Genetic diversity of the novel coronavirus SARS-CoV-2 (COVID-19) in Portugal

More information at **https://insaflu.insa.pt/covid19/**

Situation Report

12th July 2022

The **National Institute of Health Doutor Ricardo Jorge, I.P. (INSA)** has analysed **38671 SARS-CoV-2 genome sequences** so far, obtained from positive samples collected in more than 100 laboratories/hospitals/institutions, across 304 municipalities.

The genetic diversity of SARS-CoV-2 has been monitored based on an average of 515 sequences/week, since the beginning of June, 2021. These sequences have been obtained from positive samples collected randomly throughout the **18 Districts of Portugal Mainland and the Autonomous Regions of the Azores and Madeira**, covering an average of 139 municipalities per week (**Figures 1 e 2**).

Figure 1. Geographic coverage (at the municipality level) of the last weekly nationwide sequencing survey, which resulted in 563 new SARS-CoV-2 genome sequences from 144 municipalities.

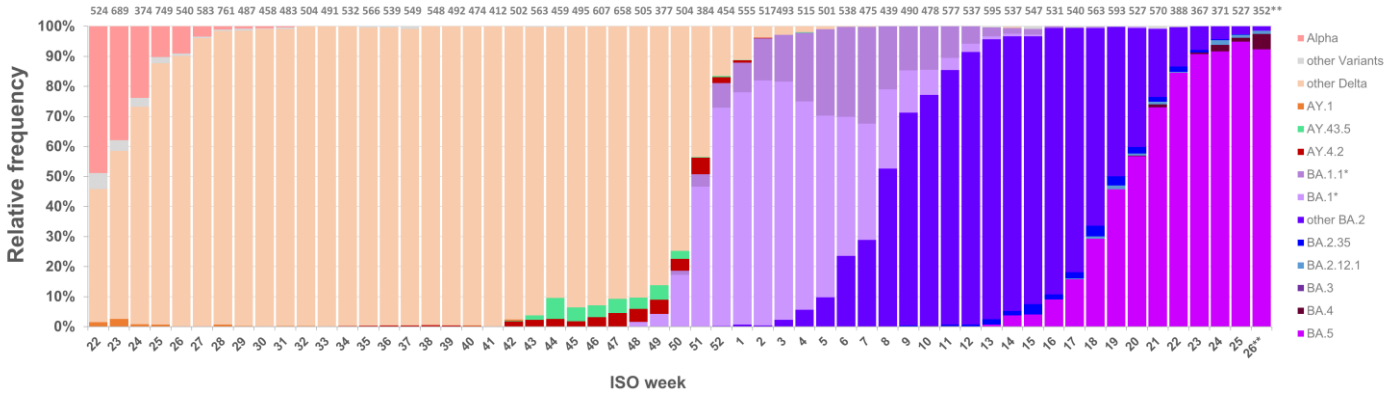

Figure 2. Evolution of the weekly relative frequency of the SARS-CoV-2 (sub-)lineages circulating in Portugal between ISO weeks 22 (31st May – 6th June, 2021) and 26 (27th June – 4th July, 2022). The values on top of each bar indicate the number of sequences analysed per week in the context of the weekly random nationwide surveys. The plot highlights: i) BA.1 (and sub-lineage BA.1.1), BA.2 sub-lineages with relative frequency ≥1% in week 25 (sampling closed), as well as the sub-lineage of interest BA.2.35 and the lineages BA.3, BA.4 and BA.5 (all classified as *Omicron* by the WHO); ii) *Delta* sublineages of interest (AY.1, AY.4.2 e AY.43.5); and iii) the Alpha variant. *BA.1 = BA.1 and sub-lineages (with exception of BA.1.1 and sub-lineages). **The frequencies presented for the last week under analysis (ISO week 26) might change in the next report, given that some data from that period is still being processed. BA.1.1 = BA.1.1 and sub-lineages.

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Main highlights:

The Variant of Concern (VOC) *Omicron*, according to the WHO classification, currently includes several (sub)lineages identified by the "BA" prefix. The nomenclature of the various sub-lineages is under constant review and refinement (https://www.pango.network/). The sequences identified in Portugal are reclassified weekly and the result are available on our website https://insaflu.insa.pt/covid19/. Whenever relevant, some of these sub-lineages will be highlighted in this report.

