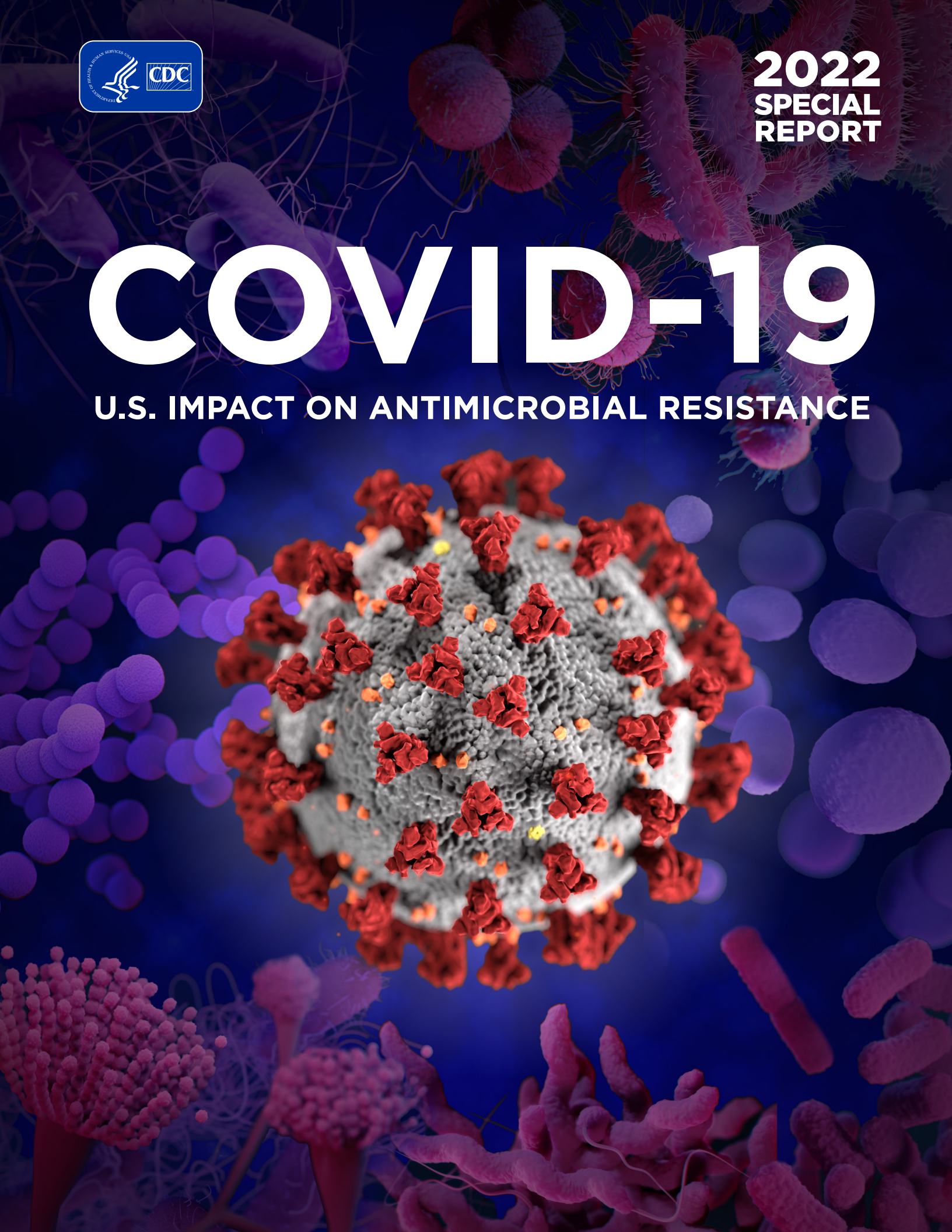
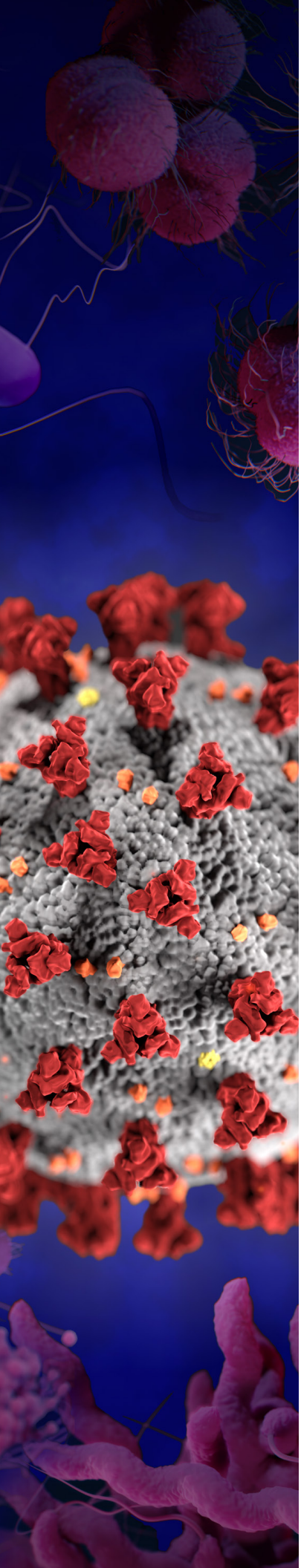
2022
SPECIAL
REPORT

COVID-19

U.S. IMPACT ON ANTIMICROBIAL RESISTANCE





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U.S. IMPACT ON ANTIMICROBIAL RESISTANCE

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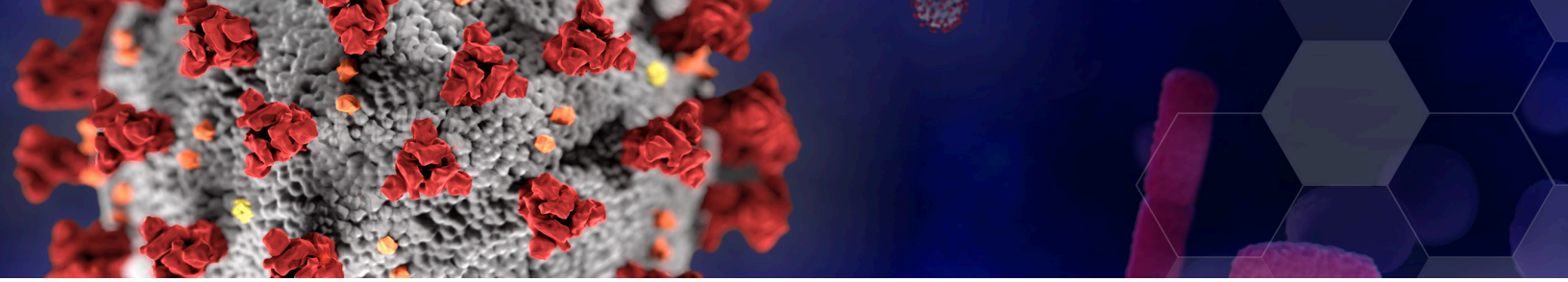


Foreword

As an infectious disease physician, I have a frontline understanding of antimicrobial resistance—when germs like bacteria and fungi defeat the drugs designed to kill them. **Antimicrobial resistance was one of our greatest public health concerns prior to the COVID-19 pandemic, and it remains so.**

Since 2013, CDC has been sounding the alarm about this potential pandemic threat in the United States across health care, the food supply, the environment, and the community. CDC showed as recently as 2019 that more than 3 million Americans acquire an antimicrobial-resistant infection or *Clostridioides difficile* infection (often associated with taking antimicrobials) each year. Nearly 50,000 people die from these threats. And a January 2022 report shows antimicrobial resistance is a leading cause of death globally, with the highest burden in low-resource countries.

After more than two years of responding to COVID-19, the threat of antimicrobial resistance is not only still present but has become an even more prominent threat. Germs continue to spread and develop new types of resistance. More investments are needed to continue addressing antimicrobial resistance while simultaneously responding to COVID-19 and other health threats.

In CDC's 2019 Antibiotic Resistance Threats Report, CDC showed that prevention is the most foundational and successful tool we have to protect people from antimicrobial-resistant infections and their spread. Between 2012 and 2017, deaths from antimicrobial resistance decreased by 18% overall and nearly 30% in hospitals. This is largely due to significant investments in U.S. prevention efforts, like improving infection prevention and control as well as antimicrobial use.

Rochelle P. Walensky, MD, MPH
Director, Centers for Disease Control and Prevention

However, as the pandemic pushed healthcare facilities, health departments, and communities near their breaking points in 2020, we saw a significant increase in antimicrobial use, difficulty in following infection prevention and control guidance, and a resulting increase in healthcare-associated, antimicrobial-resistant infections in U.S. hospitals.

In fact, CDC identified significant increases in infections across many healthcare-associated pathogens, such as carbapenem-resistant *Acinetobacter*, extended-spectrum beta-lactamase-producing Enterobacterales, vancomycin-resistant Enterococcus, and drug-resistant *Candida*. In fact, resistant hospital-onset infections and deaths both increased at least 15% during the first year of the pandemic.

Additionally, because many clinics and healthcare facilities limited services, served fewer patients, or closed their doors entirely in the face of challenges from COVID-19, there is a lack of data in 2020 for many pathogens that spread in the community, like sexually transmitted drug-resistant gonorrhea. Some laboratories experienced supply shortages, such as testing kits for sexually transmitted infections.

> These setbacks *can* and *must* be temporary. The COVID-19 pandemic has made it clear—prevention is preparedness.

In some instances, public health resources were forced to shift from tracking antimicrobial resistance to tracking COVID-19 cases.

The pandemic also greatly impacted antibiotic prescribing. Historic gains made on antibiotic stewardship were reversed as antibiotics were often the first option given to treat those who presented with a febrile pulmonary process even though this presentation often represented the viral illness of COVID-19, where antibiotics are not effective. Antibiotic and antifungal stewardship—one of our best prevention tools—remains critically important. These drugs are a shared resource, meaning that using antibiotics for one purpose or patient can impact how they work for another. We must be responsible stewards of these drugs, no matter where they are used, to prolong and preserve their efficacy and protect patients of today and tomorrow.

These setbacks *can* and *must* be temporary. The COVID-19 pandemic has made it clear—prevention is preparedness. **We must prepare our public health systems to fight multiple threats, simultaneously. Because antimicrobial resistance will not stop, we must meet the challenge.**

We must invest in the prevention-focused public health actions that we know work, such as accurate laboratory detection, rapid response and containment, effective infection prevention and control, and expansion of innovative strategies to combat antimicrobial resistance. These include alternatives to antibiotics and antifungals, new vaccines to combat infections that can develop antimicrobial resistance, and novel decolonizing agents to stop the spread of antimicrobial-resistant germs by people who may not know they are carriers.

Although we have faced many obstacles in the United States over these past few years, we must stay focused on preparing for the next public health threat, whenever and wherever it emerges. The COVID-19 pandemic has showcased that the investments CDC has made in the antimicrobial resistance infrastructure are supporting flexibility and resiliency in public health systems. If properly resourced, we can continue to build a resilient public health system to keep our nation safe. The foundational capacity we need to address antimicrobial resistance will not only slow the spread of these infections but will also serve as an investment in the critical core capacity for public health threats.

During the COVID-19 pandemic, hospitals treated sicker patients who required more frequent and longer use of catheters and ventilators. Hospitals also experienced supply challenges, reduced staff, and longer visits during the pandemic.

Unprecedented challenges could have contributed to reduced comprehensive prevention practices, which are key to stopping antimicrobial-resistant infections and their spread.

The COVID-19 pandemic has taught us all hard lessons and has reminded us that the best way to prevent a looming antimicrobial-resistance pandemic is to invest in preparedness.

Now is the time for us to address our current antimicrobial-resistant threats, while simultaneously preparing for unknown emerging threats in the future.

COVID-19 Impacts on

Antimicrobial Resistance Tracking and Data:

Enhance data systems and sharing to prevent infections and stay ahead of antimicrobial resistance

CDC uses several data sources and systems to track antimicrobial resistance in the United States and abroad. Knowing where and how changes in resistance are occurring helps us find solutions to prevent spread and slow resistance, especially in outbreak responses.[1]

Recently, the United States has been building a solid foundation for public health preparedness to address antimicrobial resistance.

- Some of thee CDC programs focused on antimicrobial resistance were repurposed during the pandemic to offer COVID-19 testing support or surge capacity to overwhelmed labs.
- Since 2016, CDC has used its Antimicrobial Resistance Laboratory Network (AR Lab Network) to detect known and emerging antimicrobial resistance in every state.
- It continued to collect isolates throughout 2020 using established processes, but some isolates remain untested due to testing backlogs.

> CDC's AR Lab Network received and tested 23% fewer specimens or isolates in 2020 than in 2019.[2]

The number of bacterial whole genome sequence (WGS) submissions to the AR Lab Network via PulseNet in 2020 was about 21% less than the average number of isolates analyzed 2015-2019 by WGS or legacy methods. This also reduced the number of sequences the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) used to predict antimicrobial resistance related to intestinal illnesses.

More resources are needed to continue establishing a resilient public health system that can maintain capacity to respond to antimicrobial resistance while also responding to other threats. Without an infrastructure and supply chains grounded in preparedness, critical antimicrobial resistance data will be delayed again when the next threat emerges. We must address gaps identified before the COVID-19 pandemic, including expanding the public health workforce, increasing local access to the best detection tools and technology, and expanding global lab capacities.

During the COVID-19 pandemic, the detection and reporting of antimicrobial resistance data slowed tremendously because of changes in patient care, lab supply challenges, testing, treatment, and the bandwidth of healthcare facilities and health departments.

Infections in the Community

- During the COVID-19 pandemic, many bacterial and fungal infections went potentially undiagnosed and untreated. The COVID-19 pandemic changed healthcare-seeking behavior and access to health care when outpatient clinics closed or limited appointments, resulting in fewer in-person visits. For example, people with mild intestinal infections that cause diarrhea may have let the illness run its course at home instead of seeking care. This may have also been the case for respiratory infections, such as those caused by *Streptococcus pneumoniae*.
- Rapid treatment can keep patients from getting sicker, prevent the pathogen from spreading, and slow the development of resistance. For example, if left undetected and untreated, gonorrhea can cause serious health complications and continue circulating in a community, increasing the chances of it developing resistance to available treatments.
- Another example is tuberculosis (TB), which is spread through the air. TB is treatable and curable, but people with TB can die if they do not get proper treatment. In 2020, reported TB cases substantially decreased in the United States, probably due to factors related to the COVID-19 pandemic, including undiagnosed cases (a result of decreased medical visits) and misdiagnosed cases. Decreases in immigration and increased use of respiratory control practices may also have contributed to the decline in cases.

Because of pandemic impacts, 2020 data are delayed or unavailable for 9 of the 18 antimicrobial resistance threats.

- *Clostridioides difficile (C. diff)*
- Drug-resistant *Neisseria gonorrhoeae*
- Drug-resistant *Campylobacter*
- Drug-resistant nontyphoidal *Salmonella*
- Drug-resistant *Salmonella* serotype Typhi
- Drug-resistant *Shigella*
- Drug-resistant *Streptococcus pneumoniae*
- Erythromycin-resistant group A *Streptococcus*
- Clindamycin-resistant group B *Streptococcus*

Available data show an alarming increase in resistant infections starting during hospitalization, growing at least 15% from 2019 to 2020.

