National Collaborating Centre for Infectious Diseases
Centre de collaboration nationale des maladies infectieuses

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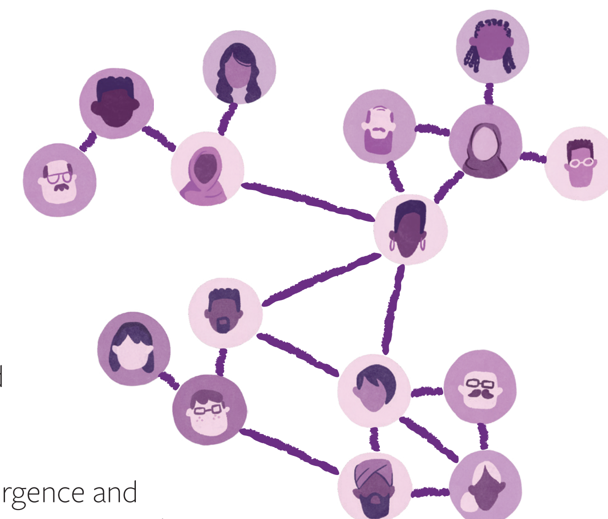
Is scientific evidence enough? Using expert opinion to fill gaps in data in antimicrobial resistance research

August 8, 2023 PLoS ONE 18(8): e0290464

Antimicrobial resistance (AMR) has had devastating effects on the health and well-being of humans, animals, and the global environment. In addition to the use of antimicrobials (AMs), cultural, social, and economic conditions also dictate why and how AMs are used. Many interventions that combat AMR are limited to single sectors and may have unintended consequences on a broader scale. These interventions may not be adopted into policy or may be met with non-compliance. Addressing the complexity of the AMR issue and its drivers requires a better understanding of the system, and how different drivers are related to and influence each other.



Simulation models have been used to explain and predict the emergence and transmission of AMR, but these models are rarely integrated across sectors and usually focus on small populations in specific settings. One of the major limitations in creating integrated models is the limited data available that can be used to capture the diverse One Health aspects of AMR. In order to improve future modelling research and to better assess interventions to combat AMR globally, professional knowledge, experiences, and opinions (tacit knowledge) may help to address existing knowledge gaps.

This study expanded on previous work in which experts from the One Health system in Europe came together at a participatory modelling workshop to co-create a causal loop diagram (CLD), which served as a visual representation of the key drivers (also called factors or nodes) and their relationships within the AMR system. The objective of this study was to use the existing qualitative descriptions of the AMR system to derive semi-quantifiable data about the drivers of AMR development and transmission in a European context.

The European One Health system integrates knowledge, surveillance, and data from human, animal, food/agricultural, and environmental domains when considering the causes of AMR to identify priorities for policy decisions.

Methods

For a previous study, seventeen experts from the One Health system in Europe participated in two 6.5-hour modelling workshops held on September 19th and 20th 2019. The participants represented a wide range of perspectives within the One Health system, with over half of participants from Sweden and the remaining from France, Italy, Spain, United Kingdom, and Belgium. The first day of the workshop consisted mostly of those who had expertise in AMR and antimicrobial use (AMU) within various areas of the overall food system (e.g., infection control, food safety, veterinary medicine). Those who participated on the second day had expertise within the broader system but are not traditionally engaged in AMR discussions (e.g., pharmaceutical law, consumer advocacy). Using open-ended questions and group discussion, the participants and facilitators mapped out major drivers of AMR (nodes) into a CLD.

In this study, participant transcripts from the workshop were re-analyzed to capture relationships between drivers in measurable terms (i.e., can increase or decrease). Transcripts from the two workshops were coded in NVIVO 12; a software used for qualitative and mixed-methods research. An adaptable codebook created to identify major AMR drivers and relationships between drivers in the existing CLD was used. For this study, additional codes were added to achieve the following:

1. Include the levels of nodes, which refers to the position of that node in Sweden based on the amount, quantity, extent, or quality compared to a referent.
2. Identify the strength (strong, weak, not mentioned) and direction (positive, negative, not mentioned) of the correlation of the relationships between the nodes.
3. Capture the source of the data related to AMR: general knowledge, personal opinion or experience, professional opinion or experience, or scientific evidence.
4. Identify the level of scientific evidence referenced: "low" for little or no data currently exists, "medium-poor" for inconsistent data or proxy data used, and "high" for good data from experimental studies, published literature or surveillance reports.

Reliability of coding was assessed between three independent researchers on 10% of the nodes (n=12) and relationships (n=20). Once satisfactory reliability had been reached, framework analysis was used to identify the level of the node and the source of the data. The framework analysis helped to inform a concept map (created in miMind version 3.13), which would capture the complexity of the relationships between nodes. In the concept map, nodes (represented as boxes) were colour coded and shaded to reflect the level (colour) and source of the data (darkness of shading). The relationships between nodes were represented by lines with varying colour and weight to depict the strength of the relationships and the type of evidence used respectively. Symbols (+/-) represented the direction of the correlation of the relationships.

