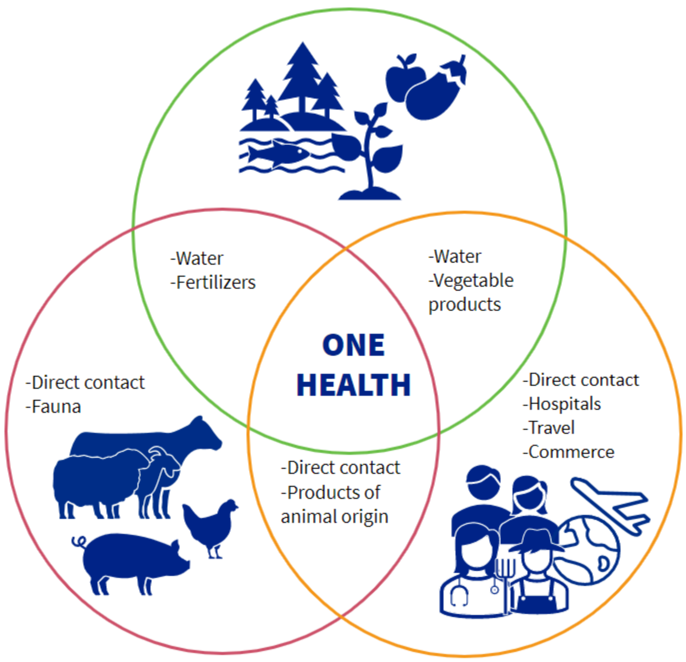
Confronting the Silent Pandemic: A Policy Framework for Addressing Antimicrobial Resistance



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Introduction

The discovery of penicillin in 1928 revolutionized modern medicine, transforming once-deadly bacterial infections into treatable conditions. Yet within two decades of penicillin's widespread use, Alexander Fleming himself warned of a looming crisis: the emergence of antimicrobial resistance. His prescient concern has materialized into what health experts now characterize as a "silent pandemic" — a global health emergency that threatens to undermine a century of medical progress (Basilio, 2025).

Antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi, and parasites evolve to no longer respond to the medicines designed to eliminate them. This includes antibiotics, antivirals, antifungals, and antiparasitics. When these drugs lose their effectiveness, common infections become difficult or impossible to treat, routine medical procedures become dangerous, and diseases once thought conquered resurge with renewed threat.

The scope of this crisis is staggering. AMR is estimated to cause hundreds of thousands of deaths annually, with projections suggesting millions more will die in coming decades if current trends continue unchecked. Drug-resistant infections already impose enormous economic burdens on healthcare systems worldwide, extending hospital stays, requiring more expensive treatments, and reducing patient productivity. Beyond individual cases, AMR threatens the foundation of modern medical practice: surgical procedures, cancer chemotherapy, organ transplantation, and care for premature infants all depend on effective antimicrobials to prevent and treat infections.

What makes AMR particularly insidious is its multifaceted nature. The problem stems not from a single cause but from interconnected factors spanning human medicine, agricultural practices, environmental contamination, and global inequities in healthcare access and regulation. Physicians overprescribe antibiotics due to diagnostic uncertainty and patient pressure. Industrial agriculture uses antimicrobials prophylactically and as growth promoters in livestock. Pharmaceutical waste contaminates water supplies in regions with inadequate environmental controls. In low- and middle-income countries (LMICs), unregulated access leads to inappropriate use while counterfeit medications further accelerate resistance.

The interactions between humans, animals, and the environment create a complex web through which resistant organisms spread. For example, a patient treated with antibiotics in one country can carry resistant bacteria across borders. Moreover, agricultural runoff containing antimicrobial residues enters water systems that supply drinking water to communities. Resistant pathogens move between livestock, wildlife, and human populations, recognizing no jurisdictional boundaries.

Current policy responses, while growing in scope and sophistication, have not kept pace with this accelerating threat. International organizations including the World Health Organization have established frameworks for coordinated action, research and development partnerships seek to revitalize the antibiotic pipeline, and antimicrobial stewardship programs aim to optimize prescribing practices. Yet gaps in implementation, enforcement, and global equity persist. Many nations lack the diagnostic infrastructure to identify resistant infections, the regulatory capacity to control antimicrobial use, or the resources to invest in alternatives.

This policy brief argues that antimicrobial resistance poses a complex, global health threat requiring stronger international coordination, improved diagnostic capabilities, and behavior-focused policy reform across healthcare, agricultural, and environmental sectors. Addressing AMR demands not just technical solutions but systemic change in how societies produce food, deliver healthcare, protect the environment, and cooperate across borders. The challenge is urgent: act decisively now, or face a future where routine infections become untreatable and modern medicine's most fundamental tools fail.

