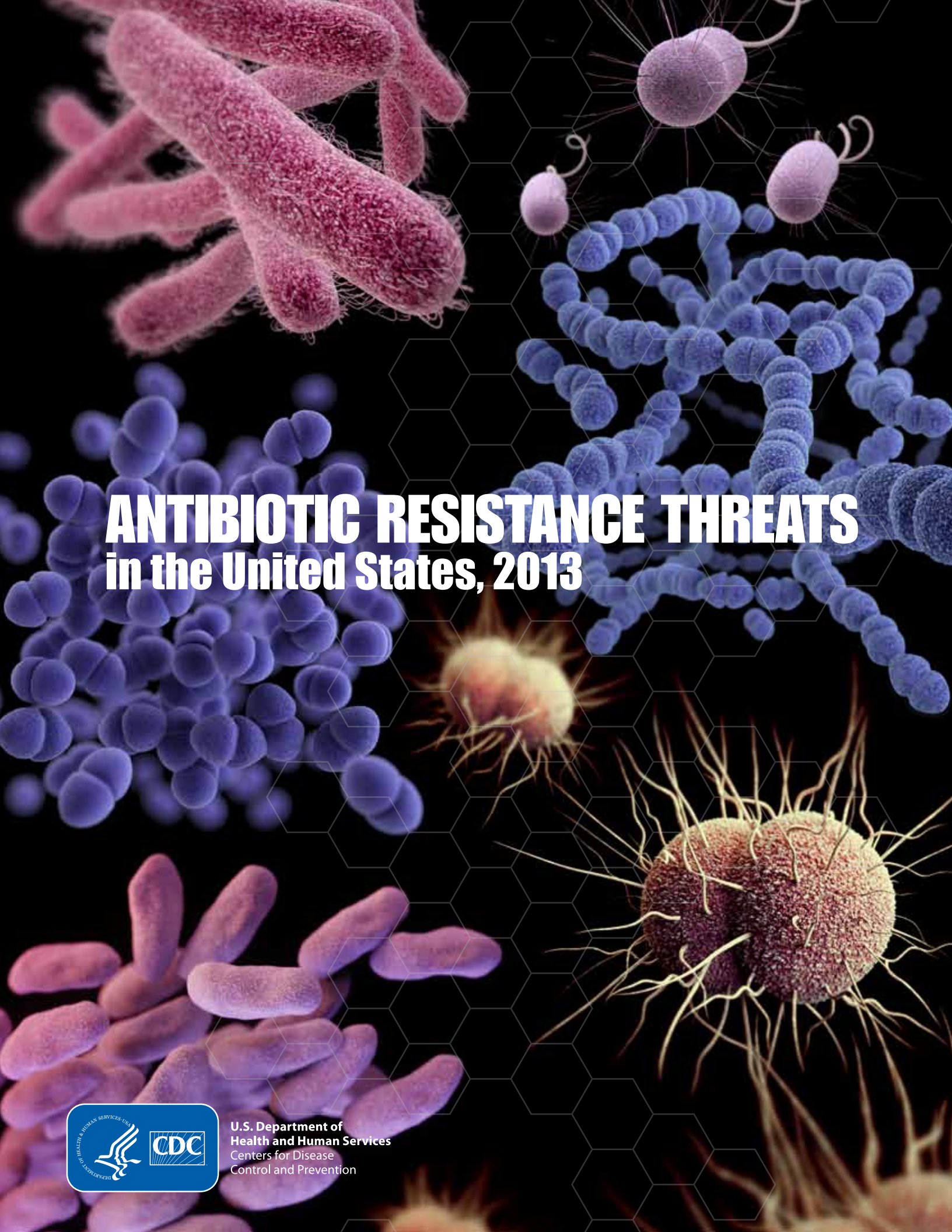
ANTIBIOTIC RESISTANCE THREATS
in the United States, 2013



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

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FOREWORD

Antimicrobial resistance is one of our most serious health threats. Infections from resistant bacteria are now too common, and some pathogens have even become resistant to multiple types or classes of antibiotics (antimicrobials used to treat bacterial infections). The loss of effective antibiotics will undermine our ability to fight infectious diseases and manage the infectious complications common in vulnerable patients undergoing chemotherapy for cancer, dialysis for renal failure, and surgery, especially organ transplantation, for which the ability to treat secondary infections is crucial.

