

# Addressing Antimicrobial Resistance to Support Sustainable Development

THEMATIC SUPPORT UNIT

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This technical note provides information on antimicrobial resistance (AMR) and guidance on how to include AMR in development programmes and policy dialogue, in particular in health, environment and food systems initiatives.

The intended audience for this technical note is Sida staff and staff at foreign missions but it may also be of interest for partner organisations.

#### INTRODUCTION

Antimicrobial resistance is a leading cause of global mortality. In 2019, an estimated 1.27 million people died of infections caused by bacteria resistant to antibiotic treatment with low-income regions and children under five experiencing the highest rates of AMR-related death<sup>1</sup>. The rising levels of AMR will hinder progress towards many of the Sustainable Development Goals (SDGs), particularly those focusing on health and well-being, poverty reduction, food security and economic growth. Given this risk, Sida prioritises integration of AMR into our programming and policy dialogue. Multiple actions by all sectors and societal levels, including governments, academia, civil society, private sector and development partners, are required to achieve the changes required for improved practices and policies to manage the AMR crisis.

Antimicrobials are medicines used to treat infectious diseases caused by microorganisms, such as bacteria, viruses, parasites, and fungi (Figure 1). They work by inhibiting the growth of the microorganisms or by killing them. Antimicrobial resistance is when microorganisms acquire the ability to withstand the drugs, making them ineffective.

The most widely used type of antimicrobials is antibiotics, which are designed for treatment of bacterial infections. Although most bacteria we encounter are harmless and crucial for maintaining healthy body functions, a minority can cause disease which may require treatment with antibiotics. This technical note focuses on antibiotic resistance (ABR) which is the



Figure 1. Resistance can develop for all types of antimicrobial medicines (antimicrobial resistance, AMR). Antibiotic resistance (ABR) is when treatment for bacterial infections becomes ineffective.

type of AMR constituting the most urgent global risk. It is also the most critical form of AMR from a One Health perspective (see below).

The rate of emergence and the negative consequences of AMR, and specifically ABR, are worst in low and middle-income countries (LMICs). This is mainly due to weak health systems, inequitable access to affordable antimicrobials, vaccines, and diagnostics of sufficient quality as well as lack of clean water, sanitation and hygiene (WASH), often concurrent with an uncontrolled sale and use of antibiotics in humans and animals.

#### **Key messages:**

- AMR jeopardises the fulfilment of several of the Sustainable Development Goals and should always be included in dialogue on health, environment and food systems. This may be achieved by strategic linking of AMR to broader development issues such as universal health coverage, sexual and reproductive health and rights, sustainable food systems, One Health initiatives, and pandemic preparedness and response.
- AMR should be mainstreamed into relevant programming in low and middle- income countries. Meaningful support to these countries can be provided through promoting public awareness, supporting research and innovation, development of systems for data generation and capacity building of professionals, including knowledge transfer, for change of practice.
- Addressing AMR requires a One Health approach recognising and integrating the interrelations between human, animal and environmental health.

<sup>1</sup> Murray C et al. <u>Global burden of bacterial antimicrobial resistance in 2019</u>: a <u>systematic analysis</u>. The Lancet (2022).

ABR is not gaining the same traction in the global discourse as the COVID-19 pandemic since the emergence of ABR is a slower pandemic and not a disease in itself. However, similar global efforts and collaboration in scientific, medical, social, and political dimensions as for the COVID-19 pandemic are needed to manage the global crisis of ABR.

# Why is a One Health approach important to tackle antibiotic resistance?

Humans and animals often share the same kind of bacteria and may be treated with the same types of antibiotics. Resistant bacteria and resistance genes can transmit between humans and animals via direct contact, food or the environment. One Health is a multi-sectorial approach that recognises these interconnections (Figure 2). Although there are several reports on how resistant bacteria transmit between animals and humans<sup>2</sup>, it is largely unknown to what extent this happens, or how much the animal sector contributes to ABR in humans. Notably, antibiotics are also used in smaller quantities in crops, fruits and vegetables for the control of bacterial plant diseases<sup>3</sup>.

While there are strong relationships between human health, animal health, plant production, food security, food safety and environmental sectors, the solutions to tackle ABR often differ between the sectors. There are, however, important interconnections requiring collaboration. Hence, applying a One Health perspective is important to find areas of synergy among the sectors to optimise outcomes.

