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Assessment of the Iran Action Plan against Antimicrobial Resistance

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ABSTRACT

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Background: The Islamic Republic of Iran provided a national action plan against antimicrobial resistance (NAP/AMR) for 2016-2021. In this study, we have dealt with the background and Iran's efforts in this way, compare Iran's NAP/AMR with other international programs, represent efficient policy options, and the evaluation indicators of each purpose of Iran NAP/AMR. The indicators of each group are represented through the consensus of three academic researchers.

Finally, our assessment reveals that performing a constant observation is highly required for a prearranged NAP/AMR. The political parties and stakeholders should punctually receive interpretable feedbacks; also, it is very important to conduct periodical assessments with the purpose of perceiving the purpose feasibility and determining the dimensions that require advancements.

Keywords: Antimicrobial resistance, National Action Plan, Iran



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Introduction

There are considerable impacts of the antibiotic resistance (AMR) infections on the health conditions of people in the world (1–3). In fact, AMR is resulted from microbe-bacteria, fungus, or virus that are associated with reduced, restricted, or inefficient drugs (4); also, there are various complex factors that lead to AMR (5,6). Widespread implications could be applied for the societies due to the dissemination ability of pathogens within the human and animal cells, as well as environmental sectors (7). The resistance bacteria transmission pathways within animals, humans, and environments could be observed in Figure 1.

Due to AMR-resulted inefficient therapies, it increases the rates of mortality and morbidity (2,6); therefore, the World Health Organization (WHO) classified it in the top ten priorities global health threats in 2019 (8). It can both eliminate the outcomes achieved through previous Millennium Development Goals (MDGs) and prevent the fulfillment of Sustainable Development Goals (SDGs) (4). There are five efficient processes that prevent the 10-million annual mortality rate and up to US\$100-trillion cost occurred by 2050 (9). Lowand middle-income countries (LMICs) incur the most losses; however, high-income countries are affected (10). According to the predictions, Asian countries will experience 4,730,000 annual mortality by 2050 (11).

There are several adverse effects on poverty and inequality, animal welfare, environment, as well as food safety and security (9,12); however, AMR is associated with wider consequences at various levels that usually tend to be ignored including the economic results that increase treatment costs (13). It is reported by the World Bank that 28.3 million people will experience AMR-resulted extreme poverty in 2050 and the major portion of this population, which is determined to be 26.2 million people, live in LMICs (9). According to the calculations, it is found that the 1.1%-3.8% reduction of global gross domestic product (GDP) will be occurred by 2050 due to avoiding action plans against AMR (9); furthermore, the annual global GDP will respectively decrease to 1.1% and 3.8% due to the low- and high-impact AMR (9). Predictions imply that by 2050, lowincome countries undergo more annual losses and up to 5% GDP reduction due to high-impact AMR (9).

As it was mentioned in SDG8, more attempts have to be carried out in order to achieve the sustainable economic growth because the above-mentioned costs, and losses are



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associated with significant adverse effects. Therefore, it could be said that AMR is considered as one of the main critical global development subjects (9) and determination of AMR-resulted multifaceted complex challenges cannot be carried out only by one person, institute, or government (7,14).

There are various AMR rates among different countries, societies, and hospitals (15). As it was illustrated through the incremental attempts against AMR, this problem is being considered as a significant challenge in the world; thus, the Global Action Plan (GAP) on AMR was implemented by the WHO in 2015. According to the mentioned plan, all of the countries in the world were asked to develop the National Action Plans (NAPs) by 2017 (16). Davies has recently concluded that although there were 117 countries that implemented AMR/NAP by 2018, only one fifth of them had the required funding in order to perform these plans (11). The selfreported data revealed that 36 countries carried out AMR/NAP; for example, although there were almost 25 African countries with NAPs, only three or four of them practically employed these plans. It could be found from the abovementioned explanations that NAPs development is the first step, while their implementation is the second step that may face various challenges including the lack of adequate human and financial resources, low-capacity health systems, and insufficient governance and adjustment (7). Figure 2 shows the timeline of international crucial events and policies of AMR, as well as efforts carried out by Iran's government.

