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Dynamics of SARS-CoV-2 lineages in French Guiana in 2020–2021: 4 epidemic waves with cross-influences from Europe and South America

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ABSTRACT

Since the first cases of SARS-CoV-2 infection in Wuhan in December 2019, this RNA virus gave rise to different viral lineages with different virological, epidemiological and immunological properties. Here we describe the dynamics of circulation of SARS-CoV-2 lineages in an Amazonian South American French overseas territory, French Guiana (FG). The data analyzed are based on the general epidemic course, and genomic surveillance data come from whole genome sequencing (WGS) as well as typing PCRs. From March 2020 to October 2021, four COVID-19 epidemic waves were observed in FG with an evolution of viral lineages influenced by virus introductions from continental France and above all by land-based introductions from neighbouring countries. The third epidemic wave from March to June 2021 was driven by a predominant Gamma introduced from Brazil and a less frequent Alpha introduced from France. This coexistence was completely substituted by Delta that initiated the fourth epidemic wave.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genomic sequences are used to monitor changes that might impact the transmission, pathogenesis, or antigenic properties of the virus.

The first variant classified as variant of concern (VOC) was detected in September 2020 in England, and was predominant in the UK by December 2020 (Covariants.Org, 2022). This VOC Alpha (Pango lineage B.1.1.7; Nextclade 20I/V1) (Genomic Epidemiology, 2022) was characterized by a higher intrinsic transmissibility than the prior variants (Volz et al., 2021; Davies et al., 2021; Obermeyer et al., 2022).

VOC Beta (Pango lineage B.1.351; Nextclade 20H/V2) was detected as early as May 2020 in South Africa and was characterized by an important immune evasion component (Garcia-Beltran et al., 2021; Hoffmann et al., 2021).

In parallel to the rise of Alpha in Europe, VOC Gamma (Pango lineage P.1; Nextclade 20 J/V3), descendant of lineage B.1.1.28. emerged in Manaus, Brazil, in mid-November 2020 (Faria et al., 2021), from where it spread to become the dominant variant in South America. One concern about P.1 was its capacity to partially evade the humoral immune response, as shown by several in vitro studies (Garcia-Beltran et al., 2021; Hoffmann et al., 2021). Consistently, both Beta and Gamma share several relevant substitutions in the spike such as the E484K, N 501Y and K417T/N in Gamma and Beta respectively. Biochemical studies identified amino acid 484 to be a dominant residue for the recognition by human polyclonal antibodies (Greaney et al., 2021). The N501Y

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mutation has been described to affect the transmission of SARS-CoV-2 by strengthening the interaction between the receptor-binding domain and the ACE2 receptor, leading to increased infectivity (Tian et al., 2021).

It has also been reported that the presence of the K417N, K417T, E484K and/or N501Y mutations results in a small but significant reduction in neutralization in individuals vaccinated or naturally infected with SARS-CoV-2 (Wang et al., 2021).

Real-world data from Manaus confirmed immune evasion capacities for Gamma, estimating that 16.5% of infections in this first gamma regional epidemic were re-infections (Prete et al., 2021; Buss et al., 2021). However, it is questionable whether the rapid spread of this VOC can be explained exclusively by immune evasion or whether this variant also has a higher transmissibility: in a model based on genomic, hospitalization and mortality data from November to January 2021 in Brazil, the increase in transmissibility was estimated at 70% to 140%, which would act in combination with an immune evasion component of 21–46% after prior infection with a non-Gamma lineage (Faria et al., 2021). A more extensive dataset, including all 2.1 million genomes available at the time worldwide, was analyzed to evaluate the growth rate of Gamma to be 1,87 [1,65; 2,1]IC95 compared to the original virus (Obermeyer et al., 2022).

Variant of interest Zeta (P.2) is another lineage descendent of B.1.1.28, that despite sharing the E484K substitution in the spike, emerged independently and earlier than P.1. It was first detected in July 2020 in the state of Rio de Janeiro (Voloch et al., 2021) and spread to become a major lineage in most parts of Brazil until December 2020 (Fiocruz Coronavirus Genomic Network, 2021), when it started to be replaced by P.1.

VOC Delta (Pango lineage B.1.617.2 and AY. sublineages; Nextclade 21A,I and J), first identified in India in October 2020 (Cherian et al., 2021), became dominant worldwide from March 2021 on and proved to outcompete pre-existing lineages, including the other VOCs Alpha, Beta and Gamma. Investigations of characteristics giving Delta fitness superior to any other variant seen so far, revealed that Delta infection is associated with higher viral load and shorter incubation time (Li et al., 2022), possibly due to more efficient viral replication (Mlcochova et al., 2021), leading to higher transmissibility. Delta growth rate was estimated [2,3-3,04]IC95, times the growth rate of the original Wuhan strain (Obermeyer et al., 2022). Additionally, Delta might have an immune escape component, as it was found to be less sensitive to neutralizing antibodies in vitro (Mlcochova et al., 2021). Additionally, real-world data from the US revealed that Delta breakthrough infections in fully vaccinated individuals were more frequent than expected, a phenomenon likely not caused by waning vaccine protection (Fowlkes, 2021; Scobie, 2021).