# What is causing the development and spread of antibiotic resistance?

ABR is a biological phenomenon that is accelerated by the misuse and overuse of antibiotics. Because all use of antibiotics contributes to the development of ABR<sup>4</sup>, it is **vital to use antibiotics rationally and only when really needed**. Inappropriate use, such as to treat infections not caused by bacteria or to prevent disease or promote growth in livestock, is a major driver of ABR. Globally, there is a massive overuse of antibiotics with around 50% of the antibiotic use considered inappropriate<sup>5</sup>. This calls for recognising that ABR is not only a biological issue, but also a complex social challenge that requires changing social norms and

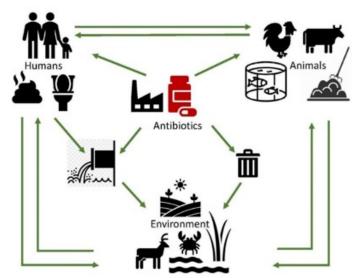


Figure 2. A One Health approach to ABR is crucial. Antibiotic use in humans and animals leads to the development and spread of ABR and results in dispersion of ABR into the environments through human and animal waste. The environment serves as a vehicle for the development and further spread of ABR to humans and animals. In addition, antibiotics enter the environment from improper disposal of unused antibiotics and from pharmaceutical production facilities.

behaviour in all of society. Efforts to reduce unnecessary demand for antibiotics may include improving basic knowledge of infections and their treatment, changing cultural beliefs, reducing misaligned financial incentives for antibiotic sales, and securing access to effective antimicrobials in resource-poor settings.

The second major cause of ABR is the spread of bacteria containing resistance mechanisms. The global spread of ABR does not respect borders and is facilitated by a number of factors, such as:

- Lack of access to WASH;
- Insufficient infection prevention and control measures:
- Weak human and animal health systems;
- Global travel and trade.

Another factor contributing to ABR emergence is the decreasing options for treatment of multi-resistant bacteria. For decades, the development of antibiotics with new mechanisms of action has declined, and the lack of effective treatment options promotes continued emergence of ABR.

<sup>2</sup> Hoelzer K et al. Antimicrobial drug use in food-producing animals and associated human health risks: what, and how strong, is the evidence? BMC Vet Res (2017).

<sup>3</sup> Taylor & Reeder. Antibiotic use on crops in low and middle-income countries based on recommendations made by agricultural advisors. CABI Agric Biosci (2020).

<sup>4</sup> World Health Organization (2015), <u>Global Action Plan on Antimicrobial</u>
<u>Resistance.</u>

<sup>5</sup> Centers for Disease Control and Prevention (2020), Antibiotic Prescribing and Use

## What are the consequences of ABR and actions needed?

Curbing ABR is a vital component for sustainable development<sup>6</sup>. Existing reports estimating the consequences of ABR indicate that in addition to human suffering, the global economy may lose nearly four percent of the annual gross domestic product by 2050<sup>7</sup>. Losses will be greater in LMICs and may push millions of people into poverty, causing increased suffering and increased health care costs, as well as loss of animals, with impacts on livelihoods and food security<sup>8</sup>.

Mitigation of ABR will also benefit from other general systems strengthening initiatives. Investments in prevention and preparedness save money and reduce the economic and societal costs of response to the ABR crisis. General examples include strengthening of WASH provisions, biosecurity measures in livestock production and along the food chain, sound chemical and waste management and regulation and control of the supply of first-line medicines. However, more ABR-specific actions are also needed such as strengthening and harmonising of ABR-relevant policies and regulatory frameworks; improvements in awareness and understanding of ABR; enhancement of supply chains for quality-assured antibiotics; inclusion of ABR into research and innovation and into food safety systems. Both types of investments and actions should be included in the dialogue with governments and partner organisations.

# In dialogue with partners on multi-sectoral action, the following questions are key:

What is the status of the implementation of the National Action Plan (NAP) against AMR? Are personal and financial resources allocated that allow implementation of the NAP? Which are the major barriers, and how could development partners assist? Are there successful approaches that can be shared?

ABR impacts human health and animal health and is affected by environmental factors, and therefore, systems transformation in all three sectors are needed both by targeted sector-specific measures, and in applying a collaborative One Health approach.



