

ARE WE OVER-PRESCRIBING ANTIBIOTICS – AND WHAT COMES AFTER?

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Introduction

In the winter of 1928, Alexander Fleming returned to his laboratory at St. Mary's Hospital in London to find something peculiar. A petri dish of *Staphylococcus* bacteria, which he had accidentally left uncovered, had been contaminated by a mold. Around the mold, the bacteria had died. That mold was *Penicillium notatum*, and Fleming had just discovered the world's first antibiotic. What followed was nothing short of a medical revolution. Penicillin, and the antibiotics that came after it, transformed once-deadly infections into minor inconveniences. Childbirth became safer. Surgery became routine. Cancer chemotherapy became possible. Antibiotics became the invisible scaffolding upon which modern medicine was built.

Yet, less than a century later, that scaffolding is cracking. The very drugs that saved millions are now being undermined by their own success. According to the World Health Organization's 2025 Global Antibiotic Resistance Surveillance Report, one in six laboratory-confirmed bacterial infections worldwide were

resistant to antibiotic treatments in 2023 . Between 2018 and 2023, antibiotic resistance rose in over 40% of the pathogen-antibiotic combinations monitored, with an average annual increase of 5-15% . The Centers for Disease Control and Prevention (CDC) reports that more than 2.8 million antimicrobial-resistant infections occur in the United States each year, killing more than 35,000 people .

We are witnessing the slow-motion collapse of one of medicine's greatest achievements. The question is no longer whether we are over-prescribing antibiotics — the evidence overwhelmingly says we are — but rather, what comes next? How do we preserve the antibiotics we still have while racing to develop alternatives that can fill the widening gap? This article explores the scale of over-prescription, its consequences, and the emerging frontier of therapies that may define the post-antibiotic era.

The Scale of Over-Prescription: A Global Snapshot

The overuse of antibiotics is not a single problem but a constellation of interconnected issues spanning human medicine, agriculture, and environmental policy. Understanding the scale requires looking at multiple dimensions simultaneously.

Human Medicine: The Prescription Paradox

In clinical settings, antibiotics are frequently prescribed for conditions where they provide no benefit. Viral respiratory infections — colds, influenza, most sore throats, and bronchitis — account for a significant portion of inappropriate prescriptions. Studies consistently show that 30-50% of antibiotic prescriptions in outpatient settings are unnecessary or suboptimal . The reasons are complex: diagnostic uncertainty, patient expectations, time pressures on physicians, and defensive medicine practices all contribute.

The COVID-19 pandemic exacerbated the problem dramatically. As healthcare systems were overwhelmed, antibiotic prescribing shot up as doctors sought to treat or preempt secondary bacterial infections in severely ill patients. CDC data reveal that six antimicrobial-resistant hospital-acquired infections increased by a combined 20% during the pandemic compared to pre-pandemic levels, peaking in 2021 and remaining elevated in 2022 . At the same time, *Candida auris*, a drug-resistant fungus that spreads in healthcare facilities, increased nearly five-fold from 2019 to 2022 .



Figure 1: The World Health Organization identifies multiple drivers of antibiotic resistance, with over-prescribing in human medicine and overuse in agriculture leading the list. (Source: WHO)

Agriculture: The Hidden Majority

Perhaps the most underappreciated dimension of antibiotic overuse occurs not in hospitals or clinics, but on farms. Globally, the majority of antibiotics are administered to animals rather than humans. In the United States alone, approximately 70% of medically important antibiotics are sold for use in animal agriculture. These drugs are used not only to treat sick animals but also as growth promoters and for disease prevention in crowded, industrial farming conditions.

This agricultural overuse creates a massive reservoir of resistant bacteria that can transfer to humans through food, water, and environmental exposure. The 2024 UN General Assembly's political declaration on antimicrobial resistance explicitly recognized this connection, calling for a "One Health" approach that integrates human, animal, and environmental health.

Global Disparities in Access and Overuse

The antibiotic crisis presents a cruel paradox. While overuse drives resistance in wealthy nations, many low- and middle-income countries struggle with inadequate access to life-saving antibiotics. The WHO report found that resistance is highest in the South-East Asian and Eastern Mediterranean regions, where one in three reported infections were resistant, compared to one in five in Africa. These

regions often lack the diagnostic infrastructure to distinguish bacterial from viral infections, leading to both overuse and underuse simultaneously.