The sections that follow examine the drivers of AMR in detail, assess the public health and economic consequences, review current policy efforts, and propose evidence-based recommendations for meaningful intervention. This is not simply a medical problem requiring medical solutions, but a policy challenge demanding coordinated action across disciplines, sectors, and nations.

Causes and Drivers of Antimicrobial Resistance

Understanding antimicrobial resistance requires examining the multiple pathways through which resistant organisms emerge and spread. AMR is not an inevitable biological phenomenon but rather the consequence of human decisions and practices across healthcare, agriculture, and environmental management. Four primary drivers accelerate the development and dissemination of resistance: medical misuse, agricultural practices, global inequities, and environmental contamination.

Medical Misuse and Overprescription

Healthcare settings represent the most direct pathway for AMR development. When antimicrobials are prescribed unnecessarily or used incorrectly, they create selective pressure that favors resistant organisms while eliminating susceptible bacteria. Several factors contribute to inappropriate prescribing in clinical practice.

First, diagnostic uncertainty leads many physicians to prescribe antibiotics as a precautionary measure. Without rapid, point-of-care diagnostic tests that distinguish bacterial from viral infections, clinicians often default to prescribing antibiotics for conditions that do not require them. Studies consistently show that a substantial portion of antibiotic prescriptions are either unnecessary or inappropriate for the diagnosed condition.

Patient pressure compounds this problem. Many patients expect antibiotics when they feel ill, and busy clinicians facing time constraints may find it easier to write a prescription than to explain why antibiotics are not indicated. This dynamic is particularly pronounced for respiratory infections, where viral causes predominate but antibiotic prescribing remains common.

Even when antibiotics are appropriately indicated, problems with dosing, duration, and patient adherence contribute to resistance. Incomplete courses allow partially resistant organisms to survive and proliferate. Subtherapeutic dosing creates selective pressure at drug concentrations that kill susceptible bacteria while permitting resistant variants to thrive.

Agricultural Practices and Food Systems

The agricultural sector's use of antimicrobials dwarfs medical consumption in many countries. Antibiotics are administered to livestock not only to treat infections but also prophylactically to prevent disease in crowded conditions and, in some jurisdictions, as growth promoters to increase feed efficiency and weight gain.

This practice creates ideal conditions for resistance development. Animals receive antibiotics at subtherapeutic doses over extended periods, creating sustained selective pressure. Resistant bacteria that emerge in livestock populations can transfer to humans through multiple routes: direct contact with animals, consumption of contaminated meat, and environmental spread through manure used as fertilizer.

The interconnection between human, animal, and environmental health — often termed the "One Health" approach — is nowhere more evident than in agricultural AMR. Resistant organisms and resistance genes move fluidly between these domains. A resistance gene that emerges in livestock bacteria can transfer to human pathogens through mobile genetic elements, creating new therapeutic challenges in human medicine.

Global Inequities in Access and Regulation

The global landscape of antimicrobial use reflects stark inequities that both drive resistance and limit effective response. In many LMICs, antimicrobials are available without prescription, leading to widespread self-medication and inappropriate use. Simultaneously, poor-quality and counterfeit antimicrobials containing incorrect doses of active ingredients are common in regions with inadequate pharmaceutical regulation.

These dynamics create a vicious cycle of overuse and misuse, accelerating resistance development. As resistance spreads, the effectiveness of available drugs declines, creating pressure for stronger or newer antimicrobials. Yet the same populations facing the highest burden of resistant infections often have the least access to advanced diagnostics and newer antimicrobial agents.

The economic dimensions of this inequity are significant. While high-income countries can invest in infection prevention, diagnostic infrastructure, and antimicrobial stewardship, resource-limited settings struggle with basic healthcare capacity. The result is a global system where resistance develops most rapidly in regions least equipped to respond.

Environmental Contamination and Transmission

Pharmaceutical manufacturing, healthcare waste, and agricultural runoff introduce antimicrobials and resistant organisms into the environment. Wastewater from hospitals, pharmaceutical plants, and communities contains antimicrobial residues that persist in water systems, creating selective pressure in environmental bacteria.

This environmental reservoir of resistance genes serves as a bridge between different ecosystems and populations. Waterways contaminated with resistant bacteria or resistance genes can affect communities far from the original source. Wildlife exposed to contaminated environments can carry resistant organisms across geographic barriers, complicating efforts at containment.

