

The SeqCOVID-Spain consortium: unravelling the dynamics of the COVID-19 first epidemic wave in Spain.

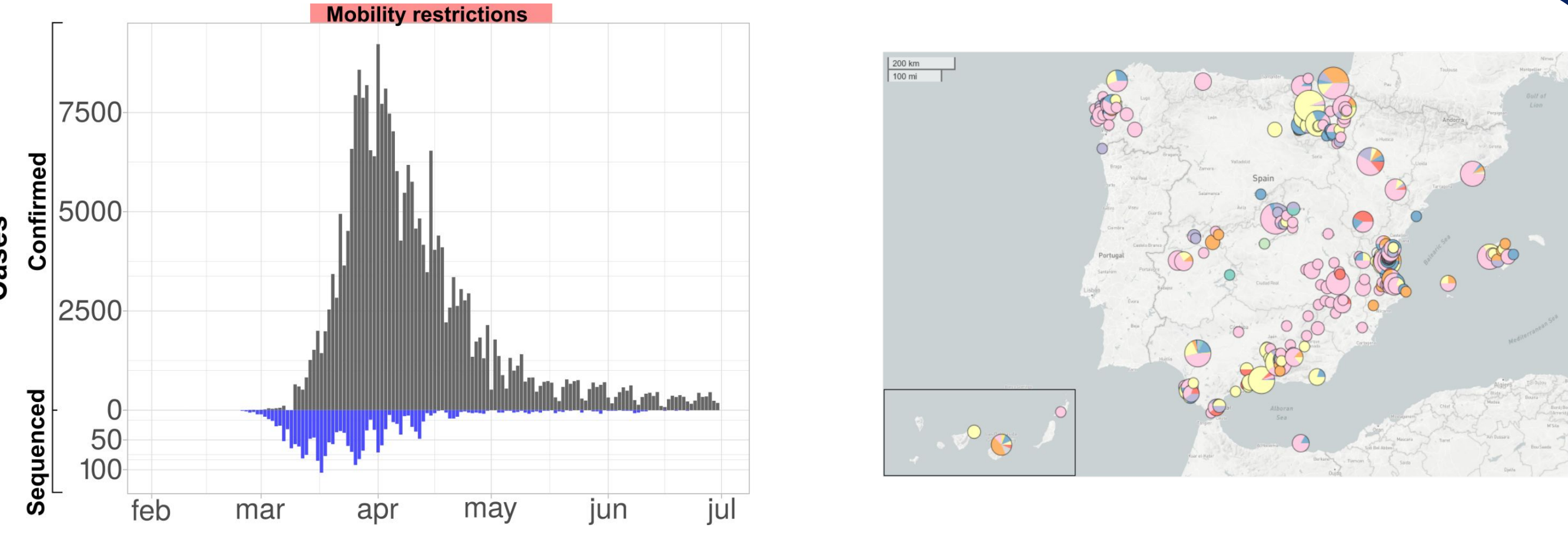
Álvaro Chiner-Oms^{1,†}, Mariana G. López^{1,†}, Darío García de Viedma^{2,3}, Paula Ruiz-Rodríguez⁴, María Alma Bracho⁵, Irving Cancino-Muñoz¹, Giuseppe D'Auria⁶, Griselda de Marco⁶, Neris García-González⁵, Galo Adrian Goig⁷, Inmaculada Gómez-Navarro¹, Santiago Jiménez-Serrano¹, Lúcia Martínez-Priego⁶, Paula Ruiz-Hueso⁶, Lidia Ruiz-Roldán⁵, Manuela Torres-Puente¹, Mireia Coscolla^{4*}, Fernando González-Candelas^{5,8*} and Iñaki Comas^{1,8*}, on behalf of the SeqCOVID-SPAIN consortium.

¹ Instituto de Biomedicina de Valencia (IBV-CSIC), Valencia, Spain | ² Servicio de Microbiología Clínica y Enfermedades Infecciosas, Hospital General Universitario Gregorio Marañón, Madrid, Spain | ³ CIBER Enfermedades Respiratorias (CIBERES) | ⁴ Instituto de Biología Integrativa de Sistemas, I2SysBio (CSIC-Universitat de València), Valencia, Spain | ⁵ Joint Research Unit "Infection and Public Health" FISABIO-University of Valencia I2SysBio, Valencia, Spain. | ⁶ FISABIO, Servicio de Secuenciación, Valencia, Spain | ⁷ Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland | ⁸ CIBER in Epidemiology and Public Health | [†] Equal contribution | * Corresponding author