French Guiana (FG) is a French overseas territory located on the northern part of South America, bordering Brazil and Suriname. The population, an estimated 300,000 inhabitants, is concentrated on the coast in the three main cities (Cayenne, Kourou and Saint-Laurent du Maroni), whereas the rest of the country is covered by Amazonian rain forest and scarcely populated. Apart from the low population density, FG has a particularly young population and less economic resources than mainland France.

This work analyses the period from the beginning of the Covid-19 pandemic and until end of September 2021, during which four epidemic waves hit FG (Fig. 1). The first SARS-CoV-2 infection in FG was identified on March 4, 2020. As the first epidemic wave started in mainland France in March 2020, a strict national lockdown was implemented in all French territories from mid-March until mid-May. This lockdown likely delayed the start of the first epidemic wave in FG until May 2020 (Andronico et al., 2021), with only a small number of isolated family clusters observed. In April and May 2020, the first community clusters appeared, which diffused to form the first epidemic wave in Saint-Georges de l'Oyapock, the border town to Brazil, in May 2020. This first wave reached central FG in June 2020. The second epidemic wave at the end of 2020 was of smaller impact. The third wave started in March 2021, peaked in May and was characterized by a slow decrease. In August 2021 a fourth wave initiated shortly after the peak of the third wave. From all epidemic waves in FG until September 2022, the third and fourth had the highest impact in terms of ICU admissions and deaths. The following very steep fifth wave driven by Omicron attained its maximum incidence in mid-January 2022, but had only a low impact on hospital and ICU admissions. The sixth epidemic wave with a majority of BA.5 peaked in the beginning of July 2022 (Fig. 3A).

The maximum incidence rate attained 542/100000 in the fourth and 3822/100000 in the fifth epidemic wave in FG. The impact of the epidemic in this very young population was lower than in mainland France (Andronico et al., 2021), with 1415 hospital admissions per 100,000 inhabitants from 1st of March (week 2020–10) until 19th of September (week 2021–37), and 82.6 deaths per 100,000 inhabitants.

The French national vaccination campaign started in mid-January 2021: vaccination was open to the Guianese adult population since April 19, 2021. BNT162b2 was the only vaccine administered in FG due to the dominance of S:E484K-bearing P.1 and P.2 variants (Alter et al., 2021; Barros-Martins et al., 2021). Although vaccination is free and easily accessible, FG has a very poor vaccination coverage compared to France.

The immunization status of a population influences viral spread. Three consecutive seroprevalence studies had been conducted in FG. The first one estimated in mid-July 2020 (when the first epidemic wave

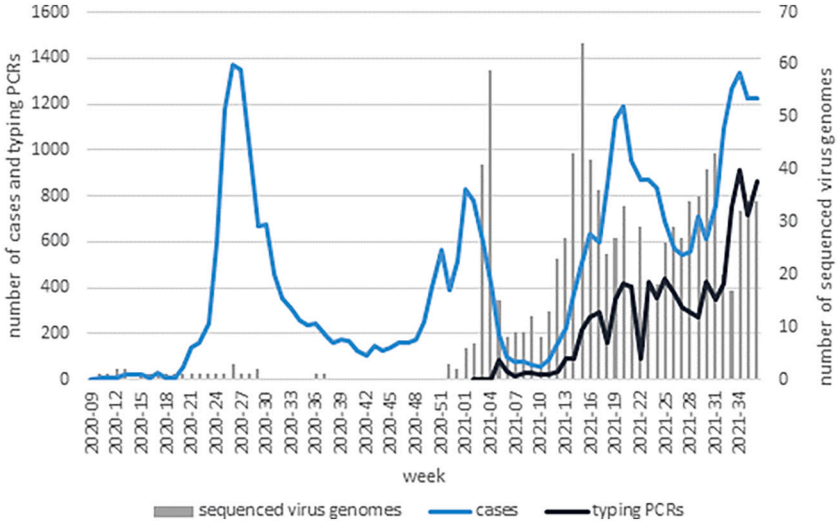


Fig. 1. The first four epidemic waves of SARS-CoV-2 in French Guiana and coverage by genomic sequencing and typing PCRs. Epidemiological curve showing the progression of weekly COVID-19 numbers in French Guiana. Four epidemic waves have been registered, with the first peaking in June/July 2020. The grey bars show the overall sampling of SARS-CoV2 genomes, while the black curve depicts the number of samples (among the positives) tested for variant key mutations by typing PCRs. The sudden fall of typing PCR numbers in week 21–22 is due to the time laboratories needed to switch from the old type of typing PCR kits to the new one.

had just finished) an overall seroprevalence of 15.4% (Flamand et al., 2021). The second one estimated in early October a seroprevalence of 23.4%. In August 2021, close to the peak of the fourth epidemic wave, anti-spike SARS-CoV-2 IgG, induced by a natural infection or vaccination, were present in 63.9% of the population (preliminary data, unpublished to date).

