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Article

Antimicrobial resistance surveillance system mapping in different countries

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HIGHLIGHTS

- Extensive use of antibiotics resulted in the rising cases of AMR against various organisms.
- The success of one health exercise depends on how far it is achieved by the countries.
- One Health has gained a lot of attraction throughout Europe, Taiwan and India.
- The One Health strategy is currently being promoted in Europe mostly in regard to antimicrobial resistance (AMR).
- Taiwan has successfully accomplished the major objectives formed for combating AMR situation.

Abstract: Antibiotics are in excessive use that has extensively increased antimicrobial resistance worldwide which has become the major public concern among the countries. To control this threat proper monitoring of the antimicrobial usage along with the increasing rate of antimicrobial resistance (AMR) is required. Further, surveillance of both the parameters is highly recommended for comparing the differences in distinct countries. Moreover, alternatives for antibiotics are also surveyed and are being researched for quick use in the near future. AMR is an issue that needs immense attention from various sectors. Thus, intervention of multisector is highly encouraged for better outcomes. One Health is one of the approaches that play a vital role in resolving this issue. In this research paper, six different European countries are discussed in terms of antimicrobial usage and AMR in the human and livestock sectors with the help of literature study and various reports published by different organizations. Data study has been conducted to collect the data for comparison study. Data sources of AMR and antimicrobial usage are analyzed and a thorough comparison of both antimicrobial use and AMR are conducted. Also, the application of One Health is studied for a balanced system. This article provides about various surveillance systems that are formed only to keep a track on the upcoming situation of AMR and the consumption of antimicrobials by the humans as well as animals. The article does not provide about all the details required to monitor the AMR issue but firmly allow the readers to get acknowledged with the broad information about the antimicrobial resistance across the six countries of Europe. The regular data collected by the different organizations play a vital role in monitoring the status of AMR and antimicrobial usage by humans and in live stocks. These annual reports have highly helped the government to decide for alternatives and have focused in many training activities to combat the AMR situation globally. AMR prevention is linked to the One Health concept. As antibiotic resistance genes persist on an interface between environment and animal and animal health, an approach is required in all three areas that stress the concept of 'One Approach to Health.'

Keywords: AMR; Surveillance; One Health Approach; Alternative Antibiotics; Comparative Medicine; Phage Therapy

1. Introduction

In the last few decades extensive use of antibiotics has result in the rising cases of antimicrobial resistance against various organisms. From narrow spectrum, people shifted to broad spectrum antibiotics which eventually increased the high resistance rates. Multidrug-resistant (MDR) bacterial infections are rapidly emerging and spreading over the world, posing a severe threat to global healthcare. Carbapenem-resistant Enterobacteriaceae (CRE), a type of Gram-negative bacteria that has evolved resistance to all or virtually all current antibiotics, is one cause for concern. Likewise, various other antibiotics are also becoming resistant against the microorganisms causing immense threat among the population. This global threat comprises of both commensal and pathogenic bacteria. The similarities between human and animal diseases, as well as the interactions between animals and humans who come into contact with them, have long been recognized. Human and veterinary medicine diverged in the twentieth century. During the same time span, our understanding of infectious diseases and antibiotics grew dramatically. The necessity for partnerships between the human health and veterinary sectors to prevent and control zoonotic illnesses and antibiotic resistance grew in the second half of the twentieth century (AMR). The notion of ecosystem health was developed toward the end of the twentieth century, extending the integration and collaboration of human and animal medicine to the environment. Later on, the phrase "One Health" was coined to describe a holistic approach to improving human, animal, and environmental health through multidisciplinary cooperation and communication. Several global plans have been established to combat the AMR epidemic, including the World Health Organization's (WHO), Global Action Plan (GAP), the new European One Health Action Plan against AMR and the Central Asian and Eastern European Surveillance of Antimicrobial Resistance network (CAESAR). (1) Surveillance and monitoring systems for AMU and AMR in humans and animals are critical for assessing and controlling global trends in antimicrobial use and antimicrobial susceptibility patterns of bacteria in various populations. In the context of a One Health strategy, zoonotic and indicator microorganisms are especially important. A strategic framework for reducing infectious disease risks at the animal-human ecosystem interface was published in 2008, adopting and promoting the One Health concept. The One Health approach has been supported and implemented by a wide number of national and international institutes since 2008. Research on the human animal environment interaction is critical to supporting the call for a One Health approach to AMR and infectious illnesses. Furthermore, training and extension initiatives are critical for promoting the One Health idea and facilitating its application among various stakeholders. (2, 3) Several governments and international organizations have now included a One Health Approach in their antimicrobial resistance action plans. Improvements in antimicrobial use, better regulation and policy, improved surveillance, stewardship, infection control, sanitation, animal husbandry, and identifying antimicrobial alternatives are all necessary efforts. This report summarizes research and educational activity in the field of One Health in Western Europe, with an emphasis on infectious diseases. It might act as a springboard for future collaborations and projects.

2. Materials and Methods

2.1. Data Sources

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We conducted a database study for collecting major characteristics of surveillance and monitoring systems on antimicrobial use and AMR in cattle and people, as well as AMR systems in food, in this publication. Countries such as Spain, Germany, France, The Netherlands, Norway, and the United Kingdom were considered for this project. The literature search in the recent times has been carried out to understand and collect the data from different grey reports and other AMR databases. The database study has been conducted by searching about the term 'Antimicrobial Resistance', 'Antibiotic Usage', 'One Health Approach', on PubMed and desired research papers or data sheets annually published by different agencies are studied for collective data, required for this research article. Additionally, information about One Health Approach in these countries were also investigated for obtaining the results. One Health policy publications issued by international organizations and countries also provided background information on the One Health program and European One Health projects. Moreover, Google research on One Health with its associated activities and trainings among these countries were conducted for acquiring more relevant outcomes. Alternative antibiotics for resolving the issue of AMR were also researched which focuses on better solution for AMR and antimicrobial usage. One of the renowned projects also known as ARDIG (Antimicrobial Resistance Dynamics the Influence of Geographic origin) together collects and gather data related to antimicrobial resistance and usage of antimicrobials from both human and veterinary sectors. The stipulated graph depicts the significant increase in the usage of antibiotics and AMR globally in the recent times. (**Figure 1**) This helps us to portray the comparison study of all the data collected for different countries along with the Asian countries. In addition, all the surveillance system for monitoring AMR in different countries of Europe has been explained thoroughly in this article. The prime reason for tracking the reports of European countries is because One Health has gained a lot of attraction throughout Europe. The One Health strategy is currently being promoted in Europe mostly in regard to antimicrobial resistance (AMR). Many nations have adopted the One Health concept in their anti-AMR policies, and funding opportunities for AMR research have considerably increased. In the areas of zoonotic diseases and One Health, the number of national and international multidisciplinary research networks is growing. (1)

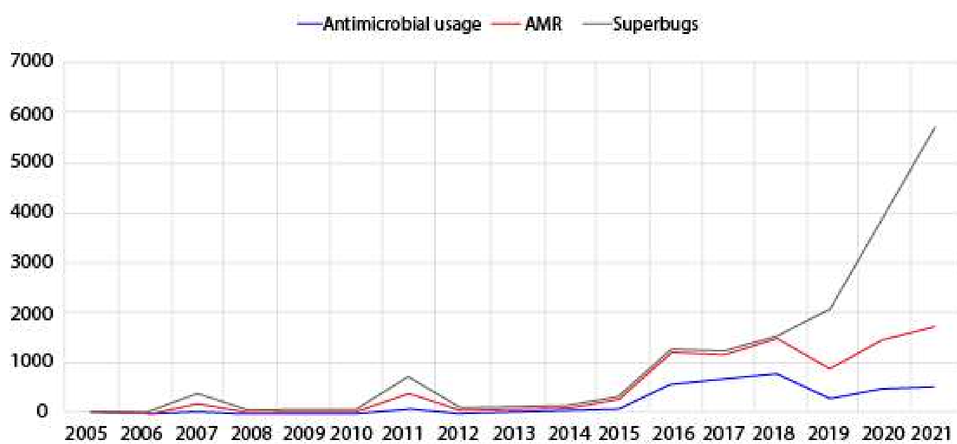

Figure 1. The stipulated graph depicts the significant increase in the usage of antibiotics and AMR globally in the recent times. **X-axis** denotes the year and **Y-axis** denotes the increasing values for AMR, Antimicrobial usage and Superbugs.