Abstract

The COVID-19 pandemic has shaken the world since the beginning of 2020. Spain was among the European countries with the highest incidence of the disease during the first pandemic wave. We established a multidisciplinary consortium to monitor and study the evolution of the epidemic, with the aim of contributing to decision making and stopping the rapid spread of the virus across the country. We present the results of the analysis for 2170 sequences from the first wave of the SARS-CoV-2 epidemic in Spain, representing 12% of diagnosed cases until March 14. This effort allowed us to document at least 500 initial introductions, between early February-March from multiple international sources. Importantly, we document the early rise of two dominant genetic variants in Spain (Spanish Epidemic Clades), named SEC7 and SEC8, likely amplified by superspreading events. In sharp contrast to other non-Asian countries those two variants were closely related to the initial variants of SARS-CoV-2 described in China and represented 40% of the sequences analyzed. The two dominant SECs were widely spread across the country compared to other genetic variants with SEC8 reaching a 60% prevalence just before the lockdown. Employing Bayesian phylogenetic analysis, we inferred a reduction in the effective reproductive number of these two SECs from around 2.5 to below 0.5 after the implementation of strict public-health interventions in mid-March. The effects of lockdown on the genetic variants of the virus are reflected in the general replacement of pre-existing SECs by a new variant at the beginning of the summer season. Our results reveal a significant difference in the genetic makeup of the epidemic in Spain and support the effectiveness of lockdown measures in controlling virus spread even for the most successful genetic variants.

Sampling

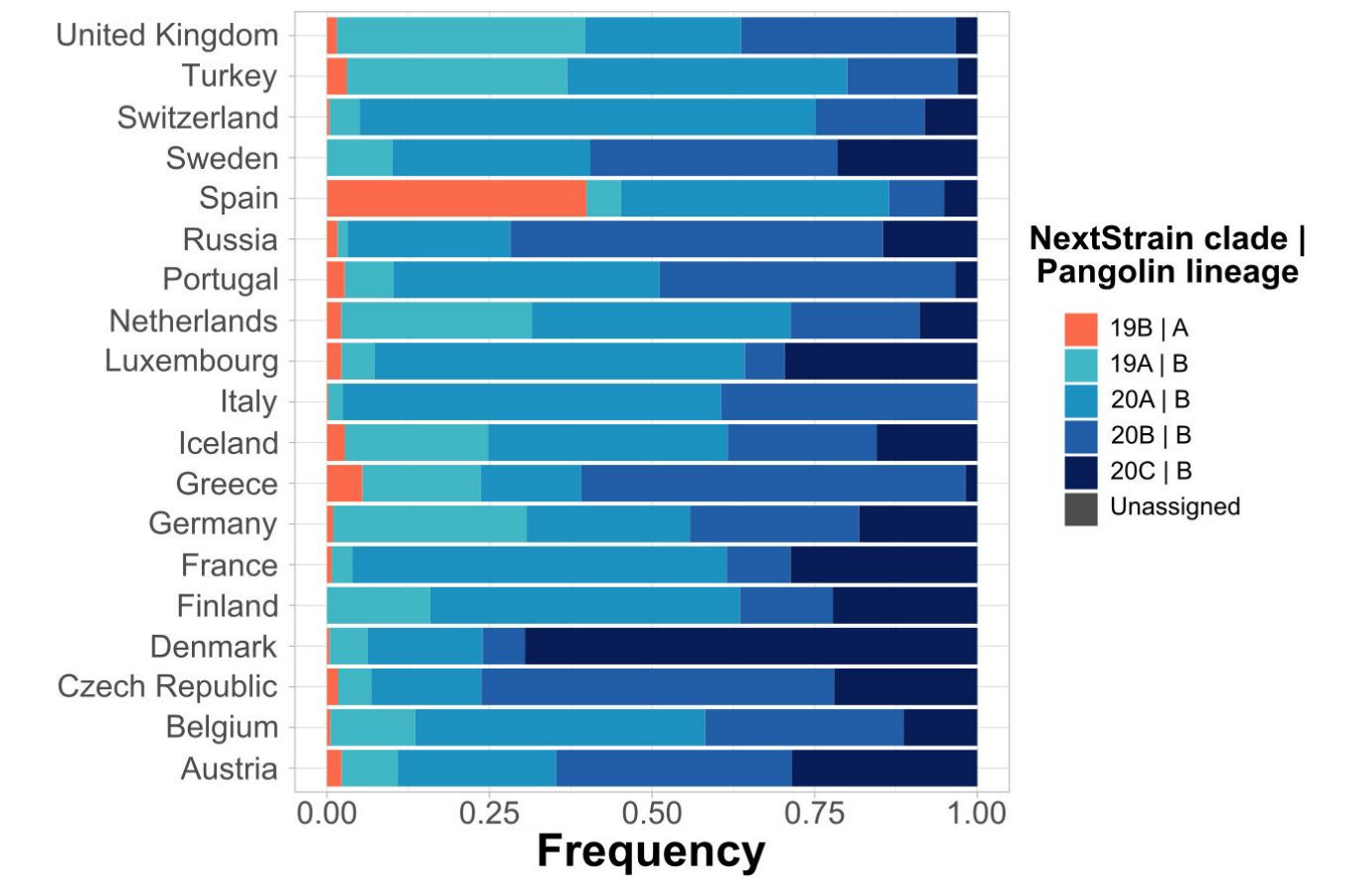


~1% of the cases reported from February to June 2020 from all over the country have been sequenced (n=2,170).

