly time step, O(t) and N(t) are the observed number of Omicron BA.2 cases and total samples at time t, p_0 is the initial Omicron BA.2 frequency, r_1 and r_2 represent the growth rate of BA.1 and BA.2 sub-lineages, and p(t) is the predicted frequency of BA.2 at time t. Our analysis is restricted to those regions with at least one detected case of Omicron BA.2 and showing an exploitable growth trend to bring the model to convergence. The initial Omicron BA.2 frequency p_0 is assigned in each region to the week preceding the first week of BA.2 sequence data and fitted jointly with the growth rate. We use an exponential distribution for r_2 and a uniform distribution for p_0 as prior distributions. For sensitivity, we fit the model considering data from January 10 onwards, using the effective reproductive number estimated in the week of January 10 as initial condition for BA.1.

RESULTS

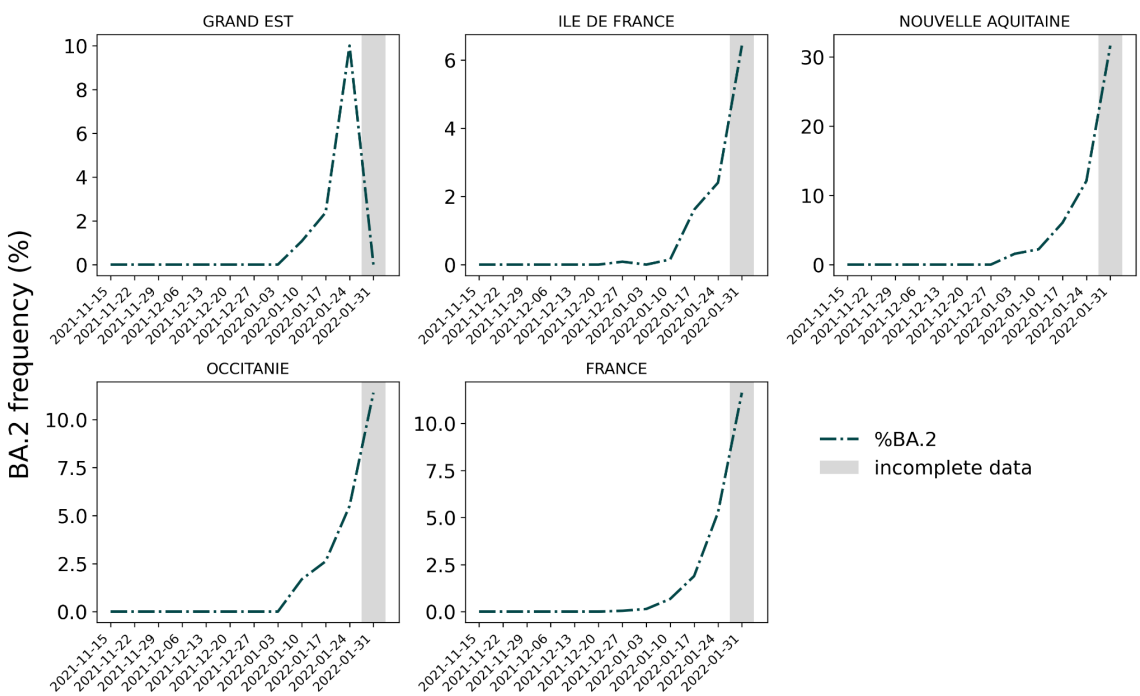

Figure 1. Omicron variant in France. Point-estimates of Omicron BA.2 sub-lineage frequency over time, based on sequence data. In the week of January 31 sequence data are still partial; the corresponding frequency, not yet consolidated, is not used in the fit.

Table 1. Estimated Omicron BA.2 frequency in France.

Week	GRAND EST	ÌLE DE FRANCE	NOUVELLE AQUITAINE	OCCITANIE	FRANCE
January 24	10.0%	2.4%	12.1%	5.5%	5.3%
January 31*	0.0%	6.4%	31.6%	11.4%	11.6%

