



Tackling the antibiotic resistance crisis

With deaths from AMR having increased by over 80% among adults aged 70 and older between 1990 and 2021, and an estimated 4.71 million deaths associated with bacterial AMR in 2021, AMR remains a global crisis

By Aleksandar Ruzicic

Bacteria are rapidly developing resistance to the antibiotics they are exposed to. Alexander Fleming discovered penicillin in 1928, and during his Nobel lecture on 11 December 1945, he had already warned about the potential dangers of antibiotic resistance, saying: “It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.”

Nearly a century later, these predictions have become a reality. The widespread and often indiscriminate use of antibiotics in human medicine and agriculture has driven the emergence and rapid spread of

antibiotic-resistant genes. Bacteria have evolved sophisticated mechanisms to evade antibiotics, including limiting drug uptake, degrading drugs, modifying targets and forming biofilms.

In 2021, an estimated 4.71 million deaths were associated with bacterial antimicrobial resistance (AMR), based on an estimation from 22 pathogens, 84 pathogen-drug combinations and 11 infectious syndromes across 204 countries and territories. Between 1990 and 2021, deaths from AMR increased by over 80% among adults aged 70 and older.

If left unchecked, drug resistance threatens to undo many of the medical advancements of the past century. Routine infections could become significantly harder to treat and common surgeries could carry much greater risks. In a worst-case scenario, the world may face a return to the pre-penicillin era, where even minor infections could be fatal.

Human actions have allowed the crisis to escalate over recent decades. On the supply side, regulatory barriers and market dynamics have made antibiotic R&D economically unattractive compared to high-priced drugs for chronic conditions. On the demand side, the widespread availability of low-cost generic antibiotics has led to overuse and misuse in both human medicine and agriculture. Alarming, over 70% of medically important antibiotics are used in agriculture, driving resistance through the transmission of resistant pathogens to humans and the excretion of active pharmaceutical ingredients by animals.

Before exploring potential solutions, we must first assess the current state across three key areas:

1. Inadequate infection management
2. Inappropriate antibiotic use
3. Barriers to innovation.

Infections continue to spread widely due to limited infection control measures. In many healthcare systems, funding is not directly tied to infection prevention or responsible antibiotic use, allowing resistant pathogens to proliferate unchecked.

The misuse of antibiotics remains a major driver of resistance. Broad and untargeted use, including general prophylaxis, accelerates the problem. Individuals often misuse antibiotics – particularly in regions where they are sold without prescriptions – by taking them for viral infections or failing to complete prescribed treatments.

In addition, insufficient R&D investment threatens the development of new antibiotics. Even when novel antibiotics gain approval, regulatory success alone does not ensure a sustainable market. Reserve antibiotics – intended only for infections resistant to older drugs – lack the pricing incentives necessary to sustain innovation. Contrasting the reality of how AMR thrives with the ideal approach of controlling AMR highlights the significant transformation needed (table 1).

How do we transition from the current state in which AMR thrives to a future where AMR is effectively controlled? Three proven strategies can drive this change:

- 1** Regulations to curb resistance development.
- 2** Push incentives to stimulate antibiotic R&D.
- 3** Pull incentives to enhance commercial viability.

Preventing infections is essential in tackling the antibiotics crisis. Leading nations implement stringent antibiotic stewardship, pathogen monitoring and healthcare reimbursement tied to programme goals. Effective infection control starts with basics like handwashing stations, enforced hygiene procedures and access to sanitation, clean water and soap – key measures to curb resistance development. Antibiotic production and disposal must be managed to prevent pharmaceutical pollution in water sources.

In agriculture, antibiotics should no longer serve as growth promoters and prophylactic use should be strictly limited – potentially through absolute use targets (mg/kg of animal/year) or taxation. The focus should be on treating sick animals while minimising overall antibiotic use.

Push incentives lower drug development costs, encouraging participation from small and medium-sized enterprises (SMEs). Given that anti-infectives, including antibiotics, have high late-stage success rates, early funding can drive marketable innovations. Examples include open research access, direct funding, tax incentives, product development partnerships (PDPs) and more. Additionally, regulatory frameworks could allow post-approval studies to demonstrate superiority for resistant infections.

Pull incentives boost demand for reserve antibiotics effective against resistant bacteria. Governments are implementing prize-based mechanisms that decouple revenue from sales volume, reflecting the insurance value of these drugs.

Table 1: How AMR thrives vs. How to control AMR

How AMR thrives	How to control AMR
<i>Infection management</i>	
● Inadequate infection control accelerates the spread of infections	● Healthcare systems and populations adhere to strong infection control practices
● Healthcare funding is not tied to infection control or responsible antibiotics use	● Healthcare funding is structured to support and enforce antimicrobial stewardship
<i>Antibiotic use</i>	
● Antibiotics are widely used in a non-specific manner, including for general prophylaxis	● Antibiotics use is limited to necessary cases, and tailored to the bacterial pathogen
● Individuals misuse antibiotics for non-bacterial infections or incomplete treatment	● Individuals use antibiotics only when necessary for bacterial infections, and complete treatment
<i>Innovation</i>	
● Insufficient R&D funding weakens the antibiotic pipeline	● Public and private sectors invest in antibiotic R&D to replenish the pipeline
● Regulatory approval alone does not justify an adequate price	● Regulatory and market access frameworks prioritise public health considerations