2.2. Surveillance Strategies of Antimicrobial Resistance and Monitoring System

2.2.1. Data Collection and Data Analysis

Different European countries have various surveillance strategies and monitoring systems for controlling the rising threat of antimicrobial resistance. Additionally, multiple organizations are coming together for putting joint efforts require combating this situation. A complete summary of the data collected are represented in a tabular form for better understanding of the data gathered.

2.2.2. France

AMR data related to agricultural, food, and the environment is monitored by the French Agency for Food, Environmental, and Occupational Health and Safety (ANSES). The French monitoring network for antibiotic resistance in pathogenic bacteria of animal origin (RESAPATH) and the Salmonella network are coordinated by this agency. The Salmonella network is a surveillance system designed to keep non-human Salmonella under control throughout the food chain. The Investigation and Surveillance of Nosocomial Infection Network (RAISIN) coordinates the nosocomial infection surveillance coordination centers across the country. BMR-RAISIN, a private RAISIN module for multi-drug resistant bacteria, reports on AMR data in the community. Healthy animals, food, and the environment are all sampled. The RESAPATH voluntary surveillance system compiles AMR data for primary bacterial species and general isolates from sick animals from each animal sector in the annual RESAPATH report. (8)

2.2.3. Germany

Clinical AMR data from companion and food-producing animals is collected in Germany through the German veterinary monitoring system (GERM-VET). The AMR-testing in the Zoonosis-Monitoring System (ZOMO) report includes data on zoonotic and commensal bacteria in various food chains, as well as AMR-data on Salmonella from national control programs, which are also reported to the EFSA. Antimicrobial Resistance Surveillance (ARS) is the human medicine's national AMR surveillance system. It gathers routine susceptibility data for all bacterial species from any sample site, including hospital and outpatient care facilities. The Hospital Infection Surveillance System (KISS) is a nosocomial infection surveillance system made up of multiple sub-systems that collect AMU and AMR data in hospitals. SARI gathered data on antimicrobial sensitivity for selected pathogenic microorganisms and the creation of AMU-AMR on a volunteer basis. (1)

2.2.4. Spain

To keep track of AMR, the Spanish Veterinary Antimicrobial Resistance Surveillance Network (VAV) was formed. VAV provides non-clinical data to the European Food Safety Authority (EFSA), which is included in the agency's annual reports. According to EU legislation, this report contains information on zoonotic infections and diseases in animals, humans, and food, as well as data on AMR in select zoonotic bacteria and indicator bacteria.(1, 6)

2.2.5. Norway

The three AMR surveillance programs in Norway are the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM), Norwegian Veterinary Antimicrobial Resistance Monitoring (NORM-VET), and the Norwegian Surveillance System for Communicable Diseases (MSIS). This annual report contains updated information on AMU and AMR prevalence and distribution in the human, animal, and food sectors. (10, 11)

2.2.6. The Netherlands

The "Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands" (MARAN), which brings together the Food and Consumer Product Safety Authority's AMR food database, is the Netherlands' AMR monitoring system for animals and food. It disseminates information on foodborne pathogen resistance as well as commensal indicators from animals and food. The Infectious Disease Surveillance Information

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System on Antibiotic Resistance (ISIS-AR) monitors AMR in key pathogens in the human sector.(12)

These surveillance systems are extremely helpful in tracking down the situation caused by antimicrobial use and antimicrobial resistance. The various features of different organizations built by the agencies have successfully helped the researchers in providing the necessary data for handling the threat worldwide. In addition to strengthening the AMR surveillance, numerous policies have been prepared by WHO, and other agencies which apparently help in working with the solution of either decreasing or avoiding the AMR situation. For teaching and training, surveillance and risk assessment, and research, the AMR Coordinating Office emphasizes a One Health approach. Political commitment, policy formation, sustainable finance, Programme creation, knowledge sharing, institutional collaboration, capacity enhancement, civil society involvement, and active community participation are all part of the framework for effective One Health implementation. One health is a straightforward and strong idea with complex processes. The national response to zoonoses must be revised, food safety must be improved and environmental integrity guaranteed. The transformation must be driven by the senior leadership. Strong, ongoing lobbying by international development partners in particular: the FAO, the OIE and the WHO should be shared with the leading national leadership, disseminating the evidentiary results, predicted economic benefits and best practice globally. The interconnected sustainable development goals offer a unique opportunity for advocacy and an integrated approach to development. The effectiveness of One Health Implementation depends on the extent to which institutional cooperation, common planning and coordinated thorough monitoring for early detection and prevention of zoonoses are achieved. The key planning, implementation and surveillance are data and science. Initial efforts for rapid tracking should be performed quickly in order to create multisectoral capacity across various organizations. The theory and practice of one health should be fully integrated and visible in the educational curriculum as well as in the constant upgrading of skills for all subjects for long-term implementation.

2.2.7. United Kingdom

In the United Kingdom, the EU Harmonized surveillance system (a native UK system) collects mandatory AMR data on indicator commensal *Escherichia coli* and/or *Campylobacter spp.* from meat and fecal content of healthy animals (chicken, beef, turkey, and pigs). There are also Salmonella National Control Programs in the United Kingdom that are hosted in the EU Harmonized Surveillance System. In Scotland, the Scotland's Rural College Veterinary Services and Capital Diagnostics (SRUC) surveillance system collects clinical isolates from animals. In England monitoring surveillance system Vet Pathogens APHA collects AMR data from infected animals that veterinarians proactively offer for diagnostic services, covering all relevant bacteria and animal species. On the human aspect, the British Society for Antimicrobial Chemotherapy's (BSAC) Resistance Surveillance Program provides antibiotic resistance data from cooperating labs in the UK and Ireland for a variety of clinically relevant bacteria from community-acquired respiratory illnesses. AMR data is collected through the Electronic Communication of Surveillance in Scotland (ECOSS) network from participating NHS and reference laboratories in Scotland.(1, 9).

3. Results

The accomplished research revealed that various surveillance systems are actively working to follow a trail of the upcoming situation of AMR and antimicrobial consumption by the humans as well as animals. These surveillance systems of European countries are jointly contributing in statistically analyzing the rising situation of antimicrobial resistance and the prominent measure taken by different organizations for implementing One Health Approach. Moreover, various training institutes and alternative measures for

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preventing AMR are firmly encouraged in these six European countries along with Taiwan and in India.