More than 50 institutions integrate SeqCOVID-Spain. The consortium is the **main contributor** of Spanish SARS-CoV-2 sequences to public repositories and databases. For the present analysis, we generated **2,170 sequences** from February to June (2020), trying to maximize the spatial and temporal diversity of the samples.

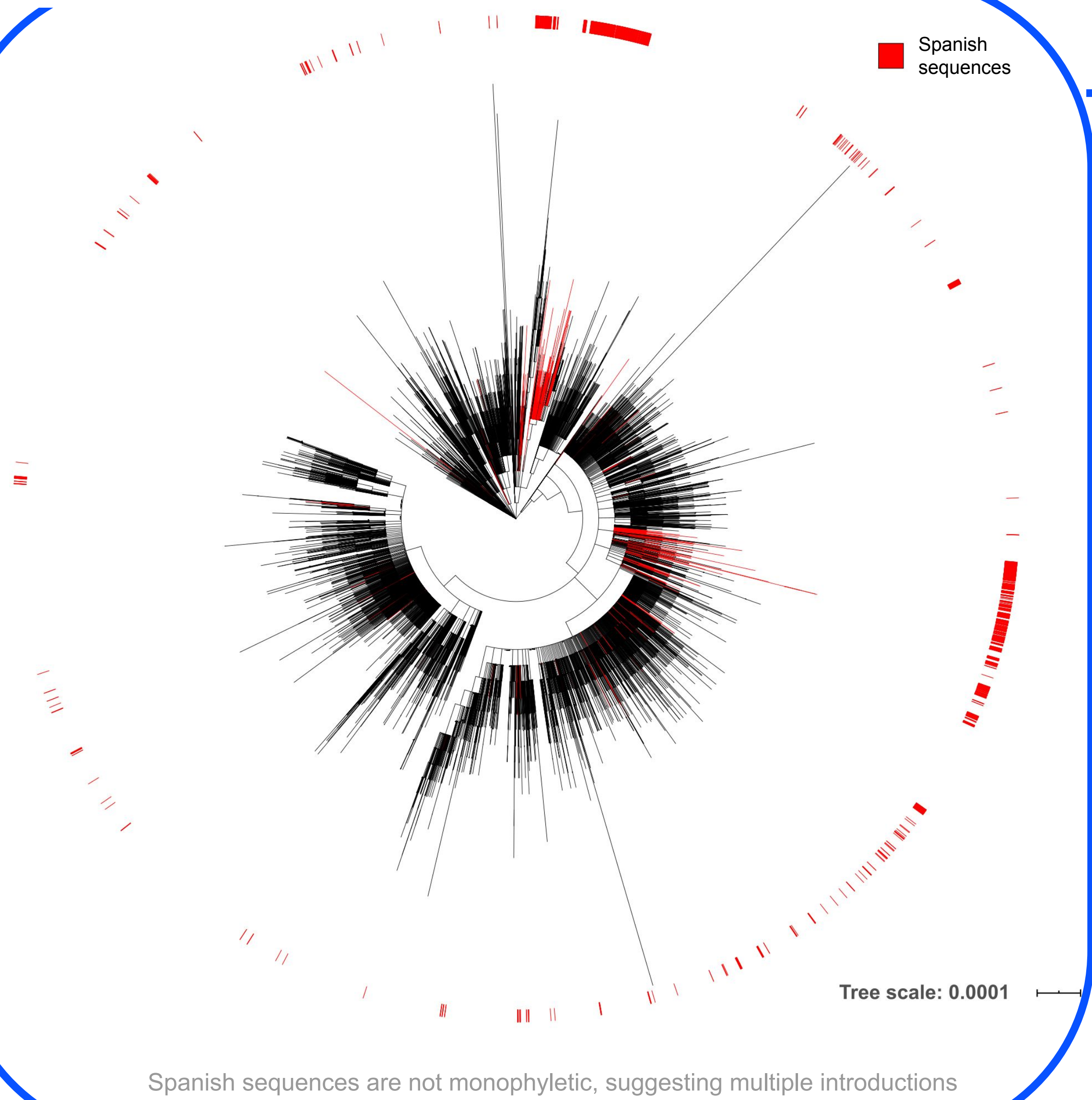
Spain had an **abundance of lineage A** (Pangolin classification) sequences, which were abundant in Asian countries but uncommon in the European region during this period.

Structure



Spain has a lineage profile different from the rest of European countries, with an overrepresentation of clade A strains (absence of D614G).