<sup>7</sup> Interagency Coordination Group on Antimicrobial Resistance (IACG), (2019). No time to wait: securing the future from drug-resistant infections.



Sweden in collaboration with WHO is working with AMR prevention in Rohingya refugee camps in Cox's Bazaar, Bangladesh. Photo: Daniel Novak.

#### Human health

Bacterial infections are a major cause of morbidity and mortality worldwide. Antibiotics have been hugely successful in improving health outcomes, and alongside improvements in nutrition, WASH, and vaccination provision, have aided in a significant global reduction of under-5 mortality and an increase in life expectancy. The positive impact of antibiotics on health, however, is threatened by inequitable access to these essential medicines. While misuse and overuse of antibiotics drive increasing levels of ABR in some parts of the world, other parts suffer from lack access to basic antibiotics.

Common infections like pneumonia, urinary tract infections and wound infections cause significant suffering affecting both children and adults across the world. WHO estimates that 14% of child mortality under five years of age globally is accounted to pneumonia, causing more than 740,000 deaths annually. Most of these could be averted by effective antibiotic treatment. According to an international survey, over half (54%) of surveyed physicians believe that infection due to a resistant pathogen is the top reason for treatment failure of bloodstream infections in newborns<sup>10</sup>.

Antibiotics are indispensable medicines for all human medical care. They are used at all levels and all specialities of a health system ranging from infection treatment in basic primary health care to highly specialised care including surgery, cancer treatment and organ transplantation. Access to effective

<sup>8</sup> World Bank (2017), <u>Drug-Resistant Infections: A Threat to Our Economic</u> Future.

World Health Organization (2022), Key facts on pneumonia.

<sup>10</sup> ReAct (2020), Treatment of newborn sepsis is threatened: Effective antibiotics are essential for childrens' survival.

antibiotics is also crucial to address sexual, reproductive, maternal, newborn and child health.

A special case of ABR is tuberculosis (TB), which is a major problem globally. Treatment requires combinations of several antibiotics and multi-drug resistance is common. The problems with TB are further complicated by co-infections with HIV, increasing treatment length, severity of disease and mortality.

When considering the broader AMR perspective, drug resistance to antiviral treatment for HIV can be found in up to 20% of new cases before starting treatment, resulting in increased numbers of HIV infections and HIV-associated morbidity and mortality.

Malaria resistance to first-line chloroquine-based therapy is spread all over the world where malaria is endemic. Resistance to second-line artemisinin combinations is also widely spread and poses a major threat if its prevalence increases further.

## Entry points for dialogue with partners in human health programmes

The following questions may be asked:

- What initiatives are in place to improve sanitation, infection prevention and control in health care facilities?
- Is access to effective antimicrobials, vaccines and diagnostics part of universal health coverage reforms? Do national drug procurement programmes and policies ensure the availability, quality and adequate distribution of antimicrobials and promote their rational use?
- Are there national campaigns to inform the public to increase knowledge and awareness and change behaviour?
- Do sexual and reproductive health and rights (SRHR) programmes include aspects on AMR? Do education programmes for midwifes, obstetricians, gynaecologists and paediatricians address AMR?

#### Animal health

Most of the global antibiotic consumption is in live-stock and aquaculture<sup>11</sup>. This is driven by widespread inappropriate use to prevent disease and promote growth. The largest share of antibiotics is used in animals intended for food production (e.g. cattle, poultry, pigs, fish and seafood). Given the justified and increasing demand for animal source foods in LMICs, it is critical that the expanding livestock and aquaculture production use antibiotics in a medically rational and responsible way, and apply other disease preventive measures than antibiotics.

Effective antibiotics are needed to cure animals from bacterial diseases. This is important both for animal welfare and economic reasons. The alternative, to not use antibiotics and cull diseased animals,

11 Boeckel T, et al. Reducing antimicrobial use in food animals. Science (2017).

would be an unethical and unsustainable use of natural resources such as increased greenhouse gas emissions without any return of nutritious animal food source for humans.

Emerging ABR has resulted in reduced alternatives for treating diseased animals, for example udder infection in milking cows and diarrhoea in young pigs<sup>12</sup>. For animal producers, ABR leads to financial losses both through higher animal death and cost of alternate drugs, and through reduced production and growth. Eventually this increase in treatment failure jeopardises livelihoods and contributes to food insecurity by increased price of animal source foods and commodities for the end consumer. The World Bank has projected that AMR may result in up to 10% loss in livestock production in low-income countries – where the need for animal source foods is the largest – by 2050<sup>8</sup>.