Analyzing data of antimicrobial resistance solely do not arise from only consuming antibiotics. There are multiple more aspects such as food habits of the humans, food chains maintained by the healthy animals and the environment together exhibit the importance of surveillance systems for AMR as these features put up the AMR issue topmost. The European Food Safety Authority (EFSA) is in charge of providing risk managers and the general public with impartial scientific advice and communication on food chain concerns. Annually, the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) collect AMR data on humans, food, and healthy animals from EU States and some affiliated countries. (4) The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals, and food is prepared and published by the European Food Safety Authority (EFSA). Also, some non-governmental organization such as European Animal Health Study Centre (CEESA) is also contributing by researching about AMR and forming relevant systems to perform the activities efficiently.(5) Precisely, the organization is working in monitoring the antimicrobial susceptibility of the bacterial pathogens that have the potential of causing diseases among the animals along with the foodborne pathogens in animal's food. These organizations are not the only aide for this surveillance system hence a prime system also called as The European Antimicrobial Resistance Surveillance Network (EARS-Net) mainly helps in the surveillance of AMR data. This is an antimicrobial resistance surveillance network established in compliance with European Union and European Economic Area legislation. The European Centre for Disease Prevention and Control (ECDC) collects AMR data from EU States through EARS-Net and publishes the annual EARS-Net report. On that account it is extremely crucial to compare the percentages of antibiotic usage and AMR which will help in displaying the numbers accurately acquired from different organizations and relevant measures will be implemented for better solution. Similarly, acknowledging this, two joint inter agency for antibiotic consumption and the analysis of AMR were published that clearly demonstrate the effects of using extensive antibiotics on humans and animals and the data were compared to AMR reports for better understanding. This report is jointly published by the European Medicines Agency (EMA), the European Food Safety Authority (EFSA), and the European Center for Disease Prevention and Control (ECDC). The European Center for Disease Prevention and Control (ECDC) and EARS-Net requires other platforms to jointly work for this. (**Fig. 1**) Every country from Europe has their own surveillance system for AMR which they follow, and prepared reports are further provided to EFSA. The AMR surveillance system is developed distinctly for humans and live stocks. (1)

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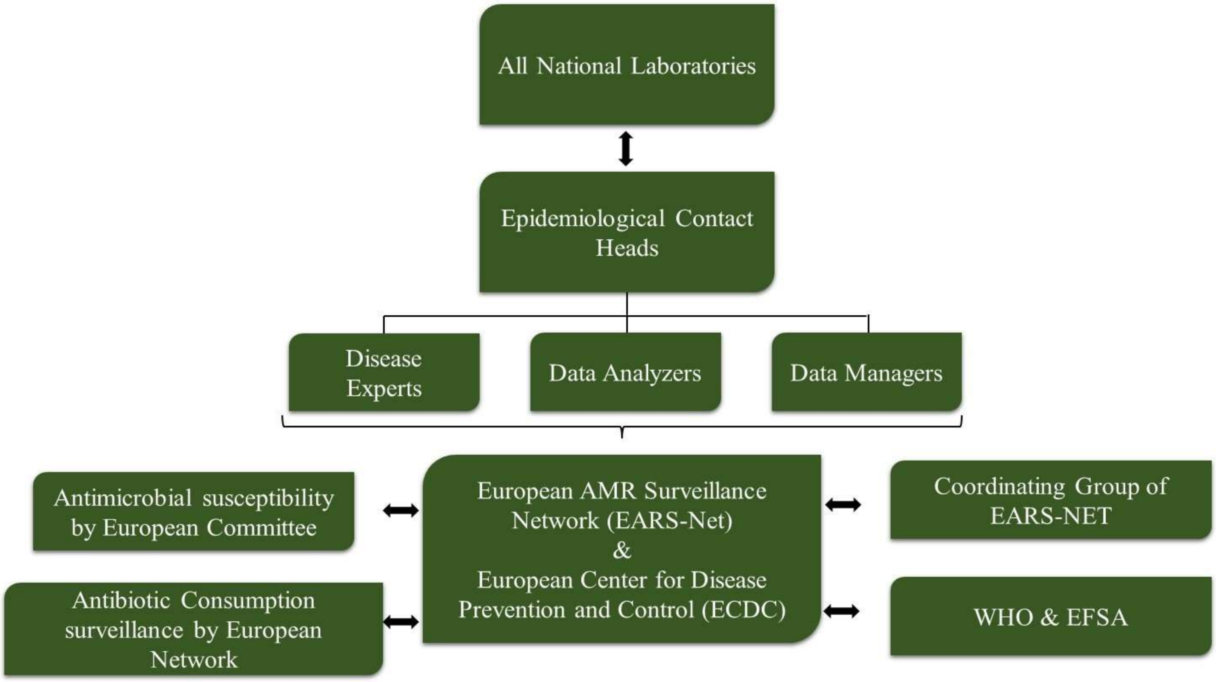

Figure 1. Different Organizations jointly working together to provide data to EARS-Net and ECDC.

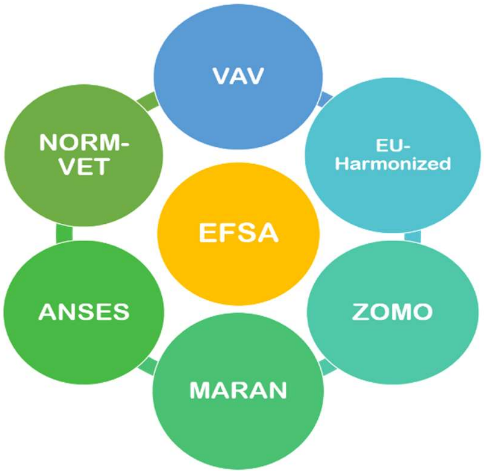

Figure 2. AMR surveillance systems for live stocks of different countries reporting the data to EFSA. **VAV**: The Spanish Veterinary Antimicrobial Resistance Surveillance Network (VAV); **MARAN**: Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands; **ZOMO**: Zoonosis-Monitoring system; **NORM-VET**: Norwegian Veterinary Antimicrobial Resistance Monitoring system; **ANSES**: The French Agency for Food, Environmental and Occupational Health & Safety; **EU-Harmonized**: The EU harmonized surveillance system.

Different systems of the country contribute in forming the reports which is eventually published by EFSA or ECDC. (**Fig.2**)

Similarly, AMR surveillance system for humans is also analyzed by different organizations formed in these six European countries. The following figure depicts the organizations that are being established for keeping the record of the AMR surveillance. (**Fig. 3**) (6)

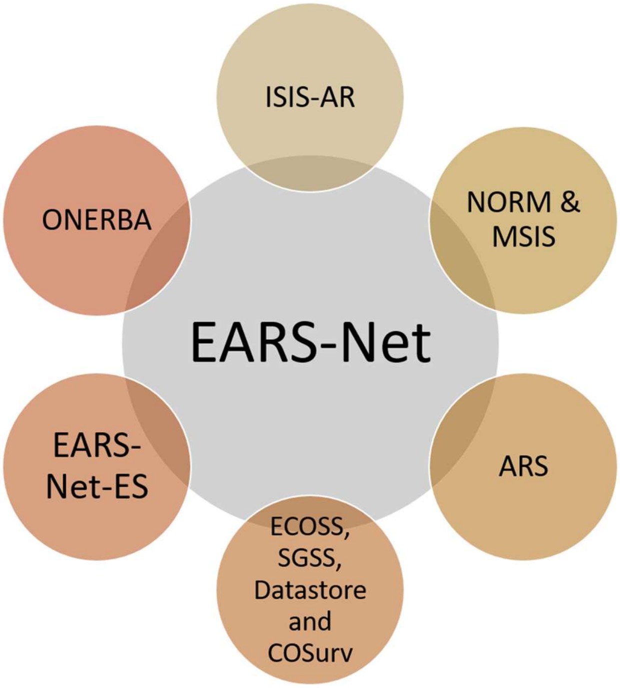

Figure 3. AMR surveillance systems for humans of different countries reporting the data to EFSA. **ISIS-AR:** Infectious Disease Surveillance Information System on Antibiotic Resistance; **NORM & MSIS:** Norwegian Veterinary Antimicrobial Resistance Monitoring; **ARS:** Antimicrobial Resistance Surveillance; **EARS-Net-ES:** European Antimicrobial Resistance Surveillance Network; **ONERBA:** National Observatory of the Epidemiology of Bacterial Antibiotic Resistance; **ECOSS, SGSS, Datastore and COSurv:** The Electronic Communication of Surveillance in Scotland, Second Generation Surveillance System.

