R&D for **Antimicrobial Resistance**

How new tools can transform the fight

GHTC global health technologies coalition

Antimicrobial resistance (AMR) occurs when microbes evolve to no longer respond to treatment. The World Health Organization considers it one of the top global health threats, given it puts the gains of modern medicine at risk and threatens progress against some of the world's deadliest diseases. In recent years, governments have increased action to reinvigorate the antimicrobial research pipeline and tackle major drivers of AMR, such as antimicrobial misuse and overuse, but much work remains to be done. The current clinical pipeline for products to address priority pathogens is insufficient, and growing resistance to antibiotics, antivirals, antifungals, and antiparasitic drugs is steadily reducing our arsenal of treatments for common threats. To confront this crisis, we need new antimicrobials and antimicrobial alternatives, as well as new diagnostics and vaccines to improve surveillance and prevention.

5 million
deaths associated with AMR every year

$100 trillion
projected cost of AMR to global economy from 2014 to 2050

1 in 5
cancer patients in treatment are hospitalized due to an infection

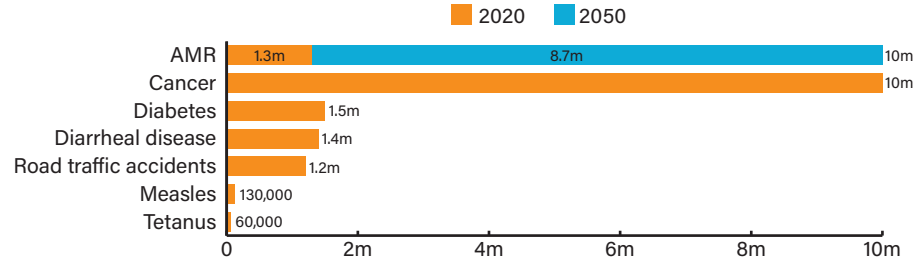
Research successes

New technologies are aiding the fight against AMR:

- Cifiderocol and sulbactam-durlobactam were approved by the FDA in 2020 and 2023, respectively, as **new antibiotics for hospital-acquired and ventilator-associated bacterial pneumonia**, providing additional treatment options for bacterial strains prone to resistance.
- Several **new antibiotics**, including pivmecillinan, vaborbactam, plazomicin, and cefiderocol, have been approved by the FDA in recent years to **treat urinary tract infections**, providing new options for those with infections unresponsive to existing drugs.
- Pretomanid, a **new drug for highly drug-resistant tuberculosis** (TB) developed with USAID and NIH support, was approved by the FDA in 2019 as part of a combination regimen that has dramatically improved treatment outcomes and reduced treatment times.
- **Pneumococcal vaccines for children**, first introduced in the 2000s, have saved millions of lives while also **reducing the use of antibiotics**. Universal coverage of these vaccines could prevent 11.4 million days of antibiotic use per year in children under five.
- **New tests that identify whether infections are resistant to certain treatments** have been introduced, including a BARDA-supported panel test that detects 13 resistance genes and rapid, automated molecular tests for drug-resistant TB.

Deaths from drug-resistant infections set to skyrocket

Predicted mortality from antimicrobial-resistant* infections versus today's common causes of death (in millions)



* resistant to antibiotics, antivirals, antifungus, and antiparasitics. Source: Bracing for superbugs 2023 (UN Environmental Programme)

Key missing tools

To control AMR, we need innovative tools to prevent, diagnose, and treat drug-resistant infections, including:

- Novel **antimicrobials** to treat priority pathogens.
- Expanded **antimicrobial options designed for children and infants.**
- **Oral formulations of existing and investigational antimicrobials**, which are easier to administer in outpatient settings and can improve treatment adherence to prevent further resistance.
- **Rapid, point-of-care diagnostic tests** that identify infections and determine if they are resistant to ensure appropriate treatment and prevent the misuse or overuse of existing antimicrobials.
- **Vaccines and other prevention options** to avert infections in the first place.
- **Alternatives to antimicrobials**, such as bacteria-targeting viruses called bacteriophages, anti-virulence therapies, and innovative approaches to manipulate the gut microbiome.

