

# Study of the Behavior of the pair *K. pneumoniae* | Carbapenems in several European Countries by Clustering Health Data Time Series With The Generalized Affinity Coefficient

Ana Paula Nascimento <sup>1,2</sup>, Mónica Vieira <sup>1,3</sup>, Cristina Prudêncio <sup>1,3</sup>, Helena Bacelar-Nicolau <sup>4,5</sup>

## Affiliations

1-RISE-Health, Center for Translational Health and Medical Biotechnology (TBIO), Escola Superior de Saúde (E2S), Polytechnic of Porto (P. Porto), R. Dr. António Bernardino de Almeida, 400, 4200 - 072, Porto, Portugal.  
 2-Biomatemática, Bioestatística e Bioinformática, E2S/P. Porto, R. Dr. António Bernardino de Almeida, 400, 4200 - 072, Porto, Portugal.  
 3-Ciências Químicas e das Biomoléculas, E2S/P. Porto, R. Dr. António Bernardino de Almeida, 400, 4200 - 072, Porto, Portugal.  
 4-Faculty of Psychology, University of Lisbon (FPUL), Lisboa, Portugal  
 5-Institute of Environmental Health, Faculty Medicine, University of Lisbon (ISAMB-FMUL), Lisboa, Portugal

## Abstract

Antimicrobial resistance constitutes a major public health and economic burden in contemporary society. The aim of this work is to identify patterns and trends associated with resistance behavior of *Klebsiella pneumoniae* to carbapenems across several European countries.

Data on *K. pneumoniae* resistance to carbapenems across several countries from 2005 to 2021 (with data available up to 2023) were retrieved from the public ECDC website in 2023. Agglomerative hierarchical cluster analysis based on the generalized Affinity coefficient was applied to the estimated ARIMA models representing the data.

The Dendrogram at the cut-off presented four clusters, first cluster with Slovenia, Luxembourg, Italy and Estonia, second Cluster with Romania, Malta, Greece, Portugal and Spain, third Cluster Denmark, France and Czechia and finally fourth cluster with Lithuania, Cyprus, Finland, Austria, Belgium and Slovakia. Although the resistance values show a more visible increasing trend over the years in Clusters II and III, the increase is more pronounced.

The application of data analysis, using agglomerative hierarchical cluster analysis based on the generalized Affinity coefficient, allows the evaluation of patterns among different regions, and gives the possibility to identify alarming groups that need urgent intervention.

## Introduction

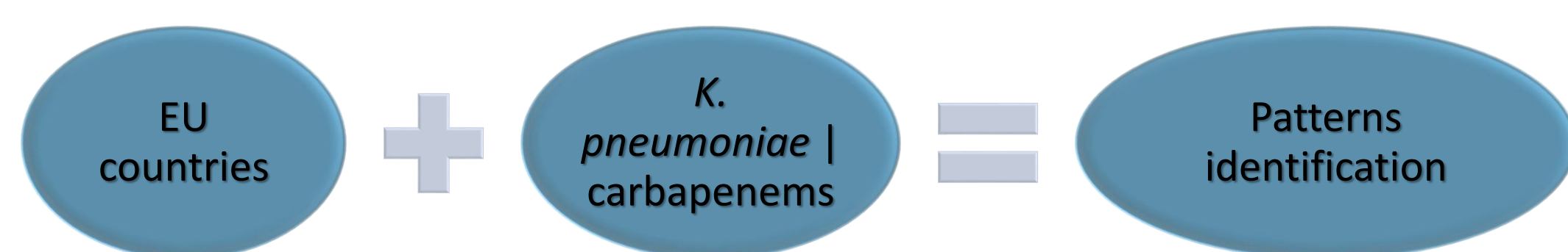
Antimicrobial resistance (AMR) constitutes a major public health and economic burden in contemporary society.