Table 1: Global Antibiotic Resistance Burden by Region (2023)

Region	Resistant Infections (%)	Primary Drivers	Key Resistant Pathogens
South-East Asia	~33%	Over-the-counter availability, poor sanitation	<i>E. coli</i> , <i>K. pneumoniae</i>
Eastern Mediterranean	~33%	Conflict zones, weak health systems	<i>Acinetobacter spp.</i> , MRSA
Africa	~20%	Limited diagnostics, agricultural use	<i>Salmonella</i> , <i>Shigella</i>
Europe	~15-18%	Hospital-acquired infections	<i>E. coli</i> , <i>Enterococcus</i>
Americas	~16-17%	Outpatient over-prescribing	<i>S. aureus</i> , <i>S. pneumoniae</i>

Data synthesized from WHO Global Antibiotic Resistance Surveillance Report 2025

The Mechanisms of Resistance: How Bacteria Fight Back

Antibiotic resistance is not a modern invention — it is basic evolution, accelerated by human behavior. Bacteria have been producing antibiotic compounds and developing resistance mechanisms for billions of years. What has changed is the selective pressure we have applied through mass antibiotic use.

The Evolutionary Arms Race

When a patient takes an antibiotic, the drug kills susceptible bacteria, clearing the field for any naturally resistant variants to multiply. These resistant survivors then pass their resistance genes to offspring through vertical transmission and to other bacteria through horizontal gene transfer — a process by which bacteria share genetic material, including resistance genes, across species boundaries.

The speed of this process is alarming. While developing a new antibiotic takes more than 10 years and costs over a billion dollars, bacteria can develop resistance within months of a drug's introduction. This asymmetry means that, without intervention, we are destined to lose the evolutionary race.

The Rise of Superbugs

The WHO report highlights that the greatest threat comes from Gram-negative bacteria, which are notoriously difficult to kill and resistant to multiple drug classes. Among these, *Escherichia coli* and *Klebsiella pneumoniae* — common causes of bloodstream and urinary tract infections — show alarming resistance levels. Globally, more than 40% of *E. coli* and 55% of *K. pneumoniae* strains were resistant to

third-generation cephalosporins, the first-line treatment for many serious infections. In parts of Africa, resistance levels exceeded 70% .

These multidrug-resistant organisms, often called “superbugs,” are forcing clinicians to turn to last-resort antibiotics such as carbapenems and colistin. These treatments are costly, complex, and often unavailable in lower-income countries, narrowing treatment options and increasing mortality .



Figure 2: The European Centre for Disease Prevention and Control estimates that antibiotic resistance causes approximately 33,000 deaths annually in Europe alone, comparable to the passenger capacity of over 100 medium-sized airplanes. (Source: ECDC)

The Human Cost: Beyond the Statistics

Behind every statistic on antibiotic resistance lies a human story. For infectious disease specialist Dr. Helen Boucher, dean of Tufts University School of Medicine, the threat is deeply personal. “I have had the sad duty to have to tell a patient that we couldn’t offer chemotherapy for their cancer, or give them a joint replacement or a heart transplant, because they had an infection that was resistant to antibiotics,” she recounted .

This scenario is becoming increasingly common. Antibiotics are not merely treatments for infections; they are the foundation that makes modern medicine

possible. Common procedures like C-sections, hip replacements, prostate biopsies, and organ transplants all rely on functional antibiotics to prevent or treat associated infections . Without them, the risk of these procedures becomes unacceptably high.

The Economic Toll

The economic implications are staggering. Without urgent action, experts project that resistant infections could cause an estimated \$3 trillion in global GDP losses per year by 2030 . A major review commissioned by the UK government projected that antimicrobial resistance could lead to 10 million deaths every year by 2050 – more than the current global toll of cancer . The economic impact could exceed \$100 trillion due to lost productivity and increased healthcare spending .

Table 2: Estimated Annual Impact of Antimicrobial Resistance

Impact Category	Current Estimate (Annual)	Projected Estimate (2050)
Direct Deaths	1.27 million	10 million
Deaths (Contributing Factor)	~5 million	Unknown
U.S. Infections	2.8 million	Increasing
U.S. Deaths	35,000+	Increasing
Global GDP Loss	Significant	\$3 trillion/year
Healthcare Costs	Billions USD	\$100 trillion cumulative

Stewardship and Prevention: Preserving What We Have

While the development of new therapies is critical, the most immediate priority is preserving the effectiveness of existing antibiotics through antimicrobial stewardship and infection prevention.

Hospital Stewardship Programs

Antibiotic stewardship is defined as using the right antibiotic at the right time at the right dose for each patient. In the United States, approximately 96% of hospitals had implemented the CDC’s seven core elements of an antibiotic stewardship program by 2023 . These elements include leadership commitment, accountability, pharmacy expertise, action tracking, reporting, and education.

The results have been promising. Prior to the COVID-19 pandemic, dedicated prevention and infection control efforts in the U.S. had reduced deaths from antimicrobial-resistant infections by 18% overall and by nearly 30% in hospitals . However, much of this progress was lost during the pandemic, underscoring the fragility of these gains.