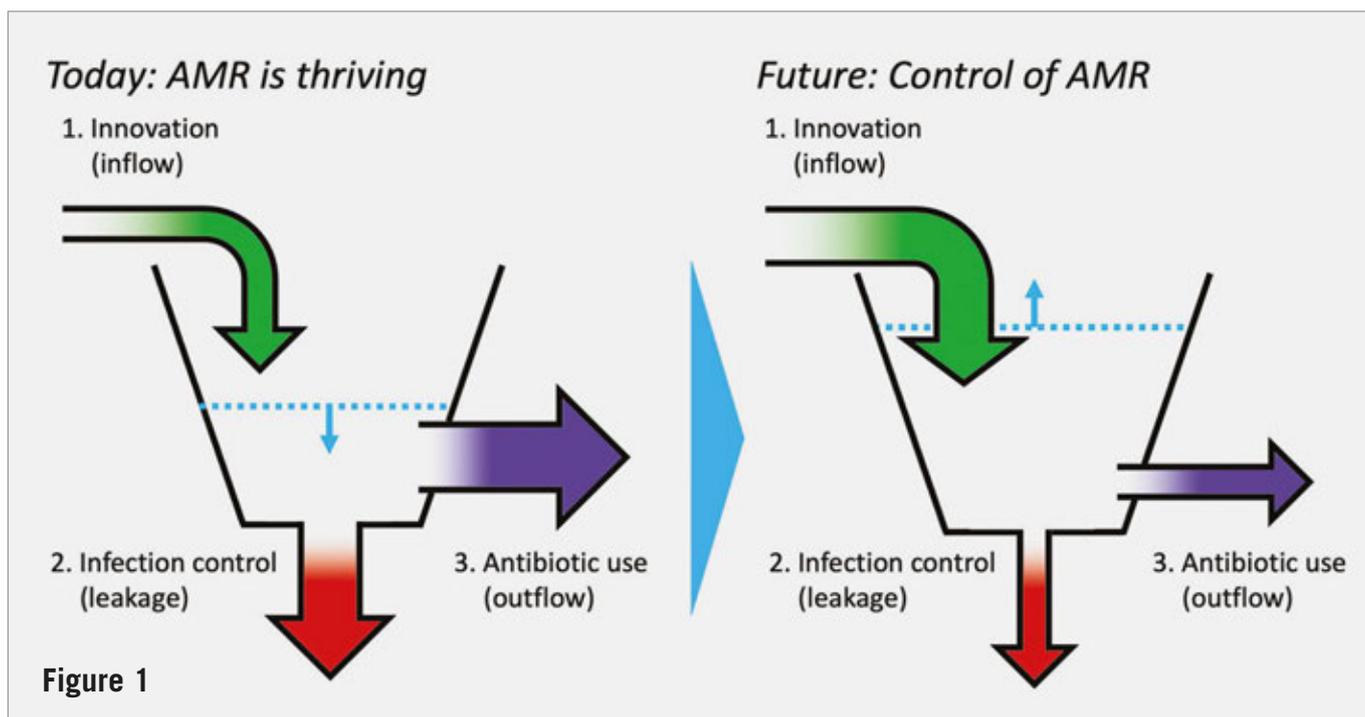


Figure 1

The UK leads with its antibiotic subscription pilot, now set for expansion. Japan has proposed a similar model, while the US advances the Pasteur Act to support market entry payments. In the EU, a multi-year initiative is designing a multi-country pull incentive scheme.

A balanced approach combining regulations, push incentives, and pull incentives is essential to combat and control AMR. Maintaining a robust antibiotic portfolio amid rising resistance resembles water management:

- 1 Inflow:** push and pull incentives, along with regulatory adjustments, drive innovation in novel antibiotics.
- 2 Leakage:** effective regulations in healthcare, agriculture and pharmaceutical production curb the spread of resistant bacteria.
- 3 Outflow:** responsible antibiotic use is ensured through antimicrobial stewardship and volume-decoupled incentives, preserving antibiotics effectiveness.

Today, AMR continues to thrive because innovation in novel antibiotics has not kept pace with the rise of resistance, driven by antibiotic misuse and poor infection control. As a result, the portfolio of effective antibiotics is steadily shrinking (see figure 1, left-hand side). To regain control over AMR, we must significantly improve infection prevention and ensure responsible antibiotic use. This will create an environment where innovation can outpace resistance,

ultimately expanding the arsenal of effective antibiotics and securing long-term solutions against resistant pathogens (see figure 1, right-hand side).

‘The widespread availability of low-cost generic antibiotics has led to overuse and misuse in both human medicine and agriculture’

Several major global initiatives are making significant strides in combatting AMR holistically:

- 1** The WHO Global Action Plan on AMR (GAP-AMR), launched in 2015, sets a global framework for coordinated action.
- 2** The Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerated (CARB-X), a public-private initiative founded in 2016, funds early-stage antibiotic research.
- 3** Also established in 2016, the Global Antibiotic Research & Development Partnership (GARDP) is a non-profit working to develop new treatments for drug-resistant infections.
- 4** The AMR Industry Alliance, launched in 2018, brings together pharmaceutical and biotech companies to drive responsible antibiotic use and innovation.

In 2022, the Food and Agriculture Organization (FAO), the World Organization for Animal Health (WOAH), the UN Environment Programme (UNEP), and the WHO formalised their partnership through the Quadripartite Collaboration for One Health. This initiative focuses on AMR, emerging zoonotic diseases and strengthening global health systems to address interconnected health challenges across human, animal and environmental sectors.

Overcoming the antibiotic resistance crisis is a formidable challenge. Traditional economic models and historic healthcare, pharmaceutical and agricultural regulations have exacerbated the problem, depleting the stock of effective antibiotics as resistance grows. However, a strategic combination of regulations, push incentives and pull incentives can help achieve the desired state in combatting and controlling AMR.

To rebuild and sustain a strong antibiotic portfolio, we must integrate strict infection management, responsible antibiotic use and continuous innovation. While bacteria are remarkably adaptable and resilient, thriving in diverse environments, our collective human intelligence must create an ecosystem that ensures long-term control over resistant bacteria.

References are available on request.

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