When first-line and then second-line antibiotic treatment options are limited by resistance or are unavailable, healthcare providers are forced to use antibiotics that may be more toxic to the patient and frequently more expensive and less effective. Even when alternative treatments exist, research has shown that patients with resistant infections are often much more likely to die, and survivors have significantly longer hospital stays, delayed recuperation, and long-term disability. Efforts to prevent such threats build on the foundation of proven public health strategies: immunization, infection control, protecting the food supply, antibiotic stewardship, and reducing person-to-person spread through screening, treatment and education.

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Director, U.S. Centers for Disease Control and Prevention
Meeting the Challenges of Drug-Resistant Diseases in Developing Countries
Committee on Foreign Affairs Subcommittee on Africa, Global Health, Human Rights, and International Organizations
United States House of Representatives
April 23, 2013

ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES, 2013

Executive Summary

Antibiotic Resistance Threats in the United States, 2013 is a snapshot of the complex problem of antibiotic resistance today and the potentially catastrophic consequences of inaction. The overriding purpose of this report is to increase awareness of the threat that antibiotic resistance poses and to encourage immediate action to address the threat. This document can serve as a reference for anyone looking for information about antibiotic resistance. It is specifically designed to be accessible to many audiences. For more technical information, references and links are provided.

This report covers bacteria causing severe human infections and the antibiotics used to treat those infections. In addition, *Candida,* a fungus that commonly causes serious illness, especially among hospital patients, is included because it, too, is showing increasing resistance to the drugs used for treatment. When discussing the pathogens included in this report, *Candida* will be included when referencing "bacteria" for simplicity. Also, infections caused by the bacteria *Clostridium difficile (C. difficile)* are also included in this report. Although *C. difficile* infections are not yet significantly resistant to the drugs used to treat them, most are directly related to antibiotic use and thousands of Americans are affected each year.

Drug resistance related to viruses such as HIV and influenza is not included, nor is drug resistance among parasites such as those that cause malaria. These are important problems but are beyond the scope of this report. The report consists of multiple one or two page summaries of cross-cutting and bacteria- specific antibiotic resistance topics. The first section provides context and an overview of antibiotic resistance in the United States. In addition to giving a national assessment of the most dangerous antibiotic resistance threats, it summarizes what is known about the burden of illness, level of concern, and antibiotics left to defend against these infections. This first section also includes some basic background information, such as fact sheets about antibiotic safety and the harmful impact that resistance can have on high-risk groups, including those with chronic illnesses such as cancer.

CDC estimates that in the United States, more than two million people are sickened every year with antibiotic-resistant infections, with at least 23,000 dying as a result. The estimates are based on conservative assumptions and are likely minimum estimates. They are the best approximations that can be derived from currently available data.

Regarding level of concern, CDC has — for the first time — prioritized bacteria in this report into one of three categories: urgent, serious, and concerning.

Urgent Threats

- *Clostridium difficile*
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Drug-resistant *Neisseria gonorrhoeae*

Serious Threats

- Multidrug-resistant *Acinetobacter*
- Drug-resistant *Campylobacter*
- Fluconazole-resistant *Candida* (a fungus)
- Extended spectrum β-lactamase producing Enterobacteriaceae (ESBLs)
- Vancomycin-resistant *Enterococcus* (VRE)
- Multidrug-resistant *Pseudomonas aeruginosa*
- Drug-resistant Non-typhoidal *Salmonella*
- Drug-resistant *Salmonella* Typhi
- Drug-resistant *Shigella*
- Methicillin-resistant *Staphylococcus aureus* (MRSA)
- Drug-resistant *Streptococcus pneumoniae*
- Drug-resistant tuberculosis

Concerning Threats

- Vancomycin-resistant *Staphylococcus aureus* (VRSA)
- Erythromycin-resistant Group A *Streptococcus*
- Clindamycin-resistant Group B *Streptococcus*

The second section describes what can be done to combat this growing threat, including information on current CDC initiatives. Four core actions that fight the spread of antibiotic resistance are presented and explained, including 1) preventing infections from occurring and preventing resistant bacteria from spreading, 2) tracking resistant bacteria, 3) improving the use of antibiotics, and 4) promoting the development of new antibiotics and new diagnostic tests for resistant bacteria.