- Carbapenem-resistant *Acinetobacter* (↑78%)
- Antifungal-resistant *Candida auris* (↑60%)*
- Carbapenem-resistant Enterobacterales (↑35%)
- Antifungal-resistant *Candida* (↑26%)
- ESBL-producing Enterobacterales (↑32%)
- Vancomycin-resistant Enterococcus (↑14%)
- Multidrug-resistant *P. aeruginosa* (↑32%)
- Methicillin-resistant *Staphylococcus aureus* (↑13%)

**Candida auris* was not included in the hospital-onset rate calculation of 15%. See Data Table and Methods for more information on this pathogen.

Invest in Adaptable Programs

Established networks, like the AR Lab Network, can be tapped into during an emergency, offering foundational strength and flexibility when challenges arise.

The seven regional labs in CDC's AR Lab Network supported each other during the pandemic to maintain critical national testing for antimicrobial resistance. Some labs offered tests outside of their typical regions when others were challenged by supply shortages or staff and equipment were diverted to COVID-19 testing.

The National Tuberculosis Molecular Surveillance Center used its AR Lab Network sequencing capacity to study SARS-CoV-2, the virus that causes COVID-19. The lab sequenced more than 4,700 SARS-CoV-2 genomes in 2020 to support contact tracing and help stop the virus from spreading. These collaborations display the flexibility of the AR Lab Network and how CDC's antimicrobial resistance investments can be adapted during a crisis.

The AR Lab Network sequenced more than 4,700 SARS-CoV-2 genomes in 2020 to support COVID-19 contact tracing and help stop the virus from spreading.

ARLABnetwork

What's Next: CDC is exploring investments in the U.S. infrastructure to better respond to the challenges of antimicrobial resistance and emerging threats simultaneously.

- Supporting uninterrupted laboratory supplies and equipment for patient care, infection control, and data tracking during emergencies and surge outbreaks.
- Merging strategies to respond to COVID-19 and antimicrobial resistance, such as using telehealth for contact tracing, supporting specimen self-collection, or offering express clinics that allow walk-in testing for sexually transmitted infections.
- Expanding the use of automated data to the National Healthcare Safety Network (NHSN) to reduce manual data collection and submission, which would allow healthcare facilities to send information on antibiotic use and antimicrobial resistance.

Pandemic-related challenges hindered many infection prevention and control practices like hand hygiene, cleaning equipment, separating patients, and using personal protective equipment (PPE)—undoing some progress on combating antimicrobial resistance.

COVID-19 Impacts on
Preventing Infections:

Prevent infections and reduce the spread of germs

Antimicrobial-resistant infections are amplified in health care. Germs spread among patients and across facilities. The inpatient population in 2020 was very different from the pre-pandemic population—hospitals saw higher numbers of sicker patients (hospitalization could not be avoided) who needed an extended length of stay. This increased their risk for resistant infections.

When done consistently and correctly, preventing infections is one of our greatest tools for combating antimicrobial resistance and saving lives.[3] We must continue building the national capacity for infection prevention and control to ensure these practices are put into action consistently.

As of 2017, dedicated infection prevention and control efforts in the United States contributed to reduced deaths from antimicrobial-resistant infections by 18% overall and by nearly 30% in hospitals.[4] However, the pandemic has undone much of this progress.

- Resistant hospital-onset infections and deaths both increased at least 15% during the first year of the pandemic. In a 2021 analysis, CDC also reported that, after years of steady reductions in healthcare-associated infections (HAIs), U.S. hospitals saw significantly higher rates for four out of six types of HAIs in 2020.[5] Many of these HAIs are resistant to antibiotics or antifungals.
- There were more and sicker patients during the pandemic who required more frequent and longer use of catheters and ventilators. This may have increased risk of HAIs and spread of pathogens, especially when combined with personal protective equipment and lab supply challenges, reduced staff, and longer lengths of stay.
- Acute care hospitals also saw more *Candida auris* cases, including in COVID-19 units.[6] *C. auris* has previously been a threat in post-acute care facilities (e.g., long-term care). The increased spread in hospitals could be a result of staffing and supply shortages and changes in infection prevention and control practices.

The United States has been building a solid foundation for public health preparedness and health systems resilience to address antimicrobial resistance. Before 2020, CDC highlighted the need for a strong foundation for health departments and healthcare facilities to rapidly identify and contain threats before they can spread. Prior to the pandemic, the *U.S. National Strategy for Combating Antibiotic-Resistant Bacteria* (CARB National Action Plan) set a goal that CDC double its investments in health departments to increase infection control and other prevention efforts.[7] In 2021, the U.S. government provided temporary funding to health departments through the COVID-19 pandemic that addresses some of these gaps. However, health departments will need sustainable resources to ensure these capacities can continue.

Preventing infections is one of the greatest tools for combating antimicrobial resistance—saving lives and reducing healthcare costs.

6 of the **18** most alarming **antimicrobial resistance** threats cost the U.S. more than **$4.6 billion annually**[8]

Vancomycin-resistant ***Enterococcus (VRE)***

Carbapenem-resistant ***Acinetobacter species***

Methicillin-resistant ***Staphylococcus aureus (MRSA)***

Carbapenem-resistant **Enterobacterales (CRE)**

Multidrug-resistant (MDR) ***Pseudomonas aeruginosa***

Extended-spectrum cephalosporin resistance in Enterobacterales suggestive of extended- spectrum β-lactamase **(ESBL)** production

Investing in Healthcare Training & Education

It is essential to train anyone working in a healthcare setting on infection prevention and control and to maintain these practices to protect themselves, their coworkers, and their patients. CDC's Project Firstline was developed at the start of the pandemic to meet the infection control educational needs of the diverse U.S. healthcare workforce. Investing in healthcare workers, health departments, and programs like Project Firstline:

- Strengthens capacity to prevent, detect, and contain outbreaks of COVID-19 and antimicrobial-resistant infections.
- Expands infection prevention and control training and education to all types of healthcare staff.
- Allows local jurisdictions to provide surge capacity to facilities for clinical services.

In its first year, Project Firstline and partners:[9]

- Developed more than 130 educational products on proper infection prevention and control practices for COVID-19.
- Trained 33,300 U.S. healthcare workers via 300 educational infection prevention and control events.
- Registered more than 6,500 healthcare workers in continuing education courses through CDC's online learning platform.
- Launched an initiative with the American Hospital Association and the League for Innovation in the Community College to integrate enhanced infection prevention and control content into healthcare training at community colleges, including addressing disparities in healthcare training and access to resources for first generation or non-English speaking students.

Assessments During the Pandemic Identified Infection Control Gaps

From January through July 2020, CDC's investments to build capacity in state and local health departments allowed them to perform 14,259 consultations in response to potential COVID-19 outbreaks at healthcare facilities.[10]

14,259
Consultations

Outbreak consultations frequently included infection control assessments, which were conducted onsite or remotely using CDC's Infection Control Assessment and Response tools or similar tools adapted at the state or local level.

2,105
Onsite assessments

4,151
Remote assessments

Most of these assessments occurred in nursing homes or assisted living facilities.

Long-term care facilities

Infection control assessments and consultations were a critical component of the response to COVID-19 outbreaks, allowing facilities to rapidly address gaps in infection control practices and reduce the spread of COVID-19.

Closing infection control gaps

What's Next: CDC is exploring investments in the U.S. infrastructure to better respond to the challenges of antimicrobial resistance and emerging threats simultaneously.

- Continuing to extend high-quality infection prevention and control training to all healthcare professionals.
- Increasing infection prevention and control implementation in facilities beyond hospitals, such as nursing homes and other long-term care facilities.
- Communicating clearly to the public and fostering conversations on topics like how germs spread and the importance of keeping hands clean.
- Identifying barriers to implementing and developing plans to maintain quality infection prevention and control practices while supporting efforts to respond to new threats.
- Increasing investments in state and local health departments, as part of the CARB National Action Plan.

While antibiotic use throughout the pandemic varied across healthcare settings, antibiotics were commonly prescribed to patients for COVID-19 —even though antibiotics are not effective against viruses.

COVID-19 Impacts on
Antibiotic Use:

Improve the use of antibiotics wherever they are used and improve access

When a patient (human or animal) receives an antibiotic they do not need, not only does the patient get no benefit, but they are also put at risk for side effects (e.g., allergic reactions, toxicity that affects organ function, *C. diff*). Evidence suggests that 1 in 5 hospitalized patients who receive an antibiotic has an adverse drug event.[22]

When COVID-19 cases increased in hospitals, so did antibiotic use. Antibiotics were frequently started upon admission, but several studies have shown that patients who had COVID-19 were rarely also infected with bacteria when admitted.[11,12]

Antibiotics and antifungals can save lives, but any time they are used—for people, animals, or plants—they can contribute to resistance.

Antibiotic Use Varied During the COVID-19 Pandemic

Hospitals

- From March 2020 to October 2020, almost 80% of patients hospitalized with COVID-19 received an antibiotic.[13]
- Antibiotic use was lower overall as of August 2021 compared to 2019 but increased for some antibiotics like azithromycin and ceftriaxone. Approximately half of hospitalized patients received ceftriaxone, which was commonly prescribed with azithromycin.
- This likely reflects difficulties in distinguishing COVID-19 from community-acquired pneumonia when patients first arrive at a hospital for assessment.

Outpatient Settings

- Antibiotic use significantly dropped in 2020 compared to 2019 due to less use of outpatient health care and less spread of other respiratory illnesses that often lead to antibiotic prescribing.
- However, in 2021 outpatient antibiotic use rebounded. While antibiotic use was lower overall in 2021 compared with 2019, in August 2021, antibiotic use exceeded prescribing in 2019 by 3%.
- From 2020 through December 2021, most antibiotic prescriptions for adults were for azithromycin and increases in azithromycin prescribing corresponded to peaks in cases of COVID-19. After an initial peak in azithromycin prescribing in March 2020, azithromycin use decreased during the pandemic.
- By August 2021, there was still more azithromycin prescribing than in August 2019.

Nursing Homes

- Antibiotic use in nursing homes spiked alongside surges of COVID-19 cases but remains lower overall.
- However, azithromycin use was 150% higher in April 2020 and 82% higher in December 2020 than the same months in 2019. Azithromycin prescribing remained elevated through October 2020.
- In 2021, antibiotic use overall was, on average, 5% lower than 2019. This decrease might be due to fewer nursing home residents during this time.

Public health must continue educating consumers, healthcare providers, and industry on the value, risks, and best practices of antibiotics and antifungals.

- These drugs are often a treatment option for emerging infectious diseases, particularly when no other treatment options are available or known.
- While some of this prescribing can be appropriate when risks for related bacterial or fungal infections are unknown, this antibiotic prescribing can also put patients at risk for side effects and further the pressure for resistance to develop and spread.
- Healthcare workers can protect patients by ensuring antibiotics and antifungals are only used when they are effective and needed, such as to treat life-threatening conditions caused by fungi or bacteria, like sepsis.

The United States has been building a solid foundation for public health preparedness to address antimicrobial resistance.

- Prior to the pandemic, CDC's Core Elements of Antibiotic Stewardship (Core Elements) helped many hospitals improve their antibiotic use. In 2020, more than 90% of U.S. hospitals had an antibiotic stewardship program aligned with CDC's Core Elements.[14]
- As part of the CARB National Action Plan, CDC aims to continue this progress in outpatient settings.
- CDC also aims to support and encourage antimicrobial resistance preventives, such as decolonization therapies, and vaccines coming to market. This will help reduce antibiotic and antifungal use by preventing infections from occurring or offering alternative treatments to these important drugs.

NHSN
NATIONAL HEALTHCARE SAFETY NETWORK

Tracking Antibiotic Use to Optimize Prescribing Practices

CDC's NHSN allows healthcare facilities to automate monitoring antibiotic use. These data inform interventions to optimize prescribing, which improves treatment effectiveness, protects patients from harms caused by unnecessary antibiotic use, and slows antimicrobial resistance. In CDC's 2019 AR Threats Report, CDC noted that tracking antibiotic use in settings like nursing homes and long-term care facilities is often non-existent or difficult to implement.

While more work needs to be done to improve tracking antibiotic use and stewardship efforts, the number of hospitals reporting antibiotic use data from 2018 through 2021 more than doubled. This helps CDC and facilities better monitor prescribing and use.

What's Next: CDC is exploring investments in the U.S. public health infrastructure to better respond to the challenges of antimicrobial resistance and emerging threats simultaneously.

- Optimizing antibiotic and antifungal use across all healthcare settings and wherever they are used.
- Continuing to improve antibiotic and antifungalprescribing and use across healthcare settings, including encouraging use of CDC's NHSN antibiotic use module for reporting and implementing CDC's Core Elements across settings.
- Tracking antibiotic and antifungal prescribing and evaluation for improvements toward optimal use.
- Enhancing communication of the latest antibiotic and antifungal use recommendations and guidance to healthcare workers.
- Supporting the development of new vaccines to address antimicrobial-resistant pathogens and other conditions for which antibiotics and antifungals are commonly prescribed.
- Working with partners to promote optimal antibiotic and antifungal use and appropriate tracking for companion animals and plant agriculture.
- Supporting basic and applied research and development for new antibiotics and antifungals, therapeutics, and vaccines.

COVID-19 Impacts on
Environment (e.g., water, soil) and Sanitation:

Addressing antimicrobials and antimicrobial-resistant threats in the environment

Antimicrobial resistance is a One Health issue, impacting the health of humans, animals, plants, and the environment. Efforts to identify antimicrobial-resistant germs, track the spread of resistance, and measure the effect of antibiotic or antifungal use require a One Health approach to surveillance.

While more research is needed to better understand how resistance develops and spreads in the environment, we do know that people can contaminate it through fecal waste. In 2018, CDC funded the University of South Carolina (U of SC) to measure resistance genes in wastewater and in treatment plant workers at municipal wastewater treatment plants.[15]

When the pandemic started, CDC recognized that the research platform to look for resistance in wastewater could also look for SARS-CoV-2 RNA (which carries genetic information) as a marker of COVID-19 in communities. Through supplementary funding to support the COVID-19 response, CDC and U of SC built upon the initial surveillance project. This work confirmed appropriateness of existing safety precautions and informed guidance drafted by partners.

CDC is looking at ways to expand surveillance through existing systems to monitor antimicrobial resistance from multiple sources across One Health. CDC is also helping to strengthen the national infrastructure for antimicrobial resistance surveillance data by improving capacity, utility, timeliness, and the use of harmonized terminology.

Exploring New Public Health Tools to Slow Resistance

Community level wastewater surveillance can help public health detect antimicrobial resistance, including new threats, before they are detected in clinical samples.[16] Wastewater from healthcare facilities could also be a key source of resistant germs, resistant genes, and antibiotic or antifungal residues. Hospital patients can have some of the most resistant infections and are commonly prescribed antibiotics or antifungals.

Monitoring healthcare facility wastewater could provide a non-invasive approach to identifying resistance in a facility and aid in decision making, like performing screening to identify cases early and implement appropriate interventions to prevent spread. Researchers could look for genes that confer resistance, especially to last-line drugs like carbapenems and colistin, to identify resistance that might be present but not yet detected in the healthcare setting.

In 2020, researchers leveraged an existing project funded by CDC's AR Solutions Initiative focused on antimicrobial resistance to better understand the burden of COVID-19 in communities—using wastewater, also called sewage.

