



ORIGINAL RESEARCH

Scenario planning: An alternative approach to European Commission for combating antimicrobial resistance by 2050

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Abstract

Aim: Antimicrobial resistance (AMR) is one of the major health challenges of the future, but the concrete impact of counteracting measures is still unclear. To study possible outcomes within the European Union, a scenario analysis for the year 2050 was performed on the possible influence of the European Commission (EC).

Methods: Scenario planning and development of strategies based on different scenarios.

Results: Rational use of antimicrobials in animals and humans, surveillance and monitoring, new antimicrobial therapies, travel and globalization, exposure to the environment, and awareness were recognized as the main driving elements. Four Scenarios were developed: An efficient and implicated EC sorts out AMR; An implicated but unsuccessful EC withstands AMR; AMR is managed regardless of the EC disinterest; and A neutral and inefficient EC fails to manage AMR.

Conclusion: All the strategies developed on the basis of the four scenarios probe for an increase in European Union's dedication to achieve positive outcomes. These include the development of effective legislation and international coordination.

Keywords: antimicrobial resistance, European Commission, one health, scenario planning, strategies.

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Introduction

Since time immemorial, mankind has struggled with the control of infectious diseases which are one of the leading causes of death worldwide (1). The COVID-19 pandemic has brought infectious diseases as top priority on the global health agenda, but in general, most of the infections are caused by non-viral agents - the bacteria. Luckily, the development of antimicrobial agents has remarkably helped for treating these infectious diseases: antimicrobials can kill or inhibit the growth of bacteria by disrupting one or more of their essential functions. However, the indiscriminate and prolific use of antibiotics ensued a selection pressure that led to the emergence of “antibiotic resistant” organisms, resulting in antimicrobial resistance (AMR) (2). It has become a major problem given the slow pace at which new antibiotics are discovered (3). Effective antimicrobial drugs are especially needed for preventive and curative measures such as ensuring complex procedures (surgeries, cancer treatment, transplants) or protecting patients from fatal diseases (2,4).

In 2019, AMR has been named as one of the top ten threats to global health by the World Health Organization (WHO) (5). Apprehensions are rampant that AMR may follow similar patterns as seen in case of epidemic outbreaks developing into pandemics (6). AMR-associated burden can be described as its impact on health or on the economy (7). At present, AMR is estimated to cause 700,000 deaths in the world per year and a cumulative loss of over 88 trillion Euros by 2050 (2,8). Hence, global efforts have been organized to face this challenge. The 2015-WHO Global Action Plan and 2016-United Nations Political declaration on AMR are some of the latest undertaken actions worldwide (9). In the European Union (EU) 25,000 patients die annually and 1.5 billion euros are expended each year due to AMR (8). Consequently, the EU reinforced the 2001 Community strategy

against AMR through the 2011 Commission action plan. With its “One Health” approach, this action plan addresses AMR in humans and animals. Based on previous approaches, the European Commission (EC) also developed guidelines for the prudent use of antimicrobials in human health (9). AMR prevention is also a topic for research and educational projects of the EC, as for example the PREVENT IT project (Risk Management and Prevention of Antibiotics Resistance) that established a collaboration between European and Indian universities and NGOs for mutual learning (10). To introduce policy interventions, evaluations of AMR burden are performed through morbidity/mortality and economic indicators (11).

Nevertheless, these indicators are the result of AMR rather than the factors which currently influence it. Thus, to ascertain the best approaches in the EU, it is imperative to acknowledge the factors that will influence AMR by 2050. The present paper aims to determine the driving forces of AMR and establish useful strategies through the development of a series of scenarios. These scenarios will concern the influence of the EU in combating AMR by the year 2050.

Methods

Scenario planning is a technique used for anticipating alternative futures. It was originally founded by economic experts to predict large-scale changes. In fact, it is particularly convenient in circumstances with high uncertainty. This method is progressively expanding in the public health sector since it takes apart the complexity of most public health concerns (12). Accordingly, scenario planning was employed in this study to address AMR intricacy and enhancing key strategies from the EU perspective. Moreover, this method has been applied successfully in the context of EU policies earlier as well. For in-

stance, the White Paper on the Future of Europe shows five scenarios for how Europe could evolve by 2025 (13).