The third section provides summaries of each of the bacteria in this report. These summaries can aid in discussions about each bacteria, how to manage infections, and implications for public health. They also highlight the similarities and differences among the many different types of infections.

This section also includes information about what groups such as states, communities, doctors, nurses, patients, and CDC can do to combat antibiotic resistance. Preventing the spread of antibiotic resistance can only be achieved with widespread engagement, especially among leaders in clinical medicine, healthcare leadership, agriculture, and public health. Although some people are at greater risk than others, no one can completely avoid

the risk of antibiotic-resistant infections. Only through concerted commitment and action will the nation ever be able to succeed in reducing this threat.

A reference section provides technical information, a glossary, and additional resources.

Any comments and suggestions that would improve the usefulness of future publications are appreciated and should be sent to Director, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop A-07, Atlanta, Georgia, 30333. E-mail can also be used: hip@cdc.gov.

CAMPYLOBACTER

THE THREAT OF ANTIBIOTIC RESISTANCE

Introduction

Antibiotic resistance is a worldwide problem. New forms of antibiotic resistance can cross international boundaries and spread between continents with ease. Many forms of resistance spread with remarkable speed. World health leaders have described antibiotic-resistant microorganisms as "nightmare bacteria" that "pose a catastrophic threat" to people in every country in the world.

Each year in the United States, at least 2 million people acquire serious infections with bacteria that are resistant to one or more of the antibiotics designed to treat those infections. At least 23,000 people die each year as a direct result of these antibiotic-resistant infections. Many more die from other conditions that were complicated by an antibiotic-resistant infection.

In addition, almost 250,000 people each year require hospital care for *Clostridium difficile (C. difficile)* infections. In most of these infections, the use of antibiotics was a major contributing factor leading to the illness. At least 14,000 people die each year in the United States from *C. difficile* infections. Many of these infections could have been prevented.

Antibiotic-resistant infections add considerable and avoidable costs to the already overburdened U.S. healthcare system. In most cases, antibiotic-resistant infections require prolonged and/or costlier treatments, extend hospital stays, necessitate additional doctor visits and healthcare use, and result in greater disability and death compared with infections that are easily treatable with antibiotics. The total economic cost of antibiotic resistance to the U.S. economy has been difficult to calculate. Estimates vary but have ranged as high as $20 billion in excess direct healthcare costs, with additional costs to society for lost productivity as high as $35 billion a year (2008 dollars).[1]

The use of antibiotics is the single most important factor leading to antibiotic resistance around the world. Antibiotics are among the most commonly prescribed drugs used in human medicine. However, up to 50% of all the antibiotics prescribed for people are not needed or are not optimally effective as prescribed. Antibiotics are also commonly used in food animals to prevent, control, and treat disease, and to promote the growth of food-producing animals. The use of antibiotics for promoting growth is not necessary, and the practice should be phased out. Recent guidance from the U.S. Food and Drug Administration (FDA) describes a pathway toward this goal.[2] It is difficult to directly compare the amount of drugs used in food animals with the amount used in humans, but there is evidence that more antibiotics are used in food production.

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1 http://www.tufts.edu/med/apua/consumers/personal_home_5_1451036133.pdf (accessed 8-5-2013); extrapolated from Roberts RR, Hota B, Ahmad I, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. Clin Infect Dis. 2009 Oct 15;49(8):1175-84

2 http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf

The other major factor in the growth of antibiotic resistance is spread of the resistant strains of bacteria from person to person, or from the non-human sources in the environment, including food.

There are four core actions that will help fight these deadly infections:

- preventing infections and preventing the spread of resistance
- tracking resistant bacteria
- improving the use of today's antibiotics
- promoting the development of new antibiotics and developing new diagnostic tests for resistant bacteria

Bacteria will inevitably find ways of resisting the antibiotics we develop, which is why aggressive action is needed now to keep new resistance from developing and to prevent the resistance that already exists from spreading.