*incomplete / non-consolidated data

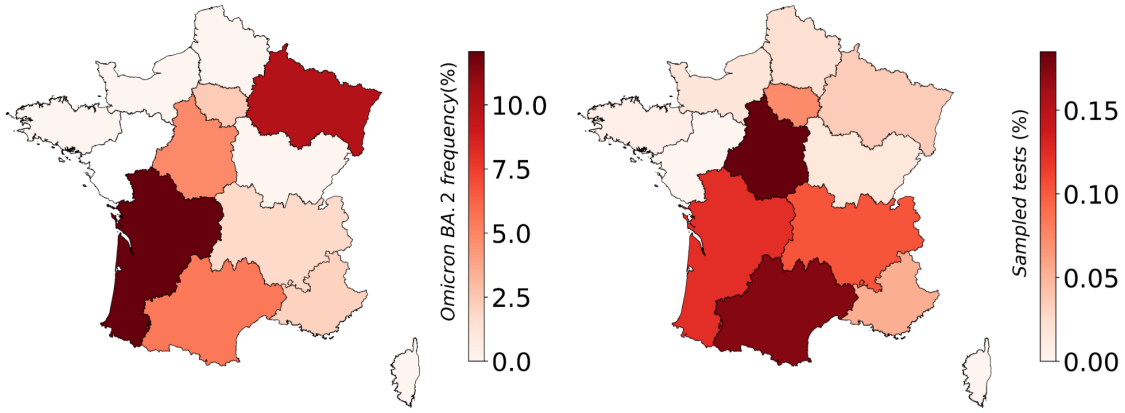

Figure 2. Estimated Omicron BA.2 frequency and sequence data sample at regional level in the week of January 24. Left: BA.2 frequency. Right: Percentage of sequenced tests among positive tests.

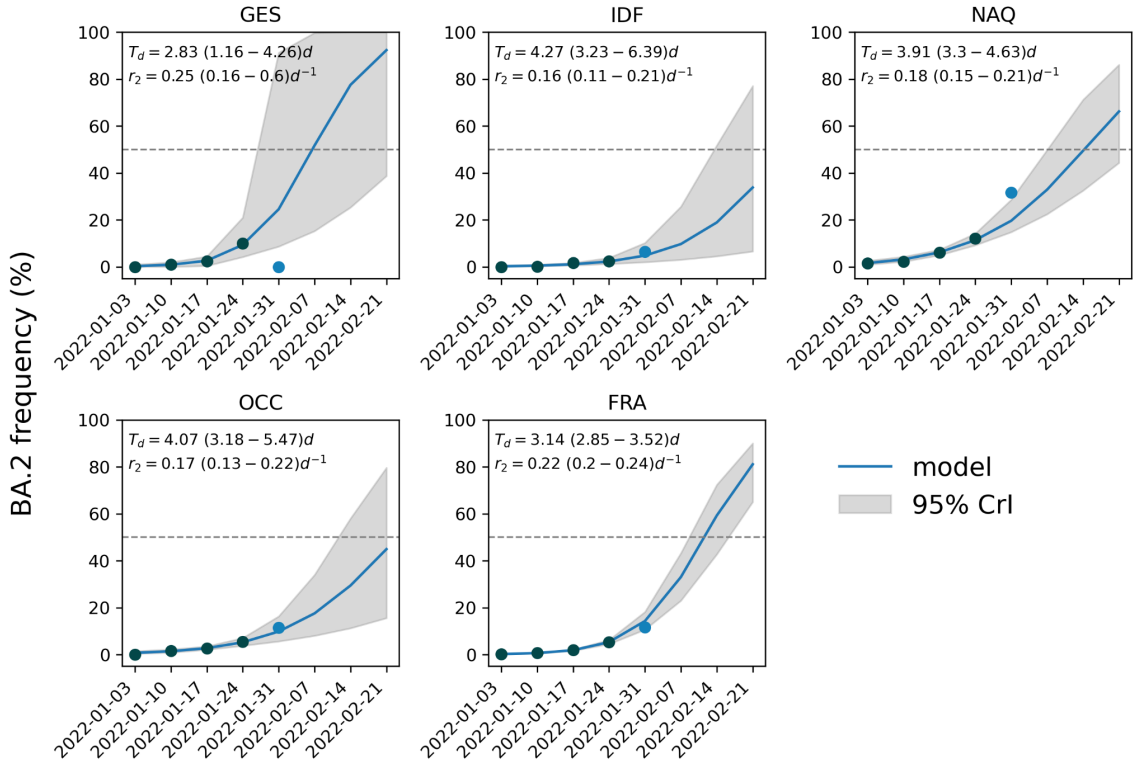

Figure 3. Estimated Omicron growth at regional and national level. Estimates of Omicron BA.2 sub-lineage frequency from sequence data and predicted frequency over time (median, blue line, and 95% credible interval, shaded area). Plots show only those regions with at least one detected case of Omicron BA.2 and for which the model reached convergence. T_d represents the doubling time of Omicron BA.2 cases growth estimated for each area (expressed in days); r_2 is the estimated daily growth rate of Omicron cases (expressed in days^{-1}). Dark blue dots represent sequence data used in the model tuning, light blue dots indicate non-consolidated data, not used by the model.