When two or more claims were made with varying levels of detail, the Sweden specific statement was selected for visual representation in the concept map. When two or more statements were using different sources of evidence, the following hierarchy was used to determine which statement would be visually represented: scientific evidence > professional > personal > general. The existing CLD which was previously validated with workshop participants was compared to the combined concept map from the two workshops to ensure consistency in the nodes and relationships identified. Nodes and relationships not found in the original CLD (nodes: n = 35, relationships: n = 74) were noted for further discussion with the research team for inclusion in the final concept map.

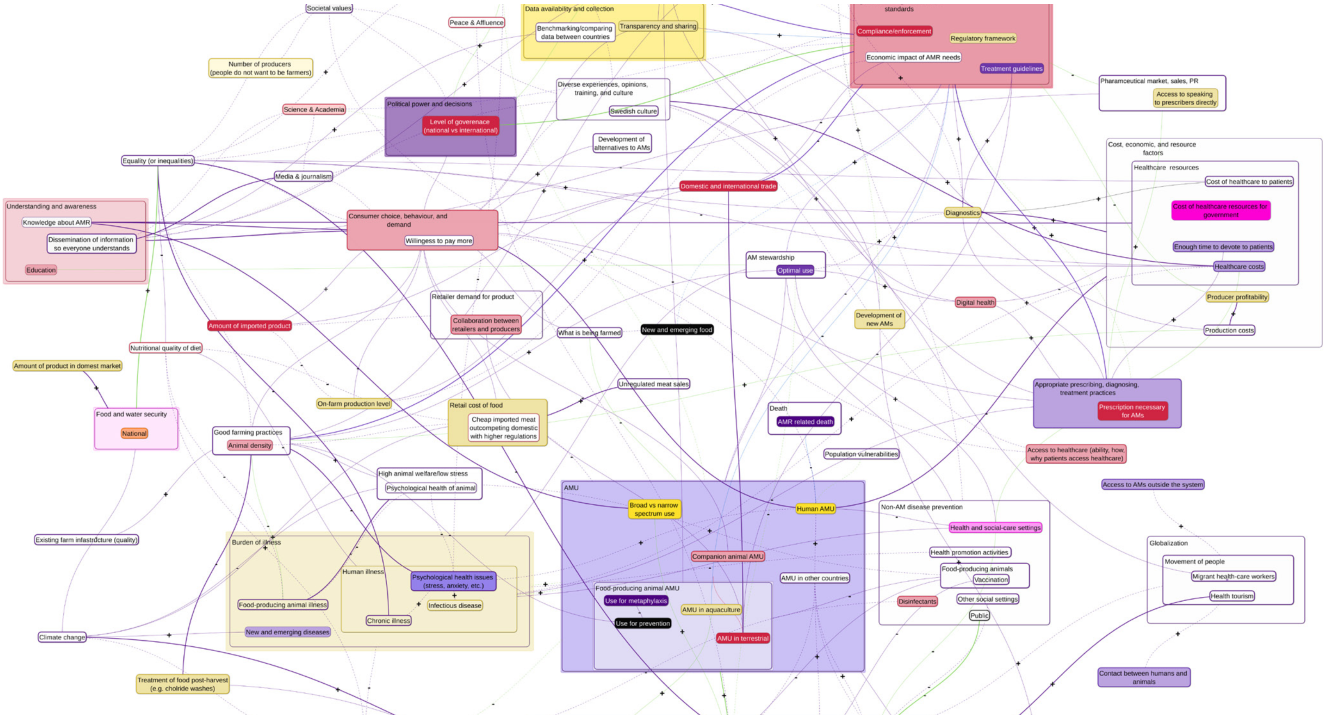


Figure 1.

Combined concept map from the two workshops in which participants described the drivers of antimicrobial resistance in a Swedish One Health system context.

Results

Framework matrix of nodes

A total of 83 nodes were included in the framework matrix: 48 from the original CLD and 35 new nodes from this analysis. These 35 new nodes emerged from:

1. New nuances about the AMR system that came to light during this analysis.
2. Existing nodes (drivers) broken down into subcategories or merged into broader categories.

Although transcripts were coded using “high”, “medium”, and “low” codes, no statements were made in the “medium” category, and thus it was dropped from the finalized framework matrix. Strong language was used to refer to both “high” and “low” levels. For example:

A participant who said that Sweden “…is a huge importer of chicken meat, beef, even pork from [name of country], which are produce under completely different conditions concerning the environment, concerning the use of antimicrobials…” implies a high or very high level of importation by Sweden, and the participant continued to discuss concerns surrounding how certain imports may increase Sweden’s exposure to AMR and AM residues.