To execute scenario planning, the process described by Neiner et al (12) was followed. According to the authors, four steps are needed to develop scenario planning in public health: (i) Define the sense of purpose; (ii) understand driving forces, key patterns and trends; (iii) develop scenario plots; and (iv) plot strategy, rehearse and converse. Briefly, first of all a relevant objective needs to be established to define the sense of purpose. In this matter, the impact of AMR on public health was considered, as it has motivated the need for action (14). After all, the EC has recognized AMR threat and works closely with WHO and other partners to accomplish AMR global action plan (15). Besides, it aims the EU to set best example globally (16). Secondly, predetermined and unpredictable forces shaping the objective need to be determined. For this purpose, a literature review was carried out. As a result, key factors, previous actions and current involvement of the EU in AMR were exposed. Next, alternative futures ought to be developed in conformity with the forces formerly established. Hereby, four scenarios were developed based on AMR progress and EC support considering the factors ascertained from the literature review. Lastly, valuable strategies should be settled irrespective of the scenario contemplated. And so, these strategies were ultimately included and argued in the discussion section (12).

Results

Driving forces, key patterns and trends

The development of resistance basically involves three major determinants: humans, animals, and the environment. Resistant bacteria arising in humans, animals, or the environment may spread from one to the other,

and from one place to another. It spans inappropriate antibiotic prescription, uncontrolled over-the-counter sale of antibiotics, disproportionate use of antibiotics in the food for animals (e.g. livestock, aquatic, pets), and poor sanitation and hygiene (17).

Of these, the rational use of antibiotics has a major influence on AMR outcomes. Common infections such as cold, flu are responsible for the majority of antibiotic prescriptions, however in reality, most of these infections are caused by viral agents against which antibiotics are ineffective (18). The use of antibiotics in these cases is not appropriate, rather it enhances the risk of AMR. Antibiotics also prevail as a prophylactic measure for minimizing the consequence of poor farming conditions and as a growth accelerator (18). To prevent misuse, the EU has published guidelines for the prudent use of antimicrobials (19). In this regard, the European Parliament and the Council of the EU issued the EU 2019/6 Regulation that prohibits the use of antimicrobial as prophylactic agent or growth promoter in animals (20). Rational use of antibiotics is a predetermined force since it has become a priority for health professionals (21).

Surveillance and monitoring are key elements of national action plans on AMR (18). For instance, at EU level, several agencies are involved in AMR surveillance: the European Centre for Disease Prevention and Control (ECDC), the European Medicines Agency (EMA), and the European Food Safety Agency (EFSA). Basically, ECDC is responsible for coordinating two surveillance networks (EARS-Net and ESAC-Net), while EMA and EFSA publish annual reports on AMR (18). These are predetermined forces - since these agencies are expected to continue with their responsibilities.

Public awareness is another key element in combating AMR. The results of Price et al (22) substantiated poor understanding of

AMR in the general population. As a matter of fact, the 2018 Eurobarometer indicated 57% of Europeans were uninformed that antibiotics are ineffective against viruses (18). This unawareness endorses antibiotics' misuse and so AMR. Hence, ECDC established the European Antibiotic Awareness Day (EAAD) which aims to support the correct use of antibiotics through national campaigns (16). Though raising AMR awareness perhaps entail a predictable force, its effectiveness is certainly unpredictable.

The discovery of new antimicrobials and diagnostic techniques will significantly impact AMR (23), therefore more investment is needed in basic science (18). For this reason, one of the main pillars of One Health Action Plan focus on boosting research, development and innovation (9). In this regard, the EU is developing in coordination with industry for development of new antibacterial agents under the COMBACTE-MAGNET project (24). Despite the investment, it is unpredictable when new antimicrobials will be ready and if so, what will be their efficacy against AMR strains.

The relevance of the interaction between chemicals (antimicrobials, heavy metals, and biocides) and pathways (industrial wastewater, animal manure) has also been emphasized in contributing to the spread of AMR. It seems that strict environmental regulations are needed in the development of AMR national action plans (25). The EU acknowledges that strong evidence is needed to counteract the incomprehension of the environment role in AMR. To fill this knowledge gap, specific actions (such as strengthening the role of the Scientific Committee on Health and Environmental Risks (SCHER) on AMR matters) have been included in the EU One Health Action Plan (9). Despite the EC engagement in the environmental area, the success of this approach is yet unpredictable.

Lastly, travel and globalization have allowed newer opportunities for cross-transmission of AMR (23). Visitors from developed countries such as USA often show colonization or infections with KPC-, VIM-, OXA-48- and especially NDM-producing Enterobacteriaceae, upon travel to countries such as Greece, Israel, Turkey and Morocco and the Indian subcontinent (26). Amongst various categories of visits, medical tourism is specifically linked to the spread of AMR. People from developed countries usually undergo several types of surgical procedures in developing countries such as India and China due to relatively low treatment costs and shorter waiting times for surgeries. Travel and globalization are unpredictable driving forces since their course and trends are likely uncertain.

Scenario plots

Four scenario plots have been developed, based on the anticipated futures resulting from AMR progress and EC support. The different scenario plots are presented in Table 1 and 2.