Purpose and scope of the research

Researches showed that considerable medicine misuse were evidenced in Iran (17-19). Soleimani.et.al found that antimicrobial drugs were prescribed for 31.5% of patients (17). Since the antimicrobial agents are extensively prescribed in the primary care clinics and animal husbandry in Iran, a fast emergence of resistant bacteria was observed (20). Sharif.et.al (2021) carried out an investigation in which they showed that the main reasons of inappropriate antibiotics prescription in Iran were lack of adequate efficient interactions and antibiotics information flow (21). The improper implementation of antibiotics leads to the enhancement of resistance, morbidity, mortality, and costs(1-3).

An approach was implemented by the WHO in the World Health Assembly (May 2014) with the purpose of developing GAP/AMR, which provides a specific framework of national action plans development such as crucial actions that have to be adopted within 5–10 years. It was

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predicted by the WHO that all of the participant countries would provide а national documentation against AMR on the basis of the above-mentioned framework by 2017. The Islamic Republic of Iran also provided a NAP/AMR 2016-2021(22), which represented the viewpoints of specialists and major stakeholders that investigated the human and animal health, agriculture, and food production in Iran (23). Despite all of the above-mentioned advances, financial and technical aspects of NAP adaption have to be focused currently in order to provide a better understanding of NAP/AMR in Iran, compare it with other international programs and consequently, represent efficient related political choices. Eventually, the evaluation indicators of purposes of employing Iran NAP/AMR are illustrated.

Experimental

This is a policy perspectives that includes several international objectives and suggestions reflected by related political decisions, Iran NAP/AMR, as well as the background literature. Moreover, all of the indicators of each group are represented through the consensus of three academic researchers.

Results

Goals of the WHO global action plan against AMR and Iran NAP/AMR are provided in table1.

There is an alignment between purposes of the above-mentioned programs and the following political issues:

- The increase of public awareness and holding training programs for professional groups.
- Observance and examination.
- Preventing and controlling the infection prevalence.
- Implementing the antimicrobial drugs properly.
- Research and development (R&D).

The required policy areas and preferred options of the national plan formulation on AMR are briefly represented in the following section. There are complex AMR drivers; therefore, the complex response and proper policy-based national plans against AMR are required (Table 2).

The observation and assessment of Iran NAP/AMR require the adequate evaluation indicators. The developments of action plans implementation and achievements are represented by indicators (21). The observation and assessment indicator groups are divided to input, process, output, outcome, and impact._

Appendix 1 represents the definition of each indicator group.

The evaluation indicators of each AMR restriction policies of Iran and the mentioned indicator group are provided in Table 3.

Findings of surveillance indicators, including the input and process indicators, could be applied for the future strategies-related discussions; however, results derived from the assessment indicators, including the output, outcome, or impact indicators, could be considered in the future allocation of resources. Therefore, both of the above-mentioned results are required.

Cooperative parties and interested stakeholders have to be aware of the mentioned results. appropriate Moreover, approaches of communication and content for the audience and clear reports have to be existed in order to improve the confidence in the national action positive plan. Confirming progress and providing public recognition regarding the participations and achievements of the participants should also be carried out.

Discussion

AMR is considered as a threatening factor of making developments in medicine, food security, and public health (10). Considerable financial and LMIC adverse effects would also be resulted globally and particularly, respectively. Current study is carried out on comprehensively collected policies, as well as related standards and indicators with the purpose achieving an efficient NAP/AMR in Iran.

One of the main reasons of AMR is antibiotics inadequate consumption (24). It was found from the preceding studies that national and international standards were not followed in Iran (25). Based on the latest inquiry from Iran Food and Drug Administration, the percentage of antibiotics-contained prescription is almost 42%. There are several socio-economic factors that can influence the adequate antibiotics consumption in the low-income countries such as Iran. These factors include the high patientdoctor ratios that prevent adequate evaluation of the symptoms of patients, as well as nonaffordable costs of diagnostic tests that inhibit doctors to order such tests for low-income patients and consequently, lead them to perform empiric treatments (26). There are also similar investigations that mention the possible incorrect results of diagnostic tests and their consequent impacts on the restricted healthcare resources (27). Furthermore, it is found that insufficient privacy in the healthcare centers can make physicians prescribe



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antibiotics without performing medical examinations for some specific cases such as gonorrhea (27). The considerations regarding prescription of antibiotics adequate are influenced by cultural norms and prospects. A large proportion of patients expect physicians to prescribe antibiotics even when they are not allowed to consume them on the basis of conducted evaluations. Another similar study showed that if complete explanations were provided, patients would have been more satisfied with prescriptions without antibiotics (27); however, it was found that physicians and pharmacies did not provide satisfactory explanations for patients (28). Ineffective communication has been introduced as one of the cultural barriers in patient education in Iran (29). Therefore, socioeconomic and cultural factors such as affordability and public norms should be carefully observed in designing AMR combating interventions.