NATIONAL SUMMARY DATA

Estimated minimum number of illnesses and deaths caused by antibiotic resistance*:

At least **2,049,442** illnesses,

23,000 deaths

**bacteria and fungus included in this report*

+

Estimated minimum number of illnesses and death due to *Clostridium difficile* (*C. difficile*), a unique bacterial infection that, although not significantly resistant to the drugs used to treat it, is directly related to antibiotic use and resistance:

At least **250,000** illnesses,

14,000 deaths

WHERE DO INFECTIONS HAPPEN?

Antibiotic-resistant infections can happen anywhere. Data show that most happen in the general community; however, most deaths related to antibiotic resistance happen in healthcare settings, such as hospitals and nursing homes.

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How Antibiotic Resistance Happens

1. Lots of germs. A few are drug resistant.

2. Antibiotics kill bacteria causing the illness, as well as good bacteria protecting the body from infection.

3. The drug-resistant bacteria are now allowed to grow and take over.

4. Some bacteria give their drug-resistance to other bacteria, causing more problems.

Examples of How Antibiotic Resistance Spreads

Animals get antibiotics and develop resistant bacteria in their guts.

George gets antibiotics and develops resistant bacteria in his gut.

Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.

George stays at home and in the general community. Spreads resistant bacteria.

George gets care at a hospital, nursing home or other inpatient care facility.

Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.

Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.

Healthcare Facility

Vegetable Farm

Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.

Patients go home.

Resistant bacteria spread to other patients from surfaces within the healthcare facility.

Simply using antibiotics creates resistance. These drugs should only be used to treat infections.

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Minimum Estimates of Morbidity and Mortality from Antibiotic-Resistant Infections*

Antibiotic-Resistant Microorganism	Infections Included in Case/Death Estimates	Infections Not Included	Estimated Annual Number of Cases	Estimated Annual Number of Deaths
Carbapenem-resistant Enterobacteriaceae (CRE)	Healthcare-associated Infections (HAIs) caused by *Klebsiella* and *E. coli* with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed until after discharge Infections caused by Enterobacteriaceae other than *Klebsiella* and *E. coli* (e.g., *Enterobacter spp.*)	9,300	610
Drug-resistant *Neisseria gonorrhoeae* (any drug)	All infections	Not applicable	246,000	<5
Multidrug-resistant *Acinetobacter* (three or more drug classes)	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed until after discharge	7,300	500
Drug-resistant *Campylobacter* (azithromycin or ciprofloxacin)	All infections	Not applicable	310,000	28
Drug-resistant *Candida* (fluconazole)	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed until after discharge	3,400	220
Extended-spectrum β-lactamase producing Enterobacteriaceae (ESBLs)	HAIs caused by *Klebsiella* and *E. coli* with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed until after discharge Infections caused by Enterobacteriaceae other than *Klebsiella* and *E. coli* (e.g., Enterobacter *spp.*)	26,000	1,700

Antibiotic-Resistant Microorganism	Infections Included in Case/Death Estimates	Infections Not Included	Estimated Annual Number of Cases	Estimated Annual Number of Deaths
Vancomycin-resistant *Enterococcus* (VRE)	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed until after discharge	20,000	1,300
Multidrug-resistant *Pseudomonas aeruginosa* (three or more drug classes)	HAIs with onset in hospitalized patients	Infections occurring outside of acute care hospitals (e.g., nursing homes) Infections acquired in acute care hospitals but not diagnosed until after discharge	6,700	440
Drug-resistant non-typhoidal *Salmonella* (ceftriaxone, ciprofloxacin†, or 5 or more drug classes)	All infections	Not applicable	100,000	40
Drug-resistant *Salmonella* Typhi (ciprofloxacin†)	All infections	Not applicable	3,800	<5
Drug-resistant *Shigella* (azithromycin or ciprofloxacin)	All infections	Not applicable	27,000	<5
Methicillin-resistant *Staphylococcus aureus* (MRSA)	Invasive infections	Both healthcare and community-associated non-invasive infections such as wound and skin and soft tissue infections	80,000	11,000
***Streptococcus pneumoniae* (full resistance to clinically relevant drugs)**	All infections	Not applicable	1,200,000	7,000