5 Benefits of Wastewater Surveillance for Antimicrobial Resistance[17]

1. **Captures silently spreading germs.** People infected with antimicrobial-resistant germs will shed these germs in their stool or wash water, whether they have symptoms or not.
2. **Operates independent of healthcare and clinical capacity.** Antimicrobial-resistant pathogens that are causing illness are still detected even if a person does not go to a healthcare professional or have access to testing.
3. **Is efficient.** One sample of wastewater can represent millions of people in a large wastewater system.
4. **Moves fast—from toilet to data in a week or less.** This allows more time to prepare a public health response compared to clinical data.
5. **Provides an early warning system.** Potentially less costly and more effective as an early warning alert system for emerging threats compared to clinical surveillance. This makes it a suitable option to provide a broad snapshot, especially for places with limited existing surveillance and resources.

AR Pathogens Cause Infections Across the One Health Spectrum

In September 2020, CDC established the National Wastewater Surveillance System (NWSS) to provide community-level data on COVID-19 infection trends by looking for markers in wastewater that tell scientists when SARS-CoV-2 is present.[18] CDC currently funds 43 public health jurisdictions to support wastewater activities across 37 states, 4 cities, and 2 territories. By May 2022, NWSS had received data from more than 59,000 wastewater samples from more than 900 sites nationwide.

The United States has been building a solid foundation for public health preparedness to address antimicrobial resistance. The CARB National Action Plan includes a One Health approach, with an expanded effort to understand antimicrobial resistance in the environment. A main challenge to implementing a One Health approach includes the need to better understand the scale and risk to human health associated with antimicrobial resistance in the environment. In addition to efforts related to wastewater surveillance, CDC is also supporting other environmental projects to better understand how antibiotics, antifungals, and antimicrobial-resistant pathogens can spread in water and soil.

Antimicrobial resistance is a One Health issue, impacting humans, animals, plants, and the environment.

What's Next: CDC is exploring investments in the U.S. public health infrastructure to better respond to the challenges of antimicrobial resistance and emerging threats simultaneously.

- Expanding the capacity of NWSS to collect antimicrobial resistance data from wastewater treatment plants and healthcare facilities to continue infectious disease surveillance.
- Studying antimicrobial resistance in community and healthcare wastewater, domestically and globally.
- Expanding global capacities to fight antimicrobial resistance in the environment, as part of the CARB National Action Plan.
- Mapping existing antimicrobial resistance ecology across One Health and monitoring shifts over time, as part of the CARB National Action Plan.

COVID-19 Impacts on

Vaccines, Diagnostics, and Therapeutics:

Invest in development and improved access to vaccines, therapeutics, and diagnostics for better prevention efforts, treatment, and detection

The COVID-19 pandemic highlighted the need to stop the spread of germs before they can cause an infection. Developing therapeutic and preventive products requires dedicated resources and policies to support research, turn discoveries into products, collect data for drug approval, facilitate clinical trials, and conduct post market evaluations on impact.

Vaccines can significantly reduce infection rates, which decreases antibiotic use and the number of resistant germs. For example, drug-resistant *S. pneumoniae* is one of the only germs listed in this report with effective vaccines to prevent infections, including pneumococcal conjugate vaccines (PCVs). The PCV13 vaccine, which the U.S. Food and Drug Administration (FDA) licensed in 2010, protects people from 13 types of pneumococcus, including resistant forms. This vaccine prevented more than 30,000 cases of invasive pneumococcal disease and 3,000 deaths from 2010 to 2013 alone.[19]

> Importantly, the PCV13 vaccine also prolonged the efficacy of the oldest antimicrobial—penicillin—by preventing more resistant forms of pneumococcus.

In 2021, two new pneumococcal conjugate vaccines were licensed for adults—PCV15 and PCV20. With additional serotypes included in these vaccines, even more cases of pneumococcal disease should be prevented.

Research on novel products, like decolonizing agents, can also help reduce the impact of antimicrobial resistance. Some people carry antimicrobial-resistant pathogens in the nose, skin, lungs, or digestive tract without becoming sick or showing symptoms, known as colonization. These germs can eventually cause an infection or people can spread these germs to others.

The CARB National Action Plan supports innovative approaches to developing and deploying diagnostic tests and treatment strategies. Limited return on investment for new diagnostics is also a significant challenge, and the development pathways for some non-antibiotic/antifungal therapeutics remain uncharted.

The COVID-19 pandemic highlighted the importance of prevention. Treatment after an infection occurs is not the only solution and should not be the only option. We need more prevention products, not just new drugs, to stop infections before they happen.

Decolonization is a Great ROI

People can carry resistant germs without symptoms of infection. CDC has invested in decolonization research and testing through CDC's AR Lab Network to stop the silent spread of these dangerous pathogens.

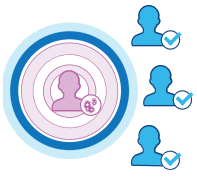
During the pandemic, CDC and the University of California, Irvine leveraged an existing regional public health collaborative with 40 healthcare facilities, including hospitals, long term-acute care hospitals, and nursing homes to conduct COVID-19 outreach to 70 Orange County nursing homes.

Facilities stopped the spread of COVID-19 by using enhanced infection prevention trainings paired with decolonization methods.[20] Staff continue to receive training and are monitoring for additional spread.

31%
fewer staff cases

43%
fewer resident cases

New decolonization agents are needed to make colonized patients less infectious and slow the spread and development of antimicrobial resistance.



INVESTING IN INNOVATION, 2016-2020

The United States has been building a solid foundation for public health preparedness to address antimicrobial resistance. Since 2016, CDC has funded more than 300 projects and collaborated with more than 100 public and private institutions.[21] Data from these projects help CDC better protect people by uncovering places resistant germs live and spread, improving outbreak response, and strengthening infection prevention and control practices. The United States must continue exploring and using innovative solutions to address the gaps identified in combating antimicrobial resistance, which will also prepare the country for new emerging threats.

Since 2016, CDC has invested more than $160 million in research to address knowledge gaps with scalable, innovative solutions such as vaccines, therapeutics, diagnostics and other prevention tools.

What's Next: CDC is exploring investments in the U.S. public health infrastructure to better respond to the challenges of antimicrobial resistance and emerging threats simultaneously.

- Supporting more innovation and research on therapeutics, vaccines, and diagnostics.
- Enhancing interagency collaborations to accelerate research for developing new antibiotics, antifungals, therapeutics, and vaccines, including working with FDA to identify ways to support decolonization products.
- Working to undo negative impacts the COVID-19 pandemic may have had on essential vaccine conversations.
- Supporting the widespread use of vaccines to prevent infections, slow the spread of resistance, and reduce antibiotic use.
- Building a vaccine data platform to inform and accelerate the development of new vaccines, stopping infections before they start, as part of the CARB National Action Plan.

COVID-19 Impacts on

18 Antimicrobial-Resistant Bacteria and Fungi

Threat Estimates

The following table summarizes the latest national death and infection estimates for 18 antimicrobial-resistant bacteria and fungi. The pathogens are listed in three categories—urgent, serious, and concerning—based on level of concern to human health identified in 2019.

	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
URGENT	Carbapenem-resistant *Acinetobacter*	8,500 cases 700 deaths	6,300 cases 500 deaths	6,000 cases 500 deaths	Stable*	7,500 cases 700 deaths **Overall: 35% increase*** **Hospital-onset: 78% increase***
URGENT	Antifungal-resistant *Candida auris*	171 clinical cases†	329 clinical cases	466 clinical cases	▲ Increase	754 cases **Overall: 60% increase**
URGENT	*Clostridioides difficile*	223,900 infections 12,800 deaths	221,200 infections 12,600 deaths	202,600 infections 11,500 deaths	▼ Decrease	Data delayed due to COVID-19 pandemic
URGENT	Carbapenem-resistant Enterobacterales	13,100 cases 1,100 deaths	10,300 cases 900 deaths	11,900 cases 1,000 deaths	▼ Decrease*	12,700 cases 1,100 deaths Overall: Stable* **Hospital-onset: 35% increase***
URGENT	Drug-resistant *Neisseria gonorrhoeae*	550,000 infections	804,000 infections	942,000 infections	▲ Increase	Data unavailable due to COVID-19 pandemic
SERIOUS	Drug-resistant *Campylobacter*	448,400 infections 70 deaths	630,810 infections	725,210 infections	▲ Increase	Data delayed due to COVID-19 pandemic‡ 26% of infections were resistant, a 10% decrease
SERIOUS	Antifungal-resistant *Candida*	34,800 cases 1,700 deaths	27,000 cases 1,300 deaths	26,600 cases 1,300 deaths	▼ Decrease*	28,100 cases 1,400 deaths **Overall: 12% increase*** **Hospital-onset: 26% increase***
SERIOUS	ESBL-producing Enterobacterales	197,400 cases 9,100 deaths	174,100 cases 8,100 deaths	194,400 cases 9,000 deaths	▲ Increase*	197,500 cases 9,300 deaths **Overall: 10% increase*** **Hospital-onset: 32% increase***
SERIOUS	Vancomycin-resistant Enterococcus	54,500 cases 5,400 deaths	46,800 cases 4,700 deaths	47,000 cases 4,700 deaths	Stable*	50,300 cases 5,000 deaths **Overall: 16% increase*** **Hospital-onset: 14% increase***

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	Resistant Pathogen	2017 Threat Estimate	2018 Threat Estimate	2019 Threat Estimate	2017-2019 Change	2020 Threat Estimate and 2019-2020 Change
SERIOUS	Multidrug-resistant *Pseudomonas aeruginosa*	32,600 cases 2,700 deaths	29,500 cases 2,500 deaths	28,200 cases 2,400 deaths	Decrease*	28,800 cases 2,500 deaths Overall: Stable* **Hospital-onset: 32% increase***
SERIOUS	Drug-resistant nontyphoidal *Salmonella*	212,500 infections 70 deaths	228,290 infections	254,810 infections	Increase	Data delayed due to COVID-19 pandemic‡ 14% of infections were resistant, a 3% decrease
SERIOUS	Drug-resistant *Salmonella* serotype Typhi	4,100 infections <5 deaths	4,640 infections	6,130 infections	Increase	Data delayed due to COVID-19 pandemic‡ 85% of infections were resistant, a 10% increase
SERIOUS	Drug-resistant *Shigella*	77,000 infections <5 deaths	215,850 infections	242,020 infections	Increase	Data delayed due to COVID-19 pandemic‡ 46% of infections were resistant, a 2% increase
SERIOUS	Methicillin-resistant *Staphylococcus aureus*	323,700 cases 10,600 deaths	298,700 cases 10,000 deaths	306,600 cases 10,200 deaths	Stable*	279,300 cases 9,800 deaths Overall: Stable* **Hospital-onset: 13% increase***
SERIOUS	Drug-resistant *Streptococcus pneumoniae*	12,100 invasive infections 1,500 deaths†	See pathogen page if comparing data over time	12,000 invasive infections 1,200 deaths	Stable	Data delayed due to COVID-19 pandemic
SERIOUS	Drug-resistant Tuberculosis (TB)	888 cases 73 deaths†	962 cases 102 deaths	919 cases	Stable	661 cases Decrease‡
CONCERNING	Erythromycin-resistant group A *Streptococcus*	5,400 infections 450 deaths†	See pathogen page if comparing data over time	6,200 infections 560 deaths	Increase	Data delayed due to COVID-19 pandemic
CONCERNING	Clindamycin-resistant group B *Streptococcus*	13,000 infections 720 deaths†	See pathogen page if comparing data over time	15,300 cases 940 deaths	Increase	Data delayed due to COVID-19 pandemic

See the Data Methods section for definitions of each pathogen.

†CDC's database allows for continuous updates for TB, *C. auris*, and *Streptococcus*. Variations in historical TB data are attributable to updated information submitted in the interim by reporting areas; this report includes data reported through June 14, 2021. For *Streptococcus*, table reflects infection increase for 2017 data as of October 2021. For *C. auris*, this report reflects clinical case increase for 2018 data.

*Changes are in rates, not comparisons of counts. Data for healthcare pathogens show a significant increase in hospital-onset rates of resistant infections in 2020, likely due to smaller number of overall hospitalizations during the pandemic.

‡For TB, 2019 and 2020 death reports are not available due to a 2-year lag. For enteric pathogens, 2018-2020 death estimates and 2020 estimates of total number of resistant infections are not available at this time.

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Carbapenem-resistant *Acinetobacter*

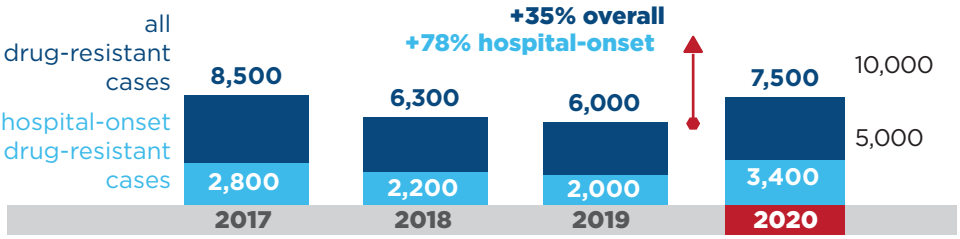
A threat to sick, hospitalized patients, often resistant to nearly all antibiotics

The rate of carbapenem-resistant *Acinetobacter* cases increased overall by 35% in 2020 compared with 2019, driven by hospital-onset cases.

U.S. healthcare facilities reported outbreaks of carbapenem-resistant *Acinetobacter* in 2020. Possible contributing factors included increased number of sicker patients, shortages in personal protective equipment, and staffing shortages.

Many carbapenem-resistant *Acinetobacter* infections tend to occur in patients in intensive care units. Due to the pandemic, hospitals saw more patients who needed an extended length of stay. This increased their risk for resistant infections.

The rates of hospital-onset carbapenem-resistant *Acinetobacter* cases decreased 2012-2017, began to plateau, then increased 78% in 2020.



Data from 2018–2020 are preliminary.

What's Next

- CDC's AR Lab Network identifies carbapenem-resistant *Acinetobacter* infections in every state and is expanding colonization screening for asymptomatic carriage of carbapenem-resistant organisms.
- CDC supports healthcare training programs like Project Firstline to help stop the spread of pathogens.
- CDC increased surveillance and infection prevention and control capacity through the American Rescue Plan Act of 2021 to strengthen efforts to reduce the spread of resistant pathogens in U.S. communities.

Antifungal-resistant *Candida auris*

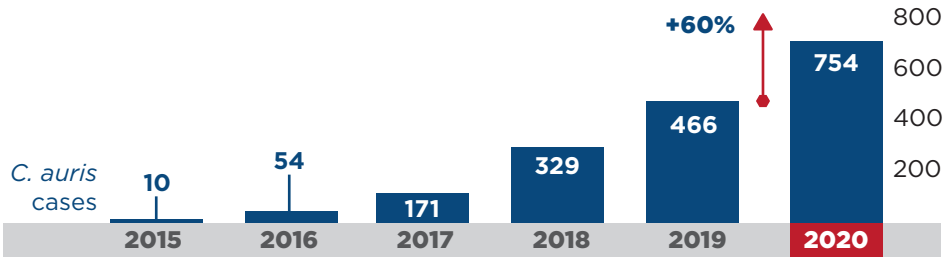
Can cause severe infections and can be resistant to all three major antifungal drug classes

***C. auris* clinical cases increased about 60% in 2020 compared to 2019. The COVID-19 pandemic likely intensified spread of *C. auris* and hindered detection of additional cases.**

Post-acute care facilities (e.g., long-term care), where most cases were identified pre-pandemic, were heavily impacted by *C. auris* during the pandemic. Acute care hospitals saw more outbreaks of *C. auris* in 2020 than previous years, especially in COVID-19 units.