The table below gives the details about all the aforementioned surveillance system followed by the distinct countries along with the features and roles they perform. (**Table 1&2**) (1, 7)

Table 1. AMR surveillance system conducted in different countries for humans.

Surveillance System	Host	Country	Roles of Surveillance System
ISIS-AR	Humans	The Netherlands	This aims at monitoring AMR in major pathogens.
			It is an AMR surveillance programs in Norway. This annual report provides updated information on AMU and AMR

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NORM & MSIS	Humans	Norway	occurrence and distribution in human beings.
ARS	Humans	Germany	It is the national human medicine AMR surveillance system. Established by the Robert Koch Institute, it collects routine sensitivity data from any sample site in the hospital and from ambulatory care institutions for all bacterial species
EARS-Net-ES	Humans	Spain	Maintains the records of AMR surveillance across Spain
ONERBA	Humans	France	AMU and AMR as well as a leading AMR network that collects data from a complex subsystem network are an annual French report, ONERBA.
ECOSS, SGSS, Datastore and COSurv	Humans	United Kingdom	The ECOSS data base gathers AMR data from participating NHS laboratories and references laboratories in

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			Scotland. Electronic communication of surveillance in Scotland (ECOSS) (SGSS) captures 98 percent of the National Health Service (NHS) laboratories across England, from routine laboratory surveillance data on infectious diseases and antimicrobial resistance.

Table 2. AMR surveillance system conducted in different countries for live stocks.

Surveillance System	**Host**	**Country**	**Roles of Surveillance System**
VAV	Live stocks & Food Habits	Spain	VAV monitors the AMR status throughout the country and is also responsible for monitoring animals and food. In addition, VAV supplies EFSA with non-clinical data.

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ANSES	Live stocks & Food Habits	France	ANSES generally monitors AMR data related to food, livestock and livestock.
ZOMO	Live stocks & Food Habits	Germany	This report also provides data on zoonotic and commensal bacteria of the different food chains reported to EFSA.
MARAN	Livestock and food	The Netherlands	Data on foodborne pathogens and commensal indicators from cattle and food are published in the annual report of The Netherlands.
NORM-VET	Animals & Food Habits	Norway	Facilitate updated incidence and distribution information on animal AMU and AMR.
EU-Harmonized	Lives tocks & Food Habits	United Kingdom	A mandatory AMR data for meat and fecal in healthy animals, using the

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			appropriate indicator *Escherichia coli* and/or *Campylobacter spp.* is collected under the European harmonized supervisory system.

Humans and animals are exposed to AMR from their food habits. Thus, a surveillance system was set up especially for the food that is being consumed by both animals and humans. A thorough monitoring of the food consumed, obtains the possibilities of getting exposed to new pathogenic organisms which could be a probable reason for the pandemic, endemic and epidemic. Again, some of the organizations similar to humans and live stocks are formed for keeping the track of rising AMR cases from food habits. (**Fig. 4**) (1)

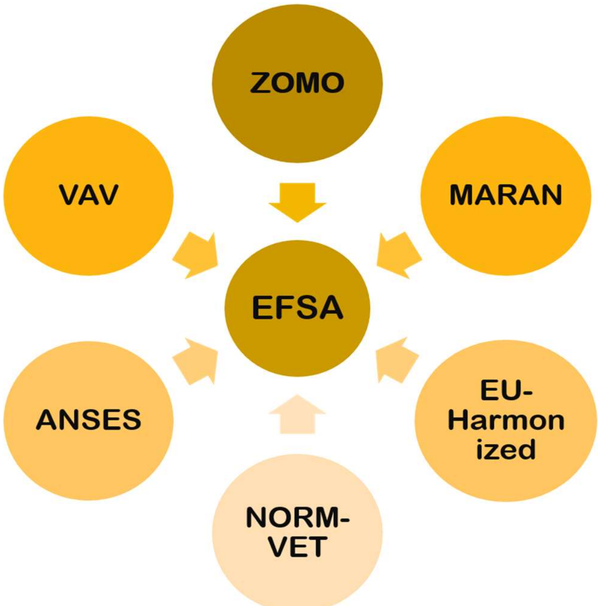

Figure 4. AMR surveillance systems for foods of different countries reporting the data to EFSA. **VAV**: The Spanish Veterinary Antimicrobial Resistance Surveillance Network (VAV); **MARAN**: Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands; **ZOMO**: Zoonosis-Monitoring system; **NORM-VET**: Norwegian Veterinary Antimicrobial Resistance Monitoring system; **ANSES**: The French Agency for Food, Environmental and Occupational Health & Safety; **EU-Harmonized**: The EU harmonized surveillance system.

The aforementioned all the organizations report their AMR data to EFSA (the European Food Safety Authority) but on the other hand, there are some organizations which don't report their AMR data to EFSA. (**Table 3**) The details of all these organizations contributing to different countries are described in the text below.(1)

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Table 3. AMR surveillance systems country wise those are not reporting data to EFSA.

Surveillance System	Country	Hosts
GERM-VET	Germany	Live stocks
RESAPATH	France	Animals
APHA-VET PATHOGENS	United Kingdom	Diseased Animals
SRUC	United Kingdom	Animals
PEG	Germany	Human Pathogens
ARMIN	Germany	Humans
BARDa	Germany	Humans
ICU-KISS, OP-KISS, SARI-KISS, MRSA-KISS	Germany	Human Pathogens
BSAC	United Kingdom	Humans
BMR-RAISINS	France	Human Pathogens

3.1. Reported Microorganisms accountable for AMR in Europe

Discussing about the surveillance systems available to control the AMR and antimicrobial usage will not be able to aware the population about the pathogenic disease-causing microorganisms accurately. Therefore, it is very important to understand the pathogens responsible for causing AMR also with the antimicrobials that are extensively used. EARS-Net received data from twenty-nine countries for all eight bacterial species under observation (*E. coli, K. pneumoniae, P. aeruginosa, Acinetobacter species, S. pneumoniae, S. aureus, E. faecalis* and *E. faecium*). *E. coli* was the most commonly reported bacterial species (44.2%), followed by *S. aureus* (20.6%), *K. pneumoniae* (11.3%), *E. faecalis* (6.8%), *P. aeruginosa* (5.6%), *S. pneumoniae* (5.3%), *E. faecium* (4.5%), and *Acinetobacter species* (4.5%). (1.7 %). (**Fig. 5**) In 2019, more than half of *E. coli* isolates reported to EARS-Net were resistant to at least one antimicrobial group under surveillance, and more than a third of *K. pneumoniae* isolates were resistant to multiple antimicrobial groups. In general, resistance percentages in *K. pneumoniae* were higher than in *E. coli*. While carbapenem resistance was uncommon in *E. coli,* carbapenem resistance rates in *K. pneumoniae* were reported to be more than 10% in numerous countries. Carbapenem resistance was also found in larger percentages in *P. aeruginosa* and *Acinetobacter species* than in *K. pneumoniae.* The increase in the percentage of vancomycin-resistant *E. faecium* isolates in the EU/EEA from 10.5 percent in 2015 to 18.3 percent in 2019 is a cause for concern. The results of antimicrobial susceptibility testing (AST) from invasive (blood or cerebrospinal fluid) isolates of eight bacterial species are provided in this paper. *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter species, Streptococcus pneumoniae, Staphylococcus aureus, Enterococcus faecalis, and Enterococcus faecium* are all important bacteria for public health in Europe. In 2019, the estimated national population coverage of data provided to EARS-Net ranged from 11% to 100%, with more than a third of the nation reporting a population coverage of 80% or above. (13)