Antibiotic-Resistant Microorganism	Infections Included in Case/Death Estimates	Infections Not Included	Estimated Annual Number of Cases	Estimated Annual Number of Deaths
Drug-resistant tuberculosis (any clinically relevant drug)	All infections	Not applicable	1,042	50
Vancomycin-resistant *Staphylococcus aureus* (VRSA)	All infections	Not applicable	<5	<5
Erythromycin-resistant Group A *Streptococcus*	Invasive infections	Non-invasive infections including common upper-respiratory infections like strep throat	1,300	160
Clindamycin-resistant Group B *Streptococcus*	Invasive infections	Non-invasive infections and asymptomatic intrapartum colonization requiring prophylaxis	7,600	440
Summary Totals for Antibiotic-Resistant Infections			2,049,442	23,488
***Clostridium difficile* Infections**	Healthcare-associated infections in acute care hospitals or in patients requiring hospitalization	Infections occurring outside of acute care hospitals (e.g., nursing homes, community) Infections acquired in acute care hospitals but not diagnosed until after discharge	250,000	14,000

*See technical appendix for discussion of estimation methods.

†Resistance or partial resistance

Limitations of Estimating the Burden of Disease Associated with Antibiotic-Resistant Bacteria

This report uses several methods, described in the technical appendix, to estimate the number of cases of disease caused by antibiotic-resistant bacteria and fungi and the number of deaths resulting from those cases of disease. The data presented in this report are approximations, and totals, as provided in the national summary tables, can provide only a rough estimate of the true burden of illness. Greater precision is not possible at this time for a number of reasons:

- Precise criteria exist for determining the resistance of a particular species of bacteria to a specific antibiotic. However, for many species of bacteria, there are no standard definitions that allow for neatly dividing most species into only two categories—resistant vs. susceptible without regard to a specific antibiotic. This report specifies how resistance is defined for each microorganism.
- There are very specific criteria and algorithms for the attribution of deaths to specific causes that are used for reporting vital statistics data. In general, there are no similar criteria for making clinical determinations of when someone's death is primarily attributable to infection with antibiotic-resistant bacteria, as opposed to other co-existing illnesses that may have contributed to or caused death. Many studies attempting to determine attributable mortality rely on the judgment of chart reviewers, as is the case for many surveillance systems. Thus, the distinction between an antibiotic-resistant infection leading directly to death, an antibiotic-resistant infection contributing to a death, and an antibiotic-resistant infection related to, but not directly contributing to a death are usually determined subjectively, especially in the preponderance of cases where patients are hospitalized and have complicated clinical presentations.

In addition, the estimates provided in this report represent an underestimate of the total burden of bacterial resistant disease.

- The methodology employed in this report likely underestimates, at least for some pathogens, the impact of antibiotic resistance on mortality. As described in the technical appendix, the percentage of resistant isolates for some bacteria was multiplied by the total number of cases or the number of deaths ascribed to that bacterium. A number of studies have shown that the risk of death following infection with a strain of resistant bacteria is greater than that following infection with a susceptible strain of the same bacteria. More accurate data for all bacteria would be necessary to estimate the extent of the differential risk for death associated with a resistant infection vs. the risk of death associated with a susceptible infection. But, lacking that data, the lower, more conservative estimate has been used. That estimate is the approximation of the number of deaths derived by applying the proportion of resistant isolates to the estimated total number of deaths caused by that pathogen.

- For several pathogens, complete data from all types of infections are not available since tracking is limited to the more severe types of infections. For some pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), only cases due to invasive disease are counted. For other pathogens, where resistance is predominately limited to healthcare settings, only disease occurring in acute care hospitals, or requiring hospitalization, are counted.

The actual number of infections and the actual number of deaths, therefore, are certainly higher than the numbers provided in this report.

This report does not provide a specific estimate for the financial cost of antibiotic-resistant infections. Although a variety of studies have attempted to estimate costs in limited settings, such as a single hospital or group of hospitals, the methods used are quite variable. Similarly, careful work has been done to estimate costs for specific pathogens, such as *Streptococcus pneumoniae* and MRSA. However, no consensus methodology currently exists for making such monetary estimates for many of the other pathogens listed in this report. For this reason, this report references non-CDC estimates in the introduction, but does not attempt to estimate the overall financial burden of antibiotic resistance to the United States.