There are four main levels specified for the policy making and decision making, which could be considered during the implementation and analysis. These levels include meta-level, macro-level, meso-level, and micro-level. All of the public requirements are considered at metalevel including education and defense; also, the allocation of total revenue to the healthcare sector is determined at this level (30). The programs conceptualization and their costeffectivenessand public interest-based resource allocations are carried out at the second level by public health politicians of the health ministry (31). It is very crucial to determine the significance of the issue for politicians at the first step of NAP and make them allocate required budgets. It is highly required that all of the politicians and health authorities consider AMR as a threatening factor. The mentioned basic steps have to be monitored prior to NAP/AMR implementation due to the restricted allocation of financial resources to the health sector in Iran.

The above-mentioned policies and plans are implemented at meso-level. For example, relevant instructions are represented by physicians (30,31); also, the laboratories, pharmacists, veterinarian, and nurses can be considered in AMR programs implementation. Involving all of the actors and stakeholders in the processes of decision-making and joint purpose development, an efficient policy or intervention could be achieved (32). It is found that quality improvement of interactions of policy makers at macro-level and healthcare workers at meso-levels with the purpose of making participatory decisions are pivotal measures to develop an aligned atmosphere against NAP/AMR. Due to the fact



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that it is not necessary to achieve the replication of all components at the national scale, it would be more beneficial to combine local activities with multinational networks that are associated with adequate data sharing, analysis, and communication properties. More appropriate results could be achieved through considering self-organized behaviors of actors at the mesolevel (33).

The processes of decision making and behaving at the individual level are carried out at the micro-level (30). Generally, behaviors of patients corresponded knowledge. are to their preferences, expectations, and histories. The policies that aim to increase AMR public awareness are also referred at this level. The evaluation of preferences of patients and estimation of the strength of their choices, including conjoint analysis and Probability Trade Off, are carried out through specific approaches (34). The above-mentioned investigations represent data for policy makers prior to their interventions; also, training the patients is faced with several challenges including their beliefs and behaviors, their opinions about health practitioners and disease treatment, as well as their interactions that have to be considered in training programs (29).

Conclusion

Performing a constant observation is highly required for a prearranged NAP/AMR. The political parties and stakeholders should punctually receive interpretable feedbacks; also, it is very important to conduct periodical assessments with the purpose of perceiving the purpose feasibility and determining the dimensions that require advancements.

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The protocol for this study was approved by the ethics committee of Shiraz University of Medical Sciences (approval code: IR.SUMS.REC.1400.380).

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Ethical Considerations

Compliance with ethical guidelines

This study was approved by the ethical committee of the Tehran University of Medical Sciences (TUMS). All the participants accepted enrollment in the study orally and all of the data that were gathered was considered confidential.

Conflict of interest

All authors declare no potential conflicts of interest in conducting the study and publishing

the article.

Figures



Figure 1. Summary of the pathways of transmission of resistant bacteria between animals, humans and the environment. Source: Bacteria and the environment – the spread of antibiotic resistance. bioMérieux: A global approach to health (https://www.antimicrobial- resistance.biomerieux.com/popup/bacteria-and-the-env ironment, accessed 12 January 2019).

Figure 2. Timeline of national and international AMR key events and policies and Iran's efforts.