The scope of environmental contamination varies dramatically by region, with the heaviest burdens falling on areas with inadequate wastewater treatment and pharmaceutical manufacturing regulations. Yet because resistance and resistant organisms travel globally, local environmental problems become international health threats.

Understanding these interconnected drivers is essential for effective policy response. Interventions targeting only one pathway — such as reducing prescribing in human medicine — will have limited impact if agricultural use and environmental contamination continue unchecked. The challenge demands coordinated action across all sectors where antimicrobials are used and where resistant organisms emerge and spread.

Public Health Burdens and Consequences

The consequences of antimicrobial resistance extend far beyond individual patients to impose substantial burdens on healthcare systems, national economies, and global health security. Understanding the full scope of these impacts — measured in deaths, disability, economic costs, and threats to medical progress — is essential for mobilizing the political will and resources needed for effective response.

Rising Mortality and Morbidity from Drug-Resistant Infections

The human toll of AMR is staggering and growing. Bacterial AMR was directly responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths, making it one of the leading causes of mortality worldwide. To put this in perspective, AMR is the third leading cause of mortality in the world, with over 1 million deaths directly linked to bacterial AMR and 5 million deaths indirectly (WHO, 2023).

Recent comprehensive analyses reveal even more concerning trends. More than one million people died each year as a result of AMR between 1990 and 2021, indicating that this has been a persistent crisis for decades.

The trajectory of AMR deaths is deeply concerning. New forecasts suggest that bacterial antimicrobial resistance will cause 39 million deaths between 2025 and 2050, which equates to three deaths every minute (*New Forecasts Reveal That 39 Million Deaths Will Be Directly Attributable to Bacterial Antimicrobial Resistance (AMR) between 2025-2050 | News | Wellcome*, 2024). A separate study finds that the "Silent Pandemic" will, by 2050, be the largest cause of human mortality. These projections underscore the urgency of intervention.

Additionally, the age distribution of AMR deaths reveals important demographic shifts. Between 1990 and 2021, AMR deaths among children under five years old declined by 50%, while those among people aged 70 years and older increased by more than 80% (Institute for Health Metrics and Evaluation, 2024). This pattern reflects both progress — through vaccination programs and improved access to clean water and sanitation that have protected children — and emerging challenges as populations age globally. AMR poses the biggest threat to older adults, as deaths in adults aged 70 and older increased by more than 80% between 1990 and 2021, suggesting that the burden will intensify as demographic aging accelerates worldwide.

Specific drug-resistant pathogens continue to drive substantial morbidity and mortality worldwide. Bacterial, fungal, HIV, tuberculosis, and malaria resistance all contribute to the growing public health burden (WHO, 2023). Tuberculosis (TB) remains a critical concern, with an estimated 231,000 new cases annually in the United States, resulting in approximately 20,000 deaths per year. Alarmingly, one in three TB patients globally has multidrug- or rifampicin-resistant TB, complicating treatment and control efforts (WHO, n.d.). Similarly, methicillin-resistant *Staphylococcus aureus* (MRSA) and other drug-resistant bacterial infections have emerged as major contributors to preventable deaths and extended hospitalizations, highlighting the urgent need for targeted interventions.

The morbidity burden — illness that does not result in death but causes disability and suffering — compounds the mortality statistics. Resistant infections typically require longer hospital stays, more intensive treatment, and result in greater disability than susceptible infections. Patients with resistant infections face prolonged illness, repeated treatments, and higher rates of treatment failure, all contributing to reduced quality of life even when they survive.

Economic Costs: Healthcare Expenditure and Productivity Losses

The economic consequences of AMR are profound and multifaceted, affecting healthcare budgets, national economies, and global trade. The World Bank estimates that AMR could result in US$1 trillion additional healthcare costs by 2050, and US$1 trillion to US$3.4 trillion gross domestic product losses per year by 2030 (WHO, 2023).

More recent economic modeling provides additional detail on these projections. Antimicrobial resistance increases the cost of health care by US$66 billion, and this will rise to US$159 billion in a business-as-usual scenario where resistance rates follow historical trends. In more severe scenarios, if resistance rates increased at the rate of the bottom 15% of countries, AMR health costs would rise to US$325 billion and the global economy would be US$1.7 trillion smaller in 2050 (McDonnell et al., 2024)

These costs manifest at multiple levels. At the patient level, resistant infections require more expensive antibiotics, longer hospital stays, additional diagnostic testing, and more intensive nursing and physician care. A single case of drug-resistant infection can cost tens of thousands of dollars more than a susceptible infection due to extended treatment duration and complications.