- ✓ Among the 10 global public health threats facing humanity
  - Priority pathogens
- ✓ Most significant threats to human health in the 21<sup>st</sup> century
  - 12 families of bacteria pose the greatest threat to human health
- ✓ "Silent Pandemic"
  - Global (and local) response to AMR

## Materials and Methods

The aim of this work is to identify patterns and trends associated with resistance behavior of *K. pneumoniae* to carbapenems across several European countries, in order to better understand its dynamics and public health implications, since it is a pair considered by the WHO as a critical priority. To achieve this, we apply, for the first time, agglomerative hierarchical cluster analysis (HCA) using the generalized affinity coefficient in combination with Autoregressive Integrated Moving Average (ARIMA) models.

### Time series Hierarchical Cluster Analysis with the Generalized Affinity Coefficient



## Conclusions

The application of data analysis, for the first time, using HCA based on the generalized Affinity coefficient, allows the evaluation of patterns among different regions, and gives the possibility to identify alarming groups that need urgent intervention. Based on slope calculations, Spain ( $m = 1.5$ ) shows the most pronounced increase in *K. pneumoniae* resistance to carbapenems. This trend is particularly evident in Cluster II, which includes Spain, highlighting a group of countries where stronger measures are needed to control the incidence of this resistance and to reinforce dissemination prevention strategies. Although Greece and Romania exhibit lower slopes, they report the highest incidence levels of resistance. As members of Cluster II, their sustained upward trend over time also places them among the priority countries for enhanced monitoring and targeted prevention policies.

## Bibliographic References

Nascimento, A. P. M. do. (2025). Health data management based on the affinity coefficient: Applications to time series cluster analysis in biotechnology (Doctoral dissertation). International Doctoral School, Universidad de Vigo.

## Results

Country	Mean (%)	Standard deviation (%)
Austria	0.59	0.46
Portugal	4.69	4.75
Belgium	0.93	0.63
Cyprus	12.6	7.1
France	0.38	0.3
Spain	1.85	1.96
Italy	22.04	13.07
Czechia	0.29	0.28
Denmark	0.22	0.23
Estonia	0.32	0.72
Finland	0.11	0.18
Greece	55.2	13.73
Lithuania	0.63	1.11
Luxembourg	0.5	0.7
Malta	5.04	4.47
Romania	25.74	16.42
Slovakia	4.18	3.43
Slovenia	0.34	0.4

Fig. 1. Summary statistics of *K. pneumoniae* resistance to Carbapenems.

From Figure 1, it can be observed that Greece, Romania, and Italy have the highest mean resistance values. Finland presents the lowest mean (very low resistance).

The results of the agglomerative hierarchical cluster analysis (HCA), using the generalized Affinity coefficient between the Autoregressive Integrated Moving Average (ARIMA) models that best fit the resistant isolate percentage values over time, in the case of the pair *K. pneumoniae* | Carbapenems, across several EU countries, are presented below.