The first two scenarios ('An efficient and implicated EC sorts out AMR' and 'An implicated but unsuccessful EC withstands AMR') assumed a strong EC involvement, whereas in the last two (AMR is managed regardless of the EC disinterest and A neutral and inefficient EC fails to manage AMR) indicates that there is no engagement of the EC to encounter AMR. Despite the level of support provided by the EC, in the first and third scenario (An efficient and implicated EC sorts out AMR and AMR is managed regardless of the EC disinterest) it is assumed AMR has been addressed appropriately. On the contrary, the second and fourth scenario (An implicated but unsuccessful EC withstands AMR and A neutral and inefficient EC fails to manage AMR) assumed an inefficient management of AMR.

Table 1. Scenario planning for AMR in view of the EC

		An efficient and implicated EC sorts out AMR	An implicated but unsuccessful EC withstands AMR	AMR is managed regardless of the EC disinterest	A neutral and inefficient EC fails to manage AMR
Predetermined forces	Rational use in animals and humans	The EC extended the guidelines and introduced stricter measures regarding the use of antimicrobials. The broad use of antimicrobials decreased and they are uniquely provided when indicated in guidelines.	The EC extended the guidelines and introduced stricter measures for antimicrobials use. Still, professionals do not follow the guidelines and measures established. Antimicrobials are used irrationally which has resulted in an increase of AMR.	The EC did not extend the guidelines and measures regarding the use of antimicrobials. Despite this, professionals are following outdated guidelines. AMR has slightly increased but not as much as it was expected.	The EC did not extend the guidelines and measures regarding the use of antimicrobials. Besides, professionals are not following the guidelines and measures.
	Surveillance and monitoring	Surveillance and evaluation of AMR have been performed correctly. Useful information has been gathered which allowed to develop appropriate strategies to confront AMR.	Surveillance and evaluation of AMR have been performed correctly and more agencies have been involved to complete this task. Despite the information gathered, it has not been used appropriately to develop useful strategies to approach AMR.	Surveillance and evaluation of AMR have failed to provide useful information. However, policymakers have been able to use the little information gathered to improve some strategies and developed useful interventions.	Surveillance and evaluation of AMR have failed to provide useful information. The EC has lost interest in monitoring AMR, there is no pressure from the European Parliament or the EC. The real status of the AMR situation is not known.

Table 2. Scenario planning for AMR in view of the EC

		An efficient and implicated EC sorts out AMR	An implicated but unsuccessful EC withstands AMR	AMR is managed regardless of the EC disinterest	A neutral and inefficient EC fails to manage AMR
Unpredictable forces	AMR awareness	The EC encouraged MS to raise effective awareness among the population through the increase of national campaigns. People are conscious of the use of antibiotics and follow accurately healthcare professionals' instructions.	The EC supported MS in developing multiple national campaigns to raise AMR mindfulness. Even so, the interventions did not have the desired impact and the public still use antimicrobials indiscriminately.	The EC did not encourage MS to increase the number of national campaigns to raise AMR awareness. However, the general public is more conscious about the AMR problem and they use antibiotics less indiscriminately, although misuse still exists.	The EC failed to encourage and support MS to raise AMR awareness through sufficient and effective national campaigns. Citizens misuse antibiotics which have increased the number of resistant pathogens.

New antimicrobial therapies	The EC has constantly been investing in AMR research. The investment has provided good results, new antibiotics have been discovered and new diagnostic technologies developed. AMR exists but there are effective resources to deal with it.	The EC has constantly been investing in AMR research. However, the development of new antimicrobials and diagnostics has not improved considerably. New advances have been made but not sufficiently to solve the problem.	The EC decreased the investment in research in AMR. The development of new therapies and diagnostics has slowed down. Despite this, new technologies developed for other health problems have been useful to deal with AMR and reduce its impact.	The EC stopped the investment in research, and no new development has been achieved. Old Antimicrobials are still used as first and second-line treatments. Health professionals have to deal with new AMR pathogens.
AMR exposure to the environment	The EC has been working to involve environmental regulators in AMR national action plans. Also, their coordination with stakeholders has improved. The degradation of antimicrobials in wastewater is strictly controlled and treated. No antimicrobials are released to the environment.	The EC has been working to get environmental regulators to be more involved in AMR national action plans. However, their coordination with stakeholders is still insufficient. New regulations are considered to be implemented regarding wastewater, but no steady action has been yet taken.	The EC did not boost the involvement of environmental regulators in AMR national action plans. Nonetheless, there is coordination between environmental regulators and other stakeholders. They achieved to develop strategies to minimize AMR impact in the environment.	The EC did not boost the involvement and coordination between environmental regulators and stakeholders. National action plans did not include AMR's impact on the environment. Antimicrobials are constantly released to the environment since there is no regulation to control it.
Travel and globalization	Tourism increased in the last years. The EC has been working to endorse early screening and control measures to tourist arriving from AMR endemic areas. These measures have been successfully applied and so, fewer AMR pathogens have been spread.	The EC encouraged new control measures and provided additional guidance on early screening for tourists returning from AMR endemic areas, yet they were not strongly followed, and several AMR strains have been locally spread.	The EC has not considered the need of new guidelines regarding early detection or additional measures in tourists. Nonetheless, healthcare professionals have been able to detect certain carriers and limit the spread of imported AMR strains.	There EC ignored tourism as a AMR threat and consequently, no measures have been considered nor proposed to supervise the transit of tourist arriving from AMR endemic areas. This situation has boosted the spread of AMR strains to different regions.