In terms of AMR, widespread resistance to the anti-parasitic drug acaracides is of particular importance in livestock and the tropics. The increasing resistance to acaracides fails to protect livestock from massive tick infestations which weakens the animals and contribute to further transmission of vector-borne diseases.

## Entry points for dialogue with partners in food and agriculture programmes

The following questions may be asked:

- Do livestock and aquaculture farmers have access to skilled veterinary services to support good animal health and disease prevention and are these services affordable?
- What measures are taken to regulate sales and use of antibiotics in livestock farming and aquaculture, including incentives for veterinarians not over-prescribing antibiotics?
- Are there any positive incentives in place for farmers to invest in disease prevention, rather than using antimicrobials to compensate for poor animal management?
- Are there systems in place to generate information and awareness about antibiotic use and the AMR problem in animals and food?

#### **Environment**

The effect of ABR on the environment and the benefits to humans provided by ecosystems (ecosystem services) is largely unexplored. However, it is well known that the environment facilitates the development and spread of resistant bacteria and resistance genes, rather than the environment itself being under threat<sup>13</sup>. A major problem is poor management of

<sup>12</sup> Bengtsson B. & Greko C. Antibiotic resistance—consequences for animal health, welfare, and food production, Upsala Journal of Medical Sciences (2014).

<sup>13</sup> Larsson J & Flach CF. Antibiotic resistance in the environment. Nat Rev Microbiol (2021).

excreta and wastewater containing antibiotics and resistant bacteria and their spread into the environment. The use of inadequately treated manure as fertilisers in agriculture introduces resistant bacteria into the environment with the risk of spreading back to humans and animals. Thus, ABR and the quality of WASH are closely intertwined. This is because improvements in WASH both reduce infectious diseases – and thereby the need for antibiotic treatment – and exposure to resistant bacteria through, e.g. drinking water of adequate quality. In addition, effluents generated in antibiotic manufacturing can contaminate the environment through wastewater. Contamination also occurs through the improper disposal of unused and expired antibiotics.

# Entry points for dialogue with partners in climate and environment programmes

The following questions may be asked:

- Are there systems in place to generate information and understanding of the ABR problem in the environment?
- What are the environmental controls to prevent and limit the transmission of resistant organisms?
- What measures are taken to improve the management of waste from pharmaceutical production and medical facilities?
- How can management of waste from animal farming and humans be improved to limit pollutants and ABR spread?
- What measures are taken to reduce faecal contamination of water?

# How does antimicrobial resistance link to the Sustainable Development Goals?

Rising levels of AMR will make it more difficult to achieve several of the SDGs, in particular those for good health, poverty reduction, food security and economic growth (Table 1).

At the same time, progress towards achieving the SDGs will contribute to mitigating AMR. For example, improvements in wastewater treatment from antibiotic production, human and animal waste (SDG 12 and 6) will reduce the risk of AMR development (less pollution of both drugs and bugs into aquatic environments). Additionally, improved access to WASH (SDG 6) will reduce the spread of infectious disease, the subsequent use of antibiotics and the spread of AMR. Investments into research and innovation (SDG 9) are vital for the development of vaccines, new antibiotics and diagnostics. Recent evidence suggests that changes occurring in the natural environment due to climate change (SDG 13) will increase the spread of infectious disease, including drug-resistant infections<sup>14</sup>. Thus, enhanced globally concerted efforts to

manage the climate crisis will also reduce the risk for increasing AMR emergence. Stronger institutions and governance (SDG 16) will contribute to implement National Action Plans (NAPs) on AMR, strengthen human and animal health systems and the supply chains of quality medicines. Finally, enhanced collaboration and partnerships across sectors and levels (SDG 17) are crucial to efficiently tackle AMR.

Table 1. Sustainable Development Goals threatened by AMR

#### **SDGs**



- People living in poverty are more prone to infectious diseases, including those caused by antibiotic resistant bacteria.
- High costs for treatment of infections due to AMR will push more people into poverty.
  Increased disease burden will reduce the ability to earn people's livelihood.