Healthcare systems bear substantial costs from AMR through increased hospital occupancy, higher staffing requirements, infection control measures, and the need for more expensive antimicrobial agents. AMR creates need for more expensive and intensive care, affects productivity of patients or their caregivers through prolonged hospital stays, and harms agricultural productivity. These direct medical costs represent only part of the economic burden.

Broader economic impacts include lost productivity when patients miss work due to illness, reduced labor force participation when people become chronically ill or disabled, and decreased economic output in affected sectors. AMR puts strain on vulnerable health systems and national economies, creating the need for more expensive and intensive care.

Agricultural impacts further amplify economic consequences. Livestock production, an essential source of protein and livelihood for millions, faces threats from AMR in animal pathogens. AMR could result in production losses in the livestock sector equivalent to the consumption needs of 746 million people, or more than two billion people in a more severe scenario by 2050 (AGDAILY Reporters, 2024). Such losses would affect food security, agricultural employment, and international trade.

Threat to Modern Medical Procedures

Beyond the direct burden of resistant infections, AMR threatens the foundation of modern medical practice. Many routine procedures and advanced treatments depend on effective antimicrobials to prevent and treat infections that would otherwise make these interventions too dangerous to perform.

Surgical procedures of all types rely on prophylactic antibiotics to prevent surgical site infections. As resistance increases, the risk-benefit calculus for many surgeries shifts unfavorably. Complex procedures such as organ transplantation, cardiac surgery, and joint replacement all become significantly more hazardous when prophylactic antibiotics lose effectiveness.

For example, cancer chemotherapy suppresses the immune system, leaving patients highly vulnerable to infections. Routine medical procedures become unsafe, including surgery and cancer treatment, thus reversing many of the gains made in modern medicine. If resistant infections cannot be effectively treated, cancer cure rates will decline and some chemotherapy protocols may become too risky to administer.

Similarly, premature infants in neonatal intensive care units, patients in intensive care, and individuals with compromised immune systems all depend on effective antimicrobials. Rising resistance rates in hospital-associated pathogens particularly threaten these vulnerable populations, for whom even common bacterial infections can be fatal without effective treatment.

Dialysis, management of chronic diseases like diabetes with its associated infection risks, and countless other aspects of modern healthcare all assume the availability of effective antimicrobials. The erosion of antibiotic effectiveness thus threatens not just treatment of infections but the entire infrastructure of modern medicine.

Implications for Global Health Security and Equity

AMR is a problem for all countries at all income levels. Its spread does not recognize country borders, making this inherently a global challenge requiring coordinated international response.

However, people living in low-resource settings and vulnerable populations are especially impacted by both the drivers and consequences of AMR. LMICs face higher rates of resistant infections while having the least capacity to respond through infection prevention, antimicrobial stewardship, or development of new treatments.

This inequity creates a global health security risk. Resistant pathogens emerging in any location can spread internationally through travel, trade, and migration. A resistance mechanism that develops in one country's hospitals or agricultural systems can rapidly disseminate globally, threatening populations worldwide. Effective response therefore requires not only that each country address AMR within its borders but that the international community supports capacity building and infrastructure development in regions with the greatest needs.

Current Policy Landscape

Efforts to address antimicrobial resistance (AMR) have intensified in recent years, reflecting recognition of AMR as a critical threat to global health, economies, and medical progress. International initiatives, research and development programs, and antimicrobial stewardship frameworks collectively aim to slow resistance, improve treatment outcomes, and strengthen global preparedness. However, implementation remains uneven, and gaps persist in surveillance, regulation, and capacity across countries.

International Coordination Efforts

- **Global Action Plan** (GAP) on Antimicrobial Resistance: Coordinated by the WHO, the GAP provides a framework for countries to develop national action plans addressing AMR across human health, animal health, agriculture, and the environment.
- **World AMR Awareness Week** (WAAW): Annual awareness campaign led by WHO to educate stakeholders and the public about AMR risks and mitigation strategies.
- **Quadripartite Joint Secretariat on AMR**: Collaboration between WHO, FAO, OIE, and UNEP to promote a One Health approach to AMR, integrating human, animal, and environmental health.

Research and Development Initiatives:

- **Global Antibiotic Research & Development Partnership** (GARDP): Supports development of new treatments for drug-resistant infections, particularly in low- and middle-income countries.
- **AMR Action Fund & CARB-X**: Provide funding and technical support to accelerate antibiotic research, close gaps in the drug pipeline, and incentivize innovation for hard-to-treat infections (WHO, 2023).
- Investment in surveillance systems is prioritized to improve detection and response to emerging resistant pathogens, with several programs extending support to LMICs.