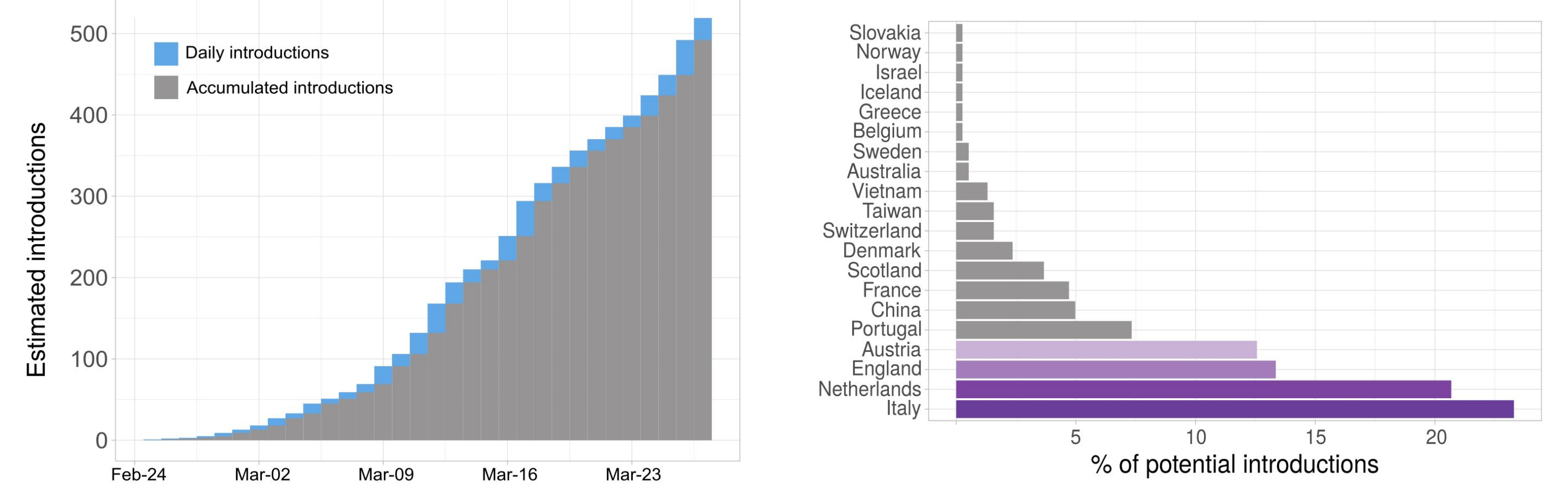
Spanish cases in a global context



If we place the Spanish sequences in a global phylogeny, they do not share a common ancestor, suggesting **multiple introductions**.