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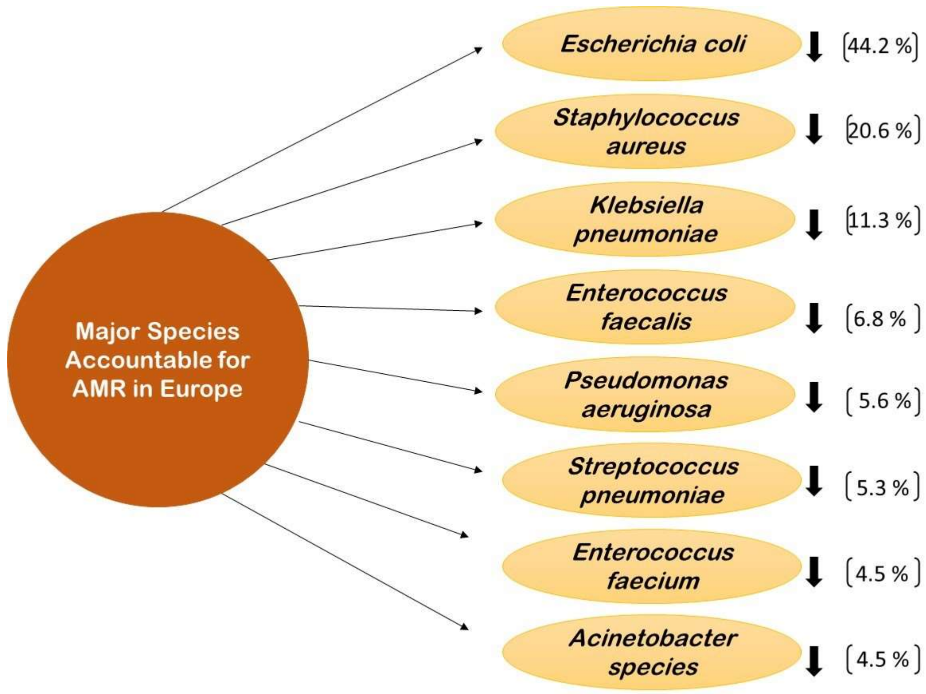

Figure 5. Major species responsible for AMR in Europe.

3.1.1. Escherichia coli

In Europe, *E. coli* is a common cause of bloodstream infection. Infections caused by antimicrobial-resistant *E. coli* account for the majority of AMR cases in the EU. The percentages of AMR reported in 2019 were substantially higher than in 2002, underlining the need for more antimicrobial stewardship and infection prevention and control activities. According to the latest data from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), there are large inter-country variations in the use of broad-spectrum antimicrobials, indicating a need for increased antimicrobial stewardship and the potential for further antimicrobial consumption reductions. (14). ***Pseudomonas aeruginosa***: Although *P. aeruginosa* is naturally resistant to a wide range of antimicrobials; acquired resistance complicates the treatment of P. aeruginosa infections. Because *P. aeruginosa* is still one of the most common causes of healthcare-associated illness in Europe, the public health consequences of AMR in *P. aeruginosa* should not be overlooked. (13). ***Klebsiella pneumonia:*** The European Union's *K. pneumoniae* resistance issue. Although carbapenem resistance has increased more than seven-fold since 2006, it has been more moderate in the last five years than in earlier eras. The WHO believes that novel drugs targeting third-generation cephalosporin- and carbapenem-resistant Enterobacterales, such as *K. pneumoniae* and *E. coli*, are urgently needed.

3.1.2. Staphylococcus aureus

Many nations have created and implemented national MRSA prevention recommendations and guidance documents, emphasizing on enhanced infection prevention and control as well as sensible antibiotic usage. Despite this progress, MRSA remains a significant pathogen in Europe. *S. aureus* is one of the most frequent bacteria that cause bloodstream infections, with a significant morbidity and fatality rate. MRSA surveillance in animals and food is currently voluntary and only carried out in a few countries. This monitoring, however, reveals an ever-changing situation, including the detection of livestock-associated MRSA (LA-MRSA), healthcare-associated MRSA, and community-associated MRSA from companion animals and/or livestock. LA-MRSA has recently received increased attention as a zoonotic risk, particularly for those who work in close proximity to

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livestock. ***Acinetobacter species***: *Acinetobacter species* have the widest inter-country range in resistance percentages of any bacterial species under EARS-Net surveillance. Depending on the reporting country, the percentage of isolates resistant to at least one of the antimicrobial groups under surveillance (fluoroquinolones, aminoglycosides, or carbapenems) ranged from 0% to 95.8 percent in 2019. Because *Acinetobacter species* is naturally resistant to many antimicrobial agents, acquired resistance complicates treatment of *Acinetobacter species* infections. Multidrug-resistant *Acinetobacter species* are a problem in the healthcare environment because they can survive for long periods of time in the environment and are notoriously difficult to eradicate once established. ***Streptococcus pneumonia:*** In addition to EARS-Net, the enhanced surveillance program for invasive pneumococcal disease (IPD), which is also supervised by ECDC, collects additional data on IPD cases from reference laboratories across the EU/EEA. The frequency of resistance to penicillin and erythromycin grew somewhat in all countries that consistently supplied antimicrobial susceptibility data, according to data from this surveillance project. (14) ***Enterococcus faecalis and Enterococcus faecium***: There are grounds for concern that *E. faecium is* fast and constantly increasing in the percentage of vancomycin resistance in the EU. The ECDC study on AMR's health burden estimated that vancomycin-resistant enterococci (VRE) infections and fatalities virtually doubled. A large issue for infection prevention and an important cause for dietary-related illnesses remain high levels of antimicrobially-resistant enterococci. In addition to being difficult to cure infections caused by resistant strains, enterococci are easily spread in medical settings. (13)

3.2. Overview of the antimicrobials resistant against the reported microorganisms

The above-mentioned subsequent organisms have been tried to be treated with multiple antimicrobials which has not benefitted the healthcare. The initial treatment method implemented against these species were applying single antimicrobial, later on due to non-observance of the former antimicrobials, healthcare sector switched to provide double antimicrobials treatment to the patients for more efficient results but to our surprise, the species were found to be successfully resistant against them. Recently, combination of antimicrobials is applied to fight against the resistance that is acquired by the organisms but eventually extensive using of multiple antimicrobials have not only triggered AMR globally but have also shown significant amount of increase in multi-drug resistance (MDR) cases worldwide. (**Table 4**) (13-15)

Table 4. Bacterial species and the antimicrobial groups to which they are resistant.

