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REVIEW

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AMR and Sustainable Development Goals: at a crossroads

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Abstract

Antimicrobial resistance (AMR) poses a significant global health threat, primarily stemming from its misuse and overuse in both veterinary and public healthcare systems. The consequences of AMR are severe, leading to more severe infections, increased health protection costs, prolonged hospital stays, unresponsive treatments, and elevated fatality rates. The impact of AMR is direct and far-reaching, particularly affecting the Sustainable Development Goals (SDGs), underscoring the urgency for concerted global actions to achieve these objectives. Disproportionately affecting underprivileged populations, AMR compounds their vulnerabilities, pushing them further into poverty. Moreover, AMR has ramifications for food production, jeopardizing sustainable agriculture and diminishing the livelihoods of farmers. The emergence of antibiotic-resistant bacteria in underprivileged areas heightens the risk of complications and mortality. Climate change further contributes to AMR, as evidenced by increased instances of foodborne salmonellosis and the development of antibiotic resistance, resulting in substantial healthcare costs. Effectively addressing AMR demands collaboration among governments, entrepreneurs, and the public sector to establish institutions and policies across all regulatory levels. Expanding SDG 17, which focuses on partnerships for sustainable development, would facilitate global antimicrobial stewardship initiatives, technology transfer, surveillance systems, and investment in vaccine and drug research. The World Bank's SDG database, tracking progress towards sustainable development, reveals a concerning picture with only a 15% success rate till 2023 and 48% showing deviation, underscoring a global gap exacerbated by the COVID-19 pandemic. Tackling AMR's global impact necessitates international cooperation, robust monitoring, and evaluation methods. The five priorities outlined guide SDG implementation, while impoverished countries must address specific challenges in their implementation efforts. Addressing AMR and its impact on the SDGs is a multifaceted challenge that demands comprehensive and collaborative solutions on a global scale.

Keywords Antimicrobial Resistance (AMR), Sustainable Development Goals (SDGs), One Health, Antimicrobial Stewardship, Socio-Economic Impacts, Alternatives to Antibiotics

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Introduction

When microorganisms are repeatedly exposed to antimicrobial substances, they can develop the ability to overcome the treatments meant to eliminate them. Antimicrobial resistance (AMR) can arise from a long-term accumulation of adaptations to withstand antibiotic exposure (Lomazzi et al., 2019).The phenomenon of Antimicrobial Resistance (AMR) is inherently evolutionary, but the widespread abuse and overuse of antimicrobials in veterinary settings and public health care systems pose a serious and escalating danger [34]. Over time, AMR, with its significant impact on the ecosystem, human, and animal health, has evolved into a global health threat [58]. The future of healthcare is increasingly uncertain, as many contagious diseases are becoming resistant to antimicrobial treatments, posing a considerable challenge to effective medical interventions [23]. The repercussions of AMR are far-reaching, encompassing more severe infections, increased health protection costs, extended hospital stays, unresponsive treatments, and elevated fatality rates. The overuse of second-line drugs due to AMR further strains the public health system [27]. Unfortunately, the discovery of new antibiotics has markedly declined in recent years, exacerbating the urgency of the situation [18]. Moreover, the effectiveness of currently employed antibiotics is diminishing as they succumb to the challenges posed by AMR [58]. This underscores the critical need for concerted efforts to address the multifaceted issue of AMR and preserve the effectiveness of antimicrobial treatments in healthcare.

The World Health Organization (WHO) introduced the Global Action Plan (GAP) on Antimicrobial Resistance (AMR) in May 2015, garnering the support of over 115 countries that subsequently launched their National Action Plans. However, a significant challenge has been the struggle for adequate funding to effectively implement these plans, as reported by WHO in 2019 [106]. The financial constraints hinder the comprehensive execution of strategies aimed at addressing AMR on a global scale. The impact of AMR extends beyond public health, significantly affecting global socio-economic development. A 2019 report by the Centers for Disease Control and Prevention (CDC) in the United States revealed that AMR has increased the direct cost of healthcare by 20 billion dollars, not accounting for an annual yield loss of approximately 35 billion dollars. Furthermore, the same CDC report highlights the human toll, with approximately 23,000 deaths occurring annually among two million people who fall ill due to antimicrobial-resistant diseases in the USA [20]. These figures underscore the urgent need for sustained global efforts, both in terms of funding and coordinated action, to mitigate the impact of AMR on public health and socio-economic well-being.

In 2020, WHO raised alarm about AMR rates, reporting data from 78 countries in their surveillance report [38]. The gravity of the situation is underscored by a World Bank evaluation, which warns that failure to control AMR could lead to a decline in the global domestic product (GDP) by 1.1% to 3.8% by the year 2050. To avert this scenario, an estimated annual expenditure of about 9 billion US dollars would be required [11]. Policymakers face a substantial challenge in responding to the development and dissemination of pathogens resistant to antibiotics. They must navigate the transformation of health systems, transitioning from ones that allow easy access to these medications to systems that ensure access to the right antimicrobial treatment while concurrently mitigating the risk of the emergence and spread of resistance [15]. This dual objective requires strategic planning, international collaboration, and sustained efforts to address the multifaceted challenges posed by AMR.

The Global Goals, also known as SDGs, are internationally designed objectives aimed at ensuring a habitable world, eradicating poverty, and ensuring that all of humanity lives in harmony and prosperity going forward [63]. The precursor to SDGs was the Millennium Development Goals (MDGs), introduced by the United Nations in September 2001, as a set of broad objectives for global associations to achieve by 2015 [33]. The concept of MDGs drew inspiration from the development movements of the 1980s and 1990s [102]. MDGs comprised 18 targets with 8 defined goals to address issues related to malnutrition, poverty, education, infectious diseases, pollution, global development cooperation, maternal and infant mortality, and gender disparities [30]. The MDGs served as a critical framework to guide global efforts toward addressing these pressing challenges and improving the well-being of populations around the world.

The SDGs acknowledge the interconnectedness of eradicating income inequality and poverty, promoting inclusive economic growth, and safeguarding the environment, recognizing that each of these elements is closely related to population health. The SDGs also emphasize the reciprocal and dynamic interactions among these components. A fundamental aspect of the SDGs is their significant positive impact on health [46]. The SDGs' agenda revolves around the evolution of social, environmental, and economic factors, encapsulated by the concept of the 5P's: "Planet, Peace, Partnership, People, and Prosperity." Contrasting with the agenda of the Millennium Development Goals (MDGs), which primarily focused on issues such as malnutrition and poverty, the SDGs place greater importance on promoting equal human rights and women's empowerment [8]. This shift reflects an expanded and more comprehensive approach to sustainable development, encompassing a broader range of factors that contribute to the well-being and equality of individuals and communities globally.

As we entered the twenty-first century, it became abundantly clear that Antimicrobial Resistance (AMR) had evolved into a significant challenge in human therapeutics. This concern has been extensively discussed, with researchers emphasizing the adverse outcomes of AMR. In contrast, the SDGs aims to transform the world by addressing poverty, inequality, environmental preservation, and providing health, justice, and prosperity for everyone (Organization, 2017).

The aim of this review is to underscored AMR as a global public health emergency, emphasizing its widespread impact on SDGs. Regrettably, the escalating issue of AMR directly hampers the ability of SDGs to achieve their objectives, as noted by various researchers [37]. The hindrance caused by AMR in the realization of SDGs was a focal point, highlighting the specific challenges posed by antimicrobial resistance. According to the United Nations Environment Programme (UNEP) it is imperative to tackle the environmental dimensions of AMR to maintain global progress towards the SDGs. Thus, fighting AMR is essential not only to keep people and animals healthy, but also to achieve sustainability (UNEP, 2023). The intertwining of AMR with the broader objectives of sustainable development underscores the urgency of comprehensive and coordinated efforts on a global scale. This review also discussed global actions and strategies necessary to achieve these goals while effectively addressing the critical issue of AMR.

Research methodology

The study analyzed previous peer-reviewed research that addresses pre-formulated research questions using a literature review approach. This method allows for an efficient and comprehensive synthesis of the body of existing literature by offering an in-depth overview of the state of knowledge on the subject today. This approach made it possible to identify knowledge gaps, extract important insights, and formulate well-informed judgments. The Electronic Databases (EDs) that are specifically used for this purpose are those offered by well-known publishers such as PubMed, Google Scholar, ScienceDirect, and Scopus. We executed a comprehensive search in all database fields by using the following terms (Sustainable Development Goals OR SDG'S), (Agenda 2030), (AMR and SDG's) and (Health and Agenda 2030).

This search approach was established to identify relevant studies that addressed the relationship between AMRs and SDG's. The mentioned databases were selected due to their broad coverage of academic literature in many domains, guaranteeing access to a diversified range of peer-reviewed papers, journals, and research publications that are crucial for carrying out an exhaustive evaluation. We carefully analyze articles referencing the Sustainable Development Goals and AMR, ensuring they directly address the research topic. This rigorous approach not only ensured relevance and coherence but also made sure to stick to the problem statement in our review and enhance the quality and precision of our findings.

Antimicrobial resistance (AMR): a pressing global health crisis

Naturally occurring compounds known as antimicrobials play a crucial role in either killing or inhibiting the growth of microorganisms. Their significance in human medicine is profound, as they have significantly improved medical practices such as surgeries and the treatment of infections. Beyond human health, antimicrobials also play a vital role in supporting the economic well-being of millions of farmers and livestock keepers globally. They contribute to the health of animals, enhance agricultural productivity, and ensure food safety. The availability and effectiveness of antimicrobials have increased, leading to improvements in agricultural productivity, overall food safety, and animal welfare [75]. However, this widespread use of antimicrobials has introduced challenges, particularly in the form of antimicrobial resistance (AMR).