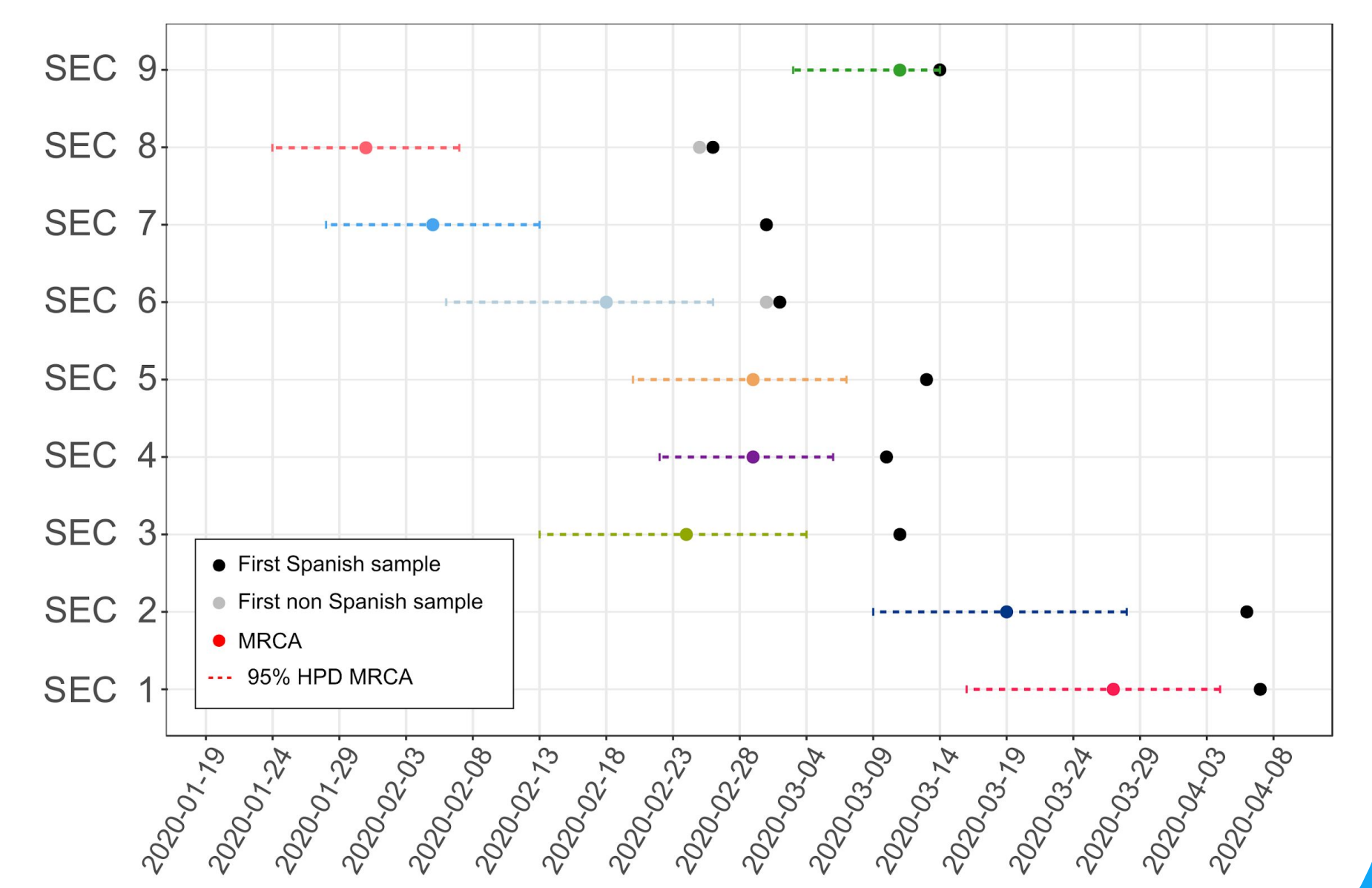
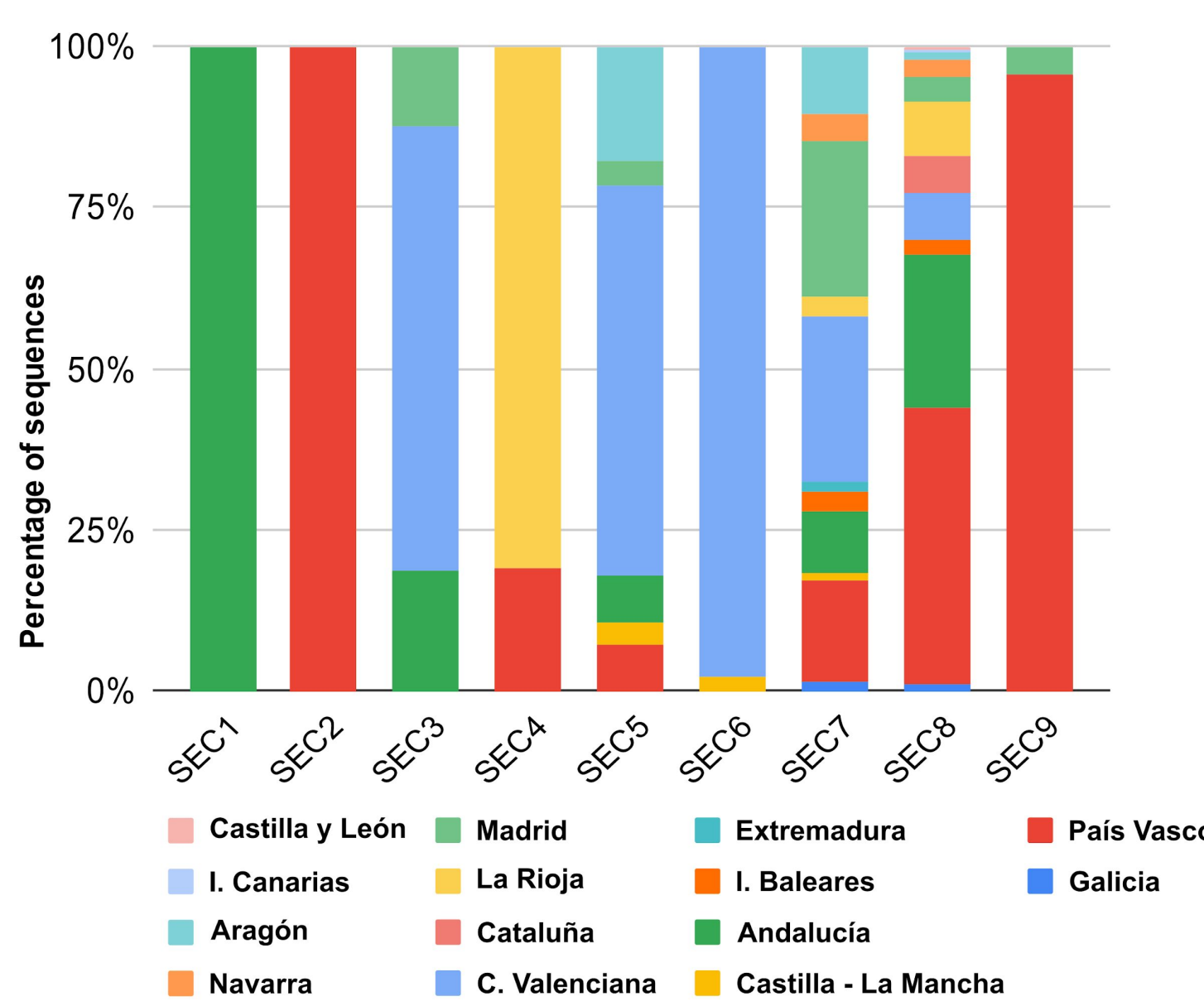
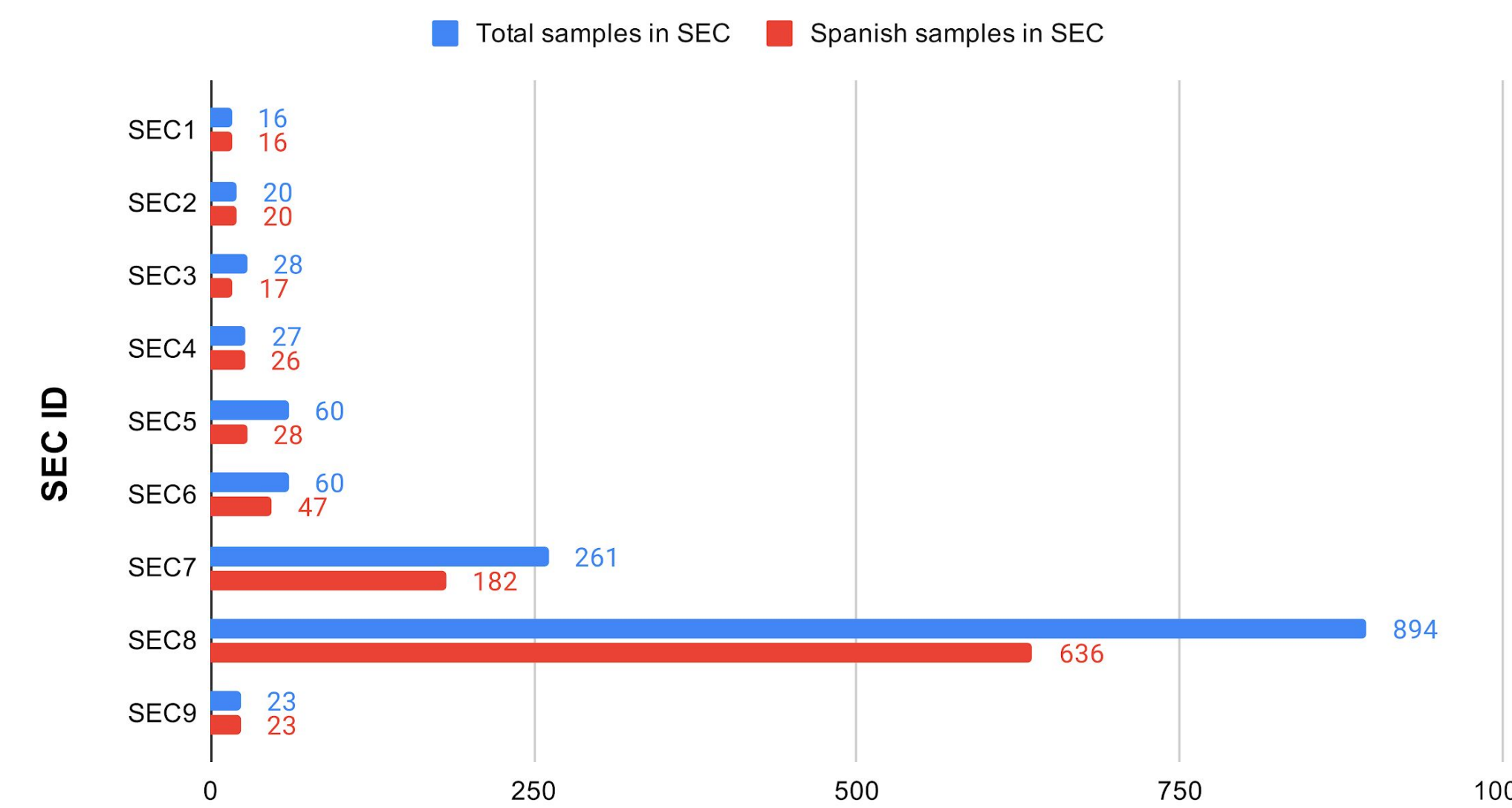
Using the phylogeny, we have calculated a minimum of **500 independent introductions from different countries, mainly Italy as suggested by epidemiological information**. Most of them ended up generating transmission clusters in Spain (191), while for some others (328) no posterior transmission was detected.