Discussion

The ongoing COVID-19 pandemic has taught us a big lesson that how devastating nontreatable infectious diseases can be (27). On similar league, AMR bears the proficiency of attacking us as an epidemic or pandemic. An estimate by WHO suggests that approximately 10 million deaths will happen due to

AMR by 2050. Although just a forecast, some of the scenarios described could be associated with this number of deaths. To decrease the odds of these deaths becoming a reality, actions must be taken on priority. Therefore, the potential influence of driving forces has been described in the scenario

plots to better understand the ways to combat AMR.

Encouraging legislators to introduce standards and procedures to assure sensible use of antimicrobials will be useful (19). Antibiotics could be restricted with a similar approach narcotics and psychotropics are controlled (regulated by the Single Convention on Narcotic Drugs of 1961 and the Convention on Psychotropic Substances of 1971). The development of these “Antibiotic Conventions” could shift the prescription of antibiotics as a first-line treatment to every possible infection. Nevertheless, to achieve this type of covenant a high level of international agreement is required. Stakeholders would clearly benefit from this consensus and of these, society also plays a fundamental role. Public awareness is an influential factor on AMR. Thus, further efforts should be considered to increase population’s consciousness about AMR threat: diversification of AMR campaigns in diverse channels such as TV, radio, or social media that could successfully raise public awareness.

In light of newer antibiotics, the development of effective antibiotics against resistant strains is the need of the hour. A fixed amount of money provided by the EC to industry could be established as funding to foster new antibiotics discoveries. Promoting partnership with industries will also improve the likelihood of developing better diagnostics to determine the etiologic agents of the diseases and, consequently, prescribe antibiotics only when necessary. Likewise, the use of artificial intelligence in AMR surveillance and monitoring would allow to analyze existing data more precisely and consequently improve outcomes through strategies adapted to each circumstance.

Tourism also represents a relevant threat to the spread of AMR strains: tourists may acquire AMR pathogens in their journeys and subsequently spread them in their country of

origin. Early detection of carriers and control measures, in combination with international cooperation are strategies which could be beneficial, if they are successfully applied (23,28). On the other hand, it is necessary to emphasize the connection between AMR and the environment. On this ground, legal measures could be established to control wastewater treatment, followed by regular inspections to assure that legislation is properly applied.

In general, the strategies developed from each scenario imply that the outcomes would likely be beneficial if there is an increase of commitment and coordination between stakeholders, especially from the EC. Some of the strategies established have been compared with conventions already applied to other health challenges, such as the Psychotropic and Narcotic Drug Conventions. Nonetheless, to achieve these methods, further collaboration and coordination are needed not only among Member States but also at international level. The EU-India collaboration contributing to this global perspective (10). The global position also emphasizes the important role the EU plays in this global health challenge and the advantageous outcomes that could be achieved if the EU is fully involved in slowing down AMR.

On the other hand, the results have shown that the EC could address the driving forces of surveillance and monitoring, environmental AMR, treatment innovation, and tourism by introducing new legislation. EU legislation can have a significant impact, not only within the Member States but also outside its borders. In fact, the EU is currently endorsing AMR measures in third countries through different actions, like promoting AMR-related standards in its bilateral Free Trade Agreements (FTAs) (9). These actions underpin the role of the EU as a global actor in the

AMR challenge and highlights, again, the importance of developing and reinforcing international collaboration.

Limitations: The initial inquiry necessary for determining the trends and driving forces was not based on a systematic literature review. Scenario planning is a method based on assumptions and therefore subject to bias, yet the non-systematic research of driving forces increases the risk of bias. Besides, some of the driving forces, though acknowledged, were not included in the scenario planning as

per the scope of this paper. For instance, the use of vaccination has shown positive effects in reducing AMR, although its success has been historically under-recognized so far (29). Lastly, the mutual influence between driving forces were not considered since none of the driving forces would uniquely impact AMR but also influence one another. Therefore, further scenarios and strategies should be developed in the future, including additional driving forces along with their reciprocal interaction/s.

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