AMR existed in nature before humans began using antimicrobial agents, and its development is driven by natural selection. Resistant microorganisms thrive in environments exposed to antimicrobials. Enzyme activity plays a significant role in many forms of AMR, as resistant bacteria transfer genes to the next generation. Some bacteria employ methods for intergenerational genetic exchange, complicating the dynamics of the AMR process [14]. The intricate relationship between antimicrobials, resistance, and microbial dynamics underscores the importance of responsible and judicious use to ensure their continued efficacy.

Antimicrobial resistance (AMR) is experiencing a sharp rise, exacerbated by the obsolescence of many standard antibiotic treatment regimens (Fig. 1). This trend poses the risk of patients in critical conditions requiring palliative care, yet the prescribed drugs are no longer clinically effective [4]. Antibiotic-resistant bacteria employ various strategies, including enzyme degradation, enzymatic scaffold modifications, efflux pumps, alterations to targets, adjustments to cell membrane permeability, and changes in the expression of the intended target. Some bacteria limit membrane or wall permeability to prevent antibiotics from entering the cell, while others create variations of selective prions that inhibit prion expression [43]. The multifaceted mechanisms of antibiotic

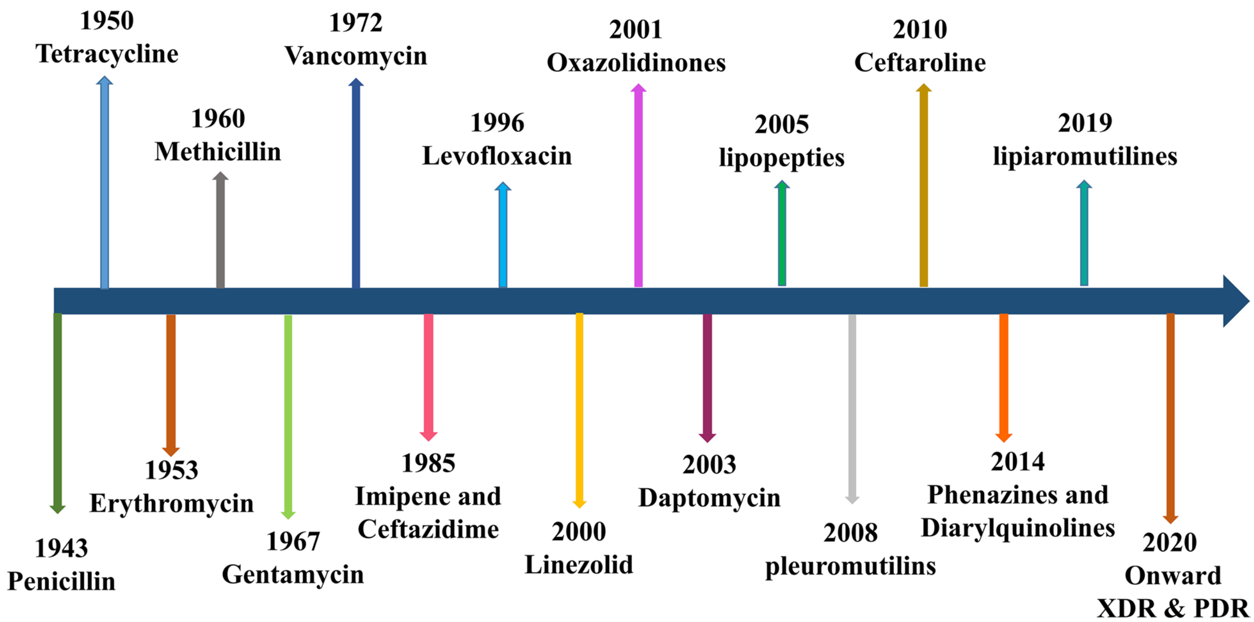

Fig. 1 Development of antibiotic resistance overtime

resistance underscore the urgent need for comprehensive strategies to address this global health challenge.

The Centers for Disease Control and Prevention's 2019 antibiotic resistance danger assessment reveals alarming statistics, with over 2.8 million cases of Antimicrobial Resistance (AMR), resulting in over 35,000 fatalities annually in the United States. The study categorizes carbapenem resistance as urgent, emphasizing the severity of the issue. The assessment further classifies risks into categories such as serious, urgent, worrying, and watch list. Of particular concern is the emergence of carbapenem-resistant bacteria, as these are considered "last-resort" medications for treating multidrug-resistant illnesses. The rise of such resistance poses a significant threat to public health. The assessment by Jim O'Neill underscores the profound impact of antimicrobial resistance, highlighting it as a major contributor to the global burden of illness [67] (Fig. 2). Addressing the challenges posed by AMR requires concerted efforts and innovative solutions to ensure the continued efficacy of antibiotics and safeguard public health.

As the crisis of Antimicrobial Resistance (AMR) reaches its zenith, experts are warning that the era of having no effective antibiotics is fast approaching [93]. Collaborative research is under consideration to discover new antibiotic combinations that can overcome resistance and enhance the effectiveness of last-resort medications [65]. The pace of new antibiotic research and development has significantly slowed since the late 1990s, with only three new antibiotics approved by the FDA in the past 30 years [90]. Recent WHO studies on clinical and preclinical drug development highlight a limited pipeline for antibiotic drugs, raising concerns about the global efforts to control drug-resistant diseases. Among the 50 antibiotics undergoing clinical trials, most offer modest advantages, and of those in preclinical development, 252 are still in the early stages of research [104]. This scarcity of new and potent antibiotics poses a serious threat to our ability to combat drug-resistant infections and underscores the urgency for increased research and development in this critical area of medicine.

From household to economy: socio-economic ramifications of AMR

Antimicrobial Resistance (AMR) imposes substantial clinical and economic burdens on healthcare systems and patients. In the United States, the annual cost of AMR amounts to $55 billion, with $20 billion spent on healthcare and an additional $35 billion lost due to decreased productivity [2]. World Bank research suggests that the impact of AMR may be more pronounced in low-income nations, potentially exacerbating poverty rates. By 2050, there could be a 1% decline in global GDP, with poorer nations experiencing a 5–7% drop, leading to losses ranging from $100 to $210 trillion. By 2007, drug-resistant tuberculosis alone was estimated to cost the world $16.7 trillion. AMR further amplifies global inequality by widening the gap between wealthy and poor nations, with impoverished populations being the most severely affected due to the high incidence of infectious diseases.

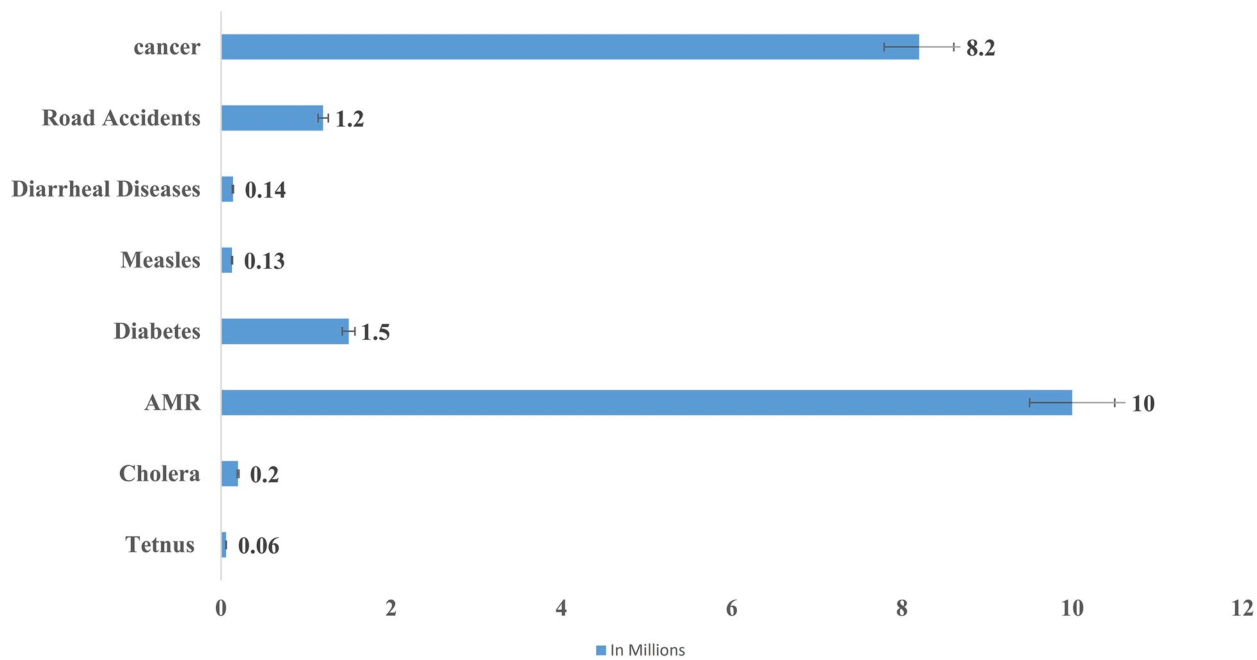

Fig. 2 Estimated death count by different diseases till 2050

Moreover, AMR has implications for workforce productivity, reducing it due to illness and premature mortality [45]. The ongoing COVID-19 pandemic adds an additional layer of complexity to the global economy by adding more expenditures in context to antibiotics usage. A review indicates that 72% of 2,010 COVID-19 patients received broad-spectrum antimicrobial therapy, even though only 8% experienced bacterial and fungal co-infection. The World Health Organization (WHO) discourages the inappropriate use of antibiotics, especially among mild COVID-19 patients [74]. The intertwined challenges of AMR and the COVID-19 pandemic underscore the critical need for judicious use of antimicrobials and global collaborative efforts to address these complex health issues.