Apart from the general national lockdown from mid-March to mid-Mai 2020, the Guianese health authorities opted for a plan in which sanitary measures depended on the respective epidemiological situation. During periods of high viral circulation and hospital saturation, the restrictions were more severe, and alleviated in low-incidence periods. These restriction measures in FG included curfews, Sunday lockdowns and the closing of all restaurants, sports, touristic as well as cultural venues. Travel was completely prohibited over land (from Brazil and Suriname) during the complete period analyzed here. Furthermore, air travel was restricted: Flight connections to Brazil were suspended from April 2020 on. For flights from Paris and the French Antilles, testing and quarantine was implemented, and a proof of compelling reason became mandatory for travelling.

The aim of this work is to provide an overview of the succession and diffusion of SARS-CoV-2 viral lineages during the four epidemic waves in FG. The isolation and small population of this territory allow comprehensive contact tracing and make it a good model for following the dynamics of introduction and spread of SARS-CoV-2 lineages.

2. Material & Methods

2.1. Covid-19 biological analyses database

All laboratory results of SARS-CoV-2 qRT-PCR and variant typing PCRs, as well as results of rapid antigenic tests performed in pharmacies are integrated into the French national Covid-19 testing information system (SIDEP). For every test, sociodemographic data of the patient (notably sex, birth date, place of residence) as well was the testing institution are also collected. Thereafter, the DATA service (Direction Appui, Traitements et Analyses des données) of Santé publique France (SpF) provided anonymized and treated data, which were used for determining Covid-19 general epidemic indicators as well as the circulation of variants.

2.2. Viral genomic surveillance system

By the end of 2020, three VOC were disseminating rapidly worldwide, making health authorities understand the need to establish reliable systems for genomic surveillance of the virus. In January 2021, the French ministry of health instructed that all SARS-CoV-2 positive samples be submitted to an additional typing PCR step, which allowed to distinguish VOCs (Alpha, Beta and Gamma) from non-VOCs.

All SARS-CoV-2-positive samples from private medical laboratories were submitted to typing PCRs between February and September 2021. Results from typing PCR as well as viral genome sequencing are collected in the SIDEP database, and were available to SpF by the intermediate of the DATA service.

As typing PCRs only screen for variant footprint mutations, it needs to be complemented by sequencing of the viral genome. Whereas in 2020 only “samples of special interest” were sequenced, from December 2020 on, WGS capacities were upscaled for sequencing of a weekly selection of representative samples from all over FG. For guaranteeing the surveillance of viral lineages from the large Guianese territory, a SARS-Cov-2 genomic surveillance network was organized between laboratories: Whole genome sequencing (WGS) of a weekly selection of representative samples sent by different laboratories, including the clinical laboratories of the 3 hospital centers, was carried out by the National Reference Center for respiratory viruses (NRC-RV) either in FG ($N = 1029$) or in Paris ($N = 434$). This permitted us to have a representation of samples from hospitalized patients as well as from mildly symptomatic patients, from different geographical origins, from specific clusters, from cases with travel history and from possible breakthrough infections. Besides, the NRC-RV in FG collected sociodemographic and clinical data for the sequenced samples.

2.3. NGS methodology and phylogenetic analysis

Genome sequences were generated from SARS-CoV-2 positive nasopharyngeal samples with Ct values below 28. Viral RNAs were amplified using a highly multiplexed PCR amplicon approach (ARTIC primers V1 to V3 according to the date of analysis). Libraries were then prepared to be sequenced either on an Illumina NextSeq500 at the Mutualized Platform for Microbiology at Institut Pasteur, Paris, or on a MinION (Oxford Nanopore technologies) according to the ARTIC nCoV-2019 sequencing protocol (https://www.protocols.io/view/ncov-2019-sequencing-protocol-v2-bdp7i5rn) at Institut Pasteur, Cayenne. Nanopore sequencing reads were basecalled with Guppy 3.4.5 + fb1fbfb and analyzed with the Nanopolish workflow provided by the Artic Network (https://github.com/artic-network/artic-ncov2019.git, commit ddfb2dc87a4f442f821787ef90a92625f6bd6a09). Consensus sequences were then submitted to Nextclade (O'Toole et al., 2021) (https://clades.nextstrain.org/) and Pangolin (https://pangolin.cog-uk.io/) in order to assign them to the different clades and lineages (O'Toole et al., 2021).

We used the Nextstrain (Hadfield et al., 2018) ncov pipeline to infer a global phylogeny including all SARS-CoV-2 sequences from FG, and contextualized using a subsampling of sequences available on the GISAID EpiCoV database (Shu and McCauley, 2017). The acknowledgment of contributing and originating laboratories for all sequences used in the analysis is provided in Supplementary Table 2.