Assessment of Domestic Antibiotic Resistance Threats

CDC conducted an assessment of antibiotic resistance threats, categorizing the threat level of each bacteria as urgent, serious, or concerning. The assessment was done in consultation with non-governmental experts in antibiotic resistance who serve on the Antimicrobial Resistance Working Group of the CDC Office of Infectious Diseases Board of Scientific Counselors (http://www.cdc.gov/oid/BSC.html). CDC also received input and recommendations from the National Institutes of Health (NIH) and the U.S. Food and Drug Administration (FDA). Threats were assessed according to seven factors associated with resistant infections:

- clinical impact
- economic impact
- incidence
- 10-year projection of incidence
- transmissibility
- availability of effective antibiotics
- barriers to prevention

The assessment was focused on domestic impact, but the threat of importing international antibiotic-resistant pathogens was taken into account in the 10-year incidence projection. Because antibiotic resistance is a rapidly evolving problem, this assessment will be revised at least every five years. Examples of findings that could result in a change in threat status are:

- Multidrug-resistant and extensively drug-resistant tuberculosis (MDR and XDR TB) infections are an increasing threat outside of the United States. In the United States, infections are uncommon because a robust prevention and control program is in place. If infection rates of MDR and XDR TB increase within the U.S., this antibiotic-resistant threat will change from serious to urgent, because it is transmissible through respiratory secretions, and because treatment options are very limited.
- MRSA infections can be very serious and the number of infections is among the highest of all antibiotic-resistant threats. However, the number of serious infections is decreasing and there are multiple effective antibiotics for treating infections. If MRSA infection rates increase or MRSA strains become more resistant to other antibiotic agents, then MRSA may change from a serious to an urgent threat.
- *Streptococcus pneumoniae* (pneumococcus) can cause serious and sometimes life-threatening infections. Antibiotic resistance significantly affects the ability to manage these infections. A new version of the pneumococcal conjugate vaccine (PCV13), introduced in 2010, protects against infections with the most resistant pneumococcus strains and rates of resistant infections are declining. The extent to which this trend will continue is unknown, but a significant and sustainable drop in resistant infection rates could result in this threat being recategorized as concerning.

In general, threats assigned to the urgent and serious categories require more monitoring and prevention activities, whereas the threats in the concerning category require less. Regardless of category, threat-specific CDC activities are tailored to meet the epidemiology of the infectious agent and to address any gaps in the ability to detect resistance and to protect against infections.

HAZARD LEVEL
URGENT

These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

Clostridium difficile (C. difficile), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

HAZARD LEVEL
SERIOUS

These are significant antibiotic-resistant threats. For varying reasons (e.g., low or declining domestic incidence or reasonable availability of therapeutic agents), they are not considered urgent, but these threats will worsen and may become urgent without ongoing public health monitoring and prevention activities.

Multidrug-resistant *Acinetobacter,* Drug-resistant *Campylobacter,* Fluconazole-resistant *Candida* (a fungus), Extended spectrum β-lactamase producing Enterobacteriaceae (ESBLs), Vancomycin-resistant *Enterococcus* (VRE), Multidrug-resistant *Pseudomonas aeruginosa,* Drug-resistant Non-typhoidal *Salmonella,* Drug-resistant *Salmonella* Typhi, Drug-resistant *Shigella,* Methicillin-resistant *Staphylococcus aureus* (MRSA), Drug-resistant *Streptococcus pneumonia,* Drug-resistant tuberculosis (MDR and XDR)

HAZARD LEVEL
CONCERNING

These are bacteria for which the threat of antibiotic resistance is low, and/or there are multiple therapeutic options for resistant infections. These bacterial pathogens cause severe illness. Threats in this category require monitoring and in some cases rapid incident or outbreak response.

Vancomycin-resistant *Staphylococcus aureus* (VRSA), Erythromycin-resistant *Streptococcus* Group A, Clindamycin-resistant *Streptococcus* Group B

Although *C. difficile* is not currently significantly resistant to antibiotics used to treat it, it was included in the threat assessment because of its unique relationship with resistance issues, antibiotic use, and its high morbidity and mortality.