Potential introductions



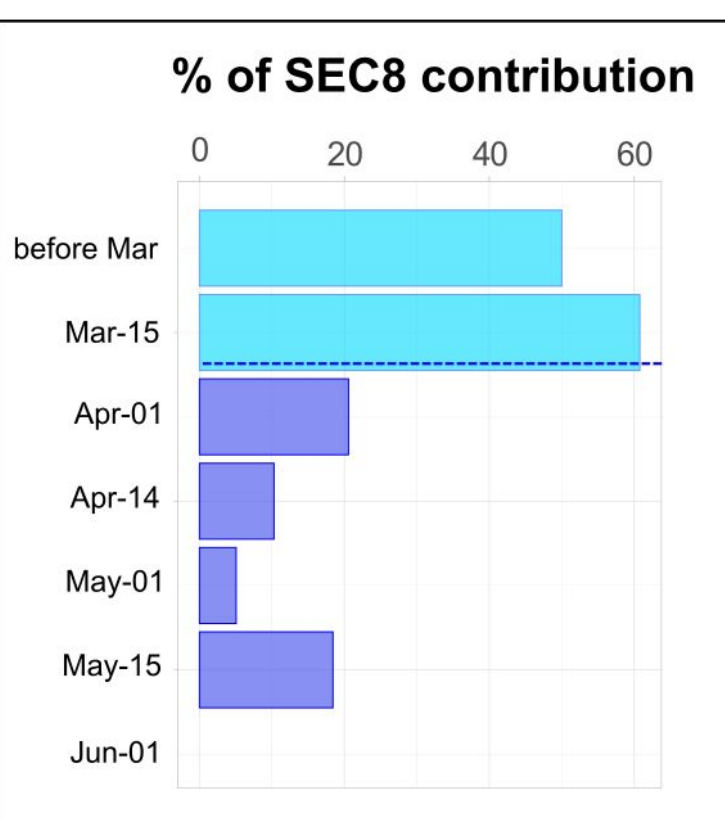
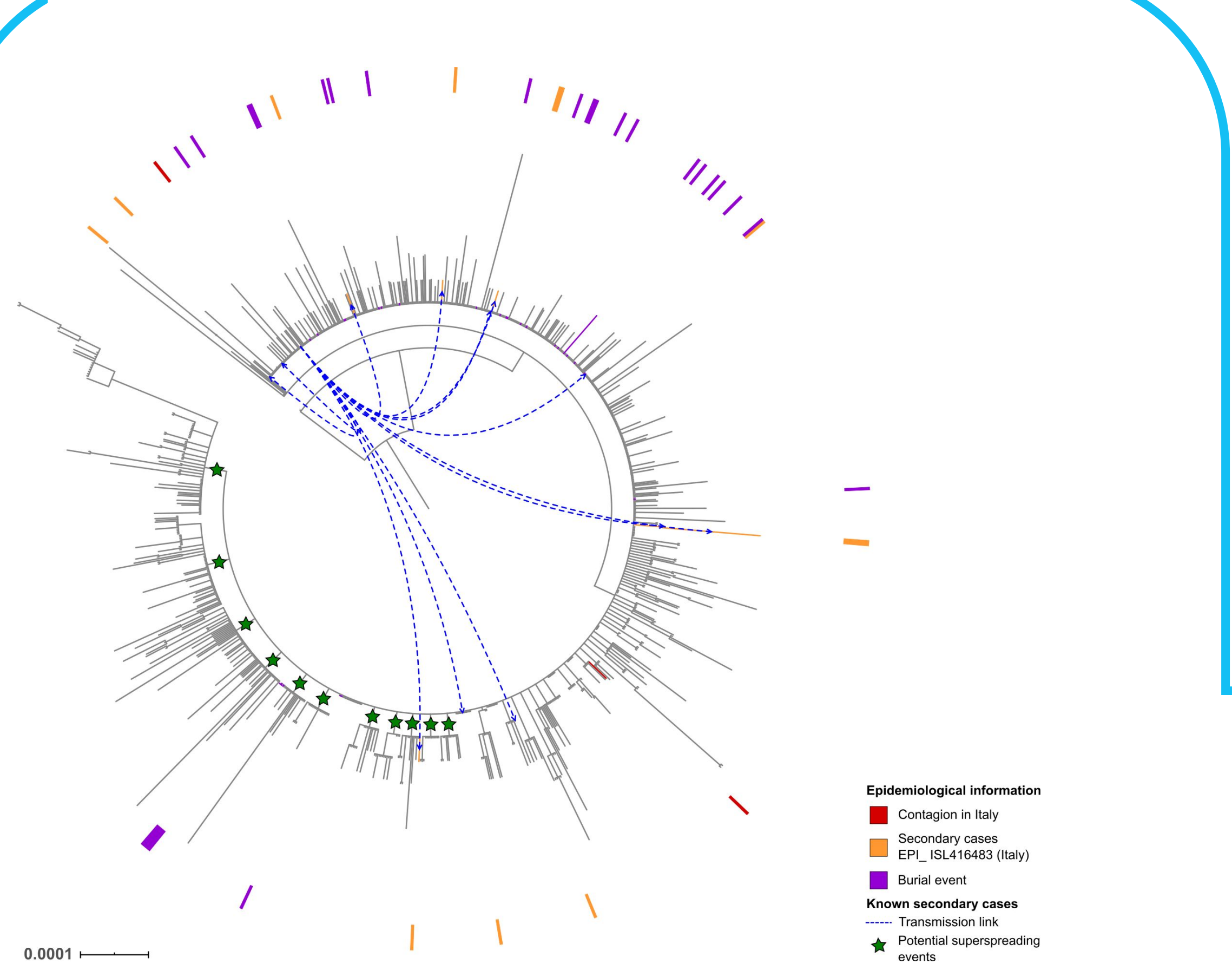
At least 500 introductions, estimated from the phylogeny, from different countries.