Antimicrobial resistance (AMR) has far-reaching consequences that extend to the workforce, significantly impacting population size and the quality of human capital. Researchers have developed a theoretical model to project the economic effects of AMR on the workforce in the future. Comparing a non-AMR baseline with current trends and potentially worse alternatives, their findings suggest that without intervention, the world's working-age population could decline by two years within a decade, with Eurasia experiencing the most significant impact [22]. If the trends of AMR continue unabated, the global economy could face an annual GDP loss of approximately $28 billion over the next ten years. In this scenario, the European Union and Organization for Economic Cooperation and Development (OECD) countries would bear a significant portion of the loss, with a $20 billion reduction in GDP [92]. The impact of AMR is particularly pronounced in developing countries, where high infectious disease cases and a reliance on labor income contribute to elevated healthcare expenditures. Challenges such as poor implementation, lack of regulation enforcement, low antibiotic awareness, and inadequate distribution of treatment recommendations make effective therapy challenging to obtain in these nations, especially in low- and middle-income countries [9, 15]. Addressing AMR is not only a healthcare imperative but also a critical component of sustaining global economic health and workforce productivity.

Decoding AMR: unraveling the primary contributing factors

Addressing the complex nature of Antimicrobial Resistance (AMR) and implementing comprehensive strategies to mitigate its impact requires a thorough understanding of the primary contributing factors (Fig. 3). The rapid development of Antimicrobial Resistance (AMR) is largely attributed to the overuse and misuse of currently available antimicrobials. Global antibiotic usage increased by 65% between 2000 and 2015 [50]. The improper use of antibiotics is prevalent in both general and acute care settings, particularly among healthcare providers working with infants and young patients. In South Africa, up to 55% of primary care physicians

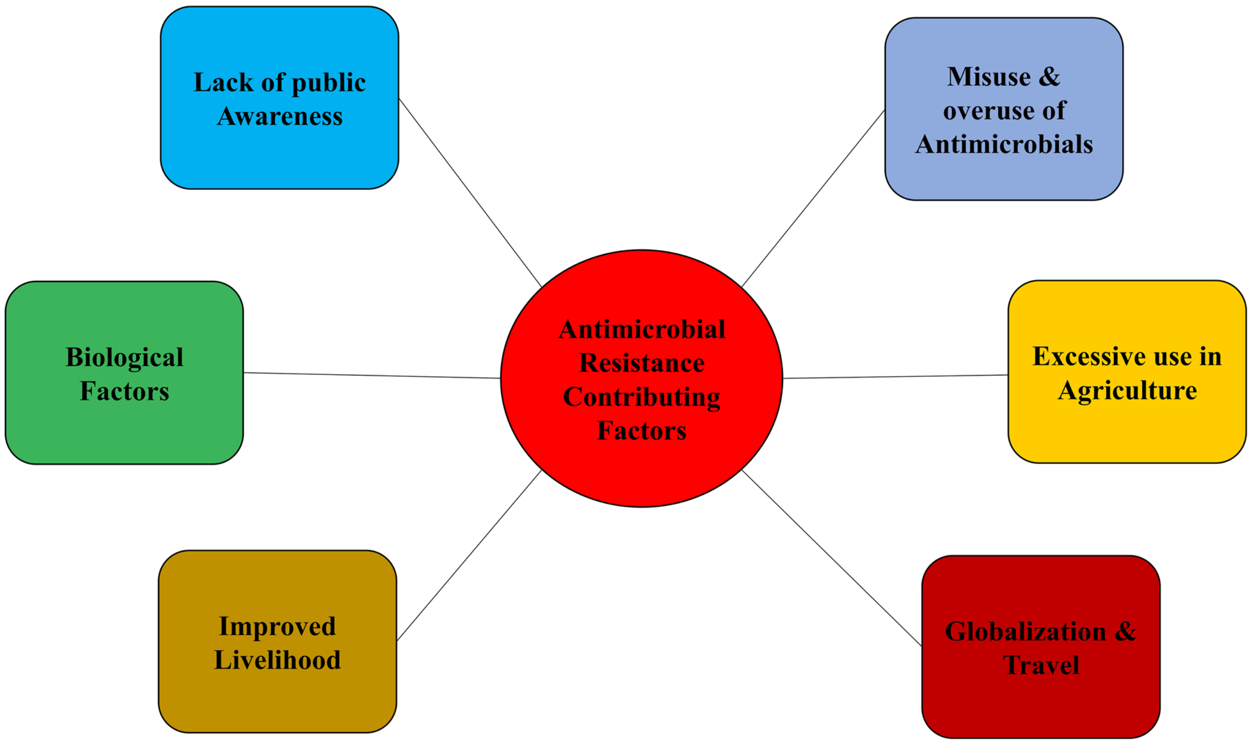

Fig. 3 Antimicrobial resistance contributing factor

misuse antibiotics, while the figures are 88% in Pakistan, 61% in China, and 15.4% in Canada. The reliance on prescription medication, especially antibiotics, for patient care is widespread in developing nations due to a lack of adequate diagnostic tools. Another common form of antibiotic misuse is administering them when they are not truly needed for therapy [22]. In Louisiana, up to 60% of antibiotic prescriptions were written for inappropriate purposes [14]. The abuse and overuse of antibiotics significantly increase the likelihood of the emergence of AMR, particularly among bacteria classified as WHO priority pathogens [101] (Fig. 4). Addressing these practices is crucial to curbing the escalation of AMR and preserving the effectiveness of existing antimicrobials.

During the COVID-19 pandemic, a rise in antibiotic prescriptions for prophylaxis has been observed in treatment plans, contributing to an increase in antimicrobial resistance (AMR) pathogens [47]. Another significant factor in the increasing AMR ratio is the extensive use of antibiotics in agriculture for disease prevention; in the US, 80 percent of all antibiotic sales are dedicated to treating animal feed. In 2010, 63,200 tons of antibiotics were used in cattle production, surpassing the quantity used for human consumption [21]. Antibiotics are administered to drinking water and nutritious animal feed to keep animals healthy, increase herd size, and enhance feed efficiency. Colistin, a crucial last-line antibiotic for treating serious infections in humans, is frequently used in animal husbandry [53]. While the European Union (EU) banned the use of antibiotics for growth promotion in 2003 [70], the FDA made it illegal to provide antibiotics to cattle without a veterinarian's prescription in 2012 [91]. Despite these measures, 26 out of 160 countries still used antibiotics as growth enhancers in agriculture in 2019 [31]. The modern and easily accessible travel routes have played a significant role in the global spread of antimicrobial resistance. Travelers may be exposed to resistant pathogens, increasing the likelihood of returning colonized and infected individuals [27].). For instance, European tourists to India, with no contact with the Indian healthcare system, tested positive for carbapenemase-producing Enterobacteriaceae (CPE) after returning from their trip indicates potential acquisition of bacteria during the trip. The overuse of antibiotics in developing nations, often associated with growing income linked to GDP growth and improvements in living standards in low- and middle-income countries, is a major driver of the global rise in antibiotic usage [79]. Addressing antibiotic use in both healthcare and agriculture is crucial to combat the growing threat of antimicrobial resistance.

Critical

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

High

- *Enterococcus faecium*, vancomycin-resistant *Staphylococcus aureus*, methicillin-resistant, vancomycin-intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter* spp., fluoroquinolone-resistant
- *Salmonellae*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, cephalosporin-resistant, fluoroquinolone-resistant

Medium

- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant
- *Shigella* spp., fluoroquinolone-resistant

Fig. 4 Priority pathogen list by WHO for developing new antibiotics

As developing countries experience economic growth, their dietary patterns shift towards higher consumption of animal protein, increasing demand for livestock production. This intensification frequently involves packed and unsanitary conditions, increasing the risk of disease propagation among animals, leading to more antibiotic use to maintain production levels and prevent outbreaks [98]. Over the past decade, there has been a global shift in antibacterial use patterns, with low- and middle-income countries (LMICs), including Turkey, Tunisia, Algeria, and Romania, having the highest rates in 2015. It is expected that, in the coming years despite LMICs currently having lower rates of antibiotic use as compared to first world countries, these rates will eventually surpass or even converge with those of high-income nations [50]. Bacterial evolution and mutation can lead to spontaneous antibiotic resistance, with insertion sequences and transposons providing plasmids access to resistance genes [81]. The transfer of these plasmids can spread antibiotic resistance to other species [89]. Currently, only 42 nations collect comprehensive data on antibiotic usage in healthcare and animal husbandry, contributing to the ongoing trends of AMR [102]. Additionally, there is a significant lack of knowledge among individuals regarding the appropriate usage and potential risks associated with antibiotics, as indicated by national questionnaires in various developed and developing nations, including the US, Sri Lanka, Japan, Australia, and the Gulf Cooperation Council. This lack of awareness serves as a vital contributing factor to AMR [27]. Addressing antimicrobial resistance requires a comprehensive, interdisciplinary strategy involving the medical, agricultural, and environmental sectors. By adopting this approach, stakeholders can develop long-lasting solutions to ensure the effectiveness of our antibacterial arsenal for future generations.