Running Out of Drugs to Treat Serious Gram-Negative Infections

Among all of the bacterial resistance problems, gram-negative pathogens are particularly worrisome, because they are becoming resistant to nearly all drugs that would be considered for treatment. This is true as well, but not to the same extent, for some of the gram-positive infections (e.g., *Staphylococcus* and *Enterococcus)*. The most serious gram-negative infections are healthcare-associated, and the most common pathogens are Enterobacteriaceae, *Pseudomonas aeruginosa,* and *Acinetobacter*. Treating infections of either pan-resistant or nearly pan-resistant gram-negative microorganisms is an increasingly common challenge in many hospitals. The table below describes the drug classes used to treat these infections and a description of important drug resistance and other limitations. The classes are in order of most likely to be used to less likely to be used.

Drug Class	Important Characteristics	Resistance and Other Limitations
β-lactams	A large class of broad-spectrum drugs that are the main treatment for gram-negative infections. The subclasses are listed below and are presented in an order from narrow-spectrum (penicillins) to broad-spectrum (carbapenem) β-lactam drugs.	Gram-negative bacteria have developed several pathways to β-lactam resistance. Perhaps the most concerning are β-lactamases, enzymes that destroy the β-lactam antibiotics. Some β-lactamases destroy narrow spectrum drugs (e.g., only active against penicillins) while newer β-lactamases (e.g. carbapenemases found in carbapenem-resistant Enterobacteriaceae or CRE) are active against all β-lactam antibiotics.
β-lactam subclass:		
Penicillin, aminopenicillins, and early generation cephalosporins	Among the first antibiotics developed for treatment of bacterial infections. In the absence of resistance, these drugs are active against a broad range of bacterial pathogens.	Resistance among gram-negative bacteria is widespread. These drugs are rarely recommended as treatment for serious gram-negative infections.
β-lactamase inhibitor combinations	These drugs are still active against gram-negative bacteria that have β-lactamases with limited activity for destroying β-lactam antibiotics.	These drugs are important for treatment of serious gram- negative infections but resistance is increasing. Bacteria that are resistant to extended-spectrum cephalosporins and carbapenems are usually resistant to these drugs as well. New β-lactamase inhibitor combination drugs in development have the potential to overcome some, but not all, of resistance from the most potent β-lactamases such as those found in CRE.
Extended-spectrum Cephalosporins	These drugs have been a cornerstone for treatment of serious gram-negative infections for the past 20 years.	Resistant gram-negative infections first emerged in healthcare settings but now are also spreading in the community. When resistance occurs, a carbapenem is the only remaining β-lactam agent.

Drug Class	Important Characteristics	Resistance and Other Limitations
Carbapenems	A broad-spectrum β-lactam antibiotic that is considered the last resort for treatment of serious gram-negative infections.	CRE infections are spreading in healthcare facilities throughout the United States and the world. It is reasonable to expect that this resistance will expand to bacteria that circulate in the community, as witnessed by extended-spectrum β-lactamase producing bacteria. Carbapenem resistance can also be found among other gram-negative bacteria including *Pseudomonas* and *Acinetobacter spp*. Once bacteria become resistant to carbapenems, they are usually resistant to all β-lactams.
Fluoroquinolones	These are broad-spectrum antibiotics that are often given orally, making them convenient to use in both inpatients and outpatients.	Resistant bacteria develop quickly with increased use in a patient population. Increased use is also associated with an increase in infections caused by fluoroquinolone-resistant, hyper-virulent strains of *Clostridium difficile*.
Aminoglycosides	These drugs are often used in combination with β-lactam drugs for the treatment of serious gram-negative infections.	Despite growing resistance problems, these drugs continue to be an important therapeutic option. However, clinicians rarely use these drugs alone because of concerns with resistance and side effects.
Tetracyclines & Glycyclines	Tetracyclines are not a first-line treatment option for serious gram negative infections; however, with increasing resistance to other drug classes, tetracyclines are considered as a treatment option. Glycyclines (i.e., tigecycline) are often considered for treatment of multidrug-resistant gram-negative infections.	Tigecycline is a drug that does not distribute evenly in the body, so it is often used in combination with other drugs depending upon the site of infection. Resistance to tigecycline has emerged but it is still relatively uncommon.
Polymyxins	These drugs are an older class that fell out of favor because of toxicity concerns. Now they are often used as a "last resort" agent for treatment of multidrug-resistant gram-negative infections.	Because these are generic drugs, there are limited contemporary data on proper dosing. In addition, resistance is emerging, but there are limited data guiding the accurate detection of resistance in hospital labs. As a result, use of these drugs present significant challenges for clinicians. In the absence of a drug sponsor, FDA and NIH are funding studies to fill these critical information gaps.