Bacterial Species	**Antimicrobial Groups**
Escherichia coli	✓ Amoxicillin, Ampicillin Resistance ✓ Third Generation Cephalosporin Resistance (Cefotaxime, Ceftazidime, Ceftriaxone) ✓ Carbapenem Resistance ✓ Fluoroquinolone Resistance (Ciprofloxacin, Levofloxacin, Ofloxacin) ✓ Gentamycin, Tobramycin Resistance

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	✓ Combined Resistance acquired to all the drugs (Cephalosporins+ Fluoroquinolones+ Aminoglycosides)
Staphylococcus aureus	✓ MRSA (Methicillin Resistant *Staphylococcus aureus*)
Klebsiella pneumoniae	✓ Third Generation Cephalosporin Resistance (Cefotaxime, Ceftriaxone, Ceftazidime) ✓ Carbapenem Resistance ✓ Aminoglycoside Resistance ✓ Fluoroquinolone Resistance (Ofloxacin, Levofloxacin, Ciprofloxacin ✓ Acquired Combined resistance against third generation drugs and fluoroquinolones and aminoglycosides
Enterococcus faecalis	✓ Highly resistant against high level of Gentamicin.
Pseudomonas aeruginosa	✓ Ceftazidime Resistance ✓ Carbapenem Resistance ✓ Piperacillin + Tazobactam Resistance ✓ Fluoroquinolone (Ciprofloxacin, Levofloxacin) Resistance ✓ Aminoglycoside Resistance ✓ Combined Resistance against all the drugs
Streptococcus pneumoniae	✓ Resistant to Macrolides (Azithromycin, Erythromycin, Clarithromycin) ✓ Combine resistant against the Penicillin and Macrolides

Enterococcus faecium	✓ Resistant against Vancomycin
Acinetobacter species	✓ Carbapenem Resistance (Meropenem, Imipenem) ✓ Aminoglycoside Resistance (Netilmicin, Tobramycin) ✓ Fluoroquinolone (Ciprofloxacin, Levofloxacin) ✓ Combined resistance against fluoroquinolones+ aminoglycosides+ carbapenems

3.3. One Health Approach and Training Programs regulating AMR

One health largely emphasizes the collaboration between human and animal health issues today, but also other disciplines should be merged, such as the environmental and social sciences. These One Health Training agreements are notably integrated more into veterinary schools than into medical training, as the review of One University Training projects in Western Europe shows. Moreover, multidisciplinary and global health research and training activities must be undertaken, as zoonotic illnesses and AMR do not stop at national borders. Increasing emergent human infectious diseases of zoonotic origin and microorganism resistance to antimicrobial medicinal products have demonstrated that there is a need for cooperation between the human, animal and environmental sectors. Increasingly, the One Health concept is recognized by politicians and scientists all across the world. In this overview, research and training efforts have been assembled with the aim of focusing on infectious diseases in the One Health in Western Europe, particularly in France, Spain, The Netherlands, UK, Germany and Norway. It can serve as a basis for future projects and partnerships. This summary indicates that One Health in Europe is widely recognized, even though most recent educational activities are. In Europe, the One Health strategy in respect to antimicrobial resistance is now being pushed (AMR).

Many nations have included the One Health strategy in their anti-AMR policy and there have been considerable increases in funding options for AMR research. The number of multidisciplinary national and international research networks on zoonotic diseases and One Health has grown. This summary indicates that One Health in Europe is widely recognized even though most recent educational activities are. In Europe, the One Health strategy in respect to antimicrobial resistance is now being pushed (AMR).

Many nations have included the One Health strategy in their anti-AMR policy and there have been considerable increases in funding options for AMR research. The number of multidisciplinary national and international research networks on zoonotic diseases and One Health has grown. European institutes have researched on the topic of One Health Approach and many minor projects and training activities are being conducted in the countries of Europe for spreading the awareness of the importance of One Health Approach to fight against AMR and figure out a solution for it. The table below depicts the information related to One Health Approach conducted or training activities performed in the Western countries of Europe. (3, 16)

Table 5. European Institutes which researched on One Health Approach and also published article on this topic.

Country	Research Institute	Topic
France	OIE	Advocating the One Health Approach in general and in relation to rabies and Rift valley fever.
Germany	Freie Universitate Berlin	Publication on AMR and zoonoses in the food chain such as *Vibrio* and *Campylobacter*
United Kingdom	The Royal Veterinary College London School of Hygiene and Tropical Medicine University of Cambridge University of Liverpool University of Edinburgh	Research of AMR Advocating the One Health concept and research of zoonoses and AMR Research on zoonotic diseases such as emerging zoonosis and neglected zoonosis Research on zoonosis such as Japanese Encephalitis Virus and rabies.
Norway	Norwegian Veterinary Institute	EU's Horizon 2020 One Health Project
The Netherlands	Netherland Centre for One Health	Netherland Centre for One Health Project
Spain	Center for Veterinary Health Surveillance (VISAVET)	Project on One Health

Various training activities for One Health are conducted in the universities of Europe. Students have also acted in One Health in recent years. Some countries have one health student associations or public health veterinary organizations and networks, such as Holland and the United Kingdom Extension activities are part of several European research projects. An annual One Health Workshop and One Health for Near Generation project is organized for instance in anticipating a Global Onset of Novous Epidemics (ANTIGONE). (3, 17)

Table 6. Training Activities conducted in the European Counties on 'One Health'.

Country	Institute	Type of Training
Spain	Veterinary School of the Universitat Autonoma de Barcelona	Masters on zoonoses and One Health
The Netherlands	Utrecht University	Honours Program One Health, One Health Track
United Kingdom	Royal Veterinary College (RVC)/London School of Hygiene & Tropical Medicine (LSHTM), London Royal (Dick) School of Veterinary Sciences, Edinburgh, University of Bristol	Masters in One Health Honours Program population medicine and One Health.
France	Nantes-Atlantic National College of Veterinary Medicine, Food Science and Engineering, in partnership with the University of Nantes' Department of Medicine and the University of Angers' Department of Medicine	Master 'Manimal' as training

3.4. One Health Approach regulating AMR in India

A National Plan for controlling antimicrobial resistance has been formed in India. The plan suggests targeting a number of critical components of AMR in both the human sector and the non-human one, including agriculture, fishing, animal husbandry, environment. The strategy addresses all the five main GAP goals and provides a further goal of boosting India's AMR leadership. There are certain priorities that are being maintained to address all the issues. Below are the main objectives of the plan. Enhance awareness of AMR through effective communication, training and education; Enhanced surveillance knowledge and evidence; Reduce infection incidence by efficient infection, prevention

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and control; Optimize the use of antibiotics in all industries; Promoting AMR investment, research and innovation activities; Enhance India's AMR leadership through international, national and sub-national collaborations on AMR.

The Indian NAP for AMR is a well-designed global planning plan which incorporates all of the key GAP goals and pledges to address critical antibiotic policy and regulatory problems within the "One Health Approach." Implementation was delayed but all parties needed a major push. Failure to achieve separate funding remains the major hurdle to implement NAPs and/or state action plans, not just in India. (25) The mapping of the surveillance system set up for antimicrobial resistance in India is described below. (**Figure 6**)