Figure 3: Antimicrobial stewardship programs in hospitals focus on optimizing antibiotic use through leadership commitment, accountability measures, and pharmacy expertise. (Source: The Hospitalist)

Diagnostic Innovation

A critical barrier to appropriate prescribing is the inability to rapidly distinguish bacterial from viral infections. Traditional bacterial cultures take 24–72 hours — an eternity when a patient is critically ill. New rapid point-of-care molecular tests, which can identify pathogens and their resistance profiles within hours, represent a game-changing tool. WHO Director-General Tedros Adhanom Ghebreyesus has emphasized the need to “innovate with next-generation antibiotics and rapid point-of-care molecular tests” .

Vaccines and Infection Control

Prevention remains the most effective strategy. Vaccines against bacterial pathogens such as *Streptococcus pneumoniae* and *Haemophilus influenzae* type b have dramatically reduced the incidence of infections that would otherwise require antibiotics. Similarly, improved sanitation, hand hygiene, and infection control in healthcare settings can prevent infections from occurring in the first place.

The Post-Antibiotic Frontier: Emerging Alternatives

As resistance outpaces the development of new traditional antibiotics, researchers are increasingly turning to alternative therapies. These approaches do not seek to replace antibiotics entirely but to supplement them and provide options when conventional drugs fail.

Bacteriophage Therapy: Nature’s Predators

Bacteriophages, or phages, are viruses that infect and kill bacteria. They are the most abundant biological entities on Earth and have been co-evolving with bacteria for billions of years. Unlike broad-spectrum antibiotics, phages are typically highly specific, targeting only one or a few bacterial strains while leaving beneficial microbiota intact.

Scientists discovered phages in the early 1900s and developed them into medicines, but the technology was difficult to standardize and scale without modern tools. When antibiotics were discovered and industrialized in the mid-1900s, phage therapy was largely abandoned in the West .

Today, however, phage therapy is experiencing a renaissance. In October 2025, France became the first country to authorize a personalized phage-based treatment platform for veterinary use — a groundbreaking regulatory innovation. Unlike traditional drug approvals that authorize a single fixed formulation, France’s platform approach establishes a validated framework for producing tailored phage combinations. As bacteria become resistant, new phages can be rapidly integrated without starting the approval process from scratch .

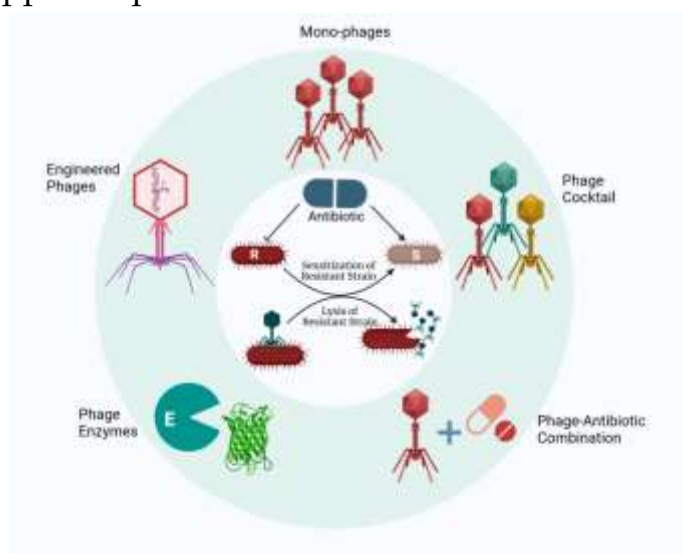


Figure 4: Modern phage therapy employs multiple strategies including mono-phages, phage cocktails, engineered phages, phage enzymes, and phage-antibiotic combinations to combat resistant bacteria. (Source: BioRender)

Antimicrobial Peptides (AMPs)

Antimicrobial peptides are short chains of amino acids produced naturally by virtually all living organisms as part of their innate immune defense. They work by disrupting bacterial membranes, a mechanism that makes resistance development more difficult. AMPs are being investigated both as standalone therapies and as adjuncts to traditional antibiotics. Research indicates that AMPs and nanotechnology are among the most extensively investigated alternatives .

CRISPR-Based Therapies

The gene-editing technology CRISPR offers a novel approach to combating resistance. Researchers are developing CRISPR systems that can specifically target and destroy resistance genes within bacteria, effectively resensitizing them to existing antibiotics. While still in early stages, this precision approach could revolutionize how we manage resistant infections.