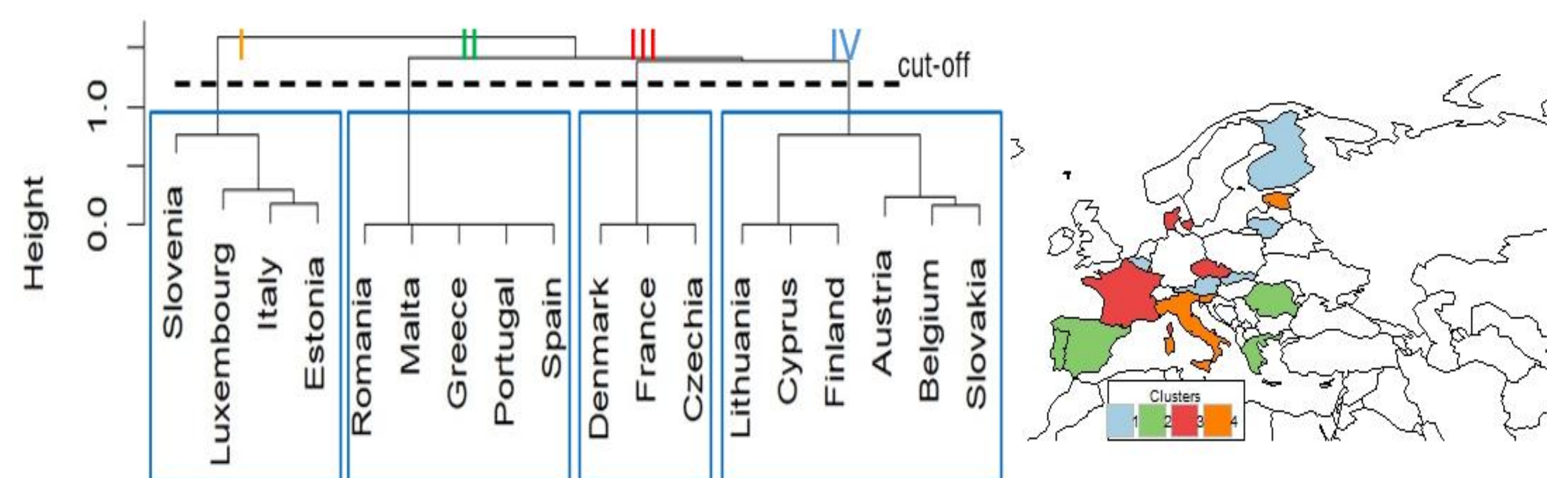


Fig. 2. Dendrogram and map representing the four clusters from cluster analysis in *K. pneumoniae* | Carbapenems resistance context

The Dendrogram at the cut-off presented four clusters (Fig. 2). Although resistance values show an increasing trend over years in all clusters, this increase is more pronounced in Clusters II and III. In fact, the data were standardized, and the slopes of the lines obtained between the years 2012 and 2020 were calculated for Clusters II and III. For Clusters I and IV, this was not possible due to the irregularity of the curves. The slopes are higher in the countries belonging to Cluster II. Specifically, the slopes for Cluster II's countries (Fig. 3) are  $m = 0.29$ ,  $m = 1.5$ ,  $m = 0.06$ ,  $m = 0.11$ , and  $m = 0.26$  for Portugal, Spain, Greece, Malta, and Romania, respectively, whereas for Cluster III's countries (Fig. 4), the slopes are  $m = 0.02$ ,  $m = 0.08$  and  $m = 0.001$  for France, Czechia and Denmark, respectively. It is also worth noting that within Cluster II, Portugal, Romania and Spain show a steeper increase, with Spain showing the most pronounced growth. It is imperative that these countries strengthen their capacity to address this issue.

