MULTIVARIATE ANALYSIS OF ANTIMICROBIAL RESISTANCE IN THE ANIMAL-FOOD-HUMAN CHAIN AND ITS CORRELATION WITH THE LEVEL OF DEVELOPMENT OF NATIONAL ACTION PLANS IN EUROPEAN COUNTRIES.

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INTRODUCTION

The One Health paradigm is essential for understanding and controlling antimicrobial bacterial resistance (AMR): a complex multi-factorial problem.

In the era of big data, nevertheless, the main challenge goes beyond the first and necessary step of constructing and updating public databases with relevant, harmonised and curated databases on AMR. Turning data into useful knowledge and insight is still an open challenge. There is a clear need for mathematical tools and analysis in order to infer predictions, cause-effect relationships or at least correlation or ranking of the relevance of the main antimicrobial drivers using current databases. Moreover, the analysis should iterate with data, detecting misleading and missing information to drive the re-design of databases in the following years.

Multivariate analysis is one of the main tools used to retrieve information from databases. It studies how different and multiple variables (features) interfere with one another and how they work in combination. Recent attempts to statistically analyse public databases of AMR focused on foodborne pathogens Zhang, et al., 2019 (10.3390/ijerph16101811) and Yang, et al., 2020 (10.3390/ijerph17020472).

METHODOLOGY

We apply multivariate analysis methods to a dataset gathering information on antimicrobial resistance in the animal-food-human chain for each country of the EU with three groups of variables:

- Human AMR quantitative variables (HUMAN VARIABLES) consisting of the ECDC 2018 percentage of strains resistant to antibiotics found in humans (E. coli resistant to Fluoroquinolones, Staphylococcus aureus resistant to Meticillin, Enterococcus faecium resistant to Aminopenicillins, Pseudomonas aeruginosa resistant to Carbapenems). Data were retrieved from the Surveillance Atlas of Infectious Diseases from ECDC (https://atlas.ecdc.europa.eu/public/index.aspx)

- Food-related AMR quantitative variables (FOOD VARIABLES) including the 2018 resistance percentage in animals and food (ESBL resistant to Ciprofloxacin in both broilers and broiler

meat) retrived from the EFSA repository in Zenodo (https://zenodo.org/record/3628719#.YVH2TppBxPY)

- Socioeconomic-political AMR qualitative variable (POLITICAL VARIABLE) consisting of the level of development (A,B,C,D,E) , in 2017, of national AMR action plans taken from the Global Database for the Tripartite Antimicrobial Resistance Country Self-assessment Survey (TrACSS) (https:/

RESULTS

When using only the quantitative variables (FOOD and HUMAN), Principal Component Analysis captures 81.7 % of the information with just two dimensions. In this projection, the maximum variability between countries is observed in the Food variables (which are highly correlated variables), and the minimum variability in resistance to Aminopenicillins is seen in Enterococcus faecium. The Cluster Dendrogram classifies the countries into three groups:

1) northern countries (Norway, Finland, Sweden and Iceland),

2) eastern and southern countries and

3) central countries.

When the analysis includes the information for the political qualitative variable of AMR plan development, 67.8 % of the information is captured with two dimensions. The cluster dendrogram identifies groups of similarity (clusters) corresponding to four groups that correspond to countries with National AMR action plans that

1) are under development (B)

2) are developed (C)

3) have identified funding sources, are being implemented, have involved the relevant sectors and have a defined monitoring and evaluation process in place (E)

4) are approved by government and reflect Global Action Plan objectives (E), but including one country classified under B and two classified under E.

DISCUSSION

The multivariate analysis of AMR variables is fundamental to understanding the interactions between Health, Environment and Society (One Health paradigm). Moreover, the information obtained from the multivariate analysis identifies the most relevant variables and remains the bedrock for developing, in the future, dynamic models of AMR based on mechanistic insight.

In this work, we analysed resistance percentages in humans, animals for food consumption and food matrices and the level of development of the national AMR plan in order to study the animal-food-human chain and how it is affected by the development of current national AMR plans. Our analysis shows that, when the percentage of resistance is considered for each country, food-related variables are responsible for the greater variability among countries that can be clustered according to their location (northern, southern/eastern or central EU country), but not clearly by their AMR development plan. Further analysis should be conducted to demonstrate if the effectiveness of AMR plans is highly dependent on the country’s location (and implicitly culture) and to include more environmental and economical variables that could affect AMR prevalence.