The typing PCR kits used from January to May 2021 detected key mutations allowing, in accordance with national guidelines, to distinguish VOC alpha from VOC beta and gamma and non VOC. In June 2021, with the arrival of the Delta variant, the PCR typing kits were adapted to detect the key mutations E484K, E484Q and L452R.

2.4. Contact tracing

Contact tracing for investigating the source of infection with a new variant was performed by the French organism for health insurance (CGSS) in collaboration with the regional health agency (ARS Guyane). Contact tracing was done systematically in the first weeks of the introduction of a new variant, by phoning the Covid-19 positive cases. A standard questionnaire was applied, collecting information of travel history or contact with a traveler as well as of activities and possible infection scenarios in the last 14 days.

3. Results

3.1. March–September 2020

The first registered introduction of SARS-CoV-2 into FG was on the 4th of March, imported from Mulhouse (France), and a sample taken from this cluster was identified as 20A/B.1.

From March until September 2020, only 27 viral genomes were sequenced from FG samples, with the results listed in Supplementary Table 1: the first SARS-CoV-2 sequences in FG were 19A, 20A and 20C, all but one with a documented history of travel from continental France. Epidemiological investigations and virological testing suggested that the virus was kept under control in isolated clusters in FG in March and April 2020. However, from mid-April 2020 to September, 15 out of 19 sequences were 20B, a dominant lineage in Brazil, but almost absent from continental France at that period(Nextstrain, 2022). Consistently, in May 2020 the first epidemic wave kicked off at the border town to Brazil, spreading to the Cayenne metropolitan area in June (contact tracing done by SpF, unpublished data). Despite the low number of sequences, the data suggest that 20B lineage was dominant in FG from

April until September 2020.

In contrast, in continental France the dominating clades from April to September 2020 were 19A, 20A and 20C, with 20E being introduced only in August 2020 (Hodcroft et al., 2021). In FG, 20A was detected in June in border cities to Suriname. No conclusions can be drawn about the degree of viral variant diffusion across the Surinamese border, as sequencing data from Suriname are too scarce at that time point.

Although border crossings between French Guiana and neighbouring Suriname and Brazil were forbidden from mid-March 2020 until December 2021, the 600 km long Maroni and 370 km long Oiapoque border rivers are difficult to control and the populations on both river banks are closely interconnected by family and commercial ties.

3.2. December 2020–February 2021: Non-VOC, dominated by P.2

The implementation of an ample genomic surveillance system to monitor SARS-CoV-2 variants resulted in a good coverage of genomic surveillance from January 2021 onwards (Fig. 1): from January to August 2021, WGS assured coverage of 7% among the weekly positive samples, and another 42% of positives were submitted to typing PCRs.

The sequencing data show that in January 2021, two main viral lineages were circulating in FG (Fig. 2B): 20A and 20B/P.2. P.2 emerged in southern Brazil in July 2020 (Voloch et al., 2021), and started increasing in frequency in September/October to make up 25% of circulating viruses in October 2020 in the Northern region of Brazil adjacent to FG, and 75% by December 2020 in most states of Brazil (Fiocruz Coronavirus Genomic Network, 2021). Consistently with these data, P.2 in FG was found to be at a proportion of 30% in December 2020 and January 2021 and increased to reach 61% in February 2021 before a rapid decline with the last P.2 detection in April 2021.

3.3. VOC alpha and gamma (January to June 2021)

Both VOC Alpha and VOC Gamma were first detected in FG at the end of January 2021 in a context of low virus circulation, the interepidemic phase between wave 2 and 3 (see Fig. 3A and B) where the average weekly incidence remained at 50/100000 (between week 4 and week 13). Both variants were first detected in Cayenne metropolitan area and Savanes sector, and spread to Western FG two weeks later.

Epidemiological investigations showed that the first four cases of VOC Alpha were a group of travelers that had just returned from Dubai with stopover in Paris. When interrogating all Alpha cases between week 4 and 10 about the presumed place of infection, 11 out of the 15 first cases reported a recent history of air travel: most importations came from continental France or from the French Antilles. From week 11 on however, most cases were not travel-related, indicating that Alpha was starting community transmission (see Fig. 3C).

Alpha increased in prevalence to reach an average of 12%, with some minor fluctuations, over most of the3rd epidemic wave (week 13–242,021, March 21st – June 26th, Fig. 2A).