 AMR will increase costs of livestock and aquaculture production; animal infections will become untreatable, and production will decrease, threatening livelihoods and food security and availability to highly nutritious animal source foods, thus, increasing malnourishment.



- Improvement in universal health coverage requires access to effective antibiotics.
- Emerging resistance to drugs for treating bacterial infections (including tuberculosis) as well as HIV and malaria, is a key barrier to reducing the burden of these diseases.
- Reducing child and maternal mortality relies on effective antibiotics.



 AMR threatens gender equality since certain groups such as women and children are at higher risk and extra vulnerable to resistant infections.



 Increasing AMR in all environments pollutes soil and water sources and reduces access to safe drinking water.



- Increased disease and death due to AMR and resulting reduced labour supply can lower productivity, household income, and lead to losses in economic growth.
- Increased AMR rates in animal production will affect animal health and subsequent productivity and economic returns.



 AMR leads to reduced access to effective medicines, especially for the poor, migrants and other vulnerable groups.



 Irresponsible use of antibiotics and the resulting AMR exhaust the global resource of efficient drugs.



 Unregulated use of antibiotics in aquaculture increases the risk of AMR emergence below water.

<sup>14</sup> Fouladkhah A et al. The threat of antibiotic resistance in changing climate. Microorganisms (2020).

#### Focus - AMR and poverty

AMR and poverty are linked in many ways: 2.1 billion people do not have access to safe drinking water, one in three do not have a basic toilet and one in eight – about 890 million people – defecate in the open. This leads to infections spreading faster and results in an increased use of antibiotics. Inadequate WASH in combination with poor nutrition and suboptimal housing conditions, puts people living in poverty at greater risk of contracting infectious diseases and AMR. In addition, poor households commonly rear livestock in close proximity to people with inadequate measures for disease prevention, thus contributing further to infectious disease spread in humans and animals.

If effective antibiotics are available in these settings, they are often expensive, in particular second- and third-line treatment regimens, and treatments drive the poor even deeper into poverty. Conversely, increasing GDP has shown to correlate with increased antibiotic consumption in LMICs, indicating that antibiotics are used more when poverty decreases. While much of the increased use may be inappropriate when diagnostics are unavailable, access to effective antibiotics actually needs to increase in LMICs to treat diseases and help people out of poverty.

It is estimated that between 500 million and 1 billion of the world's poor are dependent on livestock for their livelihood. The emergence of AMR jeopardises peoples' livelihoods through higher animal mortality and reduced production and growth. By 2050, AMR is projected to result in up to 10% loss in livestock production in low-income countries.

#### Global governance of antimicrobial resistance

AMR is featured in several health-related international agendas such as the Global Health Security Agenda, International Health Regulations, the SDGs, health systems strengthening, primary health care and universal health coverage. However, it's complex technical nature is a barrier to making a strong and sustained case and only one indicator for AMR is included in the SDG framework<sup>15</sup>. Following the endorsement of the Global Action Plan in 2015, most countries have developed multisectoral NAPs, but implementation in many countries is hampered by limited financial, material and human resources, lack of capacities and political commitments.

The Tripartite (the World Health Organization, the Food and Agriculture Organization of the United Nations and the World Organisation for Animal Health), which in 2020 was expanded to the United Nations Environment Programme, is supporting countries with the NAPs, and established in 2019 the AMR Multi-Partner Trust Fund as a multi-stakeholder initiative to catalyse the implementation of One Health NAPs<sup>16</sup>. In 2020, the Global Leaders Group on Antimicrobial Resistance was founded.

## The Swedish development focus on antimicrobial resistance

Sweden is at the global forefront in providing high quality human healthcare and productive livestock with low use of antibiotics. This has been possible through long-term government supported strategic and multilevel partnerships to reduce AMR and has generated one of the lowest levels of antibiotic use and resistance in humans and animals in Europe. The Swedish approach to guide interventions with reliable and transparent antibiotic use and resistance data, and our focus on disease prevention as means to reduce antibiotic use has proven to be effective<sup>17</sup>.