- **Lineage BA.5**
  - Lineage BA.5 presents several genetic traits of interest, such as the presence of the mutations **L452R** and **F486V in Spike** (both affect Spike regions that interact with the human cells and mediate adherence/immune evasion). BA.5 also presents the deletion del69-70 in Spike, which is responsible for the SGTF profile, so this laboratory indicator has also been used as a proxy to estimate its frequency. However, due to the recent decrease in the number of tests performed with the *TaqPath – ThermoFisher* methodology (allowing the monitoring of the proportion of samples with "SGTF" profile) by the different laboratories, SGTF data now lack robustness and, as such, are no longer used for BA.5 lineage monitoring.
    The nationwide weekly surveys by sequencing show that, since its first detection in week 13, the **lineage BA.5 is dominant in Portugal since week 19** (9th - 15th May, 2022) **and presented a relative frequency of 92.3% in the latest national sequencing survey in week 26** (27th June - 4th July, 2022) (**Figure 2**).

- **Lineage BA.2**
  - **In Portugal, BA.2 has been firstly detected in random nationwide sequencing surveys in ISO week 52** (27th December 2021 – 2nd January, 2022) (**Figure 2**), becoming dominant on week 8 (21st–27th February, 2022). After reaching a maximum relative frequency of 95% on week 13 (28th May – 3rd Abril 2022), this lineage presents a **continuous decrease in relative frequency**, having ceased to be dominant since week 19 (9th-15th May, 2022), point from which lineage BA.5 became dominant in Portugal (**Figures 2** and **3**). It's relative frequency at week 26 (*analysis ongoing*) is estimated to be 2.6%.
  - Among the **BA.2 sub-lineages,** we have been monitoring the circulation of two lineages, **BA.2.12.1 and BA.2.35**, both **characterized by an additional mutation in position L452 of Spike protein** (L452Q and L452R, respectively). Mutations in this protein site are associated with resistance to neutralizing antibodies and is also known as a marker mutation of other variants of interest/concern, such as *Delta*, *Kappa* and *Omicron* BA.4/BA.5. While lineage **BA.2.12.1** has been presenting **fluctuating relative frequencies during the last weeks** (**Figure 2**)**, with values <2%, lineage BA.2.35 has been constantly decreasing since week 19 (9th-15th May, 2022**), with no detected cases on week 26 (analysis ongoing).

- **Lineage BA. 1**
  - **BA.1** has been firstly identified in Portugal by mid November, 2021, and was dominant between ISO weeks 51, 2021 (20th-26th November) and 7, 2022 (14th-20th February), having reached its maximum circulation in week 2 (95.6%, 10th-16th January, 2022) (**Figure 2**). **The current circulation of BA.1 in Portugal is estimated to be residual** (<1% since week 16, 18th-24th April, 2022).~

- **Lineages BA.4 and BA.3**

  - Since week 19 (9th-15th May, 2022), **42 sequences of the BA.4 lineage of Omicron variant were identified in Portugal**, associated with confirmed cases in all 7 Regions (**Figure 3**). This lineage presented a relative frequency **5.1% on week 26** (27th June - 4th July, 2022). Similarly to BA.5, with which it shares multiples mutations of interest, BA.4 lineage (also classified as VOC) has a relevant circulation in some countries, in particular in South Africa. In Portugal, no BA.3 case has been detected since week 11 (14th-20th March, 2022; see Report from 29th March, 2022).

- **Recombinants**

  - The co-circulation of several lineages/variants in the community increases the possibility of the occurrence of mixed infections, i.e., the same individual being simultaneously infected by more than one of them. In this context, mixture of their genetic material might occur, resulting in a hybrid genetic profile, commonly designated as "recombinant".

  - Currently, several SARS-CoV-2 recombinants have been described at a global scale (e.g., Delta+Omicron BA.1 or BA.1+BA.2), with novel designations being assigned to the recombinants with epidemiological/functional relevance. **In Portugal, the few recombinant viruses identified so far were detected in sporadic cases** in the weekly random surveys. Among these, we highlight **cases associated with the recombinants internationally designated as XM, XN, XE, XH and XAG**, being that all are characterized by a hybrid genetic profile where an initial portion of the genome corresponds to lineage BA.1 and the remaining portion to lineage BA.2. Similarly to other recombinant SARS-CoV-2 detected so far in Portugal, there is no evidence that these recombinants might present functional differences (e.g., differences in transmissibility and immune evasion) from the parental lineages BA.1, BA.2 and BA.5.

- Dynamic tables summarizing the **frequency and geotemporal spread of the variants/lineages identified so far as well as the mutations of interest in protein Spike** in each of them are available in the website.