C. auris surveillance activities, particularly colonization screening, were negatively impacted when resources were diverted to the COVID-19 response. This likely resulted in undetected spread of *C. auris* and undercounting of 2020 cases.

C. auris clinical cases have steadily increased since 2015 and significantly increased in 2020. The increase in 2020 could be a result of staffing and supply shortages, an increased number of sicker patients, and changes in infection prevention and control practices (e.g., re-use or extended use of gowns and gloves).



What's Next

- The rapid rise in cases is concerning and emphasizes the need for continued surveillance, expanded lab capacity, quicker diagnostic tests, and robust infection prevention and control.
- CDC is expanding support to its AR Lab Network so that more states will have the capability to rapidly detect *C. auris* infections and colonization at the local level to target interventions and slow spread.
- CDC supports innovative studies to decrease *C. auris* contamination of surfaces (e.g., testing products and methods).

Clostridioides difficile (*C. diff*)

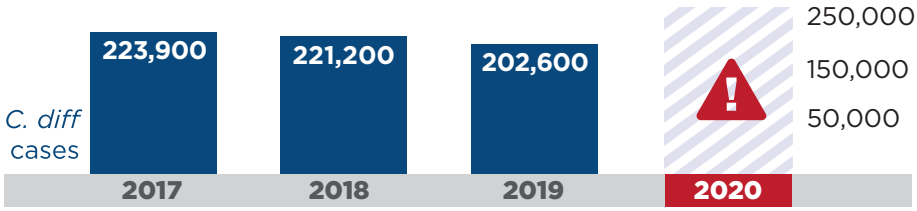
One of the most common healthcare-associated infections, affecting thousands of people every year

Other CDC data suggest a continued decrease for hospitalized *C. diff* infections in 2020 during the COVID-19 pandemic, likely driven in part by changes in healthcare-seeking behavior.

Factors that might have contributed to declines in hospitalized *C. diff* infections through 2019 include:

- Increased emphasis on diagnostic stewardship to reduce inappropriate testing
- Continued adherence to recommended infection prevention and control measures
- Continued implementation of inpatient antibiotic stewardship programs

The number of patients hospitalized with *C. diff* infections continues to decrease, building on nationwide declines since 2017. However, 2020 data were delayed by the pandemic.



The number of *C. diff* infections and deaths continued to decrease from 2017 through 2019. These estimates are not available for 2020 because data submission slowed when resources were diverted to the COVID-19 response.

What's Next

- *C. diff* is rarely resistant to the antibiotics commonly used to treat it. However, *C. diff* usually occurs in people who have taken antibiotics.
- Improving antibiotic use is an important strategy to reduce *C. diff* infections.
- CDC will continue monitoring how changes in antibiotic use may impact *C. diff* infections, including in 2020.

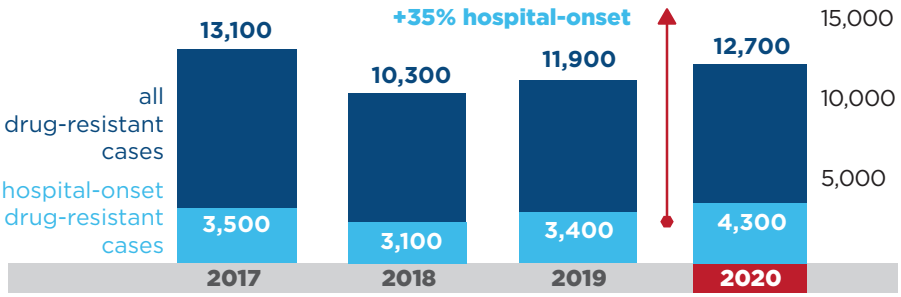
Carbapenem-resistant Enterobacterales (CRE)

Some of these bacteria are resistant to nearly all antibiotics

CRE are a major concern for patients in healthcare facilities, especially those who require devices (e.g., catheters), long courses of some antibiotics, or long stays.

Due to the pandemic, hospitals saw higher numbers of sicker patients (often when hospitalization could not be avoided) who needed an extended length of stay. This likely increased their risk for resistant infections.

The rate of CRE cases declined significantly from 2017 to 2018, but began to rise again in 2019 and continued into 2020.



Data from 2018–2020 are preliminary.

The rate of CRE infections increased 35% in hospitals in 2020, emphasizing the important role these difficult-to-treat pathogens play in hospital infections and the need to contain further spread.

What's Next

- CDC's AR Lab Network identifies CRE infections in every state and is expanding colonization screening for asymptomatic carriage of these organisms.
- CDC supports healthcare training programs like Project Firstline to help stop the spread of pathogens.
- CDC increased surveillance and infection prevention and control capacity through the American Rescue Plan Act of 2021 to reduce the spread of resistant pathogens across U.S. communities.

Drug-resistant *Neisseria gonorrhoeae*

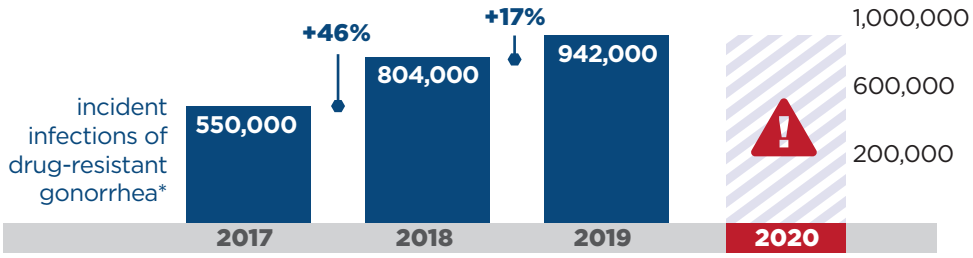
Gonorrhea rapidly develops resistance to antibiotics—ceftriaxone is the last recommended treatment

In 2020, many STD clinics and healthcare facilities limited services, served fewer patients, or closed entirely. During 2017 to 2019, data show an increase in infections caused by gonorrhea with resistance to any of the six antibiotics currently or historically recommended to treat it.

Estimates for 2020 are not available, likely due to:

- Infections going untreated
- Decreased screening for asymptomatic infections
- Staffing shortages and testing/supply shortages in labs and clinics
- Decreased access to health insurance from increased unemployment

Although cases are missed each year, there is no way to know how many were missed in the shutdown period and the months following.



*Among persons aged 15-39 years old.

The estimated number of drug-resistant gonorrhea infections is not available for 2020 due to the COVID-19 pandemic. The increase of drug-resistant gonorrhea infections in previous years remains alarming.

What's Next

Given the ability of gonorrhea to quickly develop resistance, the best public health actions continue to be:

- Slowing emergence and spread through infection prevention, rapid detection, monitoring, and appropriate treatment until new drugs or vaccines are available.
- Developing innovative vaccines and delivery mechanisms.
- Meeting people where they are to increase healthcare accessibility, including walk-in tests or treatment, and telehealth.

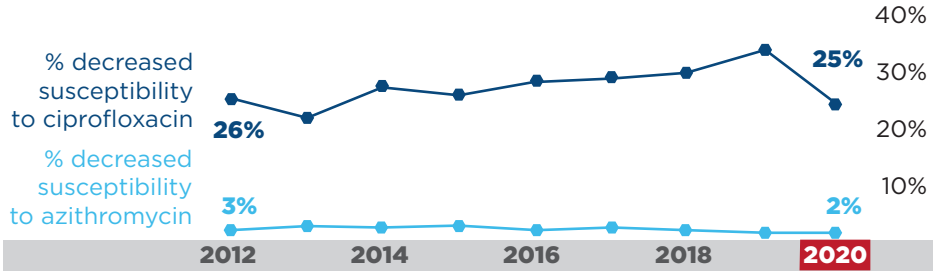
Drug-resistant *Campylobacter*

Spreads through contaminated food (especially raw or undercooked chicken), unpasteurized milk, contaminated water, and contact with animals

There were 23% fewer overall *Campylobacter* infections (susceptible and resistant) reported during 2020 compared to the average annual incidence from 2017 through 2019. These decreases could be attributed to pandemic behaviors, such as limited international travel, fewer restaurant meals, fewer emergency department visits for abdominal symptoms, and increased telehealth visits that may have reduced stool sample collection.

Understanding the full impact of the COVID-19 pandemic will require continued monitoring of data.

Most of the decreased susceptibility to antibiotics for severe *Campylobacter* infections is to fluoroquinolones, such as ciprofloxacin.



Data from 2019 and 2020 are preliminary.

In 2020, there were fewer overall reported *Campylobacter* infections, likely because of factors related to the COVID-19 pandemic. Also, 26% of *Campylobacter* had decreased susceptibility to ciprofloxacin or azithromycin—a 10% decrease from 2019.

What's Next

- Prior to the pandemic, *Campylobacter* infections with decreased susceptibility were on the rise, making it more difficult to treat the most severe of these infections.
- Continued prevention efforts are needed as the world moves beyond COVID-19, including reducing contamination along the food chain, especially for chicken.
- People can protect themselves by not rinsing raw chicken before cooking and by following food safety practices.

Antifungal-resistant *Candida*

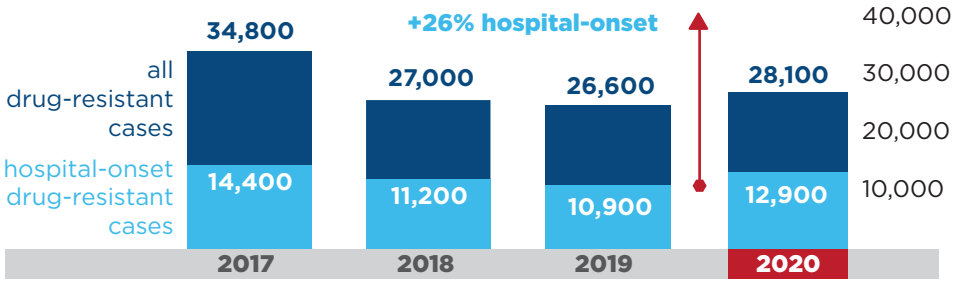
Candida species, which are types of fungi, cause infections and many are resistant to the antifungals used to treat them

After years of decreasing cases, antifungal-resistant *Candida* increased in 2020, with a 26% increase in the rate of hospital-onset cases. This is likely related to multiple factors during the COVID-19 pandemic.

Increases in cases of antifungal-resistant *Candida* in 2020 were potentially because of overcrowding patients, increased number of sicker patients, and staff shortages, which negatively impacted infection control and antifungal use.

Candida species are a common cause of life-threatening bloodstream infections in hospitals and can also cause infections in the mouth, skin, and vagina. Only three classes of antifungals are available to treat severe *Candida* infections. Many clinical laboratories cannot test *Candida* for drug resistance, limiting the ability to guide treatment and track resistance.

Drug-resistant *Candida* cases decreased until 2020, when hospital-onset cases increased during the COVID-19 pandemic.



Includes resistance to any of the three major classes of antifungals. Excludes *C. auris* cases.

What's Next

- CDC's AR Lab Network helps U.S. clinical labs identify and test *Candida* species for resistance. This helps lab professionals and healthcare providers rapidly and correctly identify resistance and treat appropriately.
- CDC supports healthcare training programs like Project Firstline to help stop the spread of pathogens.
- Continued surveillance, antifungal stewardship, and infection prevention and control will prevent *Candida* infections and their spread.

Extended Spectrum Beta-lactamase (ESBL) producing Enterobacterales

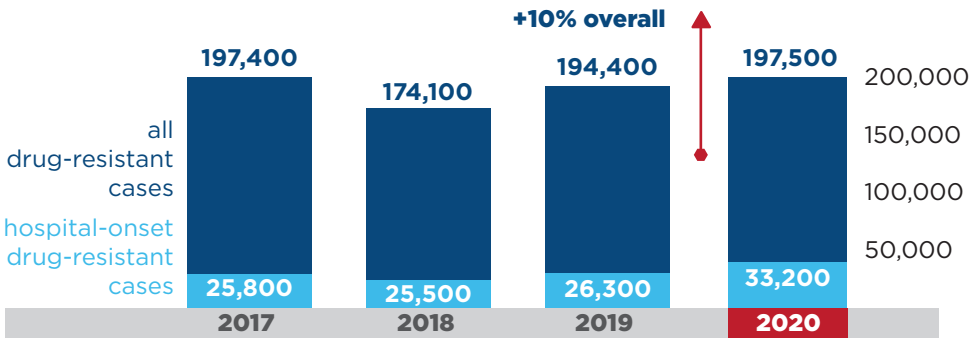
Can spread rapidly and cause or complicate infections in healthy people

The rate of ESBL-producing Enterobacterales cases increased from 2019 to 2020, with an increased rate in both hospital-onset (32%) and community-onset (7%).

Due to the pandemic, hospitals saw higher numbers of sicker patients (hospitalization could not be avoided) who needed an extended length of stay. This increased their risk for resistant infections.

Like many of the Urgent and Serious pathogens in this report, antibiotic options to treat ESBL-producing Enterobacterales infections are limited. Healthcare providers now increasingly need to use intravenous (IV) carbapenem antibiotics to treat infections that used to be treated with oral antibiotics in an outpatient setting.

Rates of ESBL cases increased an estimated 10% from 2019 through 2020, primarily driven by an increase in hospital-onset infections.



Data from 2018–2020 are preliminary.

What's Next

- More work is needed to understand the drivers of ESBL-producing Enterobacterales spreading to inform prevention efforts.
- CDC provides antibiotic stewardship education and healthcare training programs like Project Firstline to help stop the spread of pathogens.
- CDC supports new interventions, such as vaccine development for a specific type of *E. coli* that are often ESBL-producers. If proven safe and effective, it would be a critical tool to prevent infections and reduce antibiotic use.

Vancomycin-resistant Enterococcus (VRE)

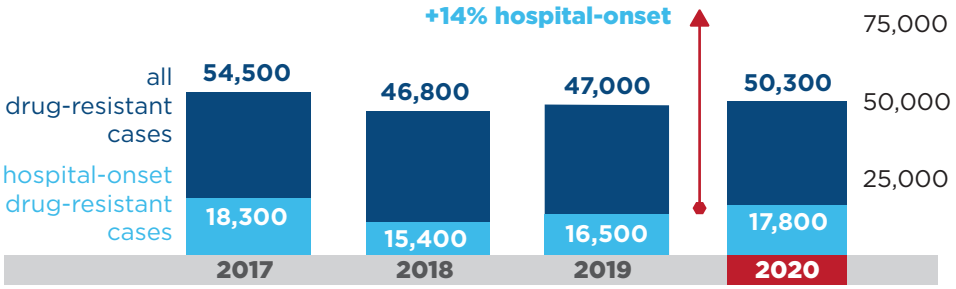
Associated with ongoing health care exposure and is resistant to vancomycin, the antibiotic of choice to treat Enterococcus

The rate of VRE cases increased 16% from 2019 to 2020, reversing substantial decreases since 2012.

Patients at high risk for VRE infections often have a weakened immune system or are receiving complex or prolonged health care.