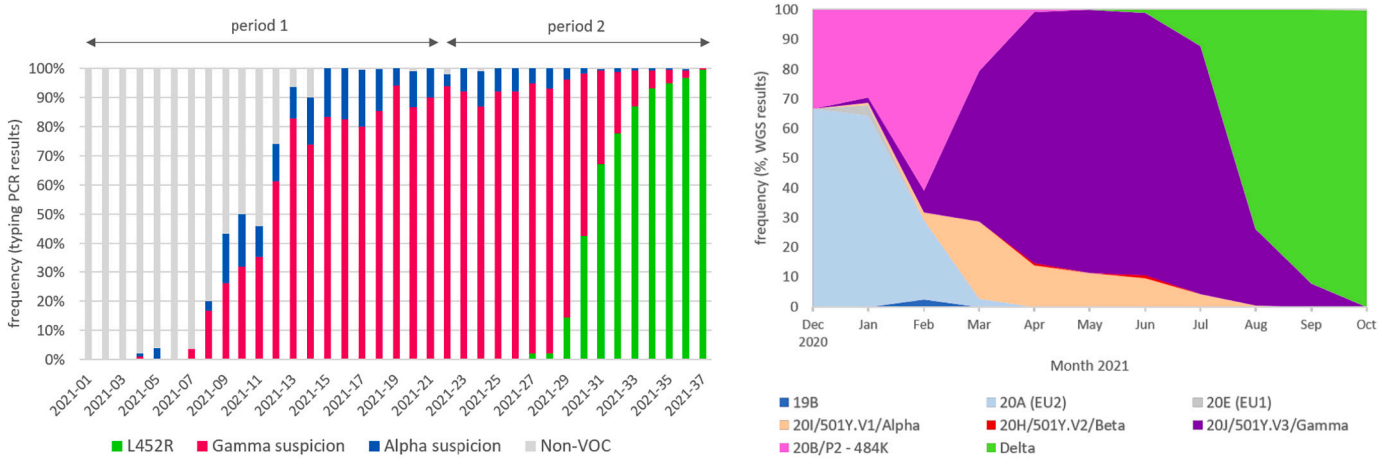
The first two Gamma variant cases in FG were confirmed in Cayenne metropolitan area at the end of January 2021 by sequencing. However, the presumed place of infection could not be identified and the interrogated patients stated not to have travelled. Direct importation from Brazil could only be confirmed for 2 cases in week 6 and 7 (Fig. 3C). However, an indication for a Gamma introduction from Brazil is that from week 4 until week 9, 17 out of the 22 Gamma cases had Brazilian names, suggesting that Gamma spread in clusters in the Brazilian community during the first weeks of its introduction. From week 10 on, when Gamma had already reached 32% frequency, it seemed to have spread into the general population, no longer limited to the Brazilian community.

The proportion of Gamma cases continued to increase, as monitored with both genomic and typing PCR data, until reaching an end-point in week 13 (Fig. 3B), by which time Gamma and Alpha had almost entirely displaced the previously circulating non-VOC virus.

A steady state defined by an average of 87% Gamma and 12% Alpha lasted over 3 months from week 13 to week 262,021.

3.4. Delta takes over (July 2021–September 2021)

The earliest detection of SARS-CoV-2 variant Delta in FG was in



(a) (b)

Fig. 2. Variant frequencies in French Guiana from December 2020 until August 2021. (a) Results from typing PCRs with 2 periods distinguished by the mutations screened: Period 1- From January to May 2021, detection of a set of key mutations as defined by French national guidelines allowed to distinguish non-VOC (in grey) from VOC variants: Alpha suspicion in blue, and Gamma suspicion in pink. Due to the absence of significant Beta circulation (sequencing results), all N501Y plus E484K positives were considered Gamma suspicions. Period 2 - From June to September 2021, the typing PCR kits detected E484K and L452R key mutations, allowing to distinguish the four VOC (the only variants still circulating during this period as confirmed by the sequencing results): Alpha suspicion (absence of E484K and L452R) in blue, Gamma suspicion (presence of E484K) in pink and Delta suspicion (presence of L452R) in green. (b) WGS data. An average of 109 samples were sequenced each month, except for December 2020 with only 3 samples. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