Antimicrobial Stewardship Programs:

- **AWaRe** (WHO): Educates and supports healthcare professionals to follow evidence-based guidelines for prescribing and administering antimicrobials (WHO, 2023).
- The **"5 D's" framework**: right Drug, correct Dose, appropriate Drug-route, suitable Duration, and timely De-escalation based on culture results (Geobel et al., 2021).
- National initiatives increasingly integrate stewardship into both hospital and community settings, aiming to optimize antimicrobial use and reduce resistance selection pressures.

Domestic Programs (United States):

Surveillance & Detection

- **National Antimicrobial Resistance Monitoring System** (NARMS): Established in 1996, NARMS is a collaborative program of the **Centers for Disease Control and Prevention** (CDC), **Food and Drug Administration** (FDA), **United States Department of Agriculture** (USDA), state and local health departments, and universities. It tracks antimicrobial susceptibility in enteric bacteria from humans, retail meats, and food-producing animals. NARMS data inform regulatory decisions, outbreak investigations, and efforts to preserve antibiotic effectiveness in both humans and animals (Center for Veterinary Medicine, 2021).
- **Antimicrobial Resistance Solutions Initiative** (AR Solutions Initiative): Led by CDC, this initiative funds laboratory networks, state and local health departments, and public-health infrastructure to detect, respond to, contain and prevent resistant infections across healthcare settings, food supply, communities, and the environment. Since 2016, the Initiative has supported testing of hundreds of thousands of isolates, genetic sequencing efforts, outbreak response, and infection-control programs (CDC, 2025).
- **Antibiotic Resistance Laboratory Network** (AR Lab Network): This network supplements local and state public-health labs by providing advanced testing capacity, resistance mechanism identification, and genomic surveillance for early detection of emerging resistant pathogens.

These programs form the backbone of the U.S. AMR response, enabling detection of resistance trends, informing public health guidance, and supporting evidence-based interventions.

National Strategy & Policy Coordination

- **National Action Plan for Combating Antibiotic-Resistant Bacteria** (2020–2025): The principal domestic blueprint for AMR mitigation. Developed by an interagency task force (HHS, USDA, DOD), the plan outlines five core goals: slowing emergence of resistant bacteria, strengthening **One Health** surveillance, promoting rapid diagnostics, accelerating development of new therapeutics and vaccines, and enhancing international collaboration (CDC, 2024)

This national framework provides policy direction, aligns agency efforts, and establishes benchmarks for stewardship, surveillance, research, and global engagement.

Stewardship, Research & Innovation Programs

- The **AR Solutions Initiative** supports grant funding and technical assistance for developing new antibiotics, diagnostics, and vaccines, and for improving stewardship and infection-control practices in hospitals, long-term care, and community health settings.
- Regulatory oversight — via FDA, USDA, and collaborating agencies — ensures that antimicrobial use in humans and animals is monitored, and that approvals of veterinary and human antibiotics incorporate resistance data drawn from surveillance systems like **NARMS** (Center for Veterinary Medicine, 2020).
- Agricultural-sector initiatives: for example, the **Animal and Plant Health Inspection Service** (APHIS) under USDA recently awarded funding to develop AMR-dashboard tools, enabling tracking of antimicrobial use and resistance patterns in livestock and domesticated animals — a crucial component of a **One Health** strategy (US Department of Agriculture, 2024).

These efforts help sustain the antimicrobial pipeline, support responsible prescribing and use, and improve data-driven management of AMR across human and animal health domains.

Policy Recommendations

Overview

Denmark is seen as one of the most successful countries in fighting AMR. with the ban on the use of growth promoters in 1998 and the introduction of the "yellow card" initiative in 2010, which established a threshold for antibiotic usage. If farmers exceed these thresholds, they receive a yellow card. Pig farmers holding a yellow card are subject to extra supervision for nine months, and the producer may be prohibited from storing antibiotics on site, with unannounced inspections by the Danish Veterinary and Food Administration. If reduction is not achieved within 12 months, the farmer receives a red card resulting in further penalties.

Yes, we could and should look at (largely) successful models in countries like Denmark and Sweden, but that doesn't mean we can replicate them. The largest problem with policy recommendations is enforcement. Denmark's success required comprehensive infrastructure including the VetStat database established in 2000 containing data on all purchased and prescribed veterinary medicines, separation of prescribing and selling functions (veterinarians can prescribe but only pharmacies can sell) (DTU National Food Institute, n.d.). and the DANMAP surveillance program collecting data since 1995 (Hammerum et al., 2007). This level of regulatory capacity, political commitment, and sustained funding over decades cannot be immediately replicated in all contexts, and thus effective policy must acknowledge these constraints.