Strengthening healthcare: approaches to addressing AMR

Antimicrobial resistance (AMR) is indeed a significant global health concern, and its implications extend to the achievement of SDGs. According to current estimates, 1.27 million deaths worldwide in 2019 were directly linked to AMR, with an additional 4.95 million deaths indirectly associated with infections related to AMR [64]. To Recognizing the severity of the issue, the World Health Organization (WHO) declared AMR a major global concern in 2014. In response, the World Health Assembly released the Global Action Plan on Antimicrobial Resistance, urging member nations to implement comparable strategies by May 2017 [103]. Measures such as the judicious use of antimicrobial drugs have been employed to reduce the prevalence and transmission of AMR. The Food and Drug Administration (FDA) in the United States has also implemented steps to assess AMR outbreaks [41]. Rapid diagnostic testing is crucial in the fight against AMR, especially in developing countries where standard microbiological methods may be insufficient. New genetic screening technologies can be utilized to generate personalized medicines for appropriate antimicrobial therapy. The One-Health concept, exploring human-animal interactions and proposing novel evaluation techniques, is considered instrumental in addressing AMR [19]. Global initiatives, such as the declaration of the 2016 high-level meeting on antimicrobial resistance at the United Nations General Assembly and the FAO/OIE/WHO Tripartite Collaboration, represent national and international efforts to combat the spread of AMR. In 2022, the Tripartite Collaboration expanded to include UNEP, forming the Quadripartite, which also involves the World Organization for Animal Health (WOAH). The Quadripartite collaborates to highlight the potential harm caused by AMR to humans, animals, plants, ecosystems, and livelihoods [68].

Antimicrobial resistance (AMR) has been a global concern for several decades, dating back to Sir Alexander Fleming's warning in the 1940s [78]. The concept of "antimicrobial stewardship" (AMS) was introduced by McGowan and Gerding in 1996 and later adopted by the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) [61, 39]. AMS is defined as an organizational or healthcare-system-wide approach aimed at fostering and monitoring the judicious use of antimicrobials to preserve their effectiveness [28]. In Europe, national programs were established to raise awareness and ensure prudent antibiotic use, and in 2016, the World Health Organization (WHO) and the United Nations (UN) endorsed the implementation of stewardship programs, emphasizing the importance of adapting strategies to local contexts [105]. The Food and Agriculture Organization (FAO) of the UN outlines four essential pillars to promote and support AMS at the national and international levels [32] (Fig. 5). These pillars likely encompass various aspects of awareness, education, monitoring, and enforcement to ensure responsible antimicrobial use. Highlighting the impact of AMS, the University of Maryland Stewardship Program demonstrated significant cost savings ranging from $200,000 to $900,000 per year. Over three years, the program reduced antibiotic spending by $3 million. Notably, after discontinuation, spending on antibiotics increased by $2 million [87]. AMS programs not only contribute to economic efficiency but also promote responsible resource use in healthcare. Additionally, they facilitate cross-border collaboration, recognizing that AMR is a global issue that requires international cooperation. The success of these programs underscores the importance of coordinated efforts to address AMR at various levels.

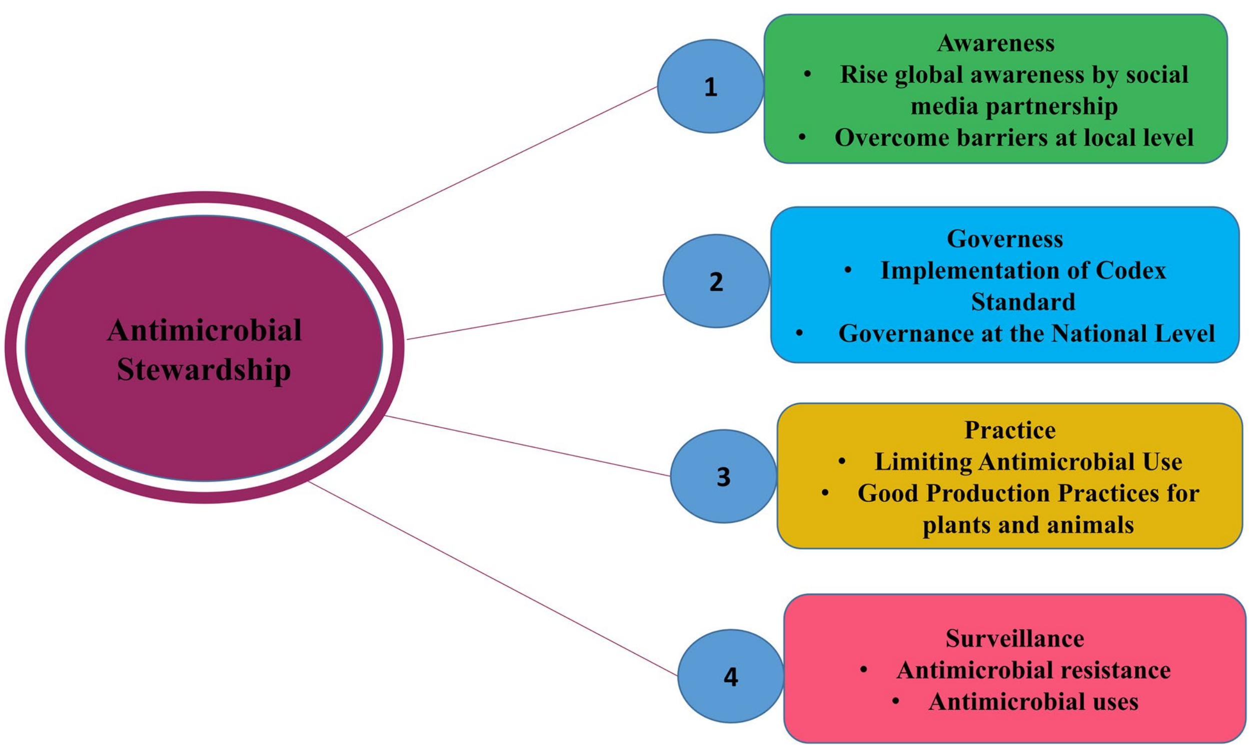

Fig. 5 Key elements of antimicrobial stewardship

To address the challenge of antimicrobial resistance (AMR), there is a need for a collaborative global effort that accelerates scientific discovery and integrates solutions into existing systems. The proposal suggests establishing a worldwide network-to-network (NTN) collaboration, which would serve as a next-generation AMR network. This network aims to train researchers for multi-team, multidisciplinary partnerships on a global scale. The envisioned NTN collaboration would involve members from both lower- and middle-income nations (LMICs) and high-income countries (HICs), ensuring representation from diverse economies, locations, climates, cultures, and resources across multiple continents [72]. An example of an organization that aligns with this vision is the Global Alliance for Rapid Diagnostics (GARD), established in 2016. GARD operates as a peer-to-peer partnership representing scientists and practitioners from various disciplines interested in AMR (https://www.egr.msu.edu/alocilja/GARD-location/global-alliance-rapid-diagnostics-gard). GARD has facilitated the formation of six regional networks, covering North America, Latin America, Southeast Asia, South Asia, East Asia, and Africa. The diagram in Fig. 6 illustrates how the proposed multidimensional, next-generation AMR network would leverage regional and disciplinary knowledge within nodes while establishing new connections between regional networks. This collaborative approach aims to enhance the capacity for research, innovation, and implementation of solutions to combat AMR on a global scale.

The integration of field data, algorithms, big data analytics, connected devices, and human input presents new opportunities for the management of Advanced Medical Devices (AMR). Leveraging digital technology and data strategically can contribute to the digital transformation of various industries, potentially mitigating the consequences of AMR [76]. The increasing availability of medical data and the application of artificial intelligence (AI) can enable rapid diagnosis of AMR, foster scientific breakthroughs, and support the development of new products and services for AMR control. These benefits can be realized at local and regional levels by compiling a comprehensive list of existing data sources and their characteristics [24]. To address the global challenge of AMR, the proposed next-generation AMR network aims to bring together diverse organizations. The network emphasizes professional development through training, research exchanges, and knowledge-sharing events. The goal is to equip the next generation with skills in communication, collaboration, and leadership, preparing them for multidisciplinary, collaborative research efforts. The Cyber Ambassadors program, funded by the National Science Foundation, offers modular and customizable training, including a "train-the-trainers" component that enables local facilitators to provide ongoing training, facilitating rapid scaling and deployment of professional development on a global scale [17]. In addition to training initiatives, researchers are exploring the creation of antibacterial substitutes as another strategy to combat AMR. This multifaceted approach underscores the importance of technological innovation, education, and global collaboration in addressing the complex issue of antimicrobial resistance.

Table1 shows some of the alternatives to antibiotics.