Breakthroughs on the brink

- Zoliflodacin, a new first-in-class antibiotic that completed Phase 3 trials, which, if approved, would become the **first new antibiotic for treating gonorrhea** in decades.
- VE303, a **new oral treatment for *Clostridioides difficile***, a potentially life-threatening bacterial infection that causes diarrhea and colon inflammation, which is undergoing Phase 3 trials with support from BARDA.
- Cefepime-taniborbactam, a **new antibiotic developed for treating complicated urinary tract infections** in adults, which completed Phase 3 trials. A pediatric formulation is also being advanced for children and newborns.
- A **protective vaccine against typhoid fever and invasive nontyphoidal Salmonellosis**, a disease caused by salmonella subspecies found almost exclusively in sub-Saharan Africa—now in first-in-human studies—could help address the estimated 70,000 deaths from the disease and 20,000 deaths from *Salmonella enetrica* serovar Typhi annually in the region.
- A **maternal vaccine to prevent sepsis in newborns** targeting *Escherichia coli,* the bacteria responsible for a large portion of sepsis infections in newborns. It is being advanced with BARDA and NIH support and would be administered to expectant mothers who pass antibodies on to their babies in utero and through breast milk.
- **Dosing validation of two existing antibiotics (fosfomycin and flomoxef) in newborns** to expand treatment options for neonatal sepsis. Forty percent of infections causing neonatal sepsis in hospitals are resistant to standard treatments.
- A portable, rapid **diagnostic test to diagnose gonorrhea infection and detect resistance** to ciprofloxacin, a former frontline oral antibiotic that can no longer treat drug-resistant infections. The test, being advanced with BARDA and NIH support, will enable doctors to treat patients with ciprofloxacin when appropriate while reserving ceftriaxone, the only other antibiotic effective against drug-resistant gonorrhea.
- A **first-of-its kind infectious disease diagnostic platform**, advanced with BARDA and NIH support, that rapidly identifies the pathogen causing an infection and profiles its antibiotic susceptibility in hours, rather than the days typically required for culture-based tests, the current standard.
- **Phage therapy**, a promising alternative to antibiotics, which uses specialized viruses called bacteriophages to target, infect, and kill bacteria. With NIH support, researchers are advancing potential phage therapies to treat TB, cholera, staph infections, and more.

US Government R&D efforts

The US government is leading efforts to advance research and development (R&D) to combat AMR through a whole-of-government approach:

- **National Institutes of Health** (NIH) conducts basic science and clinical research to advance new antimicrobials and other technologies to combat AMR and provides in-kind assistance to the global Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) nonprofit partnership.
- **Biomedical Advanced Research and Development Authority** (BARDA) supports early-stage and advanced development of antimicrobials and other products through direct R&D investments and financial support of CARB-X.
- **Centers for Disease Control and Prevention** (CDC) develops diagnostic tools, operates an AMR isolate bank to provide samples to product developers, and supports domestic and global surveillance and stewardship activities, including operating a global laboratory and response network.
- **Department of Defense** supports global surveillance activities through its overseas laboratories and supports the development of select antimicrobials to combat sepsis and the threat of drug resistance in combat wounds.
- **US Department of Agriculture** conducts veterinary surveillance and stewardship activities and advances R&D for antimicrobials and vaccines for animal populations.
- **US Agency for International Development** (USAID) advances product development and implementation research for select global threats impacted by rising drug resistance, including malaria, TB, and HIV/AIDS.
- **Food and Drug Administration** (FDA), alongside approving products for use in the United States, also cooperates the AMR isolate bank with CDC and provides guidance to product developers.

R&D for **Antimicrobial Resistance**
advancing **innovation** to save lives

Scan this code or visit
ghtcoalition.org/resources-item/healthareas
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