One participant said “…actually during 2019 WHO [World Health Organization] has tried to boil down all the resistance is to all bacteria into one score, to simplify it, and then Sweden comes out on top, [name of country] comes out in the bottom”, referring to Sweden as having low levels of AMR compared to other countries.

Based on the framework matrix, there were instances where Europe (specifically Sweden) was mentioned to have "zero" or "none" for a given category (8/83 nodes). For example, quota for meat, dairy, and eggs was identified to not play an important role in the agricultural system in Sweden. Similarly, AMU for growth promotion and (soon to be) for prevention of disease under certain conditions is banned in the European Union (EU) and post-harvest interventions for disease control (e.g., chloride washes) are not common practice; these were identified to have low importance in the agriculture system in Sweden.

The majority of statements were coded as professional experience and opinion (52/83 nodes), eight were categorized as personal knowledge, and four coded as general knowledge. In the category of statements that refer to scientific evidence for a given node (n = 33), claims coded as "scientific evidence-high" occurred for 13 nodes, while statements were coded as "scientific evidence-low" for 7 nodes. For example:

> One participant said "We don't actually have precise figure on use. Most of the figures used are based on sales from pharmaceutical companies, or from prescription figures from definitely surgeons, or doctors and so on and they are very broad aggregate figures. How many of those are actually used, we really don't know. We just assume that the sales figures are a good proxy...", which highlights that the way in which AMU in human medicine is measured is currently not an adequate or reliable measure (coded as "scientific evidence-low").

Map of drivers and relationships

In the final **concept map**, 189 relationships between the drivers of AMR were mentioned and a direction for the correlation was deciphered for 131 relationships, but the strength of the relationship was less commonly reported (32/189 deciphered, 28 = strong and 4 = weak). Personal (n = 80/189) and professional opinion and experience (n = 95/189) were often used to back up claims of relationships between nodes. Scientific evidence was used to support 24 of the relationships, of which 5 indicated the strength (all categorized as strong) of the relationships. Sometimes, statements made by one participant would refer to the strength and/or direction were followed by another participant who provided additional evidence from their own experience or knowledge to create an evidence-based statement for the relationship.

One participant provided a specific example which described how an increase in data transparency and availability to the general public (e.g., through news and media) led to a change in consumer demand (e.g., reduction in AMU in food agriculture), which in turn led to large changes in government decisions (targets for agricultural AMU to reduce by 75%), resulting in a large reduction in AMU. This claim gave insight into the strength and direction of the relationship and referenced a scientifically based indicator.

Discussion, limitations, and conclusion

There is currently a need for simulation models of the drivers and transmission of AMR to integrate data across human, animal, and environmental sectors, but empirical data is often not available. This study sought to derive semi-quantifiable data to describe major drivers of AMR and their relationships using transcripts from discussions with experts in the Swedish AMR system.

The analysis of transcripts from two workshops with AMR experts revealed that participants mainly focused on strong relationships, or measures which were coded with the level "high" or "low", but not "medium". This may be because participants would first think of relationships that have large impacts or feel that weaker relationships are not worth mentioning, even though they may still be important to the overall system. Most statements were made based on personal or professional knowledge and experience, likely because this was a secondary analysis and was not the original major objective of the workshops. These statements may also have scientific evidence to support them that was not mentioned in the workshop and should be verified with further expert engagement. Finally, it is possible that participants were framing their claims to place the Swedish ARM system in the best possible light. Although Sweden has many regulations around AMU, participants may not be aware of how other practices, such as the heavy reliance on imported meat and fish, can have an impact on the presence and exposure to AMR in Sweden.

One study limitation is that the results may differ based on the participants present and the timing of the workshops. Since perspectives may differ between experts in the same field or may change between specific time periods (e.g., during or after the COVID-19 pandemic), the final concept map is specific to the Swedish AMR system in 2019. Additionally, the original goal of the workshop discussions was not to identify the strengths of relationships between drivers or the evidence to support these statements. The described study was a secondary analysis of the transcripts which provided great insight into the different drivers of the AMR system and their relationships, but future studies would benefit from workshops designed to prompt participants for more quantitative estimates for the drivers and their relationships.

This study was able to derive-semi-quantitative data that provided insight into the past, current, and potential future states of the major drivers of AMR and highlighted the gaps in quantitative data using transcripts from a workshop with experts across the system that drives AMR. These results can be applied to future models of AMR transmission and emergence to better capture the complexity of the AMR system.

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Production of this document has been made possible through a financial contribution from the Public Health Agency of Canada through funding for the National Collaborating Centre for Infectious Diseases. The views expressed herein do not necessarily represent the views of the Public Health Agency of Canada.