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Tables

Table 1. Purposes of the WHO global action plan against AMR and Iran NAP/AMR

The WHO Global Action Plan against AMR in 2015	Iran Action Plan against AMR in 2016
The realization of AMR was developed as result of implementing the efficient communication, education, and training.	The public awareness, as well as educating and training the professional groups were increased.
The awareness and evidence were extended through performing surveys and explorations.	AMR and antimicrobial drugs consumption was observed; also, signs of AMR transformation and growth were detected.
The infection incidence was decreased due to applying efficient sanitation, hygiene, and appropriate infection prevention measures.	The increase of microorganisms resistant to antimicrobial agents and drugs was restricted because proper control and prevention plans were employed.
The implementation of antimicrobial medicines among humans and animals was optimized.	The proper application of antimicrobial agents and drugs was developed in order to improve the health care, livestock production, poultry farming, and aquaculture.
The economical factors required by all of the countries to achieve a sustainable investment were developed; also, the investments in new medicines, diagnostic tools, vaccines, as well as other interventions were enhanced.	AMR research and development (R&D) were improved.

Table 2. Appropriate policy areas and preferred options required for Iran NAP/AMRs

Policy areas

Policy options

Policy areas	Policy options
1) AMR awareness enhancement with the purpose of decreasing the improper prescription of antibiotics	 Employing the identified actions in order to increase the understanding, benefit from the public awareness campaigns, develop the public awareness, represent vulnerable groups experiences to risky ones (patient for patient education), or peer education. Implementing the measures of professional education and training within the human, animal, and environmental health sectors.
2) Strengthening surveillance, monitoring, and screening the prescription of antimicrobial drugs and the spread and change in extension in AMR	 All of the human, animal, and environmental sectors have to employ the integrated AMR surveillance systems. National surveillance systems.
3) Using the controlling and preventing programs with the purpose of preventing AMR prevalence, as well as strengthening antimicrobial stewardship to reduce the inappropriate prescribing.	 Primary care: Transforming the prescription behavior of physicians as a result of using complex non-financial measures including specifications, audits, computerized reminders, and financial incentives. Implementing the point-of-care tests with the purpose of controlling the viral infections. Making joint decisions between the clinician and patient, and educating the patient during consultations. Hospital care: Transforming the prescription behavior of caregivers through multiple-technique interventions such as holding educational meetings, performing outreach visits, implementing rules and guidelines, and restructuring the environment by physical reminders or laboratory developments.
4) Develop the appropriate implementation of antimicrobial agents and drugs for the livestock productions, fowl and aqua farming, and healthcare system.	 The vertical and horizontal combination of physician- and nurse-involving infection prevention and control (IPC) measures, such as hand hygiene campaigns, as a result of infection-related financial incentives or penalties. The WHO published evidence-based instructions in 2016 regarding IPC plans central factors.
5) Development and decrease of IPC improper antibiotic applications, respectively, in animals with the purpose of dropping the resistant pathogens prevalence among animals.	 Limited implementation of non-therapeutic and human implementable antimicrobials. Using various IPC measures including the use of higher biosecurity, improved husbandry methods, and vaccination.
6) Restricting the environmental susceptibility of AMR pathogens with the purpose of decreasing their environmental propagation.	• Observation and adjustment of the environment and related actions or products with significant effects on AMR pathogens propagation and development.
7) R&D improvement within the novel antimicrobial therapies, diagnostics, and vaccines with the purpose of altering the AMR-rendered antibiotics, decreasing irrelevant antibiotics application, and preventing the occurrence of infections.	 R&D in antibiotics: Unstable incentives of improving the novel antibiotics or subsidizing the R&D costs. Recently, the implementation of market entry rewards or options market of antibiotics has been recommended. New supranational funding initiatives are Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), as well as the Global Antibiotic Research & Development Partnership (GARDP). R&D in diagnostics: Providing a fast and straightforward test with the purpose of distinction of various bacterial and viral infections such as coordinating the regulatory standards and processes in order to decrease the duplications of clinical studies, minimize the delays and regulatory standards costs, and employ the health technology assessment (HTA) in diagnostics



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Policy areas	Policy options	
	procedures.	
	 R&D in vaccines: Performing evaluations and 	
	vaccinations are resulted from using the vaccines against	
	AMR and making decisions on vaccine development and	
	application.	
	 Coordinating research: AMR research methodology 	
	has to be multidisciplinary and holistic in order to avoid	
	research gaps and efforts duplication; moreover,	
	institutes, including the Joint Programming Initiative on	
	Antimicrobial Resistance (JPIAMR), that confirm the global	
	coordination of researches are highly important.	