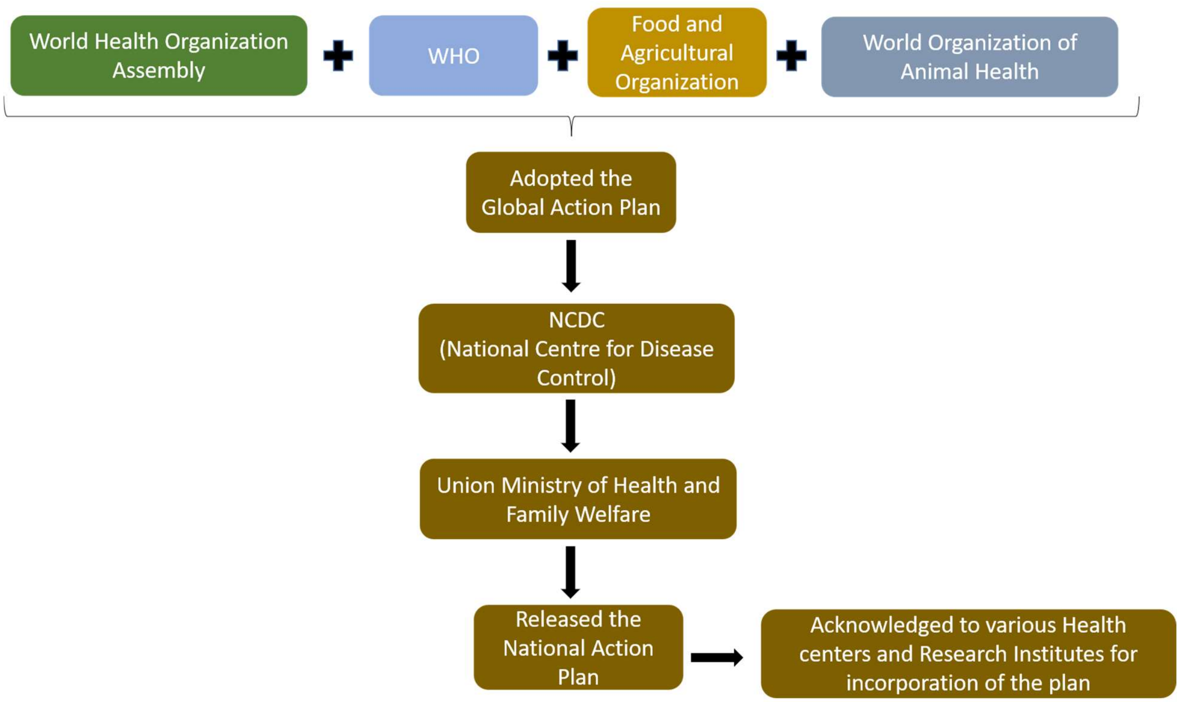

Figure 6. Mapping of the surveillance system set up in India for controlling antimicrobial resisitance.

3.5. One Health Approach regulating AMR in Taiwan

A major global crisis has developed antimicrobial resistance (AMR). Taiwan's CDC implemented the National Antimicrobial Stewardship Program, established multi-channel monitoring of multi-drug resistant organisms, hospital accreditation and hospital infection control inspections related to antimicrobial stewardship, coordinated infection control interventions and carried out antimicrobial control interventions in response to the growing threat poses by AMR. Taiwan CDC also proactively establishes relevant guidelines, e-learning materials and manual hygiene and antimicrobial awareness campaigns to encourage everyone to reduce this condition. Main Objectives are: Enhanced surveillance and control of carbapenem-resistant *Enterobacteriaceaes* of antimicrobial-resistant pathogens; In order to accredit and control hospital infections and hospital inspections, the antimicrobial stewardship of all hospitals is necessary or encouraged; To offer a number of e-learning courses to improve the understanding and consciousness of health workers on antimicrobial stewardship; To conduct national public and health awareness-raising campaigns; Cooperation on the fight against AMR with human and animal health sectors. [26] Thus, a comparative study has highlighted the fact that European countries

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and as well as Asian countries such as India and Taiwan are equally contributing in building various agencies and organizations for combating AMR by implementing various policies and many other surveillance systems which has actively increased the implementation of One Health Approach. In addition to this, after European countries, Taiwan has successfully accomplished many of their objectives which have helped the country in fighting against the AMR. Among all the above-mentioned strategies to prevent AMR, some of them are broadly explained below. (**Fig.6**) (18) The mapping of the surveillance system set up for antimicrobial resistance in Taiwan is described below. (**Figure 7**) (30) (31)

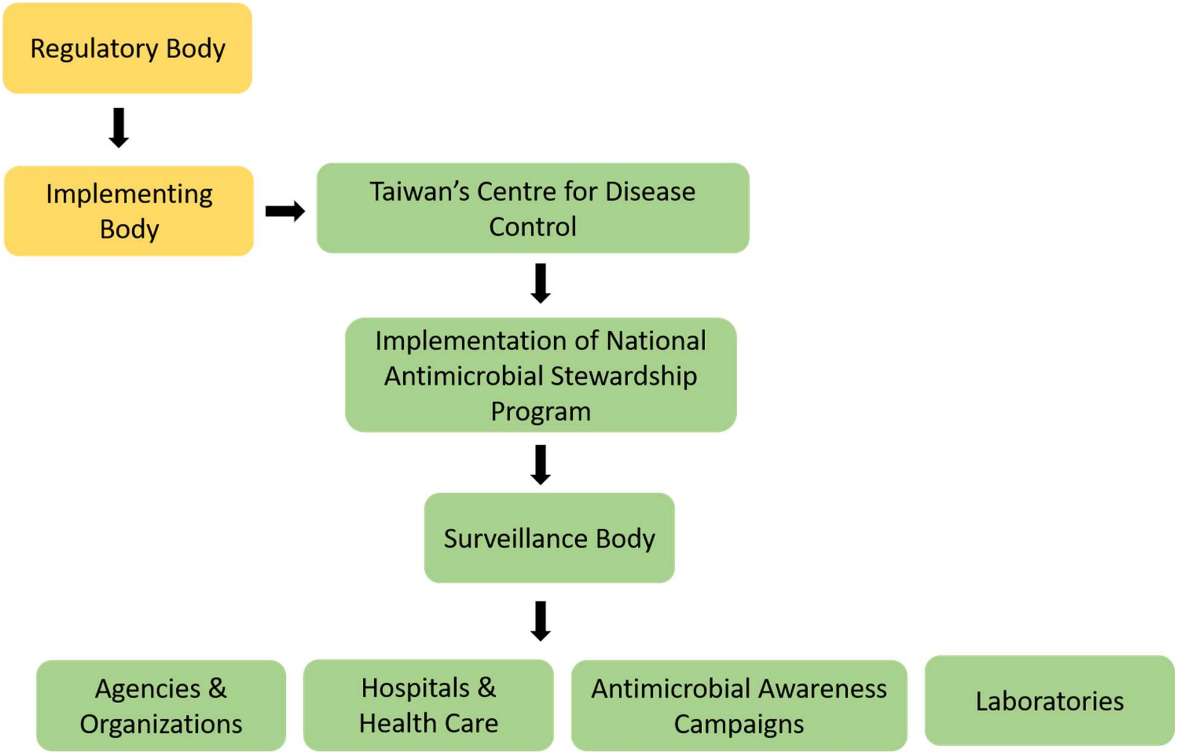

Figure 7. Mapping of the surveillance system set up in Taiwan for controlling antimicrobial resistance.

3.6. Alternatives for Antimicrobial Resistance

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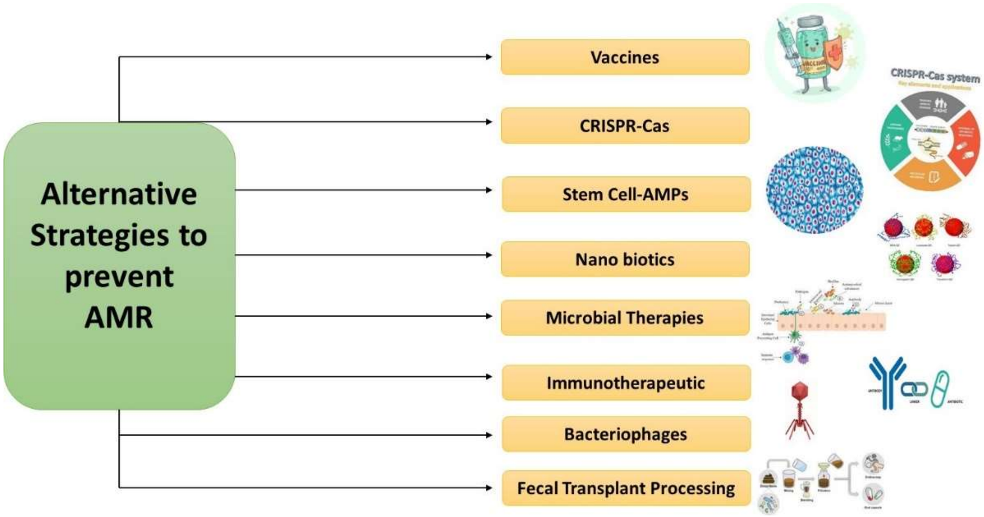

Figure 8. Possible alternative strategies to prevent AMR.

