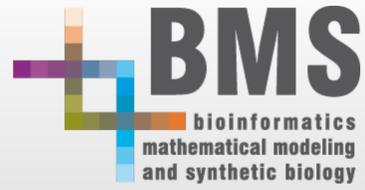




# A mixed effect multi-funnel model for country surveillance of antibiotic resistance: evidence from the WHO GLASS dashboard



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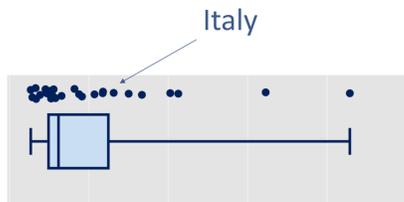
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## The threat of AntiMicrobial Resistance (AMR)

Antibiotic resistance poses a significant global health challenge [1], necessitating robust **surveillance** methods to monitor its prevalence and trends across different hospitals, regions or countries. According to [2], “Setting up country-level surveillance of resistance and consumption is vital for understanding the impact of AMR and to reduce the spread of resistant pathogens”.



WHO GLASS dashboard visualization  
2020 European region data  
Escherichia Coli resistance to Cefotaxime

## The WHO dashboard

AMR resistance data for year 2020, pertaining to the WHO European region, were acquired from the GLASS dashboard, which presents global AM consumption and resistance data for countries, territories, and areas, enrolled in GLASS (Global Antimicrobial Resistance and Use Surveillance System) [3].

For each pathogen-antibiotic pair, the GLASS dashboard provides the number of performed Antibiotic Susceptibility Tests (AST) and the corresponding resistance percentage for each country.

In the boxplot provided by GLASS, Italy does not appear to be an outlier.

## Objectives

- to develop a diagnostic tool for statistically monitoring AMR at country level, as reported in the GLASS dashboard;
- to define a model of natural variability of AMR that considers the number of performed tests and provides alarm limits;
- to obtain the distribution of AMR across countries, highlighting possible clusters of countries sharing common features.

## Methods: the Funnel Plot

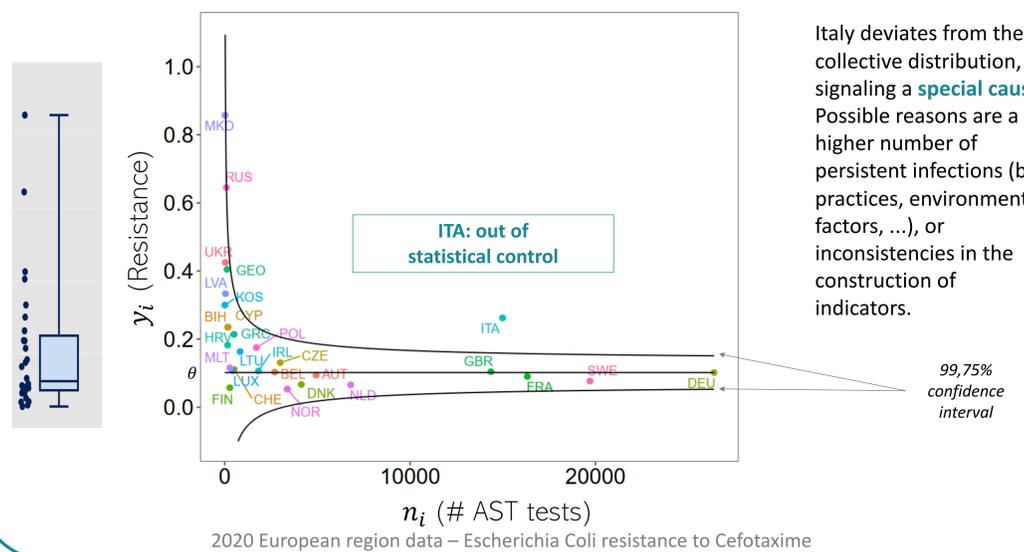
To characterize the statistical variability of antibiotic resistance as a function of AST numerosity, we propose utilizing the funnel plot methodology [4], a statistical process control approach [5] that compares the performance of units having different sizes and provides probabilistic alarm limits. In particular, the inter-unit variability is described either by multiplicative overdispersion or by a random effect model [6]. In the literature the standard funnel plot addresses only unimodal dispersion of indicators. To address multimodal distributions of antibiotic resistance observed in the dashboard, two new multi-funnel models are developed, based either on multiplicative overdispersion or the introduction of a Gaussian Mixture Model (GMM) random effect.

## Results

Pathogen - Antibiotic	Model*	$\theta$	$\sigma$	$\omega$	$\theta'$	$\sigma'$	$\omega'$
Esch. Coli - Cefotaxime	Single funnel	10%	2.1	0.01	-	-	-
Acinetobacter - Meropenem	Multi funnel	5%	0.9	0.017	81%	2.2	0.019

### Example of standard funnel - Escherichia Coli vs Cefotaxime

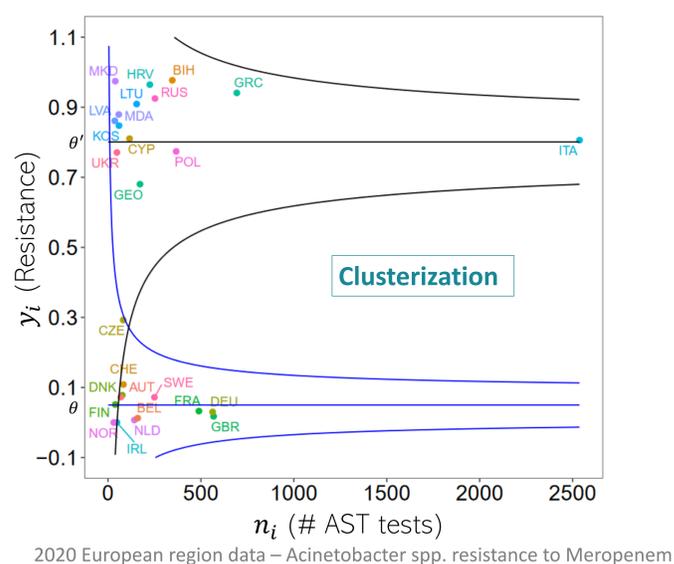
$$y_i = \theta + \eta_i + \epsilon_i, \quad \eta_i \sim N(0, \omega^2), \quad \epsilon_i \sim N(0, \sigma^2/n_i)$$



Italy deviates from the collective distribution, signaling a **special cause**. Possible reasons are a higher number of persistent infections (bad practices, environmental factors, ...), or inconsistencies in the construction of indicators.

### Example of multifunnel - Acinetobacter vs Meropenem

$$y_i = \alpha_i(\theta + \eta_i + \epsilon_i) + (1 - \alpha_i)(\theta' + \eta'_i + \epsilon'_i), \quad \alpha_i \in \{0,1\}$$



The two **clusters** (North+Center Europe and South+East Europe) reflect different ease of infections (differences in environment, public health,...) or differences in data collection.

**Conclusions:** These findings show the effectiveness of funnel models for the statistical characterization of the antibiotic resistance variability across European countries. In some cases, variability is adequately explained by a single random effect accounting for country variability, but in several other cases the variability is at least bimodal and calls for a “country effect” distributed according to a GMM, yielding the newly defined multi-funnel plots.

## References

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