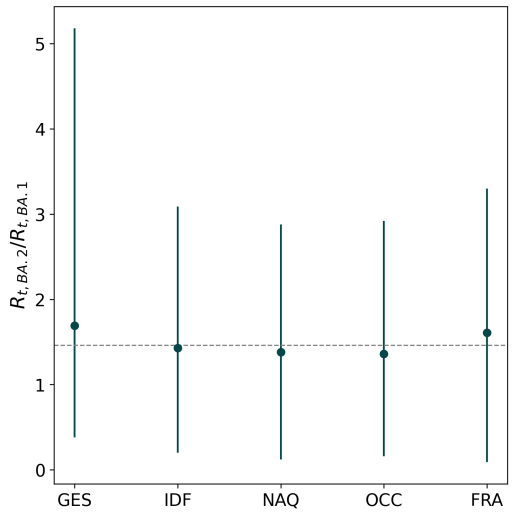

Figure 4. Estimated Omicron BA.2 spreading rate advantage at regional and national level. Estimates of spreading rate advantage of BA.2 over BA.1 at regional scale in the regions under study and at national scale. The average (horizontal dashed line) is

estimated to be 1.46 among the four regions. When analyzing metropolitan France as a whole, we find a spreading rate advantage of BA.2 over BA.1 of 1.61 (95%CrI 1.52 - 1.69).

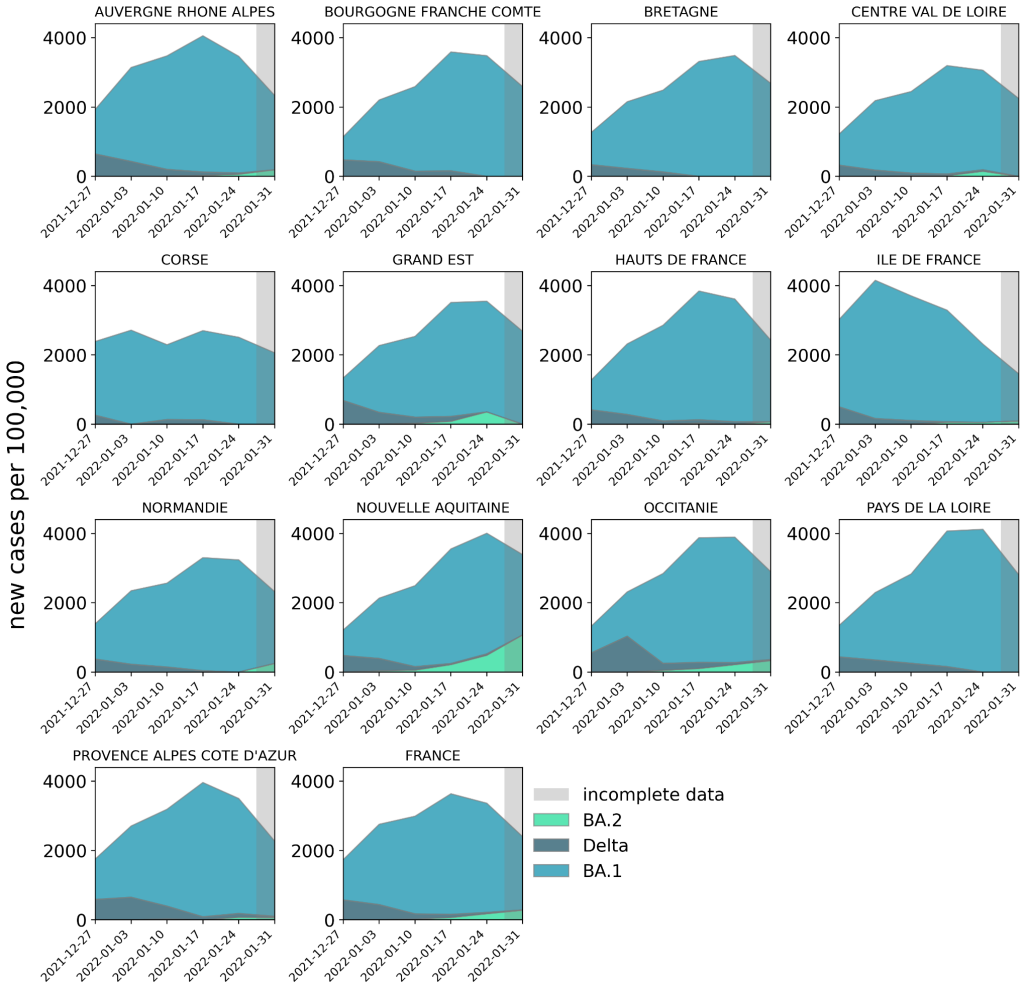

Figure 5. Estimated incidence due to Delta, BA.1 and BA.2 in January 2022.