Policies	Evaluation indicators	Indicator Group
Action promotion with the purpose of	· Increased AMR public awareness.	Outcome
increasing the public awareness of AMR policies	Increased number of websites that provide information regarding AMR propagation adverse effects	· Input
	 Social involvement in related actions. 	 Process
	 Numbers of dedicated public training programs and meetings held with the purpose of increasing AMR awareness. 	· Input
	 Increased number of online training plans held with the purpose of increasing AMR public awareness. 	· Process
	 Number of training programs held with the purpose of increasing the awareness of insured people. 	· Process
	 The number of social campaigns that increase the adequate antibiotics prescription 	· Process
	 Social involvement in social campaigns held with the purpose of increasing the adequate antibiotics prescription 	· Process
	 Increased appropriate antibiotics consumption by individuals 	· Outcome
Development of AMR-related	 Number of AMR training programs 	· Process
education and training programs	Quantity of adequate training programs	· Output
	The amount of training program-achieved awareness that is evaluated through performing related investigations	·Output
	The coverage amount of participants who completed the courses	· Process
	 The coverage amount of groups that received educational packages and integrated education 	· Process
	Quantity of individuals with certificates of attending AMR training courses	· Process
	 Quantity of AMR training packages for healthcare providers 	· Output
	 The compliance trend of healthcare providers that follow the measures of preventing and controlling various infections, microbial resistance, hand hygiene, and using personal protective equipment in five years 	· Outcome
	• Quantity of distributed educational tools provided by responsible organizations.	· Process

Table 3. The responsible and evaluation indicators of each AMR restriction policies

ſ	Policies	Evaluation indicators	Indicator Group
╞	Improving AMR monitoring systems within healthcare centers and medical	· Utilized hand hygiene solutions within hospitals	· Input
	institutes such as restricted surgery centers, day care, medical offices,	 inpatient wards Following the measures of preventing and controlling the infections within the hospitals inpatient wards 	·Outcome
	and clinics.	 Quantity of clinical measures in hospitals to control the infectious diseases 	· Output
		 The amount of clinical measures followed by hospitals to control the infectious diseases 	·Outcome
		 Delivering antimicrobial medicine without prescriptions by the community pharmacies 	· Outcome
		 Patients with drug-resistant tuberculosis and Neisseria gonorrhea 	· Outcome
		 Number of medical institutes with AMR monitoring systems 	· Input
		 Quantity of related annual investigations The paid amount of antibiotics after receiving the results of antibiotic sensitivity test reported in hospital profiles of patients 	 Output Output
		 Transformation patterns of prescribing the antibiotics Rate of the country's AEP complied patients who were admitted to hospitals to the total number of hospital admissions 	 Output Input
		 Rate of AEP-complied hospital patients paid by insurance companies to the total hospitals 	· Input
		Sessions held by infectious committees within the hospitals	· Output
		The collaborations between infectious diseases professionals and other healthcare professionals with the purpose of developing the adequate antibiotics implementation	· Outcome
		 Number of hospital-reported antibiotic consumption and AMR pattern feedbacks received by health authorities 	· Output
		Number of hospital-received antibiotic consumption and AMR pattern feedbacks of the country	· Output
		 Quantity of microbial culture tests carried out in various hospital wards 	· Output
	The surveillance of prescription and antibiotic usage trends	 Proportion of antimicrobial medicine prescribed in outpatient and inpatient healthcare centers 	· Output
		 The amount of prescribed antibiotics-contained drugs by outpatient and inpatient centers, physician specialty, 	· Output
		etc. Rate of antimicrobial usage considering the statistics	· Output
		of sold drugs · Quantity of institutes, such as insurance companies,	· Input
		that monitor the consumption of antibiotics Quantity of prescribers-delivered feedbacks of	· Output
		 prescribed antibiotics during a specified period of time Applied IT systems for the collection and integration of prescription data 	· Input
	Improving AMR observation in the areas of veterinary medicine, livestock production/poultry farming,	 Transformational trends of index strains resistance Transformational trends of index strains resistance genes 	 Output Output
	and aquaculture	 Cooperation of health and veterinary authorities, livestock, poultry farming, and aquaculture institution 	· Process
		Quantity of joint plans of health authorities and other systems beyond AMR health systems	· Output
	Normalizing and boosting the laboratory tests and operation of	 Proportion of national standards corresponded to the international ones 	· Input
	antimicrobial tests, respectively, that are applied in the laboratory	 Proportion of institutes that follow the standards Quantity of standardization training seminars 	 Input Process
	diagnosis		