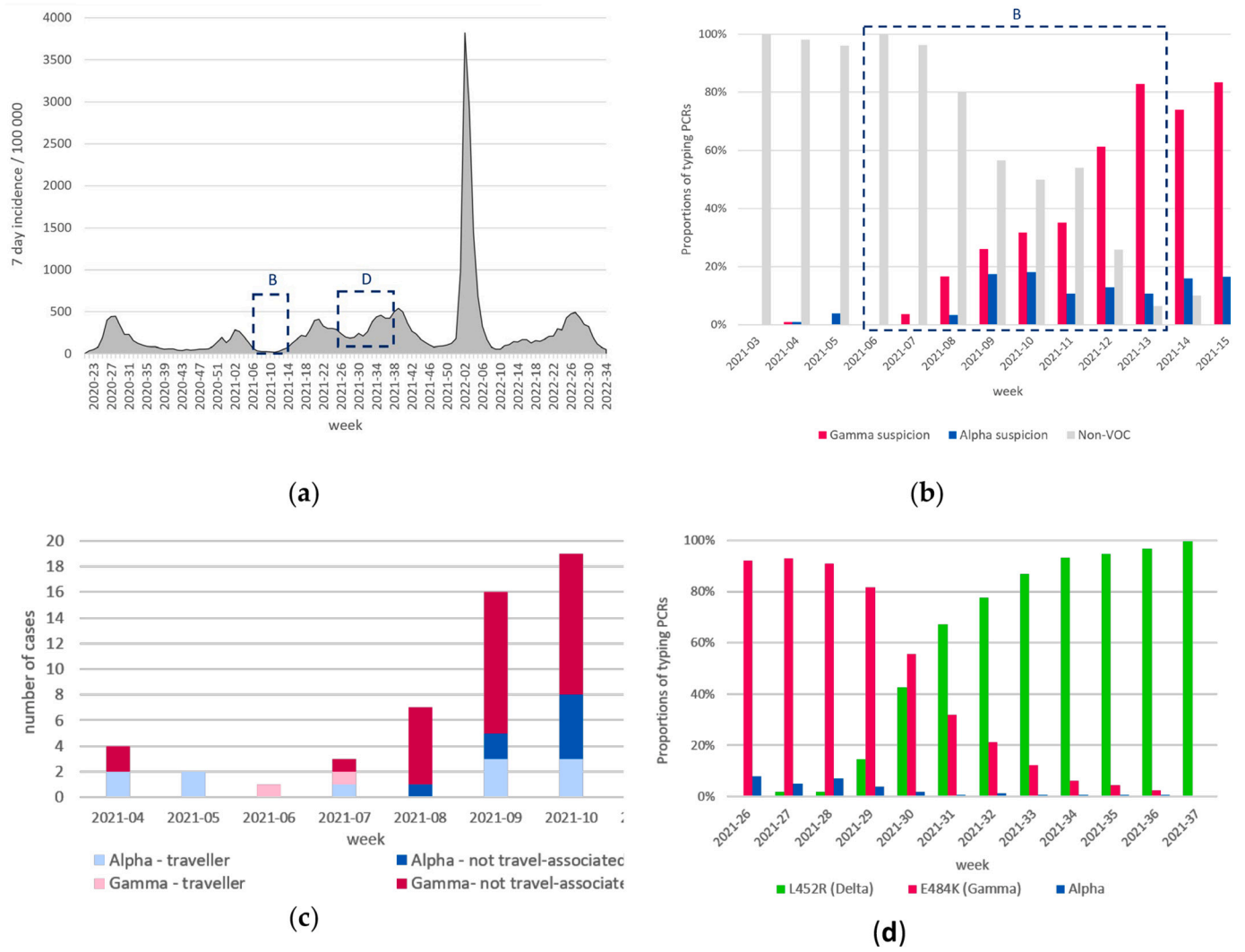


Fig. 3. The introduction of Alpha, Gamma and Delta variants. (a) 7 days incidence showing the 6 epidemic waves of SARS-CoV-2 circulation in FG between March 2020 and August 2022. Box B and D are the periods of time that is zoomed upon in Figs. 3 (b) and (d) (b) The introduction and dissemination of VOC Alpha and VOC Gamma. The underlying data are an addition of typing PCR and genome sequencing data of week 2021–03 until 2021–16. The dashed line box is the same time period as the box labelled B in graph (a). (c) Epidemiological investigation of the first Alpha and Gamma cases. Cases that confirmed a travel history in the last 14 days were distinguished from cases with presumably autochthonous infection. (d) The introduction and dissemination of Delta variant from week 2021–27 on, as shown by typing PCR data.

samples from June 8 and 162,021. A total of 14 Delta cases were identified between week 23 and week 28, when Delta frequency was still low (0–2%). Out of these 14, a history of travel was confirmed for 6, out of which 2 people had returned from France, 1 from Mali, 1 from UK, 1 from the US and 1 from Suriname. For the remaining 8 cases, 2 were contacts of an imported case, 2 reported no travel history, and 4 could not be reached. For all cases interrogated from week 29 on, infection was predominantly not travel-related.

From week 29 on, Delta frequency in FG exploded to reach 14% for week 29, 67% in week 31, and 95% in week 35 (Fig. 2B and 3D). Interestingly, infra-regional heterogeneities were observed: Delta became the main circulating variant in central FG in week 31 (69% in Cayenne and Kourou urban areas), whereas it took 2 more weeks to reach the same proportion in Western FG. By September 20th 2021, Delta had reached 100% frequency in all parts of FG.

A phylogenetic representation of the genomic surveillance of SARS-CoV-2 in French Guiana between March 2020 and October 2021 is presented in Fig. 4.

4. Discussion

Here we described the spatiotemporal pattern of introduction, diffusion and persistence of SARS-CoV-2 variants in FG.

Analysis of the 912 viral genomes detected in French Guiana between the beginning of March 2020 and October 2021 has allowed to identify eight circulating lineages by typing: 19B, 20A(EU2), 20B/P2, 20E (EU1), Alpha, Beta, Gamma and Delta (Fig. 4). For the VOCs Alpha, Gamma and Delta, we can observe rapid and successive replacements of these lineages over this period. These rapid changes may be associated with multiple introduction events as suggested by the sublineage diversity observed for example for VOCs Gamma and Delta with many genomes sampled in FG falling in distinct branches containing genomes from multiple international locations.