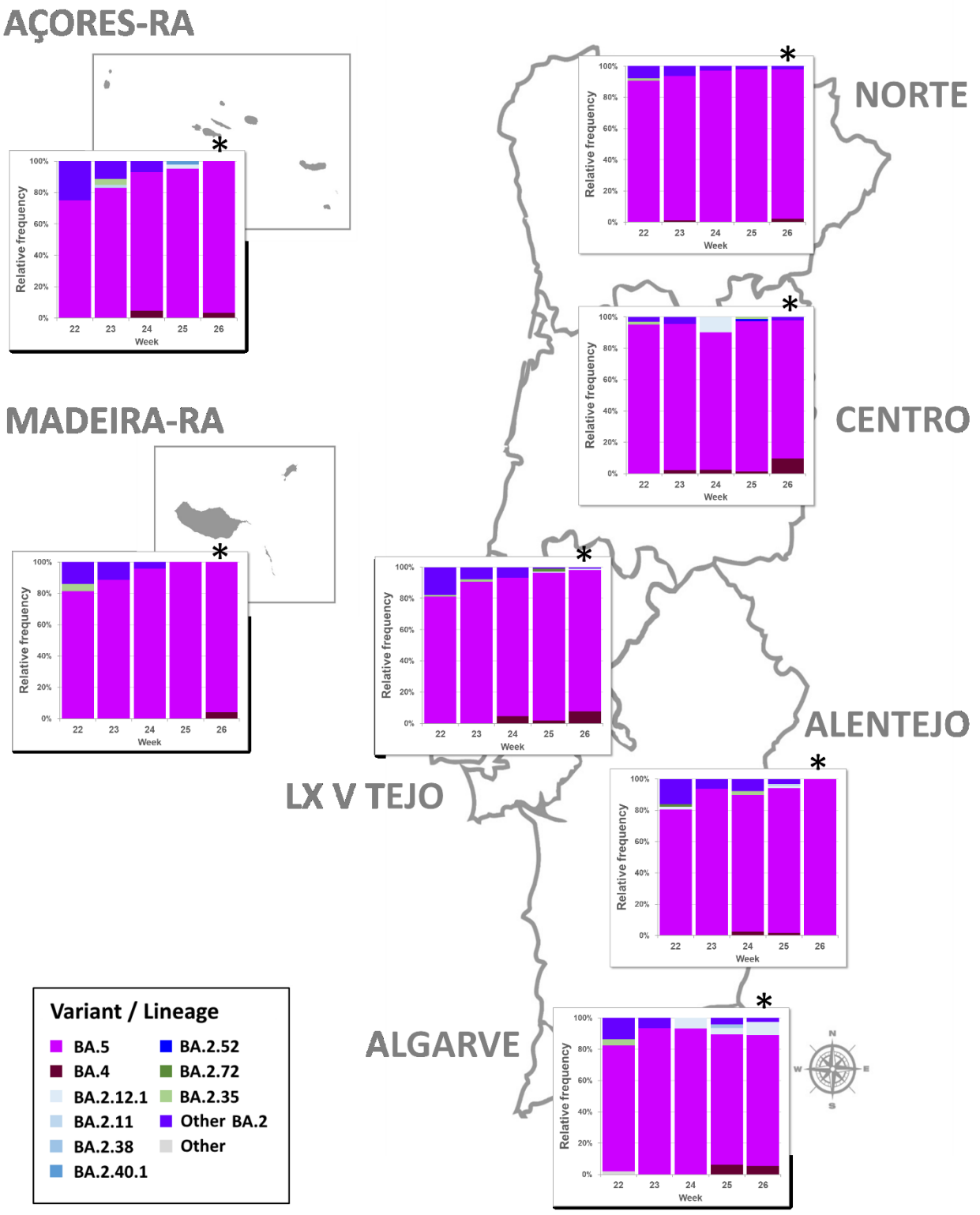

Figure 3. **Evolution of the weekly relative frequency of SARS-CoV-2 lineages in each Health Region, between ISO weeks 22** (30th May – 5th June) **and 26** (27th June – 4th July), **2022**. The plots highlight BA.2 sub-lineages with relative frequency ≥1% in at least one Region in week 24 (sampling closed), BA.4 and BA.5 (all classified as *Omicron* by WHO).

**It is expected that the frequencies presented for the last week under analysis (ISO week 26) might change in the next report, given that some data from that period is still being processed.*

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