Policy in LMICs: Surveillance and Enforcement

National action plans generally haven't been implemented at scale in LMICs, and with few exceptions, stewardship guidelines have had limited impact. Basic infection prevention and control are still inadequate in many facilities, and insufficient microbiology-laboratory capacity limits timely surveillance.

However, Kenya's experience demonstrates that progress is possible with the right approach. Kenya's NAP-AMR implementation between 2017-2022 provides a realistic model for what works—and what doesn't—in resource-limited settings. Kenya established a multisectoral National Antimicrobial Stewardship Interagency Committee (NASIC) to provide leadership and coordination for NAP-AMR implementation. Given Kenya's devolved government structure, the NAP-AMR provided for establishment of County Antimicrobial Stewardship Interagency Committees (CASICs) mirroring NASIC to oversee implementation at the county level. In 2021, Kenya developed its first M&E framework for the NAP-AMR using a multisectoral consultative process. The framework comprised 85 indicators based on 85 activities contained in the NAP-AMR—41 for human health and 44 for animal and crop sectors. Kenya established 22 AMR surveillance sentinel sites that submit data to a central data warehouse. In 2016, two model sentinel surveillance hospital laboratories were enrolled as pilot sites with US CDC support. Kenya's National AMR Surveillance and Information Centre (NASIC) developed a Central Data

Warehouse that archives AMR data from sentinel sites, with first data submission in 2018 (Mukoko et al., 2025).

Replicable Model for Other LMICs

Based on Kenya's successes and documented failures, implement the following phased approach:

Phase 1: Establish governance and pilot surveillance before attempting scale.
Key actions include:

- Establish national coordination body **(NASIC equivalent)** with representation from human health, animal health, agriculture, environment, and finance ministries, secured through formal ministerial mandate
- Develop **NAP-AMR** with realistic scope AND cost every activity using **WHO costing tool** (developed August 2021) to avoid Kenya's initial planning failure
- Create **M&E framework** with measurable indicators and scorecard for objective progress assessment
- **Identify** 2-3 pilot sentinel sites with **existing laboratory capacity** (TB reference labs, teaching hospitals, research institutions)

Phase 2: Implement at pilot scale and document what works.
Key actions include:

- **Develop stewardship guidelines** for healthcare settings, prudent antimicrobial use guidelines for animals, IPC policy and training curriculum—adapted to local context, not copied from high-income countries
- **Test data systems** (may require international support)**:** If internet connectivity fails (as in Kenya), implement dedicated mobile data at sentinel sites, establish regional data hubs for physical data delivery, create SMS-based critical alerts, accept monthly/quarterly reporting as realistic
- **Address weak laboratory-clinical interface identified in Kenya:** Train clinicians on specimen collection, establish turnaround time standards, create feedback loops with monthly antibiograms, pilot antimicrobial stewardship rounds
- **Begin limited enforcement:** Survey pharmacies in pilot urban areas, shut down 5-10% most egregious violators, partner with pharmacist associations to identify compliant "model pharmacies," implement consumer awareness campaigns

Phase 3: Scale Strategically
Key actions include:

- **Expand** to 15-25 sentinel sites, but only after confirming supply chain solutions work and data transmission systems **function consistently**
- **Expand urban pharmacy enforcement using risk-based classification:** "Good" pharmacies (reduced inspections), "Bad" pharmacies (warnings, education), "Ugly" pharmacies (fines, closure); train inspectors (target 1 per 100-200 urban pharmacies); implement progressive penalties; link pharmacist licensing to AMR education
- **Scale agricultural enforcement:** Require **veterinary prescriptions for all antimicrobials,** mandate quarterly veterinarian dispensing reports, **ban critically important antibiotics at import** (easier than farm monitoring), work through cooperatives for compliance
- **Integrate AMR into existing programs:** Embed in HIV/AIDS monitoring, TB treatment, maternal-child health, malaria case management; incorporate into annual ministry budgets; add to pre-service training curricula and licensing examinations

Phase 4: Sustain and Expand
Key actions include:

- Achieve 50%+ county coordination body coverage (exceeding Kenya's 42.5%)
- Expand enforcement to rural areas with realistic expectations of slower progress
- Demonstrate measurable impact: Track clinical outcomes (treatment failure rates, mortality) at sentinel sites, document resistance trends, conduct economic analysis of savings versus investment
- Help other countries and contribute data to WHO GLASS