Our data show that the SARS-CoV-2 lineages in FG have been predominantly determined by the circulating variants in neighbouring Brazil: this was the case for 20B, being the major clade in FG from April to September 2020, for the P.2 lineage prevailing from December until February 2021 and for P.1 (Gamma) domination from March to June 2021. These findings coincide with the epidemiological investigations

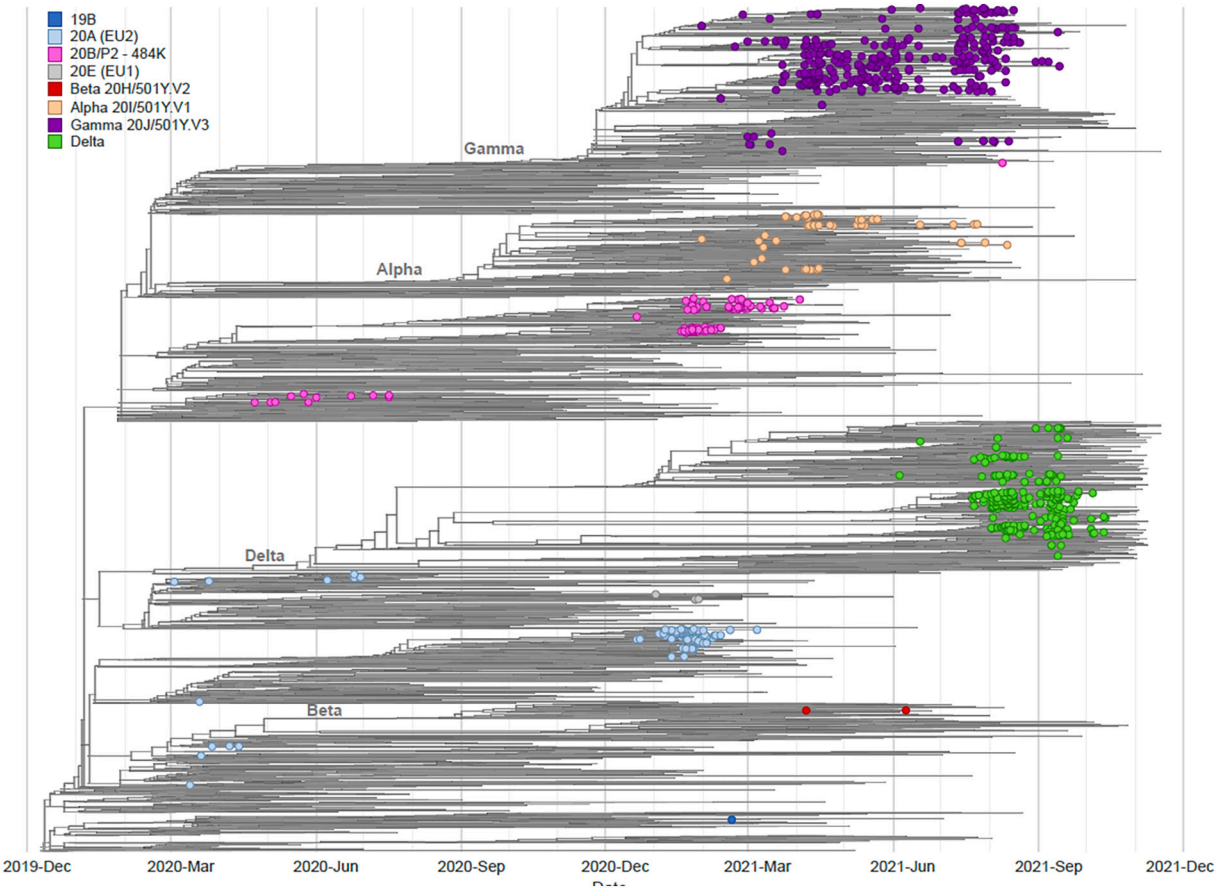


Fig. 4. Time-calibrated phylogeny of SARS-CoV-2 in French Guiana. The phylogeny was inferred using 912 complete or near complete sequences from French Guiana, with 5099 international genomes for contextualization. The tips corresponding to sequences from French Guiana are highlighted, and colored according to their clade. All SARS-CoV-2 sequences available on the GISAID EpiCov database as if January 30th, 2021 were retrieved, and included in a phylogenetic analysis using the Nextstrain pipeline (https://github.com/nextstrain/ncov). Within Nextstrain, a random subsampling approach capping a maximum number of sequences was used. The acknowledgement of contributing and originating laboratories for all sequences used in this analysis is provided in Supplemental Table 2.

revealing that the first epidemic wave in FG kicked off at the Brazilian border town of Saint Georges in May 2020 and then spread westwards into central FG and later to Saint Laurent in the West.

It might be surprising that the daily incoming flights from continental France had solely a minor influence on SARS-CoV-2 variant composition in the first 3 epidemic waves in FG, but it could be explained by the obligation of passengers to present a negative Covid-19 test, and the recommendation for them to quarantine upon arrival.