4. Discussion

This article provides an overview of various surveillance systems that are formed only to keep a track on the upcoming situation of AMR and the consumption of antimicrobials by the humans as well as animals. The article does not provide about all the details required to monitor the AMR issue but firmly allow the readers to get acknowledged with the broad information about the antimicrobial resistance across the six countries of Europe along with a comparative study between Taiwan and India. There are also a lot of debates on the themes of research covered by the term 'One Health.' Any field of research, including anthropology, sociology, pedagogies or comparative medicine, that may contribute to human, animal, or ecosystem health can be 'One Health.' Failure to treat certain infections with currently available antibiotics is a concern for biomedicine. Phage therapy as an alternative therapy against bacterial infections has been extensively investigated. Although various challenges exist, bacteriophages treatment could be used in future to replace antimicrobial agents with pathogens that are drug-resistant. The technique is now becoming popular as photographs are omnipresent, host-specific and harmless and can be administered with food orally. Antibiotic protein in target bacteria is developed for the delivery of recombinant phages. Topical treatment for open wounds or systemic infections may be performed intravenously. However, phage therapy gives rise to some serious concerns. The main thing about the host bacterium is its fine specificity. This prevents their use for acute infections as empirical therapy. The basis for their investigation was bacteriophageal lysins, the extremely specific peptidoglycan hydrolases and was also referred to as enzybiotics. Incorporated lysins represent a new therapy form that is powerful and readily available to fight antimicrobial resistance as multimedia resistant diseases are becoming increasingly common threats. (19, 20)**.**

With the emerging crisis of AMR, vaccine treatments are seen as a possible solution by health authorities, healthcare providers and drug developers. The biomolecules that boost the host immune system and give immunity against infectious agents are the immunotherapeutic. Developments in the new technology of recombinant vaccines have been essential for reducing the use of different antibiotics for primary and secondary bacterial infection. One of the most important ways to prevent infections continues to be vaccines. Increasing the internal immune system is the advantage of immunotherapeutic agents.(18) The CRISPR case is a distinguishing adaptive immune feature in archaea and bacteria, which offers protection against invasively invading bacteriophages and provides a regularly cross-sectional breast repeat. Short bacteriophages or plasmids known as spacers are inserted as a CRISPR array into the bacterial genome; the Cas proteins machine

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uses guide RNAs from spacers to target the invading nucleic acid with the same sequence. Phagemids from CRISPR-Cas9 could kill in vivo certain bacteria. CRISPR Nanosized Compounds can target the Mec- A gene that is involved in the methicillin-resistant *S. aureus* effectively. (21)

Mesenchymal stem cells (MSCs) have been intensively investigated for a variety of chronic diseases over several decades in order to develop a safe and promising therapeutical product. MSCs show promising skills in promoting immunomodulation, tissue cure and excessive inflammation control. Recently, human MSCs have been shown to synthesize antimicrobial peptide (AMP) factors that eradicate bacteria through several mechanisms including an inhibition of bacterial cell wall synthesis. Non-bacterial effects of MSCs (HUCMSCs) on drug resistant clinical pathogens like *E. coli*, S. aureus, and K. pneumonia have been detected. (22) A number of names known as fecal microbiota transplantation are known as fecal bacteriotherapy. The FMT process involves the transplantation, using various routes, including enema, nasogastric, nasoduodenal and colonoscopy, of a fecal suspension of commensal bacteria by a healthy individual donor into the intestinal lumen of the recipients. Clinical trials have found an automotive FMT (aFMT) in antibiotic-disrupted human patients that is better than probiotic therapy and that it has induced a fast and almost complete recovery of GI microbiota. (23)**.** Nanoparticulate materials may be used for the supply or may contain antimicrobial materials. The nanoparticles and antibiotics based on metal and metal oxides are seen as promising therapeutic candidates for the future applications of biomedical science, because they have lower toxicity and improved antibacterial, antivirals and cancer efficacy. They are of unique size, such as an increased volume-to-surface ratio making them efficient medicines carriers and improving their solubility, compatibility and ease of delivery.(24)**.**

Future advancing genetic engineering and next generation sequence has enabled scientists to develop future strategies, such as bioengineered probiotics or pharmabiotics that can become a bacterial infection biotherapy or prophylaxis. An option against antibiotics may be bio-engineered probiotics with diverse immunogenic properties. Ingenerated or recombinant probiotics with high competence could provide a greater degree of site specificity than common drug administration regimes to produce drugs, therapeutic proteins and gene therapy vectors.(18)

5. Conclusion

The regular data collected by the different organizations play a vital role in monitoring the status of AMR and antimicrobial usage by humans and in live stocks. These annual reports have highly helped the government to decide for alternatives and have focused in many training activities to combat the AMR situation globally. AMR prevention is linked to the One Health concept. As antibiotic resistance genes persist on an interface between environment and animal and animal health, an approach is required in all three areas that stresses the concept of 'One Approach to Health.' Finally, at any stage of life, antibiotic resistance can affect humans or animals. Alternative therapies should be developed to reduce dependency on chemical therapy. As antibiotics became part of modern medicine before seven decades, antibiotic effectiveness is decreasing. Clinical research, microbiology, genetics and computer engineering, imaging and modelling experts should work together to develop strategies to deal with this problem and to develop new therapies. Patients with normal infections should avoid unnecessary prescription and over-prescription of antibiotics and should advise patients to follow good hygiene such as hand washing and adequate infection management measures.

Abbreviations: AMR: Antimicrobial Resistance; MDR, Multi-Drug Resistance; CRE, Carbapenem-resistant Enterobacteriaceae; WHO, World Health Organization's; GAP, Global Action Plan; CAESAR, Central Asian and Eastern European Surveillance of Antimicrobial Resistance network; ARDIG, Antimicrobial Resistance Dynamics the Influence of Geographic origin; AMU, Antimicrobial Usage; EFSA, The European Food Safety Authority; ECDC, European Centre for Disease Prevention

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and Control; CEESA, European Animal Health Study Centre; EARS-Net, The European Antimicrobial Resistance Surveillance Network; EMA, European Medicines Agency; VAV, The Spanish Veterinary Antimicrobial Resistance Surveillance Network; MARAN, Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands; ZOMO, Zoonosis-Monitoring system; NORM-VET, Norwegian Veterinary Antimicrobial Resistance Monitoring system; ANSES, The French Agency for Food, Environmental and Occupational Health & Safety; EU-Harmonized, The EU harmonized surveillance system; ISIS-AR, Infectious Disease Surveillance Information System on Antibiotic Resistance; NORM & MSIS, Norwegian Veterinary Antimicrobial Resistance Monitoring; ARS, Antimicrobial Resistance Surveillance; EARS-Net-ES, European Antimicrobial Resistance Surveillance Network; ONERBA, National Observatory of the Epidemiology of Bacterial Antibiotic Resistance; ECOSS, SGSS, Datastore and COSurv, The Electronic Communication of Surveillance in Scotland, Second Generation Surveillance System; ANSES, French Agency for Food, Environmental, and Occupational Health and Safety; RAISIN, Investigation and Surveillance of Nosocomial Infection Network; SRUC, Scotland's Rural College Veterinary Services and Capital Diagnostics surveillance system; BSAC, British Society for Antimicrobial Chemotherapy's Resistance Surveillance Program; ARS, Antimicrobial Resistance Surveillance; VRE, vancomycin-resistant enterococci; MSCs, Mesenchymal stem cells; MRSA, Methicillin Resistant *Staphylococcus aureus*.

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