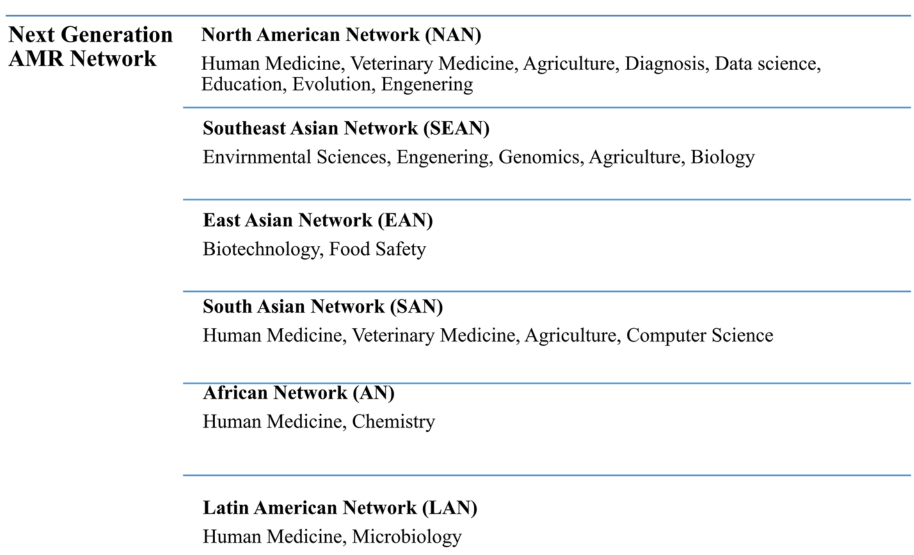

Fig. 6 Aspects of next generation AMR networking

Table 1 Alternative to antibiotics

Alternative	Properties	Advantages	Disadvantages	References
Vaccine	Easy to use Limit onset of disease	Promote Specific Immunological Protection Prevent Bacterial And Viral Infection	Limited cross-protection with some pathogens	[99]
Probiotics	Prebiotic Symbiotic Competitive exclusion	Useful for commensals gut bacterial health Prevent pathogen colonization	Mixed efficacy of a single probiotic	[36]
Predatory Bacteria	Alter and consume other bacteria	Effective against biofilm Can access recalcitrance infection	No interaction between host and commensals	[29]
Monoclonal Antibodies	Prophylactic action Pre-emptive approach	Long half-life Highly specific Do not disrupt normal flora	Limited stain efficacy	[35]
Phage Therapy	Narrow host spectrum Great diversity Bacteriolysis	Lytic activity independent of antibiotic resistance Do not infect eukaryotic cells Found naturally in environment	Potential ability to induce horizontal gene transfer by generalized transduction	[3]
Bacterial cell wall hydrolases (BCWH)	Lysozymes Autolysins Virolysins	Highly effective against antibiotic resistant bacteria Safe and well understood Immunogenicity is not a concern for their effectiveness	Non-effective against many Gram negative bacteria Some Gram positive stains also resistant to lysozymes	[69]
Nano-particles (Silver, Gold, Zinc and Zinc oxides, Nickel And Nickel oxides)	Low minimum inhibitory concentration (MIC) Unique physical and chemical properties	Can target multiple cellular pathways at once Can penetrate through cell wall and kill bacteria Used to treat multiple drug resistant bacteria	High cost of drug development Toxicity	[3]
Herbal Medicine	Phytochemicals	Efflux inhibitory activity against Gram negative bacteria Biofilm inhibitors. Quorum sensing inhibitors	Lack of standardization	[84]

Significance of SDGs: importance and implications

The Millennium Development Goals (MDGs) represent a comprehensive set of development objectives adopted by numerous countries to address their unique needs and challenges (Fig. 7) [13]. These goals provide a framework for global collaboration with the shared aim of halving world poverty, saving millions of lives, and enhancing the well-being of billions of people in a sustainable manner [83].

Efforts to achieve the MDGs have been varied globally, with a significant focus on addressing infectious diseases and improving maternal and child health. However, attention to establishing international partnerships and promoting sustainable environmental development has been comparatively limited. Despite considerable international and national efforts, progress has been uneven across different regions of the world. The rapid development of several Asian nations, including China, India, Indonesia, and Vietnam, has played a crucial role in the reduction of global poverty [54]. However, challenges persist, with 15.5% of the world's population still living in hunger, and many African countries facing difficulties in achieving the targeted two-thirds reduction in child mortality by 2015. Maternal mortality rates, particularly in Southern Asia and sub-Saharan Africa, remain high, reflecting the slow progress in these regions where 80% of the world's poorest people reside [33]. The MDGs have provided a valuable framework for international collaboration and goal-setting, laying the groundwork for subsequent initiatives such as the SDGs, which build on the achievements and lessons learned from the MDG era.

The United Nations General Assembly introduced the SDGs for the period 2016–2030 as a more comprehensive successor to the Millennium Development Goals (MDGs). Unlike the MDGs, the SDGs convey a clear message to all United Nations member countries: successful goal attainment requires collective action from every nation. The SDGs consist of 17 objectives and 169 targets, surpassing the MDGs in scope by addressing the root causes of poverty and emphasizing universal development for the benefit of all of humanity [63]. While the MDGs faced challenges, particularly in terms of funding limitations that hindered progress in poorer countries, the SDGs took a more inclusive approach.

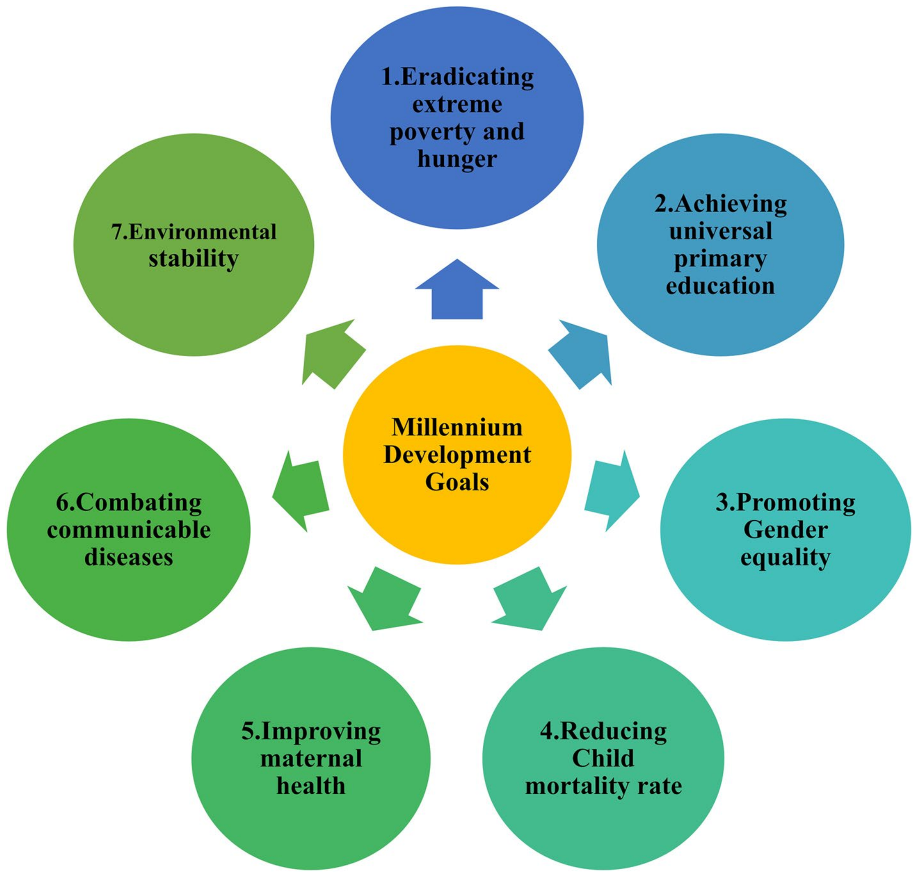

Fig. 7 Millennium development goals

They emphasize equal human rights and development for both developing and developed nations [51]. The SDGs actively involve both the public and private sectors to facilitate global sustainability. They also highlight individual behavior changes as a crucial tool for achieving environmental sustainability. Aligned with Agenda 2030, the global goals stress the importance of "mobilizing global partnerships" to foster cross-border collaboration, allowing individuals and nations to collectively address the needs of less developed countries [52]. The SDGs, with their holistic and collaborative approach, represent a more ambitious and interconnected framework for addressing global challenges compared to the earlier MDGs.

The SDGs, with their numerous objectives, targets, and supporting activities, pose a challenge for governments and international agencies due to the complexity of whole systems thinking [63]. While early mapping exercises have illustrated the interconnections between various objectives, it is evident from past performance that there may be a lack of expertise in handling trade-offs and unexpected outcomes [66]. It is crucial to set priorities among objectives and assess how they might impact other goals. The challenge lies in developing innovative solutions for contemporary issues related to energy, agricultural productivity, and commercial success in the twenty-first century. The SDGs advocate for interconnected innovation on a significant scale, emphasizing action and intelligent thinking over expansive approaches. Addressing issues such as improved ecological benefits and the development of more democratic and sustainable food systems can contribute to achieving Goal 2 (Zero Hunger) and other related objectives. The success of the SDGs requires not only a commitment to the goals but also the ability to navigate the complexities of interconnected systems and adapt strategies to achieve positive outcomes.