The first variants of concern detected in FG were Alpha and Gamma, at the end of January 2021. Both started diffusion in an inter-epidemic phase with low number of cases in February 2021. However, their path of introduction and their propagation were completely different: Alpha was introduced by air travel from continental France and from the French Antilles, while Gamma was introduced overland from Brazil. It is compelling that during the introduction period of Alpha and Gamma, many events of travel history could be confirmed for Alpha, while only 2 were confirmed for the introduction of Gamma from Brazil (Fig. 3C). With the Brazilian border officially closed at this time, people having travelled by land would be less inclined to report their unauthorized travel and to be tested than airline passengers. Thus, imported cases from Brazil were less likely detected and included in the contact tracing procedure.

It is striking that from March to June 2021, during the third epidemic wave, an equilibrium was established with 12% alpha and 87% Gamma variant and this proportion did not change for three months, even if most studies infer different fitness advantages for Alpha (transmissibility)[3]–(Obermeyer et al., 2022) and Gamma (rather immune escape)[6]–(Wang et al., 2021). It is not clear whether Alpha and Gamma had a much different intrinsic transmissibility: their intrinsic transmissibility was likely similar, with previous viral spread making the difference in terms of observed fitness. While the possibility of superspreading events cannot be ruled out, founder effects with a much higher number of introduction events for Gamma than for Alpha can also be considered in the dominance of Gamma in FG: it is indeed likely that significant undocumented border crossings between Brazil and France have occurred.

VOC Beta did not play a role in SARS-CoV-2 epidemics in FG, likely due to the geographical distance and non-existing economic links with Southern Africa: Only five importation events of Beta into FG were detected between April and June 2021, and virus control measures appear to have prevented its spread into the population.

The 4th epidemic wave driven by Delta started in FG in the beginning of August 2021, while the 3rd wave dominated by Gamma had just passed its peak. The introduction of VOC Delta into FG was first documented on June 8th in the context of rapid global progression of this variant which, due to fitness advantage, supplanted pre-existing variants and became the dominant epidemic variant globally. Direct introduction of Delta from France to FG was documented only for 2 cases and their secondary infections, as contact tracing was stopped before Delta reached 2% prevalence. However, the fact that Delta cases appeared first in Cayenne and Kourou areas, before spreading to the western part of FG, would support a predominant introduction by air travel (Cayenne being the only international airport). Massive delta importation from Suriname can be excluded as Delta prevalence in the border region to Suriname was low at a time when Delta was already predominant in

central FG. Finally, for Delta as for other variants, the transmissibility of the virus might be more important for explaining its rapid spread into the population than the number of introduction events.

The experience of SARS-CoV-2 variants in FG has shown that the frequencies and coexistence of viral lineages is influenced by virus introductions from continental France, as well as by overland introductions from Brazil.

Given that a vaccination coverage sufficient to significantly control virus epidemic waves has not been reached in any of the countries of Northern South America, and even less in FG, future variants that would be able to outcompete Delta can cause further epidemic waves of high impact in this specific territory.

5. Conclusions

Our data show that until the arrival of Delta in June 2021, the composition of SARS-CoV-2 lineages in French Guiana has been predominantly determined by the circulating variants in neighbouring Brazil, although the border to Brazil was officially closed for limiting virus spread. Nevertheless, introductions by air travel from Europe also influenced the strains circulating in FG: VOC Alpha was mainly introduced from metropolitan France, but later never exceeded 20% frequency. Furthermore, we saw that when a new VOC managed to diffuse into the Guianese population, it would rapidly kick off a new epidemic wave, with Gamma and Alpha constituting the third wave and Delta sustaining the fourth wave in 2021.

CRediT authorship contribution statement

Alexandra Miliu: Conceptualization, Formal analysis, Investigation, Visualization, Writing – original draft, Writing – review & editing. **Anne Lavergne:** Conceptualization, Formal analysis, Investigation, Data curation, Writing – review & editing. **Tiphanie Succo:** Formal analysis, Writing – review & editing. **Claire Laizé:** Investigation. **Audrey Andrieu:** Formal analysis, Investigation. **Antoine Enfissi:** Formal analysis, Data curation, Resources. **Vincent Enouf:** Formal analysis, Data curation. **Sylvie Van der Werf:** Formal analysis, Data curation. **Denis Blanchet:** Resources. **Magalie Demar:** Resources. **Jean-François Carod:** Resources. **Thierry Carage:** Resources. **Claude Flamand:** Formal analysis. **Sourakhata Tirera:** Formal analysis, Investigation, Writing – review & editing. **Etienne Simon-Lorière:** Formal analysis, Writing – review & editing. **Cyril Rousseau:** Conceptualization, Formal analysis, Writing – review & editing. **Dominique Rousset:** Conceptualization, Formal analysis, Investigation, Data curation, Resources, Writing – review & editing.

Declaration of Competing Interest

None.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.meegid.2022.105370.

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