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Policies	Evaluation indicators	Indicator Group
	· Quantity of surveillance- and assessment-derived samples on the basis of molecular epidemiology	· Input
	Proportion of unsuccessful antimicrobial tests	· Output
Implementation of incorporated healthcare systems in the human,	Providing collaborative platforms of the healthcare system with animals, environment, and food sectors	· Input
animals, environment, and food systems	Delivering monitoring reports using a uniform healthcare approach	· Output
Infection prevention and control by	· Quantity of health-related infections	· Input
healthcare systems, as well as developing the cross-sector collaboration	Quantity of universities of medical sciences with adequate regional networks of the infection prevention and control	· Input
	Proportion of pneumococcal vaccine-achieved immunity	· Output
	· Quantity of homecare-related clinical instructions	· Output
	· Quantity of standard insurance-covered homecare services	· Output
	Adhesion of care assistances to clinical instructions of infection prevention	· Outcome
Development of controlling the	· The amount of veterinary medicine-related vaccines	· Input
antibiotics usage in the livestock production, aquaculture, and agricultural products such as food	dosage · The standard adhesion of production and process control	· Output
supply chain	 Prescribed or consumed antibiotics in the livestock production, poultry farming, and aquaculture 	· Output
	 Adequate proportion of standard antimicrobial agents consumption in the livestock production, poultry farming, aquaculture, and agriculture 	· Outcome
Capability development with the	· Quantity of AMR-infected patients	· Output
purpose of controlling AMR	· Quantity of AMR prevalence educational plans	· Process
prevalence	· Quantity of adequate reactions to the prevalence	· Output
	 Instructions against AMR prevalence 	· Output
	· Administrations that act against AMR prevalence	· Output
Development of antibiotics stewardship within medical institutes	· Quantity of medical institutes that act based on the antibiotics stewardship plans	· Output
	Quantity of antibiotics stewardship asserting systems	Output
	 Proportion of electronic prescriptions Rate of the healthcare referral system-based services to the total efforced convices in the country. 	· Input · Input
	 to the total offered services in the country Adjustments of reviewing the antibiotics contained in the basic health insurance package 	· Output
	Rate of modified principles of adequate antibiotics prescription to the total available principles	· Output
	 Rate of cost-effective and prevalent antibiotics with variables that could be deducted to the total antimicrobial agents 	· Output
Assuring the reasonable antimicrobials consumption in the	· Quantity of improved or employed standards of risk management	· Output
veterinary medicine, livestock production, poultry farming, and aquaculture	 Quantity of medical institutes, livestock production, and food production centers with antimicrobial stewardship teams 	· Output
	Quantity of educational plans and booklets on the adequate implementation of antibiotics and food additives	· Process
	· Quantity of related electronic prescriptions	· Input
Research development: representing the mechanisms of AMR,	Quantity of related national grant-supported investigations	· Output
transmission, and related socio- economic effects	· Quantity of genome database-collected genomes	· Output

Policies	Evaluation indicators	Indicator Group
Research development: increasing AMR public awareness, education,	 Transformations of social trends towards AMR in a five-year period 	· Outcome
preventing & controlling the infections, antimicrobials, and drugs	 Transformations of the order of antimicrobial drugs consumption in the community during a five-year 	· Outcome
stewardship	period Quantity of the related investigations	· Process
Development of clinical studies carried out with the purpose of optimizing the available approaches of infectious diseases prevention, diagnosis, and treatment	· Related research developments	· Process
Development of activities and	Quantity of supplementary AMR educational programs	Output
researches carried out on novel approaches of prevention, diagnosis,	 Quantity of infectious disease-reducing vaccines for humans and animals 	· Output
treatment, and improving collaborations between universities, industry, and related sectors	 Quantity of AMR-related R&D national grants 	· Output
International cooperation development to investigate AMR and improve R&D with the purpose of	 Rate of general international clinical assessment booklets to improve antimicrobial drugs of humans to the total baseline booklets and periodic evaluations 	· Input
implementing novel approaches of AMR infections prevention, diagnosis, and treatment	Rate of general international booklets required for the veterinary antibiotics confirmation to the total baseline booklets and periodic evaluations	· Input



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