Pandemic challenges: impacts of COVID-19 on SDGs

The period from 2015 to 2019 witnessed global progress toward the SDGs at a rate of 0.5 percentage points annually. However, the COVID-19 pandemic has significantly hampered the achievement of the 2030 Agenda's objectives, which were originally targeted for completion by 2022. The current rate of progress has slowed down to only 0.1 points per year [80] (Fig. 8). The pandemic,

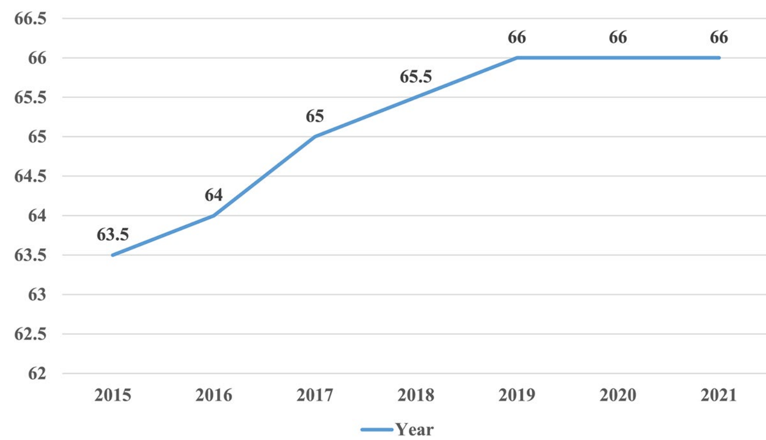

Fig. 8 SDG index score over time globally (2015–2021)

leading to six million deaths by May 2022, has had a profound impact on global health systems. It has resulted in increased poverty, with an estimated 119–124 million people falling back into extreme poverty. The global GDP per capita is predicted to decline by 4.2% [94]. The economic repercussions of the pandemic have been severe, with 225 million people losing full-time jobs, and 1.52 billion youth out of school and college due to lockdown measures. Approximately 49% of global nations are experiencing negative growth on the SDG index [109]. COVID-19 has caused a downturn in economic development by disrupting global consumption and manufacturing. The pandemic's impact has not only exacerbated economic challenges and social inequalities but has also led to a widespread increase in antibiotic use globally. The long-term consequences of this pandemic on the SDGs are still uncertain as its profound impact reverberates throughout the entire system, compelling us to navigate with resilience and innovation towards a more sustainable and equitable future [49, 77].

Leaving no one behind: SDGs and the one health approach

The term 'One Health' was coined in 2003–2004, coinciding with the emergence of SARS and the spread of H5N1. The Wildlife Conservation Society's gathering produced the "Manhattan Principles," emphasizing the interconnectedness of animal and human health and the risks they pose to economies and food supplies. These principles underscored the importance of interdisciplinary collaboration in responding to new diseases, particularly those affecting animal health [26]. The concept of One Health has deep historical roots, with origins dating back at least two centuries [6]. The most widely accepted definition, shared by the US Centers for Disease Control and Prevention (CDC) and the One Health Commission, describes it as a transdisciplinary, collaborative, multisectoral approach operating at local, regional, national, and international levels to achieve optimal health outcomes (Fig. 9). Another definition comes from the One Health Global Network, emphasizing the connections between the health of ecosystems, animals, and people [57].

Peace, prosperity, economic advancement, and social justice for everyone are the overarching goals of the SDGs. Target 3.3 within SDG3, which focuses on health and well-being, specifically aims to halt the spread of communicable diseases, neglected tropical diseases, AIDS, TB, and malaria. This ambitious target set for 2030 is designed to catalyze rapid investments and efforts to eliminate and control chronic diseases to advance global development [73]. In 2018, the Global Animal Law Association launched the United Nations Convention on Animal Health and Protection (UNCAHP), an international initiative. The primary objective of UNCAHP is to safeguard human and environmental health, ensure the welfare of animals as sentient beings, and contribute to the overall health of the planet [86]. Unlike previous animal-related initiatives, UNCAHP carries legal obligations for member nations, signifying a substantial shift from purely voluntary agreements. This change reflects an understanding of how vital animal health and well-being are on a global scale. However, it's noteworthy that animal welfare has received limited attention within the 2030 Agenda for Sustainable Development (SDGs), with explicit references in SDGs 14 (life below water) and 15 (life on land) that address the well-being of all living organisms, though the welfare criteria is not explicitly mentioned. The term "animals" appears only once in goal 2.5.5 of the 2030 Agenda for Sustainable

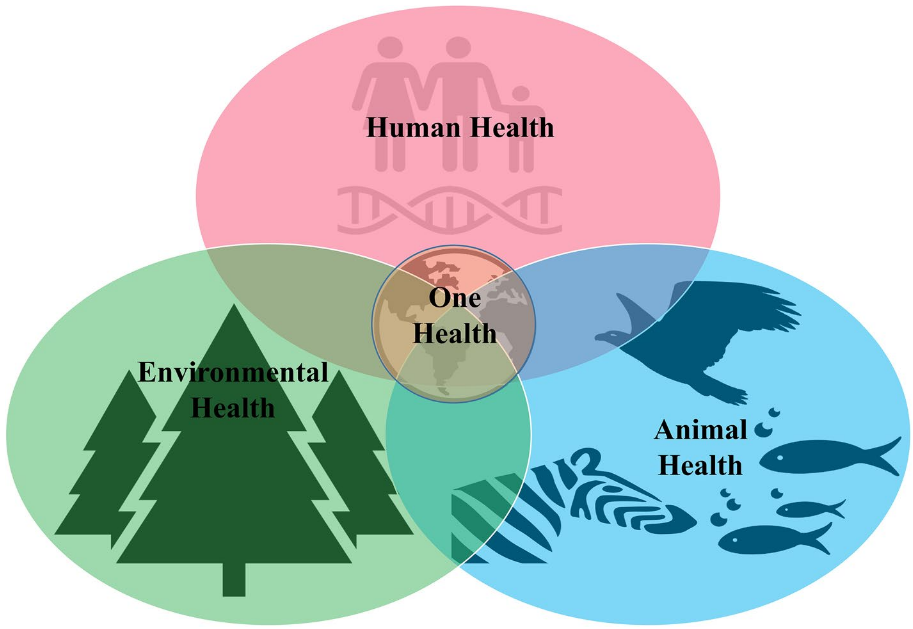

Fig. 9 One Health

Development [100]. Some advocates propose the inclusion of an 18th Sustainable Development Goal focused on animal health, welfare, and rights to comprehensively address all facets of sustainable development. The aim of such a goal would be to protect the well-being of everyone on the planet [16].

Sustainable development goal: How AMR influences SDGs

Antimicrobial Resistance (AMR) is often referred to as a silent pandemic, and its significant impact on the global economy and public health poses a threat to the achievement of the SDGs (Fig. 10). The diminishing effectiveness of antibiotics directly hinders progress toward certain

Fig. 10 Goals addressed about AMR are highlighted in red

SDGs. AMR has a disproportionate impact on underprivileged and marginalized populations, as they often lack access to basic healthcare and preventive measures. A World Bank assessment suggests that over 24 million people could fall into poverty by 2030 due to inadequate measures to combat AMR [45]. AMR significantly increases the cost of treatment, placing a greater financial burden on individuals with low incomes. This escalation in healthcare costs exacerbates the challenge of achieving SDG1, as it pushes the impoverished deeper into poverty [71]. Addressing AMR is crucial not only for public health but also for advancing the broader agenda of sustainable development.

The anticipated 50–70% increase in food production between 2010 and 2030, driven by factors such as population growth, economic expansion, and changes in consumption habits, is expected to coincide with a comparable rise in the use of antimicrobials in food production, particularly in meat, milk, and egg production [60]. R This increase in antimicrobial use in agriculture poses a serious threat to the sustainability of food production and can have negative implications for farmers' livelihoods, thereby hindering the achievement of SDG 2 (Zero Hunger) and SDG 8 (decent work and economic growth).

As of the period between 2015 and 2022, there has been a global increase in the percentage of women receiving assistance from professional health personnel during delivery, rising from 81 to 86% (Fig. 11). While this has led to a slight decrease in the global maternal mortality ratio (MMR), progress toward SDG 3 (Good Health and Well-being) is impeded by the increasing risk of serious complications and higher mortality rates associated with common illnesses, especially for vulnerable groups like women and children [71]. Antibiotics play a crucial role in modern medicine, and addressing harmful trends in resistance is essential for achieving SDG 3, which aims for good health and well-being for all at all ages [42].

The rise and prevalence of antibiotic-resistant bacteria can exacerbate public health challenges, particularly in underprivileged areas of the Global South, where additional factors such as industrial pollution and limited access to clean water and sanitary facilities come into play [48]. Antibiotic residues can be transported through water, sediments, and soil, creating gradients of varying concentrations. Even low levels of antibiotics in the environment can contribute to the selection of highly resistant bacteria. Limited access to sanitation and clean water further facilitates the spread of bacterial infections, increasing the risk of illness and mortality, particularly among children [40]. The implementation of Goal 6, which focuses on clean water and sanitation, is expected to have a positive impact by reducing the need for antibiotics through the prevention of various diseases. Furthermore, it may help curb the spread of Multi-Drug Resistant (MDR) strains into the surrounding environment, originating from sources such as animal farms or hospitals. Achieving

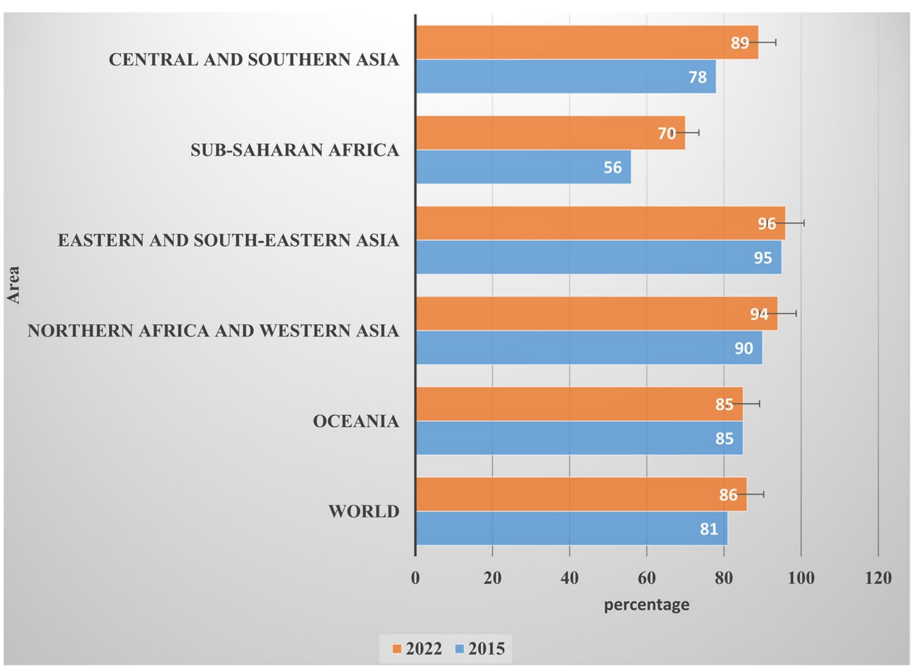

Fig. 11 Trend of births by skilled health workers over the period of six years (2015-2022)

SDG 6 can thus contribute to addressing the challenge of antibiotic resistance and promoting public health.