Enforcement Mechanisms That Work:
Phased, Targeted Approach (Not Comprehensive from Day One):

- **Phase 1 (Years 1-2):** Focus on egregious violations—pharmacies selling controlled narcotics without prescription, clearly counterfeit drugs; shut down 5-10% worst offenders to demonstrate seriousness; partner with professional associations to identify compliant "model" practitioners
- **Phase 2 (Years 3-5):** Build regulatory capacity in major cities first; implement risk-based classification of pharmacies; link professional licensing to continuing AMR education; pilot mobile authentication systems for medicine verification
- **Phase 3 (Years 5-10):** Scale to rural areas; implement electronic prescription tracking in urban centers; use progressive penalties (warnings → fines → license suspension)

U.S. Policy Recommendations

The United States possesses infrastructure, resources, and regulatory capacity that LMICs lack, enabling more sophisticated interventions. However, current AMR response remains fragmented and underfunded relative to the threat. The following recommendations provide actionable pathways for federal action.

1. Pass Modified Subscription Legislation for Antibiotic Development

Address antibiotic pipeline collapse through market-based incentives.

Key components should include:

- **Pass modified PASTEUR Act with strengthened requirements:** The **PASTEUR Act** has been introduced three times since 2019 without passage, proposing $6 billion over 5 years for subscription contracts ranging from $750 million to $3 billion per drug. However, the bill faced opposition after academics raised concerns that drugs wouldn't be required to improve patient outcomes.
- **Strengthen evidence standards:** Require proof of superiority in clinical trials or demonstrated efficacy against WHO priority pathogens based on patient outcomes, not solely microbiological endpoints to address academic concerns
- **Mandate transparency:** Require public reporting of contract values, clinical trial data, and stewardship outcomes

This approach addresses market failure where antibiotic development costs average $1.5 billion but annual sales average only $46 million (Towse et al., 2017). Policy analysis projects every dollar spent yields $6 of value in first decade, saving 20,000 American lives; after three decades, value jumps to $28 per dollar invested and 383,000 lives saved (Bonnifield & Towse, 2022).

2. Expand and Mandate CDC Surveillance Infrastructure

Strengthen national surveillance to enable data-driven interventions.

Actions should include:

- **Expand CDC AR Lab Network:** Appropriate sustained funding to expand from current 7 regional labs to 50-state coverage for comprehensive geographic representation
- **Extend to outpatient settings:** Establish surveillance in ambulatory care where majority of antibiotics are prescribed; integrate with existing Prescription Drug Monitoring Programs
- **Integrate One Health data:** Link human surveillance (NHSN) with animal agriculture surveillance (NARMS) and environmental monitoring in unified platforms accessible to public health officials
- **Require public reporting:** Make facility-level antibiotic use data publicly available through interactive dashboards to create transparency and accountability

3. Create Financial Incentives for Antimicrobial Stewardship

Tie reimbursement to stewardship quality to drive behavior change.

Centers for Medicare & Medicaid Services (CMS) should implement:

- **Startup funding for small/rural hospitals:** Provide grants for stewardship program development in facilities lacking resources for dedicated personnel
- **Reward demonstrated improvement:** Create bonus payments for facilities showing measurable reductions in inappropriate prescribing without adverse patient outcomes

4. Strengthen Agricultural Antimicrobial Restrictions

Address agricultural sector contributing to resistance development.

FDA and USDA should implement:

- **Ban remaining growth promoters:** Complete phase-out of medically important antibiotics for production purposes
- **Restrict disease prevention uses:** Prohibit routine administration to healthy animals; require veterinary diagnosis before treatment as done in EU
- **Eliminate critically important antibiotics:** Ban agricultural use of WHO highest priority critically important antimicrobials including fluoroquinolones and third/fourth generation cephalosporins
- **Strengthen Veterinary Feed Directive enforcement:** Increase inspection frequency for feed mills and farms; impose meaningful penalties for violations rather than warnings
- **Implement usage reporting:** Mandate farm-level antimicrobial use data collection similar to Denmark's VetStat system to establish baselines and track reduction progress toward EU Farm to Fork Strategy target of 50% reduction by 2030.