Due to the pandemic, hospitals saw higher numbers of sicker patients (hospitalization could not be avoided) who needed an extended length of stay. Pandemic pressures also resulted in staffing shortages, inconsistent use of contact precautions, and breaks in appropriate infection control practices. This increased risk for resistant infections.

This increase warrants further monitoring to assess if cases will continue to increase and to identify potential underlying causes, such as new dominant strains of VRE.



Data from 2018–2020 are preliminary.

What's Next

- CDC provides antibiotic stewardship education and supports healthcare infection control training programs like Project Firstline to help stop the spread of pathogens.
- CDC increased surveillance and infection prevention and control capacity through the American Rescue Plan Act of 2021 to strengthen efforts in reducing the spread of resistant pathogens across U.S. communities.

Multidrug-resistant (MDR) *Pseudomonas aeruginosa*

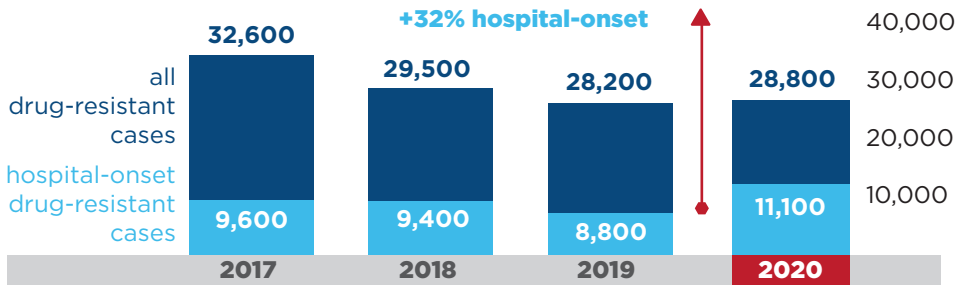
Some are resistant to nearly all antibiotics, including carbapenems

In 2020, the rate of cases of hospital-onset MDR *P. aeruginosa* increased 32% compared to 2019.

After years of decreasing cases, including a significant decline in overall drug-resistant cases in 2019 compared to 2017, MDR *P. aeruginosa* cases rose significantly in hospitals in 2020.

People who are in the hospital or with weakened immune systems are at increased risk for *P. aeruginosa* infections. It is particularly dangerous for patients with chronic lung diseases. In 2020, hospitals saw higher numbers of sicker patients (hospitalization could not be avoided) who needed extended stays. This increased their risk for resistant infections.

The increase in 2020 was driven by hospital-onset cases potentially due to longer hospitalizations and secondary bacterial infections (e.g., pneumonia) associated with COVID-19 infections.



Data from 2018–2020 are preliminary.

What's Next

- CDC provides antibiotic stewardship education and supports healthcare infection control training programs like Project Firstline to help stop the spread of pathogens.
- CDC increased surveillance and infection prevention and control capacity through the American Rescue Plan Act of 2021 to strengthen efforts in reducing the spread of resistant pathogens across U.S. communities.
- CDC investments in nationwide programs strengthen infrastructure, enhance prevention activities, and support response workforce.

Drug-resistant nontyphoidal *Salmonella*

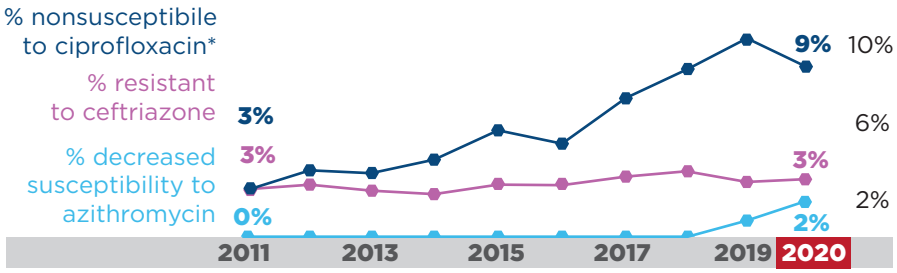
Spreads through contaminated food and water, or through contact with animals, their feces, and their environment

In 2020, 14% of *Salmonella* infections were resistant to at least one antibiotic used to treat severe infection. This was a 3% decrease from 2019. There were also fewer overall *Salmonella* infections reported in 2020, likely because of factors related to the COVID-19 pandemic.

There were 22% fewer overall *Salmonella* infections (susceptible and resistant) reported during 2020 compared to the average annual incidence from 2017 through 2019. Some of the decrease could be attributed to pandemic behaviors, such as fewer restaurant meals, fewer emergency department visits for abdominal symptoms, and increased telehealth visits that may have reduced stool sample collection.

Understanding the full impact of the COVID-19 pandemic will require continued monitoring of data.

Resistance to ciprofloxacin continued to rise from 2016 through 2019, limiting treatment options.



Data from 2018–2020 are preliminary. Excludes *Salmonella* Typhi and Paratyphi. *Fully or partially resistant to ciprofloxacin.

What's Next

- Prior to the pandemic, resistant *Salmonella* infections were on the rise, making it more difficult to treat the most severe of these infections.
- Continued prevention efforts are needed as the world moves beyond COVID-19, including reducing contamination along the food chain, especially for chicken and other meats and vegetables.
- People can protect themselves by washing hands and following food safety practices.

Drug-resistant *Salmonella* serotype Typhi

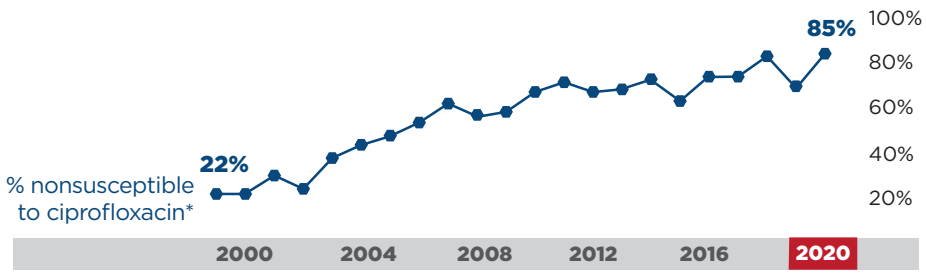
Spreads through contaminated water, food washed with contaminated water, and person-to-person contact

In 2020, 85% of *Salmonella* Typhi infections were resistant (fully or partially) to ciprofloxacin, severely limiting treatment options.

The number of reported overall Typhi infections (susceptible and resistant) in 2020 was less than half the average annual incidence from 2017 through 2019. Most typhoid cases in the U.S. are acquired during international travel. The decrease is potentially attributed to decreased exposure due to limited travel in 2020.

Although the number of cases and international travel declined in 2020, cases did continue occurring in international travelers, especially to Pakistan. Since 2018, cases of extensively drug-resistant (XDR) Typhi have been on the rise, including among people who traveled to Pakistan and those who did not.

Salmonella Typhi infections require antibiotic treatment to recover from illness. Ciprofloxacin resistance has been increasing since 2002.



Data from 2018–2020 are preliminary. *Fully or partially resistant to ciprofloxacin.

What's Next

- Increasing resistance indicates a need for increased awareness of prevention measures during travel, such as vaccination and safe eating and drinking practices. Understanding the full impact of COVID-19 will require continued monitoring of data.
- Data also highlight the critical need for continued close monitoring, because infections will increase when international travel increases post-pandemic and may continue to drive resistance levels even higher.
- Further studies are needed to understand the sources of XDR Typhi infections among U.S. residents without international travel.

Drug-resistant *Shigella*

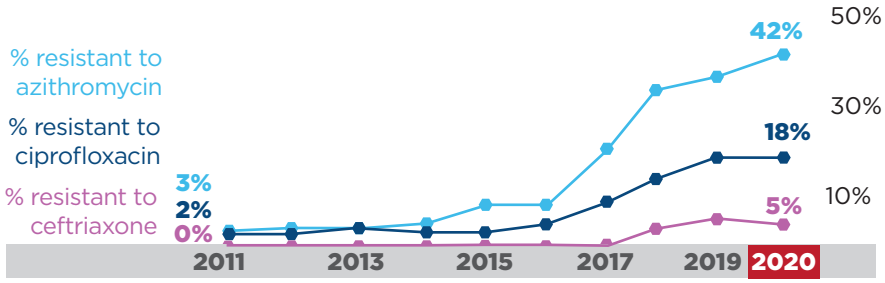
Spreads through contact with the feces of an infected person, including through sexual activity and through contaminated food, surfaces, or water

In 2020, nearly 46% of *Shigella* infections were resistant to the drugs used to treat them, a 2% increase from 2019. However, there were fewer overall *Shigella* infections reported in 2020, likely because of factors related to the COVID-19 pandemic.

There were 41% fewer overall *Shigella* infections (susceptible and resistant) reported in 2020 compared to 2017 through 2019. This may be from pandemic behaviors such as limited international travel, closed schools and daycares, fewer emergency department visits, and increased telehealth visits that may have reduced stool sample collection.

Resistant *Shigella* infections are most common in men who have sex with men (MSM), people experiencing homelessness, and international travelers. Susceptible infections are most common in kids younger than 5 years old. The increase in resistant infections could be due to continued exposure in homeless shelters and among MSM, along with less spread of susceptible *Shigella* due to closed schools and daycares.

Drug-resistant *Shigella* infections have been rising since 2016. Resistance to ceftriaxone was rare before 2018, but was 5% in 2020.



What's Next

- Understanding the full impact of the COVID-19 pandemic will require continued data monitoring.
- People can protect themselves by washing hands; avoiding sexual activity with people who have diarrhea or have recently recovered from *Shigella* infection; and following safe food and water guidelines when traveling internationally.

Data from 2018–2020 are preliminary.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

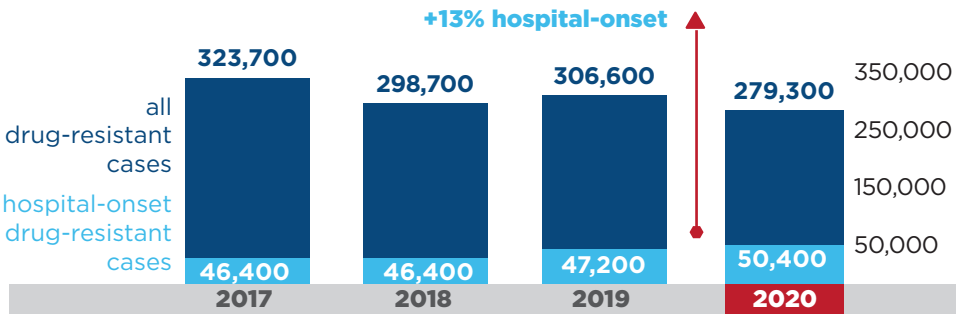
S. aureus commonly spreads in healthcare facilities and communities

After years of decreasing, the overall rate of MRSA cases stabilized in 2017 through 2020. The rate of hospital-onset cases increased 13% in 2020, while the rate of community-onset MRSA cases decreased 5% compared with 2019.

Hospital-onset MRSA bloodstream infections may be increasing. While this is a small segment of the overall MRSA cases, this increase, combined with the stabilization of overall MRSA cases, indicates that progress to prevent MRSA bloodstream infections in healthcare slowed—likely due to challenges created by the pandemic.

CDC partner studies identified interventions like MRSA decolonization to reduce the spread of pathogens in intensive care units and nursing homes, especially when combined with rigorous infection prevention and control.

The rate of hospital-onset cases increased 13% in 2020 compared to 2019.



Data from 2018–2020 are preliminary.

What's Next

- CDC provides antibiotic stewardship education and supports healthcare training programs like Project Firstline to help stop the spread of pathogens.
- CDC works with partners to determine best ways to bring decolonization products to market.
- CDC increased surveillance and infection prevention and control capacity through the American Rescue Plan Act of 2021 to strengthen efforts in reducing the spread of resistant pathogens across U.S. communities.

Drug-resistant *Streptococcus pneumoniae*

A leading cause of bacterial pneumonia and meningitis in the United States

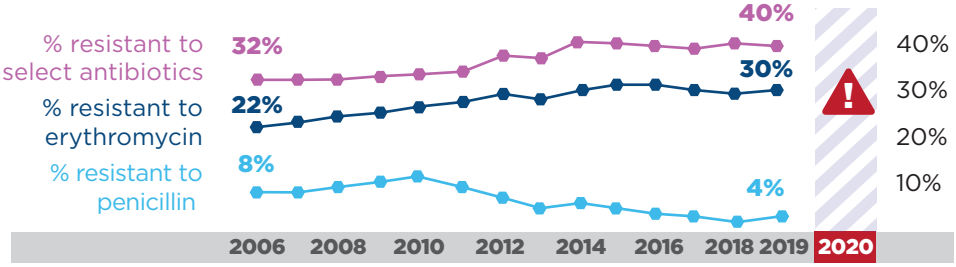
Initial data suggest fewer invasive infections caused by *S. pneumoniae* in 2020 compared to the previous 5 years.

It is not clear yet how this decrease impacted antimicrobial resistance patterns—data are not yet available due to the pandemic.

Resistance data for 2020 are not yet available because of delays in isolate submission and laboratory supply shortages, despite jurisdictions working tirelessly to maintain surveillance. The U.S. needs to continue building stronger public health infrastructure.

Drug-resistant *S. pneumoniae* is one of the only germs listed in this report with effective vaccines to prevent infections, including pneumococcal conjugate vaccines (PCVs). PCV has reduced pneumococcal infections caused by vaccine strains—most of which were resistant to antibiotics—by more than 90% in children and 60% in adults. Non-vaccine strains contribute to disease and resistance.

New vaccines will be critical for *S. pneumoniae* as resistance to some important antibiotics continues to increase.*



*Unable to compare data with 2019 report estimates, see Methods for details.

What's Next

- In 2019, *S. pneumoniae* caused around 30,300 invasive infections, resulting in 3,250 deaths. More than 40% of invasive infections were resistant to one or more clinically relevant antibiotics.
- New PCVs were recommended for adults in late 2021, targeting additional resistant strains.
- Achieving high vaccination coverage and encouraging appropriate antibiotic use will slow the spread of pneumococcal resistance.

Drug-resistant Tuberculosis (TB)

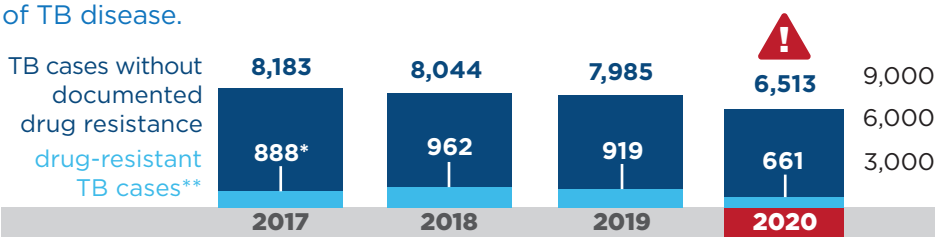
Develops when the antibiotics used to treat TB, caused by *Mycobacterium tuberculosis,* are misused or mismanaged

Drug-resistant TB cases in the United States declined 28% from 2019 to 2020, similar to an overall decline in TB cases of 19%. This is probably due to multiple factors related to the COVID-19 pandemic.