Table 2. Estimated Omicron BA.2 growth rates, doubling times and spreading rate advantage in France.

Week	Growth rate	Doubling time	Spreading rate advantage
GES	0.25 (0.16-0.6) –	2.83 (1.16-4.26) –	1.69 (1.31-3.49) –
IDF	0.16 (0.11-0.21) –	4.27 (3.23-6.39) –	1.43 (1.23-1.66) –
NAQ	0.18 (0.15-0.21) –	3.91 (3.3-4.63) –	1.37 (1.26-1.50) –
OCC	0.17 (0-13-0.22) 0.12 (0.07-0.16)*	4.07 (3.18-5.47) 5.84 (4.23-9.63)*	1.35 (1.2-1.56) 1.31 (1.12-1.49)*
FRA	0.22 (0.2-0.24) 0.17 (0.15-02)*	3.14 (2.85-3.52) 4.05 (3.51-4.64)*	1.61 (1.52-1.69) 1.63 (1.53-1.78)*

*sensitivity test, fitting only on data from January 10 onwards.
Regions with no estimates did not have exploitable data to let the model converge in the sensitivity test.

KEY FINDINGS

- Flash sequence data report a frequency of 5.3% of the Omicron BA.2 sub-lineage in France in the week of January 24 (**Figure 1**, **Table 1**). Analyses at the regional level show a high heterogeneity in the estimated Omicron BA.2 sub-lineage frequency among regions (**Figures 1, 2**). Data from the week of January 24 report a higher prevalence of the new variant in Nouvelle-Aquitaine (NAQ), Occitanie (OCC), Grand-Est (GES) and Île-de-France (IDF) regions.
- We estimated a daily growth rate of BA.2 in the range 0.20 - 0.24 /day at national level (**Figure 3**), in agreement with estimates from other countries[3]. The model indicates that BA.2 will likely become dominant in metropolitan France around mid-February.
- At regional level only four regions (Nouvelle-Aquitaine (NAQ), Occitanie (OCC), Grand-Est (GES) and Île-de-France (IDF)) reported exploitable BA.2 frequencies to assess the variant dynamics in time within the region, confirming the fast growth. The model indicates that BA.2 likely became dominant last week in Grand-Est with a growth rate similar to the national value **(Table 2)**. Growth rates of BA.2 in the other regions are estimated to be in the range of 0.13 - 0.22 / day.
- We estimate the average spreading rate advantage of BA.2 over BA.1 at 1.46 among the four regions under study (**Figure 4**). The result is consistent with relative estimations from the UK[10]. The spreading rate advantage estimated at national level is 1.61 (CrI 1.51-1.69). A sensitivity analysis initializing the model one week later (from January 10) shows that estimates are robust **(Table 2)**.
- While overall cases started to decrease, with the effective reproductive number at national level passing from 1.28 (1.28-1.29) in the week of January 3 to 0.88 (0.88-0.89) in the week of January 31, there is a clear trend of case incidence growth of BA.2 at national level, in Grand-Est, Île-de-France, Nouvelle Aquitaine and Occitanie (**Figure 5**). Based on the predicted frequency and the spreading rate advantage of BA.2 at the national level, we estimate the effective reproductive number at 0.81 (0.78-0.83) for BA.1 and 1.30 (1.22-1.39) for BA.2 in the week of January 31. In a scenario of unchanged conditions, this indicates that the overall reproductive number would increase above 1 as the frequency of BA.2 increases over time.

LIMITATIONS

- Estimates refer to the period from January 3 to the week of January 24; data in the week of January 31 are not consolidated yet. Additional data will be needed to provide estimates for a more recent period.
- The main limitation of the analysis lies in the spatial coverage. Spatial coverage of sequence data is not uniform in the territory (**Figure 2**), increasing the uncertainty of the estimates across regions.
- We estimated the effective reproductive number of BA.1 sub-lineage to inform the exponential growth model running EpiEstim package estimation on the officially reported cases. Testing

capability may have been put under stress under winter holidays, leading to time-varying underdetection in some regions, hence affecting the estimation of the effective reproductive number in the first weeks of January. A sensitivity analysis using the effective reproductive number estimated in the week of January 10 results in longer doubling times of BA.2 over BA.1 in Occitanie and metropolitan France, but estimates of spreading rate advantages remain stable (Table 2).

- Estimates on the generation time of the BA.2 sub-lineage are still preliminary. The generation time of both Omicron BA.1 and BA.2 was assumed to be 0.5 days shorter than the one estimated for the Delta variant (4.6 days). Recent evidence from the UK found a shorter serial interval for BA.2 with respect to BA.1[11].

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