Social inequalities play a direct role in antimicrobial resistance (SDG 10), particularly in underprivileged populations who are often at a higher risk of developing infectious diseases. Limited access to premium medication due to resource constraints may lead to the prevalent practice of self-medication with antibiotics in developing countries [5]. The relationship between global climate change (Goal 13) and antimicrobial resistance is also noteworthy. A 1-degree Celsius increase in ambient temperature has been linked to a 5–10% rise in the number of cases of foodborne salmonellosis, resulting in substantial costs for healthcare and the economy [85]. Moreover, antibiotic resistance in common pathogens like Escherichia coli, Klebsiella pneumoniae, and Staphylococcus aureus increases by 4.2%, 2.2%, and 3.6%, respectively, with a 1-degree Celsius rise in temperature. This highlights the significant and lasting impact of climate change on antibiotic resistance across various bacterial groups [56]. Addressing social inequalities and mitigating climate change are crucial components of a comprehensive strategy to combat antimicrobial resistance and achieve sustainable development goals.

Achieving the goals set out in SDG 17, which emphasizes global partnerships for sustainable development, is crucial for addressing antimicrobial resistance (AMR). Governments, entrepreneurs, and the public sector need to collaborate to implement global sustainability efforts at various regulatory levels, from international to local [44]. AMR poses a significant sustainability issue, and establishing institutions and policies to combat it is essential. Expanding the scope of SDG 17 can play a key role in promoting global antimicrobial stewardship initiatives rooted in scientific knowledge. This includes supporting technology transfer, improving surveillance systems, creating computerized data repositories, and encouraging international investments in vaccine and drug research. Additionally, it can facilitate the development and implementation of diagnostic tests to address AMR [59]. An AMR not only directly affects SDG goals related to health but also has far-reaching implications for equality, clean water, economic growth, poverty alleviation, hunger eradication, food production, innovation, high-quality education, and gender equality. Ignoring the threat of AMR puts the 2030 SDG agenda at risk, as potent antibiotics are essential for the achievement of these objectives. A comprehensive and collaborative approach is necessary to combat AMR and safeguard global public health and sustainable development.

International trade as an engine for achieving SDGs

Global trade is considered a cornerstone for achieving the SDGs, as emphasized in the Agenda 2030 for Sustainable Development report, which underscores its role in promoting sustainable development, poverty reduction, and economic growth [107]. The impact of global trade extends across various SDGs, contributing to different aspects of development. It plays a crucial role in advancing Goal 1 by fostering the economic growth of countries, and serving as an essential source of employment. Furthermore, international trade influences other SDGs, such as enhancing food security and nutrition (Goal 2), ensuring universal access to affordable medicine (Goal 3), and bolstering a country's revenue-generating capacity (Goal 8) [88]. The export of goods and services contributes at least 50% to the GDP of underdeveloped nations, making global trade a vital source of funding for both the public and private sectors [96]. Trade policies can be leveraged in low-income nations to boost public revenue through taxes on imported and exported goods and services, with a portion of the revenues being reinvested from the sale of commodities. These taxes have the potential to significantly contribute to the overall public revenue of these nations, making up between 10 and 25% of it. Importantly, trade policies can also address social and environmental sustainability considerations, serving as a non-financial means of fulfilling the SDGs [97].

Globalization holds the potential to uplift developing economies, but it also carries adverse environmental consequences, including alterations in land use patterns and a surge in CO2 emissions [62]. Developed nations often reap environmental benefits, but this comes at the cost of developing nations grappling with resource exploitation. Notably, from 1990 to 2008, international trade led to the transfer of a staggering 16 gigatonnes of CO2 emissions from developed to developing nations. While this helped maintain emission levels in developed countries, it tripled them in their developing counterparts. This shift is partly attributed to stringent regulations compelling pollutant-emitting industries to relocate to developing nations with lower labor costs and less stringent environmental standards [108]. Tackling these environmental repercussions necessitates international trade agreements that not only acknowledge environmental spillovers but also establish objectives based on consumption patterns [1].

From plans to reality: assessing our progress on the path to sustainability?

The World Bank's SDG database serves as the primary source for indicators tracking progress toward sustainable development (Table 2). The data selected aims to ensure sufficient coverage for low-income nations, with

Table 2 UN sustainable development goals and their indicators

	UN defined Goals	World Bank indicators
1.	End poverty in all its forms, everywhere	Poverty headcount ratio at $1.90 a day (2011 PPP) (% of population)
2.	End hunger, achieve food security and improved nutrition, and promote sustainable agriculture	Prevalence of undernourishment (% of population)
3.	Ensure healthy lives and promote well-being for all at all ages	Births attended by skilled health staff (% of total)
4.	Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all	Adolescents out of school (% of lower secondary school age)
5.	Achieve gender equality and empower all women and girls	Proportion of seats held by women in national parliament (%)
6.	Ensure available and sustainable management of water and sanitation for all	People using at least basic drinking water services (% of population)
7.	Ensure access to affordable, reliable, sustainable and modern energy for all	Access to clean fuels and technologies for cooking (% of population)
8.	Promote sustained, inclusive and sustainable economic growth, full and productive employment, and decent work for all	Adjusted net national income per capita (annual % growth)
9.	Build resilient infrastructure, promote inclusive and sustainable industrialization, and foster innovation	Manufacturing, value added (% of GDP)
10.	Reduce inequality within and among countries	GINI Index (World Bank estimates)
11.	Make cities and human settlements inclusive, safe, resilient and sustainable	PM2.5 air population, population exposed to levels exceeding WHO guideline value (% of total)
12.	Ensure sustainable consumption and production patterns	Adjusted net savings: excluding particulate emissions damage (% of GNI)
13.	Take urgent action to combat climate change and its impacts	CO2 emissions (metric tons per capita)
14.	Conserve and sustainably use the oceans, seas and marine resources for sustainable development	Total fisheries production (106 metric tons)
15.	Protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification, and halt and reverse land degradation, and halt biodiversity loss	Forest area (106 km2)
16	Promote peaceful and inclusive societies for sustainable development, provide access to justice for all, and build effective, accountable and inclusive institutions at all levels	Completeness of birth registration (%)
17.	Strengthen the means of implementation and revitalize the global partnership for sustainable development	Debt service to exports (%)

a specific focus on achieving global inclusivity [10]. The evaluation of global progress towards UN SDGs in 2023 is possible through this database. Out of the 169 targets, 138 can be assessed using data from around the world and analyses conducted by custodian organizations. However, only 15% of these targets are projected to be achieved by 2030, with 48% experiencing moderate to severe deviations from the intended trajectory. More than 37% have either shown no improvement or have declined compared to the 2015 baseline (Fig. 12) [95]. This report suggests that the world is significantly off-course from meeting the targets, and the impact of the COVID-19 pandemic has exacerbated the situation.

Step to success: targeted strategies for achieving SDG

The SDGs, anticipated to surpass the MDGs, face challenges in implementation, including the absence of fixed priorities and delays in data reporting. Successful achievement of the SDGs requires each nation to establish clear priorities, providing detailed guidance for understanding how to attain these goals (Fig. 13) [82].