Since the first Swedish NAP against ABR was published in 2000, the governance structures have developed stepwise. In the latest version of the Swedish NAP<sup>18</sup>, the objective number 7 states that Sweden should continue to show leadership in international efforts to curb ABR by sharing knowledge and experience with other countries from a One Health perspective, paying particular attention to the needs of LMIC. The Development policy from 2016 furthermore stresses the need for stronger health systems and infection prevention to curb ABR and promotes a knowledge-based development support<sup>19</sup>.

# Showcase Bangladesh - How AMR is tackled through policy and practice

In Bangladesh, single and multi-disciplinary actions are mixed in efforts to contain AMR. The National Action Plan on AMR was approved in 2017 based on the WHO Global Action Plan guidelines and is defining activities and their output indicators, responsible authorities and the timeline. Coordination of activities is supported by assigned working groups and the One Health Secretariat with staff from three ministries (human health, animal health and environment).

Sales of drugs without prescription by registered physicians or veterinarians has been prohibited and model pharmacies have been established through the Bangladesh Pharmacy Model Initiative which sets standards for drug outlet personnel, premises, dispensing, storage, hygiene, record keeping, and disposal. To improve antibiotic stewardship, physicians, veterinarians, and scientists have formed the Bangladesh AMR Response Alliance and developed trainings, treatment guidelines and mobile apps for responsible antimicrobial use in humans, livestock and aquaculture.

Although much remains to prevent AMR emergence, systems have been initiated in Bangladesh to address AMR in a more comprehensive manner. Exploring opportunities to work against AMR is also supported and stated as goal in the Strategy for Sweden's development cooperation with Bangladesh 2021–2025. A four year collaboration on a country level with WHO Bangladesh to prevent AMR was recently signed.

<sup>15</sup> SDG indicator 3.d.2: Percentage of bloodstream infections due to selected antimicrobial-resistant organisms

<sup>16</sup> The AMR Multi-Partner Trust Fund.

<sup>7</sup> Swedish work against antibiotic resistance – a one health approach.

<sup>18</sup> Swedish strategy to combat antibiotic resistance 2020-2023.

<sup>9</sup> Policyramverk för svenskt utvecklingssamarbete och humanitärt bistånd [Skr. 2016/17:60].

#### Focus - AMR and gender

Many of the risks posed by AMR are common for women and men. However, biological and socially constructed differences between women and men also cause differences in the exposure to AMR and the use of antimicrobials<sup>1</sup>. Gender differences in particular may impact a person's risk of exposure, lack of access to information, quality of care and adherence practices. Therefore, curbing AMR requires a gender responsive approach that takes different contexts and opportunities into account. For example, in the growing epidemic of drug resistant sexually transmitted diseases (STD), including HIV and gonorrhoea, health care providers may respond differently to women, men and LGBTI persons due to cultural norms, stigma or discrimination. Women and girls in particular those with lower education and resources, may have less access to sexual and reproductive health services providing them with information and protection against drug resistant STDs, or may not be able to afford the necessary treatment. On the other hand, men are less likely to adhere to prescribed antibiotic treatment for themselves and as caregivers.

In addition to gender aspects, there are also biological aspects that put women and girls at increased risk of exposure to AMR. This includes during pregnancy, abortion and childbirth. Urinary tract infections are also more prevalent in women and becoming harder to treat due to an increasing number of resistant strains. Consequences of resistant infections for those women and children who survive include infertility, social stigma and even abandonment by the spouse and thereby their livelihood.

Gender also causes differences in occupational exposure to infections. Women face higher occupational exposures to drug resistance in general as frontline health workers, in keeping livestock, and in the processing and marketing of animal products. On the other hand, men often work in dirty and dusty conditions, often combined with smoking, which causes a higher risk of respiratory tract infections and higher prevalence of tuberculosis.

1 WHO (2018), Tackling antimicrobial resistance (AMR)together: working paper 5.0: enhancing the focus on gender and equity



Curbing AMR requires a gender sensitive approach. Photo: Joachim Beijmo.

#### **RECOMMENDED READING**

World Bank (2019), Pulling Together to Beat Superbugs.

IACG (2019), No time to wait: Securing the future from drug-resistant infections.

UNSDCF (2021), <u>Antimicrobial resistance and the United</u>
Nations Sustainable Development Cooperation Framework:
guidance for United Nations country teams.

WHO (2015), Global Action Plan on Antimicrobial Resistance.

FAO, <u>The FAO Action Plan on Antimicrobial Resistance</u> 2021-2025.