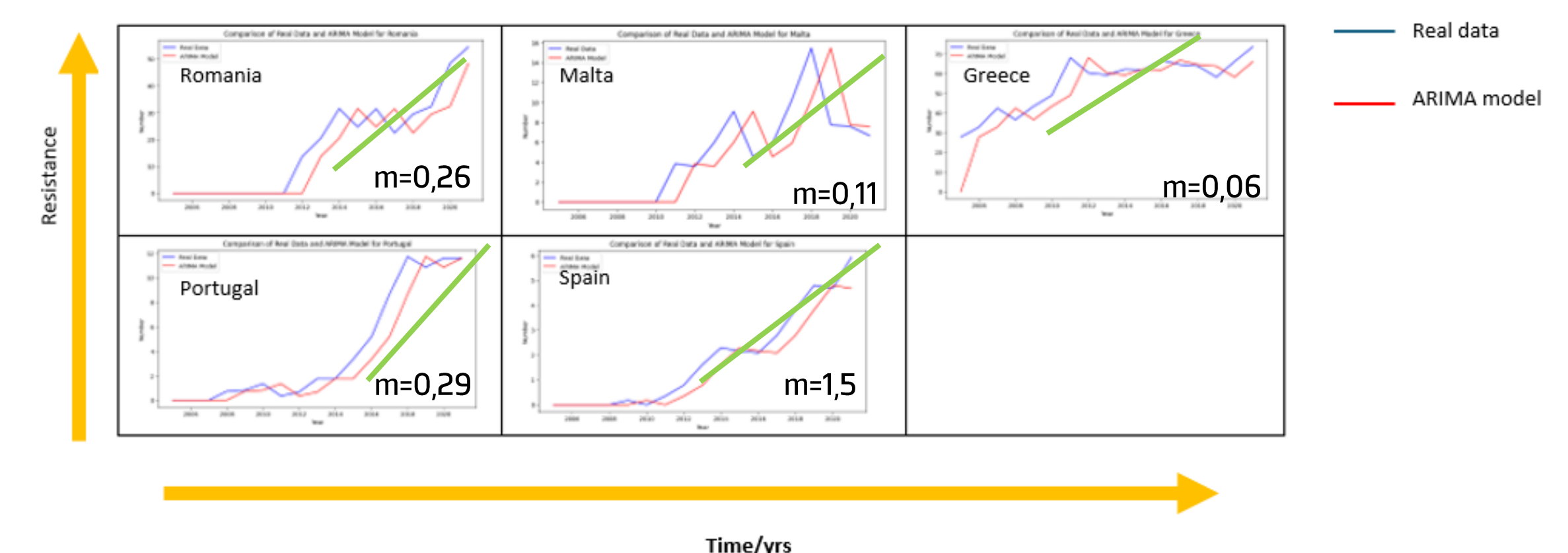


Fig. 3- Fit and forecast across countries belong to cluster II in *K. pneumoniae* | Carbapenems resistance context.

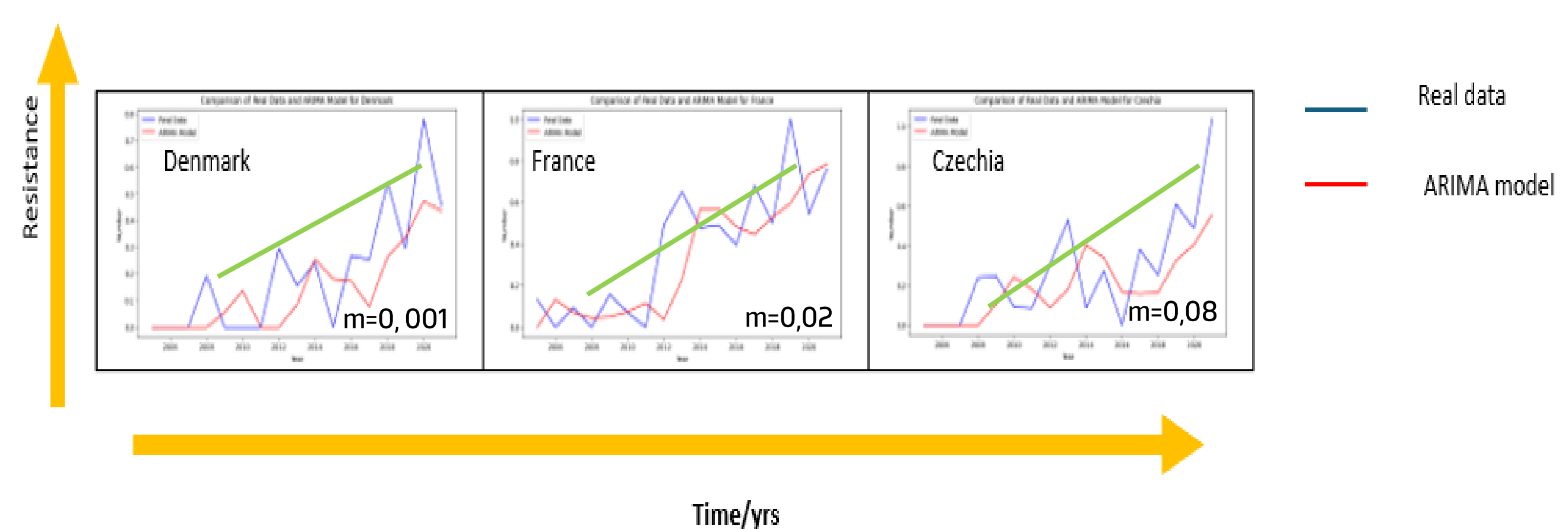


Fig. 4- Fit and forecast across countries belong to cluster III in *K. pneumoniae* | Carbapenems resistance context.