Spanish Epidemic Clades (SEC)

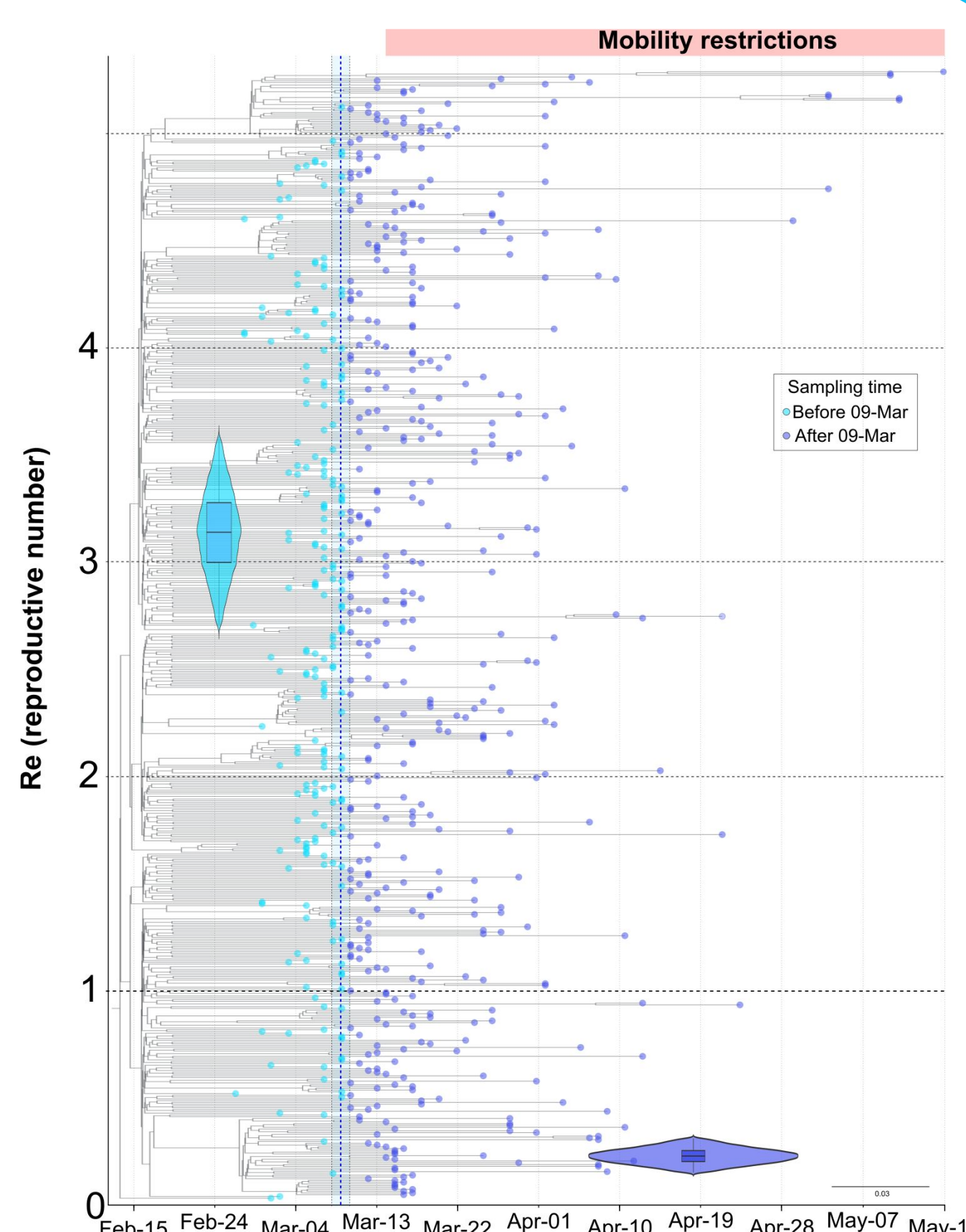


9 different Spanish Epidemic Clades (SEC) account for ~40% of the sequenced cases. These SECs had a heterogeneous distribution across the country, and were introduced on different dates.

SEC8 in detail



The success of SEC8 was facilitated by several early and multiple introductions in Spain, superspreading events and the absence of sanitary measures in a naïve population. SEC8 represented ~60% of the sequenced cases before the national lockdown, a strict intervention that was highly effective to reduce the Re.



We have epidemiological information proving that SEC8 was introduced **from Italy**, at least twice, to the Valencia city in which a big transmission cluster started. At the same time, a burial in La Rioja region acted as a **superspreading event**. We have also SEC8 sequences from the same period from Madrid, Andalucía and Basque Country. SEC8 was so successful that almost **60%** of the sequenced cases before the national lockdown belonged to this clade. Finally, the **national lockdown** that started on 14th March 2020 was **highly effective in stopping the viral transmission**. This was reflected in a **reduction of Re from 3,1 (before lockdown) to 0,2 (after the lockdown) in SEC8 strains**.

Funding

CSIC
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

GOBIERNO DE ESPAÑA | MINISTERIO DE CIENCIA E INNOVACIÓN

ISC
Instituto de Salud Carlos III

European Research Council

This work was funded by the Instituto de Salud Carlos III project COV20/00140, Spanish National Research Council project CSIC-COV19-021, Ministerio de Ciencia PID2019-104477RB-I00 and ERC StG 638553 to IC, and BFU2017-89594R to FGC. MC is supported by Ramón y Cajal program from Ministerio de Ciencia and grants RTI2018-094399-A-I00 and SEJ19/011.