5. Establish State-Level Prescriber Accountability Systems

Federal leadership should be complemented by state action to change prescriber behavior.
State legislatures and medical boards should implement:

- **Mandate continuing education:** Require all prescribers (physicians, nurse practitioners, physician assistants) to complete antimicrobial stewardship training as condition of license renewal every 2 years
  - This may be also possible **through current state programs** (ex. **Amending Section 239 of Public Health Law** in NY to include antimicrobial stewardship as component of infection control training)
- **Expand Prescription Drug Monitoring Programs:** Extend systems currently tracking opioids to flag inappropriate antibiotic prescribing patterns (multiple prescribers, excessive durations, inappropriate indications)

6. Invest in Research for Antibiotics and Alternatives

Direct federal research investment complements market incentives.

NIH and BARDA should prioritize:

- **Clinical trials optimization:** Increase funding for **Antibacterial Resistance Leadership Group** (ARLG) supporting trials that optimize dosing and duration of current antibiotics and validate new diagnostics
- **Alternative therapeutics development:** Invest in bacteriophage therapy, monoclonal antibodies, anti-virulence compounds, and immunotherapies offering non-antibiotic treatment options that don't create resistance pressure
- **Current research:** Fund studies on resistance mechanisms, host-pathogen interactions, microbiome impacts, and horizontal gene transfer to inform next-generation interventions
- **Rapid diagnostics acceleration:** Prioritize technologies enabling point-of-care pathogen identification and susceptibility testing within 30 minutes to enable precision prescribing

7. Support Global Capacity Building

U.S. policy cannot succeed in isolation given AMR's transboundary nature.

USAID, CDC, and State Department should implement:

- **Sustained LMIC funding:** Provide $1 billion+ annually for LMIC surveillance infrastructure, laboratory quality systems, and personnel training recognizing that resistance emerging anywhere threatens populations everywhere
- **Technology transfer facilitation:** Support local production of essential diagnostics and antibiotics in LMICs through voluntary licensing and manufacturing partnerships
- **Regional surveillance networks:** Fund One Health platforms integrating human, animal, and environmental data across regions (Africa, Asia-Pacific, Latin America)
- **WHO GLASS technical assistance:** Ensure U.S. support helps countries generate standardized, comparable AMR data for global monitoring and response coordination

Global investment serves U.S. interests directly: Resistance emerging in any location can spread internationally through travel, trade, and migration. Supporting LMIC capacity prevents resistance development at source and enables early detection of emerging threats before they reach U.S. borders.

Realistic Expectations

Perfect compliance is neither achievable nor necessary. The goal is not elimination of all inappropriate antibiotic use or complete prevention of resistance emergence—both are impossible. Rather, the objective is substantial reduction: moving from current levels where 30-50% of outpatient antibiotic prescriptions are inappropriate to 15-25% inappropriate; reducing agricultural antimicrobial use by half while maintaining productivity; slowing resistance emergence rates to preserve existing antibiotics' effectiveness for decades longer than current trajectory predicts. Therefore, even partial implementation yields significant returns. A 25% reduction in inappropriate prescribing prevents thousands of resistant infections annually. Slowing agricultural resistance development by half extends the useful life of critically important antibiotics. Detecting novel resistance mechanisms months earlier through enhanced surveillance enables faster containment responses. Moreover, the policy pathway exists; political will remains the limiting factor. The investment required—approximately $3-4 billion annually at peak—represents less than 0.2% of federal healthcare spending to address a threat causing tens of billions in annual costs. The question is not whether we can afford to act, but whether we can afford the consequences of continued inaction

Conclusion

Antimicrobial resistance (AMR) is an accelerating global public health threat that undermines the treatment of infectious diseases and the safety of routine and advanced medical care. Driven by inappropriate antimicrobial use in human health and agriculture, environmental dissemination, and persistent regulatory and access inequities, AMR is already responsible for over one million deaths annually and imposes substantial economic costs worldwide. As former U.S. CDC Director Tom Frieden has warned, “If we use antibiotics when not needed, we may not have them when they are most needed.” Despite the existence of international frameworks and national action plans, current responses remain insufficient due to gaps in surveillance, enforcement, and sustainable investment, particularly in low- and middle-income countries.

This policy brief outlines feasible, evidence-based interventions scaled to implementation capacity. Phased surveillance and targeted enforcement can deliver measurable progress in resource-limited settings, while high-income countries can leverage existing infrastructure to strengthen stewardship, restore the antimicrobial development pipeline, regulate agricultural use, and support global capacity building. Elimination of AMR is neither achievable nor required; sustained reductions in inappropriate use and earlier detection of resistance can preserve antimicrobial effectiveness, reduce mortality, and limit long-term costs. But, acting now is not optional—it is the only path that preserves antimicrobial effectiveness and prevents a largely avoidable public health failure from becoming irreversible.

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