Other Promising Approaches

A comprehensive analysis of global research from 2010–2023 identified several other alternatives gaining traction :

- Nanotechnology:** Silver nanoparticles and other nanomaterials can deliver drugs directly to infection sites and disrupt bacterial biofilms
- Probiotics and competitive exclusion:** Using beneficial bacteria to outcompete pathogens
- Monoclonal antibodies:** Targeted immunotherapies that neutralize specific pathogens
- Vaccines:** Both traditional and mRNA-based vaccines against resistant pathogens
- Bacteriocins:** Antimicrobial peptides produced by bacteria to inhibit competing strains

Table 3: Alternative Therapies to Antibiotics – Research Landscape

Alternative Therapy	Mechanism	Development Stage	Key Advantages	Key Challenges
Bacteriophage Therapy	Viral predation of bacteria	Veterinary approved (France); human trials ongoing	Highly specific; self-amplifying; low toxicity	Regulatory complexity; narrow host range; bacterial resistance
Antimicrobial Peptides	Membrane disruption	Preclinical/Phase I	Broad spectrum; rapid killing; immunomodulatory	Toxicity; stability; manufacturing cost
CRISPR-Cas Systems	Targeted gene editing	Early research	Precision targeting; can reverse resistance	Delivery challenges; off-target effects; ethical concerns
Nanoparticles	Drug delivery; membrane damage	Preclinical/Phase I	Enhanced bioavailability; biofilm penetration	Long-term safety; environmental impact
Monoclonal Antibodies	Pathogen neutralization	Phase II/III for some pathogens	Highly specific; long half-life	High cost; limited spectrum; resistance possible
Probiotics	Competitive exclusion	Marketed for some indications	Safe; inexpensive; microbiome-friendly	Variable efficacy; regulatory ambiguity

Based on analysis of 47,702 studies published 2010–2023

Regulatory and Economic Challenges

Developing alternatives to antibiotics faces significant hurdles beyond the scientific. The traditional pharmaceutical business model, built on blockbuster drugs prescribed to millions of patients over years, does not align well with antibiotics or their alternatives. New antibiotics are typically reserved as last-resort treatments, limiting their sales volume. This economic reality has led most major pharmaceutical companies to abandon antibiotic research.

Alternative therapies face additional regulatory challenges. Phage therapy, for instance, does not fit neatly into existing drug approval frameworks designed for single chemical entities. France's platform approach represents a promising regulatory innovation, but global harmonization remains a distant goal.

The 2024 UN General Assembly political declaration on AMR called for increased international funding for antibiotic research and development, but commitments remain insufficient. Without sustainable funding mechanisms — such as subscription models that delink revenue from sales volume — the pipeline of new treatments will remain dangerously thin.

Conclusion

We are standing at a crossroads in medical history. The antibiotic era, which began with Fleming's accidental discovery nearly a century ago, is not ending with a bang but with a whimper — the quiet erosion of drug effectiveness as bacteria outpace our ability to develop new treatments. The evidence is unequivocal: we are over-prescribing antibiotics in human medicine, overusing them in agriculture, and failing to invest adequately in the alternatives that might save us.

The statistics are sobering. One in six bacterial infections globally is now resistant to standard treatments. Resistance is rising by 5–15% annually. Without action, 10 million people could die annually from resistant infections by 2050. Yet these numbers, as shocking as they are, fail to capture the full human tragedy — the cancer patient denied chemotherapy, the transplant recipient facing an untreatable infection, the new mother at risk from a once-preventable post-surgical complication.

But despair is not a strategy. The tools to address this crisis exist, even if they remain underutilized. Antimicrobial stewardship programs have proven effective when implemented consistently. Rapid diagnostics can eliminate guesswork in prescribing. Vaccines and improved infection control can prevent infections before they occur. And on the horizon, phage therapy, antimicrobial peptides, CRISPR-based approaches, and other innovations offer genuine hope for a post-antibiotic toolkit.

What is needed now is the political will, regulatory innovation, and sustained funding to translate these possibilities into realities. The 2024 UN General Assembly declaration was a start, but declarations without action are merely words. France's pioneering regulatory framework for phage therapy shows what is possible when regulators think creatively. We need more such leadership.

The question "Are we over-prescribing antibiotics?" has been answered. The more urgent question — "What comes after?" — demands our immediate attention. The post-antibiotic era is not a distant dystopia; it is arriving in hospital wards and clinics around the world today. Whether that era is defined by a return to the pre-penicillin mortality rates of the past or by a new generation of precision therapies depends entirely on the choices we make in the next decade.

As Dr. Tedros Adhanom Ghebreyesus warned, "Antimicrobial resistance is outpacing advances in modern medicine, threatening the health of families worldwide". The time to act is not tomorrow. It is now.

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