The successful implementation of the SDGs requires the development of metrics to provide the community with informative tools. These metrics should consist of quantitative definitions with straightforward, understandable measurements that account for possible inequities. Regularly updated indices for objectives, targets, and progress-monitoring metrics can be created to facilitate tracking. Indicators serve as the foundation for monitoring progress toward the SDGs, and quantitative targets help measure this progress. Nations can choose from a list of indicators provided by the Sustainable Development Solutions Network (SDSN), tailoring the selection to their needs and capabilities. Sub-goals and intersecting objectives should be considered by developing nations for effective implementation [7]. A global partnership between government and scientific bodies is essential to develop a monitoring framework for the successful implementation of the SDGs. Comprehensive evaluation and scrutiny will help assess the effectiveness of these initiatives. Biodiversity indicators and metrics developed by the Convention on Biodiversity can be

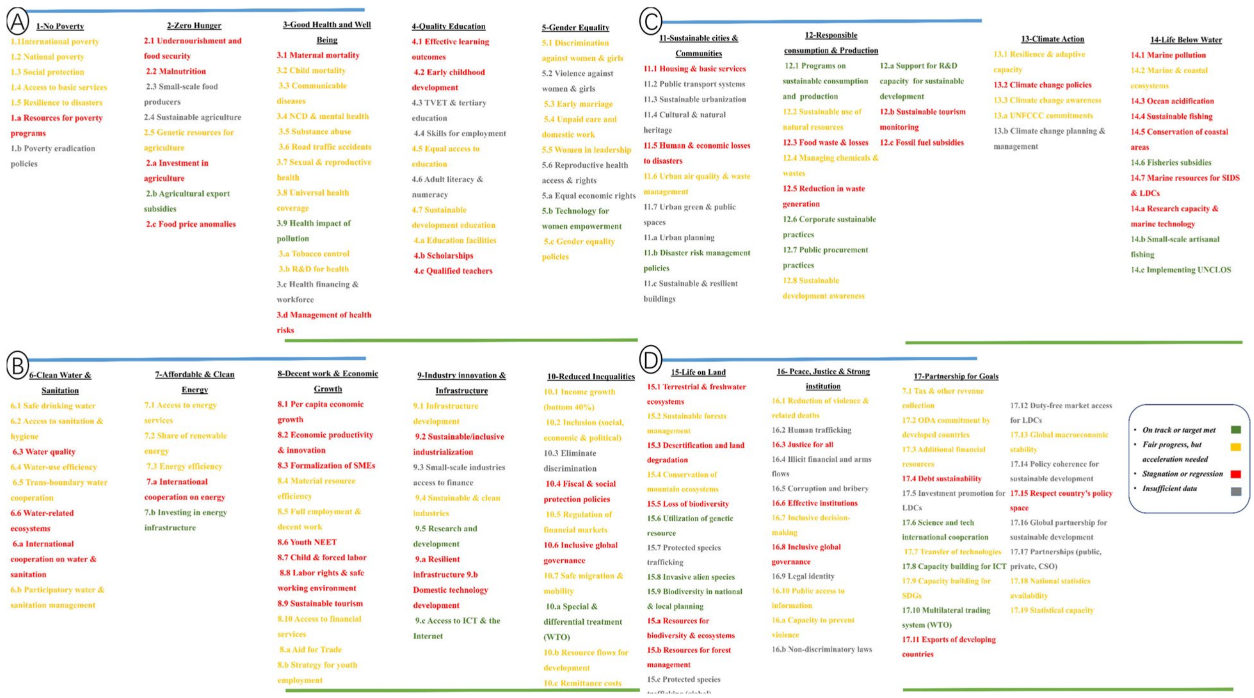

Fig. 12 SDG's progress report 2023

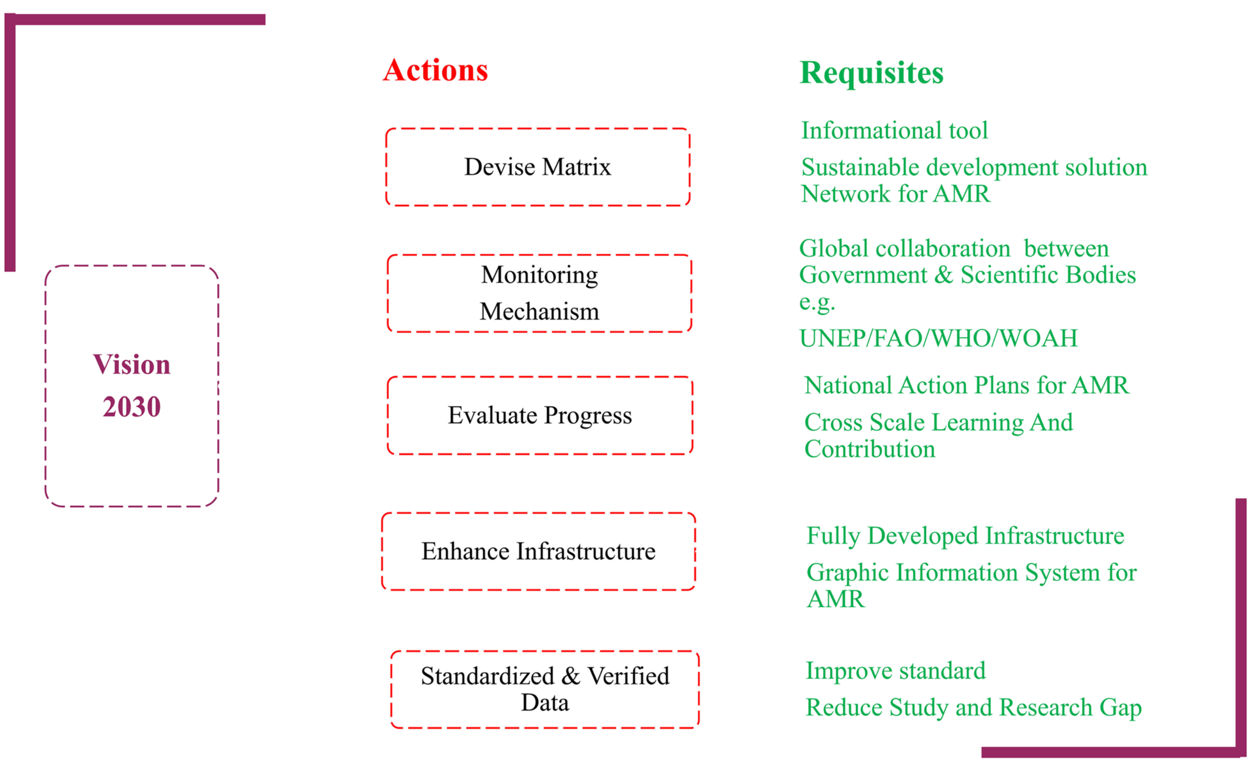

Fig. 13 Stratiges to Achieve SDGs in context to AMR

employed to monitor biodiversity status, with a focus on prioritizing accountable institutions in developing countries to ensure efficient decision-making through improved information gathering and transmission [25].

Establishing a national action plan with deadlines for assessing progress towards the SDGs is crucial. These plans should incorporate cross-scale learning and collaboration, along with periodic evaluations at different stages, mirroring global assessments [12]. Developing countries face obstacles such as inadequate infrastructure, labor shortages, and a lack of development policy in achieving the SDGs. Obtaining mapping data is particularly challenging due to expensive transportation, limited mountainous access, and deficient ground surveillance networks [55]. Dependency on external sources is common because these nations often lack the capability to analyze remote sensing data or produce high-resolution geospatial products. To address this, developing nations need to invest in key geospatial divisions, ensuring sufficient human capacity, equipment, software, and policy frameworks to integrate geospatial information infrastructure and data collection into official reporting systems [82]. Standardizing and validating SDG data to ensure timely release and open access is crucial. Nations should enhance cooperation, scrutinize reports from NGOs and the government, and foster transparency and discussions to prevent injustices. Affluent nations should provide adequate financial aid and support mechanisms to assist poor and undeveloped nations in reaching SDG objectives, creating a more equitable data system.

Conclusion

As this article clearly demonstrates, attaining the 17 SDGs and the 169 related goals outlined in the 2030 Agenda for Sustainable Development is an enormous task. However, the task is further complicated by the emergence and escalation of AMR as a pressing global health threat. AMR makes it harder to accomplish a number of SDGs, especially those that have to do with equitable growth, health, food security, and ending poverty. In addition to raising the likelihood of mortality and morbidity, the spread of drug-resistant infections puts pressure on healthcare systems, jeopardizes the safety and production of food, and hinders the achievement of universal health coverage. In addressing antimicrobial resistance (AMR), it's crucial to recognize that there isn't a singular "magic cure." As a global community, our focus should be on realistically managing the concerning levels of AMR that have already emerged.

AMR is a natural phenomenon exacerbated by the misuse of antibiotics in humans, animals, and plants. Our emphasis on the interaction between the SDGs and AMR underscores the need for a multilateral and interdisciplinary approach. The WHO and CDC have been working together to combat AMR. The WHO has launched initiatives to raise awareness, promote stewardship, and strengthen surveillance systems. The CDC has implemented targeted interventions, such as the Antibiotic Resistance Solutions Initiative and the Antibiotic Resistance Laboratory Network, to reduce healthcare-associated infections and antibiotic misuse. International collaborations like the Global Antibiotic Research and Development Partnership (GARDP) have accelerated the development of new antimicrobial agents and diagnostics. These efforts have led to decreased incidence of resistant infections, improved patient outcomes, and strengthened healthcare systems' resilience against AMR.

However, the fight against AMR remains an ongoing challenge, requiring sustained commitment, innovation, and collaboration across sectors to preserve the efficacy of antimicrobial agents and safeguard public health for future generations. A significant challenge lies in creating a unique indicator for AMR within the SDGs framework, reflecting the impediment it poses to achieving these goals. This indicator is vital for tracking the effects of antibiotic resistance and assessing the efficacy of treatments. To develop and implement comprehensive strategies for SDGs containment calls for fostering multisectorial collaborations among governments, world organizations, civil society, educational institutions, healthcare providers, veterinarians, pharmaceutical companies, and the private sector as a whole. Progress toward each SDG, especially those still distant from realization, necessitates international cooperation through well-defined policies and plans. This collaborative effort is essential to maintaining the world's trajectory toward sustainability and effectively addressing social, economic, and environmental challenges. To ensure sustainability and support human existence, policymakers must integrate monitoring and evaluation methods, a responsibility that scientists must wholeheartedly support. The five priorities outlined in this context provide a methodology for incorporating objectives, establishing incremental targets for SDG implementation, and showcasing comprehensive execution. However, for true sustainability, the developing world must carefully navigate the SDGs, requiring thoughtful consideration and concerted efforts.

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