Progress toward TB elimination has slowed in recent years and the COVID-19 pandemic strained public health services, including TB services. To continue progress in the U.S., public health must:

- Improve diagnostics and treatment for drug-resistant TB disease
- Encourage healthcare providers and TB programs to use strategies like directly observed therapy (in-person or electronic) to ensure people with TB start and complete treatment
- Expand testing and treatment for TB among people at increased risk, such as people born in countries where TB disease is more common and people living in congregate settings

Decreased medical visits in 2020 may have led to undiagnosed, delayed diagnosed, or misdiagnosed TB disease. Pandemic mitigation efforts and changes in immigration and travel may have reduced the incidence of TB disease.



What's Next

- CDC and public health partners will continue to monitor drug-resistant TB cases to better understand data trends and identify the most effective TB control and prevention strategies.
- CDC launched the "Think. Test. Treat TB" communications campaign to raise awareness of TB prevention among people at risk and healthcare providers.
- CDC published new guidance for a treatment regimen for extensively drug-resistant TB disease in 2022.

*CDC's 2019 AR Threats Report reported 847 cases of first-line drug-resistant TB in 2017; variations are attributable to updated information submitted in the interim. **Resistant to first-line TB drugs.

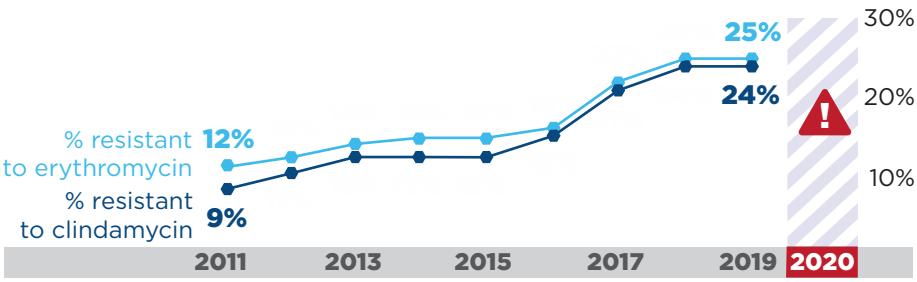
Erythromycin-resistant group A *Streptococcus* (GAS)

GAS is the most common bacterial cause of sore throats, often referred to as strep throat

Resistance data for 2020 are not yet available because of delays in isolate submission and laboratory supply shortages, despite jurisdictions working tirelessly to maintain surveillance during the pandemic. The U.S. needs to continue building stronger public health infrastructure.

Nearly 1 in 4 invasive GAS infections are now caused by erythromycin- and clindamycin-resistant strains, limiting treatment options, especially for adults with severe penicillin allergy. Azithromycin use (in the same drug class as erythromycin, often used for strep throat) increased during some peaks of the pandemic. It is unclear how these surges in use may impact resistance in GAS. Clindamycin, with penicillin, is used for severe, life-threatening GAS infections such as flesh-eating disease.

GAS resistance was already on the rise, emphasizing the need for antibiotic stewardship—especially for patients with viral infections like COVID-19 that are not treatable with antibiotics.



Initial data suggest fewer invasive infections caused by GAS in 2020 compared to the previous 5 years.

However, it is not clear yet how this decrease impacted antimicrobial resistance patterns—data are not yet available due to the COVID-19 pandemic.

What's Next

- In 2019, GAS caused about 25,050 invasive infections, resulting in 2,250 deaths. Of these, around 6,200 infections were resistant to erythromycin with 560 deaths.
- Vaccines for GAS are in development, but it will be some time before one is available for use.
- CDC continues working with patients and healthcare providers to improve antibiotic prescribing and use.

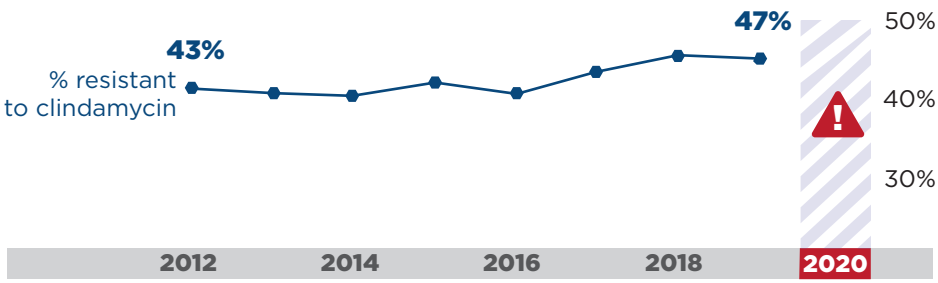
Clindamycin-resistant group B *Streptococcus* (GBS)

GBS can cause severe illnesses—including bloodstream infections, pneumonia, meningitis, and skin infections—in people of all ages

Resistance data for 2020 are not yet available because of delays in isolate submission and laboratory supply shortages, despite jurisdictions working tirelessly to maintain surveillance during the pandemic. The U.S. needs to continue building stronger public health infrastructure.

One in 4 pregnant women carries GBS bacteria in their body. Mothers who test positive for GBS during pregnancy can pass GBS to their newborns. Healthcare providers give these mothers penicillin or ampicillin during labor to prevent the spread of GBS to newborns during birth.

New vaccines will be critical for GBS as, pre-pandemic, nearly half of these infections were resistant to clindamycin—an important treatment alternative for patients with severe penicillin allergy.



Initial data suggest fewer invasive infections caused by GBS in 2020 compared to the previous 5 years.

However, it is not clear yet how this decrease impacted antimicrobial resistance patterns—data are not yet available due to the COVID-19 pandemic.

What's Next

- CDC is assessing how the COVID-19 pandemic may have impacted GBS infections and resistance.
- In 2019, GBS caused about 33,000 severe infections, resulting in 2,000 deaths.
- Vaccines are in development for mothers-to-be to prevent GBS disease in their newborns.
- It is important to continue screening all pregnant women and improving antibiotic prescribing and use to combat antimicrobial resistance.

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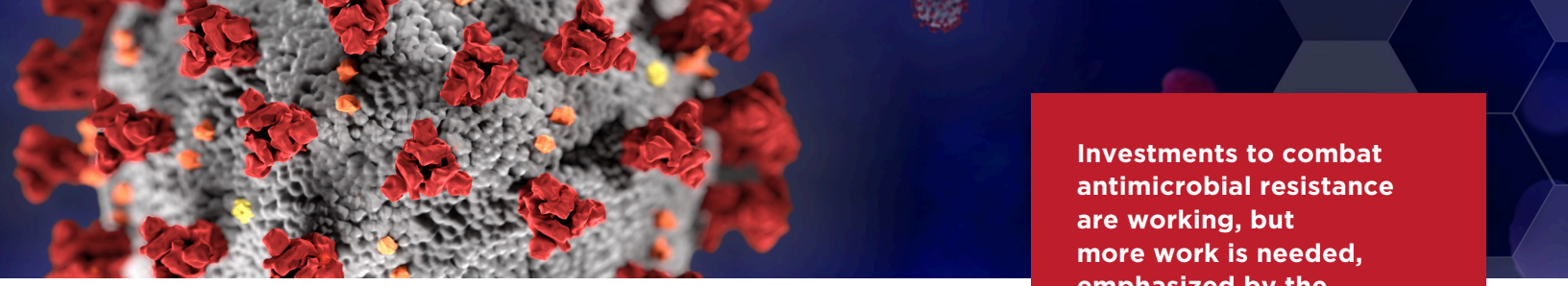


Investments to combat antimicrobial resistance are working, but more work is needed, emphasized by the COVID-19 pandemic. The United States must continue to invest in preparing public health systems across One Health to address threats from multiple angles, simultaneously, and across One Health.

Building Public Health Capacity for Antimicrobial Resistance

CDC is and will remain at the forefront of combating antimicrobial resistance, including leading infection control and response efforts. The agency makes key investments towards establishing a stable foundation for public health that slows the spread of antimicrobial resistance and prevents infections before they start. This work is transforming how the nation and world combat this threat.

First in 2013 and again in 2019, CDC highlighted gaps in knowledge related to antimicrobial resistance in its two Antibiotic Resistance Threats Reports.

It is inevitable that antimicrobial resistance will continue to emerge and spread, but the pandemic has negatively impacted core actions to limit the spread and its impact. Infection prevention and control practices were especially impacted—the most foundational and successful tool to protect people in healthcare settings and communities from getting an infection and the spread of antimicrobial-resistant germs.

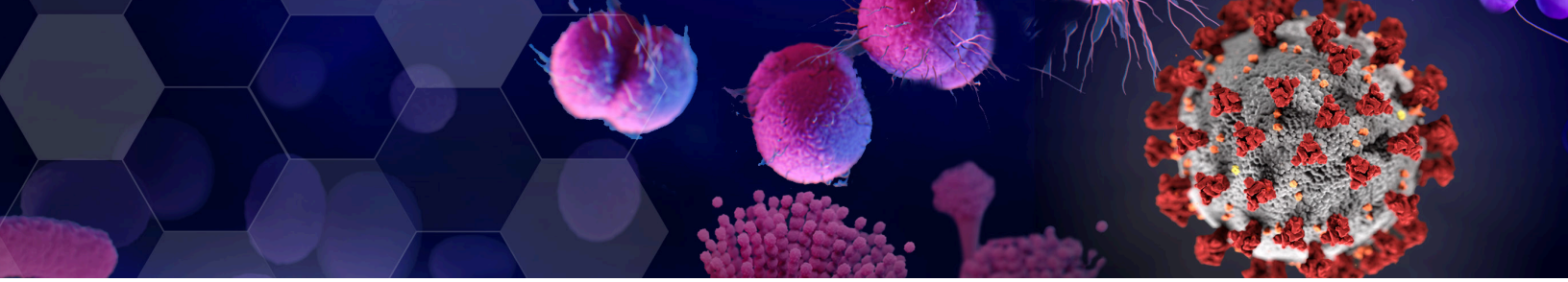
Specimen collection and testing to track resistant infections was also heavily impacted, hampering the United States' ability to understand the burden of antimicrobial resistance to inform the public health response. The pandemic also revealed that CDC's aggressive pre-pandemic investments in the national infrastructure to combat antimicrobial resistance can be flexible and resilient when protecting the nation from more than one threat. Established networks, like CDC's AR Lab Network, can be leveraged during an emergency, offering foundational expertise that can pivot easily to address other threats when challenges arise.

The United States must continue to invest in prevention-focused public health actions, such as accurate laboratory detection, rapid response and containment, effective infection prevention and control, and expansion of innovative strategies to combat antimicrobial resistance. If properly resourced, the United States can continue to build resilient domestic and global public health systems to keep our nation safe against the threats of antimicrobial-resistant pathogens.

Addressing Antimicrobial Resistance and Health Equity

Health equity is when everyone has the opportunity to be as healthy as possible. Many risks for antimicrobial-resistant infections are tied to social determinants of health—where people live, how often people engage with health care, quality of care received, and other factors. CDC is addressing health equity related to antimicrobial resistance as a part of CDC's CORE Initiative, an agency-wide strategy to increase equity across public health.

As a direct result of CDC's prevention investments through its Antimicrobial Resistance Solutions Initiative, the United States has implemented enhanced practices, new initiatives, and innovative studies. Data have shown national progress in slowing the spread of antimicrobial resistance and preventing these infections is possible.



Summary: COVID-19 Impacts on Antimicrobial Resistance

Antimicrobial-resistant infections and *Clostridioides difficile*—a bacterium that is not typically resistant but can cause deadly diarrhea and is associated with antibiotic use—cause more than 3 million infections and 48,000 deaths in the United States each year. In 2018, CDC identified five core actions integrating a One Health approach to better prepare the United States for the resistance that will continue to emerge worldwide. The pandemic has undone much of the nation's progress on antimicrobial resistance, especially in hospitals. The United States must continue to invest in the prevention-focused public health actions to combat antimicrobial resistance.

Tracking & Data

Knowing where and how changes in resistance are occurring informs solutions (e.g., outbreak response, containment) to prevent spread and slow resistance. During the COVID-19 pandemic, the detection and reporting of antimicrobial resistance data slowed tremendously because of changes in patient care, testing, treatment, and the capacity of healthcare facilities and health departments.

Preventing Infections

It is vital to prevent infections before they start. The COVID-19 pandemic undermined efforts in healthcare infection prevention and control. Antimicrobial-resistant infections are amplified in health care. Germs spread among patients and across facilities. Pandemic-related challenges hindered many prevention practices like hand hygiene, cleaning equipment, separating patients, and using personal protective equipment.

Antimicrobial Use & Access

Antibiotics and antifungals can save lives, but any time they are used—for people, animals, or plants—they can contribute to resistance. While antibiotic use throughout the pandemic varied across healthcare settings, antibiotics were commonly prescribed to patients with COVID-19. Antibiotics are appropriate to treat serious bacterial infections and life-threatening conditions like sepsis and pneumonia, but they are not effective against viruses like the one that causes COVID-19.

Environment & Sanitation

Efforts to identify antimicrobial-resistant germs, track the spread of resistance, and measure the effect of antimicrobial use require surveillance across human, animal, and plant populations and the environment. CDC is exploring how innovative solutions in wastewater surveillance can be used to improve detection and response for antimicrobial resistance.

Vaccines, Therapeutics, & Diagnostics

The COVID-19 pandemic highlighted the need to stop the spread of germs before they can cause an infection. Treatment after infection occurs is not the only solution and should not be the only option. We need more prevention products, not just new antimicrobials, to stop infections before they happen. These include alternative treatments to new antimicrobials, new vaccines to combat infections that can develop antimicrobial resistance, and novel decolonizing agents to stop the spread of antimicrobial-resistant germs by people who may not know they are carriers.

Technical Appendix

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Data Methods

Drug-resistant *Campylobacter*

Estimates of the annual number of infections from *Campylobacter* with decreased susceptibility to ciprofloxacin or azithromycin in 2018 and 2019 are reported in this report. They were derived by multiplying an estimate of the total number of *Campylobacter* infections in the United States in 2018 and 2019 by the percentage of *Campylobacter jejuni (C. jejuni)* and *coli (C. coli)* isolates with decreased susceptibility among those isolated from patient specimens in 2018 and 2019 and tested by the National Antimicrobial Resistance Monitoring System (NARMS). To estimate the total number of infections overall (susceptible and resistant), the number of illnesses caused by *Campylobacter* infection (including both culture-confirmed and those detected by culture independent diagnostic tests) reported to CDC's Foodborne Diseases Active Surveillance Network in 2018 and 2019 was scaled up to the U.S. population and adjusted for underdiagnosis; more detailed methods have been described.[1] This method could not be used to estimate total infections during 2020 due to difficulties estimating underdiagnosis of enteric (intestinal) infections during the COVID-19 pandemic. Instead, for 2020, the relative percentage change in incidence of laboratory-diagnosed infections (compared with the average during 2017–2019) was reported using data from FoodNet.[2] The absolute change in the percentage of isolates with decreased susceptibility between 2019 and 2020 was calculated. To measure decreased susceptibility, isolates were tested by broth microdilution to determine minimum inhibitory concentrations (MICs) for ciprofloxacin, azithromycin, and other antibiotics.[3] Epidemiological cutoff values (ECOFFs) established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) were used to interpret MICs for *C. jejuni* and *C. coli*.[4] EUCAST uses the term "non-wild-type" to describe bacteria with MICs above the ECOFFs and to distinguish them from "wild-type" bacteria without resistance mechanisms. Non-wild-type isolates are referred to as having "decreased susceptibility" in this report. For *C. jejuni*, decreased susceptibility to ciprofloxacin was defined as MIC ≥1 μg/mL and decreased susceptibility to azithromycin as MIC ≥0.5 μg/mL. For *C. coli*, decreased susceptibility to ciprofloxacin and decreased susceptibility to azithromycin were both defined as MIC ≥1 μg/mL. Because ECOFFs are only available for *C. jejuni* and *C. coli* (which accounted for ~97% of *Campylobacter* isolates tested by NARMS during 2018–2020), the average percentage with decreased susceptibility was assumed to be the same for other species when calculating the estimated number of infections from *Campylobacter* with decreased susceptibility.

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Candida auris

National *Candida auris* (*C. auris*) case counts were obtained through monthly CDC outreach to state health departments, which tracked cases individually as this fungus emerged. CDC began collecting data on *C. auris* cases in 2016 following a clinical alert, but some cases were identified retrospectively through laboratory data review. The earliest known U.S. case was identified retrospectively from a specimen collected in 2013. Cases were defined using the standardized case definitions for *C. auris*.[1] A clinical case is defined as a detection of *C. auris* from any body site when the specimen was collected for the purposes of diagnosing or treating disease in the normal course of care. Antifungal susceptibility testing was not available for all cases, but testing performed from July 2016 to June 2019 by the Antimicrobial Resistance Laboratory Network has shown most *C. auris* isolates are resistant to at least one of the main antifungal drug classes. Confirmatory species identification was available and antifungal susceptibility testing were performed at CDC or public health laboratories that are part of the Antimicrobial Resistance Laboratory Network.[2] Resistance rates were calculated using all *C. auris* isolates for which the Antimicrobial

Resistance Lab Network conducted antifungal susceptibility testing. CDC performed whole-genome sequencing on *C. auris* to evaluate relatedness of strains in the United States and around the world.[3,4]

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Clostridioides difficile

National estimates of the number of *Clostridioides difficile* infections (*C. difficile*, CDI) requiring hospitalization or in already hospitalized patients were obtained from data submitted to CDC's Emerging Infections Program (EIP)'s *C. difficile* surveillance program. As of 2019, 35 counties in 10 states participated in EIP CDI surveillance. A case of CDI was defined as a positive stool test (toxin or molecular assay) in a person aged ≥1 who did not have a positive test during the previous 8 weeks. Medical record review was performed on all CDI cases in 8 of 10 EIP sites and on a random sample of 33% of cases from the remaining 2 EIP sites. CDI cases were classified as community-associated if there was no documentation of an overnight stay in a healthcare facility in the 12 weeks before the patient's *C. difficile*-positive stool specimen; all other CDI cases were classified as healthcare-associated. Multiple imputation analysis was performed for missing race and epidemiologic class (community-associated versus healthcare-associated) based on the distribution of known race and epidemiologic class by age, sex, and EIP site. For the 2 EIP sites that performed sampling, CDC used the distribution of known race, age, sex, epidemiologic class, and hospitalization data among sampled cases to estimate these data for the non-sampled cases using domain analysis. The population estimates from the U.S. Census Bureau, stratified by age, sex, and race distribution of the U.S. and EIP population, were used to calculate the sampled weights to estimate the 2017–2019 national burden of CDI requiring hospitalization or in already hospitalized patients.

The estimated number of CDI deaths in 2017–2019 was calculated by multiplying the national estimate of the number of CDIs requiring hospitalization by an estimate of CDI-attributable mortality (expressed as a percentage) obtained from the literature. Although estimates of CDI-attributable mortality published since 2000 range from 4.5% to 16.7%, the attributable mortality of CDI appears higher during epidemic periods; estimates of attributable mortality range from 4.5% to 5.7% during endemic periods.[1] Because it was derived from a patient population most similar to patients with CDI requiring hospitalization, an estimate of attributable mortality of 5.7% at 180 days was used.[2]

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Erythromycin-resistant Group A *Streptococcus*

Estimates of the proportion of Group A *Streptococcus* (GAS) isolates resistant to erythromycin and clindamycin are from isolates collected through Active Bacterial Core surveillance (ABCs), which is part of CDC's Emerging Infections Program (EIP) network.[1] ABCs conducts surveillance for invasive bacterial infections, including GAS, at 10 sites located throughout the United States. In 2019, the surveillance population for GAS was approximately 34.6 million people. Isolates are collected on an estimated 88% of all cases (approximately 1200-2300 isolates per year) and sent to reference laboratories for susceptibility testing to 14 different antibiotics (ampicillin, cefazolin, cefotaxime, cefoxitin, ceftizoxime, ciprofloxacin, clindamycin, daptomycin, erythromycin, levofloxacin, linezolid, penicillin, tetracycline, and vancomycin) using Clinical and Laboratory Standards Institute (CLSI) methods until 2015.[2] Beginning in 2016,

susceptibility to antibiotics was predicted from whole-genome sequencing data.[3]

Cases and deaths were estimated by applying the 2019 resistant rate to erythromycin (24.7%) to total cases (25,050) and total deaths (2,250) reported in the 2019 report of ABCs.[4] Erythromycin and clindamycin resistance rates from 2015–2019 are based on data collected through ABCs GBS surveillance report.

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Clindamycin-resistant Group B *Streptococcus*

Estimates of the proportion of Group B *Streptococcus* (GBS) isolates resistant to clindamycin are from isolates collected through Active Bacterial Core surveillance (ABCs), which is part of CDC's Emerging Infections Program (EIP) network.[1] ABCs conducts surveillance for invasive bacterial infections, including GBS, at 10 sites located throughout the United States. In 2019, the surveillance population for GBS was approximately 37.9 million people. Surveillance isolates were collected from 7 ABCs sites until 2013; an 8th site began collecting isolates in 2014. In 2019, isolates were collected from ~88% (approximately 2300) of cases from these 8 sites. Reference laboratories performed susceptibility testing to 14 different antibiotics (ampicillin, cefazolin, cefotaxime, cefoxitin, ceftizoxime, ciprofloxacin, clindamycin, daptomycin, erythromycin, levofloxacin, linezolid, penicillin, tetracycline, and vancomycin) using Clinical and Laboratory Standards Institute (CLSI) methods until 2015.[2] Beginning in 2016, susceptibility to antibiotics were predicted from whole-genome sequencing data.[3,4] Estimates of severe disease are also from ABCs.

Cases and deaths were estimated by applying the 2019 overall resistance rate to clindamycin (46.8%) from the ABCs antimicrobial susceptibilities report to total cases (30,700) and total deaths (2,000) reported in the 2019 ABCs GBS surveillance report.[5]

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Drug-resistant *Neisseria gonorrhoeae*

Estimates of the number of incident gonococcal infections with resistance or elevated minimum inhibitory concentrations (MICs) to antibiotics,* including cephalosporins and azithromycin, are included in this report. These estimates were calculated by multiplying an estimated number of incident gonococcal infections in the United States in 2018 and 2019 by the prevalence of resistance or elevated MICs among gonococcal isolates collected and tested by the Gonococcal Isolate Surveillance Project (GISP) in those years for resistance to penicillin, tetracycline, and ciprofloxacin or elevated MICs to azithromycin, ceftriaxone, and cefixime.[1–3]

To develop the clearest picture of the burden of antibiotic-resistant gonorrhea, the estimates presented in this report were generated using a more comprehensive and robust methodology than those presented

in the 2019 Antibiotic Resistance Threats Report.[4] The current analysis uses the same datapoint for each respective year regarding the prevalence of resistance and/or elevated MICs as a multiplier. However, the analysis estimates incident gonococcal infections for each year using a mathematical modeling approach that takes into account several parameters known to impact the incidence of gonococcal infection.[1] In contrast, for the previous 2019 report, the estimated total number of incident gonococcal infections was obtained from a study that calculated the number of estimated incident infections using the formula: incidence rate = prevalence/duration.[5]

Calculating these estimates is driven by two things: 1) the percentage of GISP isolates with resistance or emerging resistance to the antibiotics tested and 2) the estimated number of total incident gonococcal infections in the United States, using data from the National Notifiable Diseases Surveillance System. Both of these factors have increased in recent years.[3,6] However, a different methodology was used to estimate the number of incident gonococcal infections between the current analysis and the 2019 Antibiotic Resistant Threats Report. For these reasons, differences in the estimates between years should be interpreted cautiously. Estimates of drug-resistant *N. gonorrhoeae* are not available for 2020.

*Data from the Gonococcal Isolate Surveillance Project (GISP). The antibiotic susceptibility criteria used in GISP in 2018 and 2019 are as follows: ceftriaxone, MIC ≥0.5 μg/ml (decreased susceptibility); ceftriaxone, MIC ≥0.125 μg/ml (elevated MIC); cefixime, MIC ≥0.5 μg/ml (decreased susceptibility); cefixime, MIC ≥0.25 μg/ml (elevated MIC); azithromycin, MIC ≥2.0 μg/ml (elevated MIC); ciprofloxacin, MIC 0.125–0.5 μg/ml (intermediate resistance); ciprofloxacin, MIC ≥1.0 μg/ml (resistance); penicillin, MIC ≥2.0 μg/ml or ß-lactamase positive (resistance); tetracycline, MIC ≥2.0 μg/ml (resistance).

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Drug-resistant nontyphoidal *Salmonella*

Estimates of the annual number of infections from nontyphoidal *Salmonella* that were resistant to at least one antibiotic used to treat severe infection in 2018 and 2019 are reported in this report. They were derived by multiplying an estimate of the total number of nontyphoidal *Salmonella* infections in the United States in 2018 and 2019 by the percentage with resistance among nontyphoidal *Salmonella* isolated from patient specimens in 2018 and 2019 and tested by the National Antimicrobial Resistance Monitoring System (NARMS). To estimate the total number of infections overall (susceptible and resistant), the number of illnesses caused by *Salmonella* infection (including both culture-confirmed and those detected by culture independent diagnostic tests) reported to CDC's Foodborne Diseases Active Surveillance Network in 2018 and 2019 was scaled up to the US population and adjusted for underdiagnosis; more detailed methods have been described.[1] This method could not be used to estimate total infections during 2020 due to difficulties estimating underdiagnosis of enteric infections during the COVID-19 pandemic. Instead, for 2020, the relative percentage change in incidence of laboratory-diagnosed infections (compared with the average during 2017–2019) was reported using data from FoodNet.[2] The absolute change in the percentage of resistant isolates between 2019 and 2020 was calculated. To measure resistance, isolates were tested by broth microdilution to determine minimum inhibitory concentrations (MICs) for ceftriaxone, ciprofloxacin, azithromycin, ampicillin, trimethoprim-sulfamethoxazole, and other antibiotics.[3] Breakpoints defined by the Clinical and Laboratory Standards Institute (CLSI) were used to categorize MICs when available.[4] Isolates with ciprofloxacin MICs categorized by CLSI as intermediate (MIC = 0.12–0.5 μg/ml) or resistant (MIC ≥1 μg/ml) were considered ciprofloxacin nonsusceptible. For azithromycin, CLSI breakpoints are established only for *Salmonella* serotype Typhi, with MIC ≥32 μg/ml categorized as resistant based on MIC distribution data and limited clinical data.[4] In this report,

nontyphoidal *Salmonella* isolates with an azithromycin MIC ≥32 μg/ml were considered to have decreased susceptibility to azithromycin. Isolates were defined as resistant to at least one essential antibiotic if they met at least one of the following criteria: resistant to ceftriaxone, nonsusceptible to ciprofloxacin, decreased susceptibility to azithromycin, resistant to ampicillin, or resistant to trimethoprim-sulfamethoxazole. *Salmonella* serotypes Typhi and Paratyphi, which cause fewer than 2% of US *Salmonella* infections, were excluded from this analysis. Data for *Salmonella* serotype Typhi are reported separately.

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Drug-resistant *Salmonella* Serotype Typhi

Estimates of the annual number of infections from *Salmonella* serotype Typhi (Typhi) that were ciprofloxacin nonsusceptible in 2018 and 2019 are reported in this report. They were derived by multiplying an estimate of the total number of Typhi infections in the United States in 2018 and 2019 by the percentage of ciprofloxacin nonsusceptible Typhi isolated from patient specimens in 2018 and 2019 and tested by the National Antimicrobial Resistance Monitoring System (NARMS). To estimate the total number of infections overall (susceptible and resistant), the number of illnesses caused by Typhi infection reported to CDC's Foodborne Diseases Active Surveillance Network in 2018 and 2019 was scaled up to the US population and adjusted for underdiagnosis; more detailed methods have been described.[1] This method could not be used to estimate total infections during 2020 due to difficulties estimating underdiagnosis of enteric (intestinal) infections during the COVID-19 pandemic. Instead, for 2020, the relative percentage change in incidence of laboratory-diagnosed infections (compared with the average during 2017–2019) was reported using data from FoodNet.[2] The absolute change in the percentage of nonsusceptible isolates between 2019 and 2020 was calculated. To measure nonsusceptibility, isolates were tested by broth microdilution to determine the minimum inhibitory concentrations (MICs) for ciprofloxacin and other antibiotics.[3] Breakpoints defined by the Clinical and Laboratory Standards Institute (CLSI) were used to categorize ciprofloxacin MICs.[4] Isolates with ciprofloxacin MICs categorized by CLSI as intermediate (MIC = 0.12–0.5 μg/ml) or resistant (MIC ≥1 μg/ ml) were considered ciprofloxacin nonsusceptible.

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Drug-resistant *Shigella*

Estimates of the annual number of infections from *Shigella* that were resistant to ciprofloxacin, azithromycin, or ceftriaxone in 2018 and 2019 are reported in in this report. They were derived by multiplying an estimate of the total number of *Shigella* infections in the United States in 2018 and 2019 by the percentage of resistant *Shigella* isolated from patient specimens in 2018 and 2019 and tested by the

National Antimicrobial Resistance Monitoring System (NARMS). To estimate the total number of infections overall (susceptible and resistant), the number of illnesses caused by *Shigella* infection (including both culture-confirmed and those detected by culture independent diagnostic tests) reported to CDC's Foodborne Diseases Active Surveillance Network in 2018 and 2019 was scaled up to the US population and adjusted for underdiagnosis; more detailed methods have been described.[1] This method could not be used to estimate total infections during 2020 due to difficulties estimating underdiagnosis of enteric (intestinal) infections during the COVID-19 pandemic. Instead, for 2020, the relative percentage change in incidence of laboratory-diagnosed infections (compared with the average during 2017–2019) was reported using data from FoodNet.[2] The absolute change in the percentage of resistant isolates between 2019 and 2020 was calculated. To measure resistance, isolates were tested by broth microdilution to determine minimum inhibitory concentrations (MICs) for ciprofloxacin, azithromycin, ceftriaxone, and other antibiotics.[3] Clinical breakpoints defined by the Clinical and Laboratory Standards Institute (CLSI) were used to categorize MICs for ciprofloxacin, azithromycin, and ceftriaxone.[4] Isolates were defined as resistant to drugs used to treat *Shigella* if they were resistant to one or more of azithromycin, ceftriaxone, or ciprofloxacin. Resistance of *Shigella* infections to ceftriaxone was not included in the 2017 Threats Report. It was added to this report due to emerging ceftriaxone resistance among *Shigella* infections since 2018.

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Drug-resistant *Streptococcus pneumoniae*

Trends in the incidence of drug-resistant *Streptococcus pneumoniae (S. pneumoniae)* per 100,000 people are from Active Bacterial Core surveillance (ABCs), which is part of CDC's Emerging Infections Program (EIP) network.[1] ABCs conducts surveillance for invasive bacterial infections, including *S. pneumoniae*, at 10 sites located throughout the United States representing a population of approximately 34.6 million people. Isolates are collected on ≥90% of all cases (approximately 2800 isolates per year) and sent to reference laboratories for susceptibility testing to 17 different antibiotics (amoxicillin, cefotaxime, ceftriaxone, cefuroxime, chloramphenicol, ciprofloxacin, clindamycin, erythromycin, levofloxacin, linezolid, meropenem, penicillin, rifampin, synercid, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin). Minimum inhibitory concentrations were determined using conventional testing (broth microdilution) or, starting in 2015, predicted from whole-genome sequencing of isolates. Clinical and Laboratory Standards Institute (CLSI) breakpoints were applied to define resistance or susceptibility.[2]

The burden of antibiotic-resistant invasive pneumococcal disease (IPD) was estimated by extrapolating 2019 IPD case counts in ABCs catchment areas to the U.S. population.[3] To estimate the number of resistant cases, CDC then applied the proportion of infections non-susceptible to clinically relevant drugs (i.e., penicillin, ceftriaxone, cefotaxime, erythromycin, levofloxacin, tetracycline, vancomycin, clindamycin, trimethoprim/ sulfamethoxazole, meropenem and linezolid) in 2019 (ranging by age group from 36 to 50%) to the total number of invasive pneumococcal infections. CDC estimated deaths by applying the proportion of infections non-susceptible to a clinically relevant drug to the total number of deaths from pneumococcal disease.

The methodology in the 2019 Antibiotic Resistance Threats Report estimated pneumococcal non-susceptible infections for both invasive disease (bacteremic pneumonia, meningitis, and bacteremia without focus) and non-invasive disease (non-bacteremic pneumonia, sinusitis, otitis media).[4] For these reasons, this report's estimates should not be compared to the 2019 report estimates.

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Drug-resistant Tuberculosis (TB)

Tuberculosis (TB) is a nationally notifiable disease; all 50 states, the District of Columbia (DC), New York City, five U.S. territories, and three freely associated states report cases to CDC's National Tuberculosis Surveillance System (NTSS). Reported cases are verified according to the TB Case Definition for Public Health Surveillance and are reported and counted according to the Recommendations for Reporting and Counting TB Cases.[1] Cases in this report are limited to those reported by the 50 U.S. states and DC. Drug-resistant TB is defined as TB resistant to any 1 of the 4 first-line antibiotics used to treat TB (isoniazid, rifampin, pyrazinamide, and ethambutol). Deaths reported to NTSS include cases diagnosed after death and deaths among patients undergoing TB treatment; death data are not available for 2019 and 2020 due to a 2-year reporting lag.

NTSS allows for continuous updates for TB. Variations in historical TB data are attributable to updated information submitted in the interim by reporting areas; this report includes data reported through June 14, 2021.

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Carbapenem-resistant *Acinetobacter,* Antifungal-resistant *Candida,* Carbapenem-resistant Enterobacteriaceae (CRE), Extended-spectrum ß-lactamase (ESBL)-producing Enterobacterales, Multidrug-resistant (MDR) *Pseudomonas aeruginosa,* Vancomycin-resistant *Enterococcus* (VRE), Methicillin-resistant *Staphylococcus aureus* (MRSA)

This section describes methods used to calculate national burden estimates for the following pathogens: carbapenem-resistant *Acinetobacter* species, drug-resistant *Candida*, carbapenem-resistant Enterobacterales (CRE), extended-spectrum ß-lactamase (ESBL)-producing Enterobacterales, multidrug-resistant (MDR) *Pseudomonas aeruginosa*, vancomycin-resistant *Enterococcus* (VRE), and methicillin-resistant *Staphylococcus aureus* (MRSA). For additional details on the methods, see *Antibiotic Resistance Threats in the United States, 2019* and Jernigan et al.[1,2]

Data Sources

Two electronic health databases were used to calculate national burden estimates: Premier Healthcare Database[3] and BD Insights Research Database.[4–7] Data from any inpatient visit in an included acute care hospital that took place between January 1, 2012–December 31, 2020, were analyzed. Because data use agreements prohibited any access to identifiers by the investigators this analysis did not constitute human-subjects research.

Hospital Cohort

A dynamic cohort of short-term acute care hospitals was created from each of the databases from 2012–2020. A hospital's data was included in the cohort for any month during which it reported at least one positive result from a microbiology culture with associated antimicrobial susceptibility testing data. The 2020 hospital cohort for this analysis comprised 589 hospitals accounting for 5.4 million discharges annually (over 17% of U.S. hospital discharges/admissions annually). Cohort hospital characteristics are similar in distribution to those of all U.S. acute care hospitals (Table 1).

Case Cohort Definition

From the hospital cohort, CDC identified a cohort of patients who had any clinical culture that yielded an isolate of an organism of interest, and that had accompanying susceptibility testing results sufficient for determining whether that isolate had the resistance phenotype of interest. CDC categorized clinical culture specimen types as either sterile, non-sterile, or surveillance based on body site. Specimens that were categorized as surveillance (i.e., cultures labeled as rectal, perirectal, or nasal) were excluded. Among clinical isolates with sufficient susceptibility testing results, those with the resistance phenotype of interest were eligible to be considered as an incident case. Only isolates from patients having no culture yielding the same resistance phenotype of interest in the previous 14 days were counted as an incident case. For patients with isolates with the resistance phenotype of interest from both a sterile and non-sterile positive culture taken within 14 days of each other, only the sterile culture was counted as an incident case. For both CRE and ESBL reporting, denominator definitions account for potential antimicrobial susceptibility cascade reporting by hospitals. Cases were defined as community-onset (CO) when the culture was obtained immediately preceding admission or within the first three days of hospitalization, and hospital-onset (HO) when the culture was obtained on day four or later.

National Estimate of Cases

For each year, CDC used a raking-procedure to determine weights for extrapolating the number of discharges included in our sample to match the distribution of discharges, stratified by bed size, U.S. census division, urban/rural designation, and teaching status, for all U.S. hospitals included in the American Hospital Association survey for that respective year.[8] Data from 2012–2020 were included, however estimates were based on the years 2018–2020.

The current data were adjusted to the 2019 Threats Report survey design to allow direct comparison between current and previous estimates. We used the 2017 data from the 2019 Threats Report to adjust weights based on imputed data from the additional database used in the previous report.[1] CDC used a generalized linear model to apply weights and calculate national rates and estimates.

Rates and Trends

Pooled rates were calculated using the weighted number of cases and discharges in each month. CDC examined temporal trends using a multivariable logistic model incorporating a survey design with the corresponding weights and hospital designation as the specific cluster.[9,10] Using monthly hospital level data from 2012–2020, CDC modeled cases per discharge or admission, controlling for hospital characteristics, month of discharge, proportion of patients in specific age group, proportion of male patients, and database. The parameter year, representing the trend, was modelled as a linear combination of independent parameters representing each year (i.e., as a categorical variable). For all pathogens, results were stratified by HO and CO as well. Trends in proportion of isolates exhibiting a resistant phenotype were calculated using the same methodology. Annual trends were compared between years: 2018 to 2017, 2019 to 2017, and 2020 to 2019.

Attributable Mortality

Estimates of 90-day attributable mortality, including in-hospital and post-discharge deaths, were derived from a retrospective cohort study of patients with an inpatient admission in the U.S. Veterans Health Administration (VHA) system between January 2007 and October 2015. CDC adapted previously published methodologies[11] using the phenotype definitions established for this report to identify cases. Using multivariable Poisson regression models with standard errors clustered at the individual level, CDC calculated the excess risk of mortality for cases compared to a matched cohort (selected using exposure density sampling matched on the day of culture[12]); CDC reported the adjusted excess risk of mortality (i.e., risk difference) for cases compared to controls as the attributable mortality.[13–15] Due to limitations in sample size, three pathogens (CRE, carbapenem-resistant *Acinetobacter* species, and MDR *Pseudomonas*) were combined to create a pooled estimate for MDR Gram negative pathogens. Using the VHA cohort, CDC calculated 90-day estimates for attributable mortality separately for HO and CO cases. CDC applied attributable mortality estimates to the corresponding burden estimates projected above to calculate the estimated annual deaths.

Table 1. Demographics for all included hospitals, stratified by Electronic Health Database, compared with the distribution of U.S. hospitals as provided by the American Hospital Association (AHA) in 2020.
*For *Candida* estimates, a subset of these hospitals were used to generate the estimates.

Characteristics	Premier: Hospitals	Premier: Percent	BD: Hospitals	BD: Percent	Combined*: Hospitals	Combined*: Percent	AHA: [8] Hospitals	AHA: [8] Percent
Total	265		324		589		4,737	
Urban	174	65.7%	237	73.1%	411	69.8%	2,923	61.7%
Rural	91	34.3%	87	26.9%	178	30.2%	1,814	38.3%
Teaching	68	25.7%	103	31.8%	171	29.0%	1,898	40.1%
Non-Teaching	197	74.3%	221	68.2%	418	71.0%	2,839	59.9%
No. of beds, <300	188	70.9%	225	69.4%	413	70.1%	3,918	82.7%
No. of beds, ≥300	77	29.1%	99	30.6%	176	29.9%	819	17.3%
U.S. Census Division								
1-New England	9	3.4%	6	1.9%	15	2.5%	179	3.8%
2-Mid-Atlantic	19	7.2%	46	14.2%	65	11.0%	395	8.3%
3-South Atlantic	85	32.1%	44	13.6%	129	21.9%	695	14.7%
4-Northeast Central	39	14.7%	53	16.4%	92	15.6%	722	15.2%
5-Southeast Central	30	11.3%	50	15.4%	80	13.6%	374	7.9%
6-Northwest Central	26	9.8%	13	4.0%	39	6.6%	680	14.4%
7-Southwest Central	42	15.8%	64	19.8%	106	18.0%	727	15.4%
8-Mountain	0	0.0%	13	4.0%	13	2.2%	421	8.9%
9-Pacific	15	5.7%	35	10.8%	50	8.5%	544	11.5%
Annual Discharges/ Admissions	2,431,895	7.7%	2,984,649	9.5%	5,416,544	17.2%	31,476,346	

Candida species

For *Candida* species, there were several differences in the methodology used. Some hospitals contributing data used in calculating estimates for bacterial pathogens did not routinely report culture results for *Candida*, and therefore estimates for *Candida* species were generated using only the subset of the hospitals that consistently reported fungal pathogen results. Weights for the extrapolation of *Candida* species infections were recalculated using the new cohort.

Only a small subset of hospitals reporting to the electronic health databases routinely submitted antifungal susceptibility results for *Candida* species, therefore CDC could not use these databases to estimate the proportion of *Candida* species that were resistant to antifungal agents. Instead, after generating an estimate of the burden of all *Candida* species (regardless of antifungal susceptibility), CDC multiplied by an estimate of the percent of *Candida* species resistant to any antifungal agent (6.9% for years 2018-2020) among blood isolates collected through CDC's Emerging Infections Program (EIP).

Attributable mortality for *Candida*-positive cultures was estimated using the Premier Healthcare Database. Adjusted risk differences from logistic regression models comparing *Candida*-positive cases with matched controls were calculated using an outcome of in-hospital deaths or discharge to hospice. Up to five matched controls were selected from the same hospital using exposure density sampling by day of an inpatient stay (i.e., the selected control must have been in the hospital with no positive *Candida* culture on the day of hospitalization that the matched case had a positive culture). Models were adjusted for patient and hospitalization characteristics. Again, CDC applied attributable mortality estimates for *Candida* to the corresponding burden estimates to calculate the estimated annual deaths.

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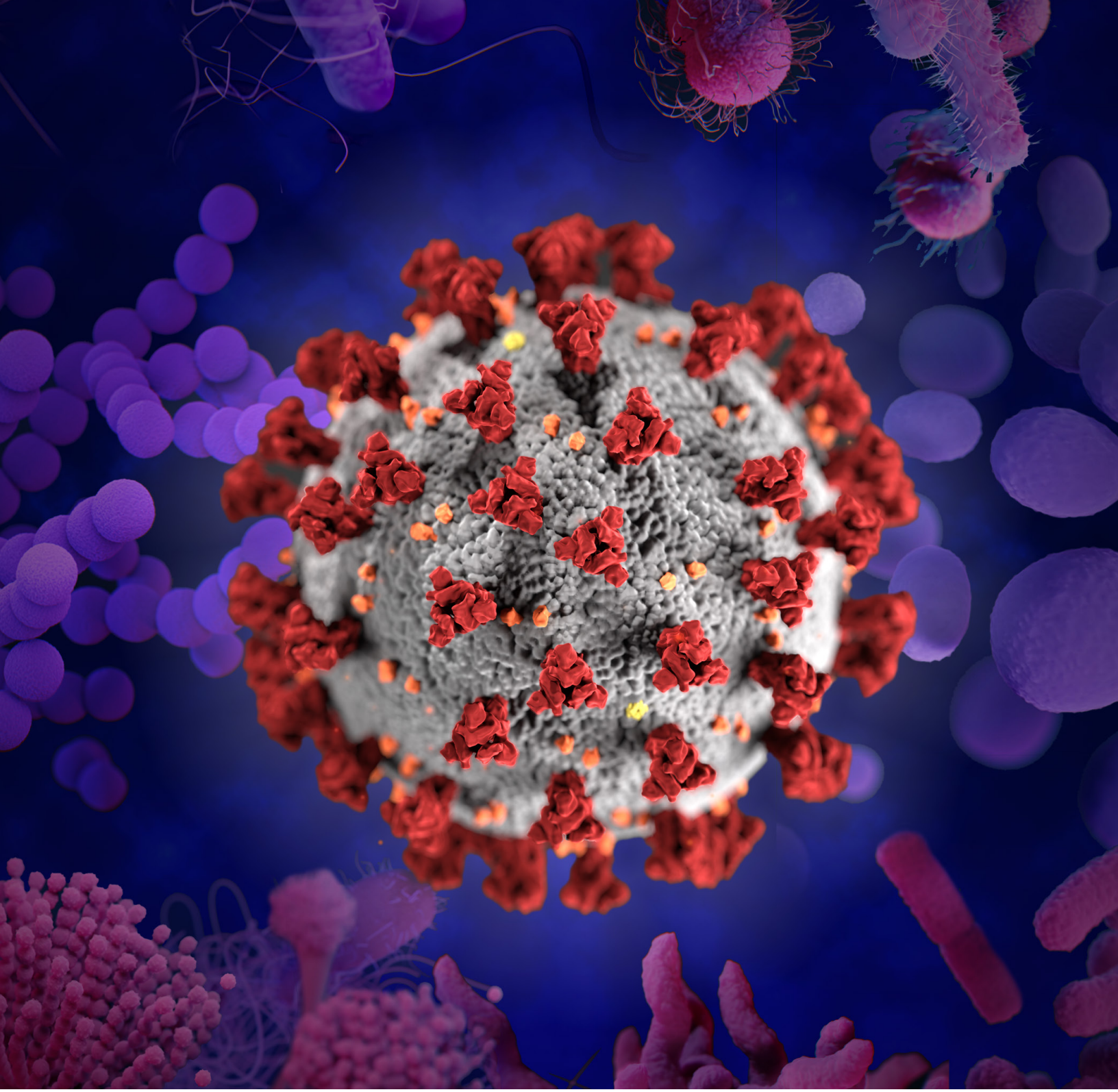

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