People at Especially High Risk

As antibiotic resistance grows, the antibiotics used to treat infections do not work as well or at all. The loss of effective antibiotic treatments will not only cripple the ability to fight routine infectious diseases but will also undermine treatment of infectious complications in patients with other diseases. Many of the advances in medical treatment—joint replacements, organ transplants, cancer therapy, and treatment of chronic diseases such as diabetes, asthma, rheumatoid arthritis—are dependent on the ability to fight infections with antibiotics. If that ability is lost, the ability to safely offer people many life-saving and life-improving modern medical advantages will be lost with it. For example:

CANCER CHEMOTHERAPY

People receiving chemotherapy are often at risk for developing an infection when their white blood cell count is low. For these patients, any infection can quickly become serious and effective antibiotics are critical for protecting the patient from severe complications or death.

COMPLEX SURGERY

Patients who receive cardiac bypass, joint replacements, and other complex surgeries are at risk of a surgical site infection (SSI). These infections can make recovery from surgery more difficult because they can cause additional illness, stress, cost, and even death. For some, but not all surgeries, antibiotics are given before surgery to help prevent infections.

RHEUMATOID ARTHRITIS

Inflammatory arthritis affects the immune system, which controls how well the body fights off infections. People with certain types of arthritis have a higher risk of getting infections. Also, many medications given to treat inflammatory arthritis can weaken the immune system. Effective antibiotics help ensure that arthritis patients can continue to receive treatment.

DIALYSIS FOR END-STAGE RENAL DISEASE

Patients who undergo dialysis treatment have an increased risk for getting a bloodstream infection. In fact, bloodstream infections are the second leading cause of death in dialysis patients. Infections also complicate heart disease, the leading cause of death in diaysis patients. Infection risk is higher in these patients because they have weakened immune systems and often require catheters or needles to enter their bloodstream. Effective antibiotics help ensure that dialysis patients can continue to receive life-saving treatment.

ORGAN AND BONE MARROW TRANSPLANTS

Transplant recipients are more vulnerable to infections. Because a patient undergoes complex surgery and receives medicine to weaken the immune system for a year or more, the risk of infection is high. It is estimated that 1% of organs transplanted in the United States each year carry a disease that comes from the donor—either an infection or cancer. Effective antibiotics help ensure that organ transplants remain possible.

Antibiotic Safety

ANTIBIOTICS ARE RESPONSIBLE FOR ALMOST

1 OUT OF 5

EMERGENCY DEPARTMENT VISITS FOR ADVERSE DRUG EVENTS

ANTIBIOTICS ARE THE **MOST COMMON CAUSE OF EMERGENCY DEPARTMENT VISITS** FOR ADVERSE DRUG EVENTS **IN CHILDREN UNDER 18 YEARS OF AGE.**

- Antibiotics are powerful drugs that are generally safe and very helpful in fighting disease, but there are times when antibiotics can actually be harmful.
- Antibiotics can have side effects, including allergic reactions and a potentially deadly diarrhea caused by the bacteria *Clostridium difficile (C. difficile)*. Antibiotics can also interfere with the action of other drugs a patient may be taking for another condition. These unintended reactions to antibiotics are called adverse drug events.
- When someone takes an antibiotic that they do not need, they are needlessly exposed to the side effects of the drug and do not get any benefit from it.
- Moreover, taking an antibiotic when it is not needed can lead to the development of antibiotic resistance. When resistance develops, antibiotics may not be able to stop future infections. Every time someone takes an antibiotic they don't need, they increase their risk of developing a resistant infection in the future.

Types of Adverse Drug Events Related to Antibiotics

Allergic Reactions

Every year, there are more than 140,000 emergency department visits for reactions to antibiotics. Almost four out of five (79%) emergency department visits for antibiotic-related adverse drug events are due to an allergic reaction. These reactions can range from mild rashes and itching to serious blistering skin reactions swelling of the face and throat, and breathing problems. Minimizing unnecessary antibiotic use is the best way to reduce the risk of adverse drug events from antibiotics. Patients should tell their doctors about any past drug reactions or allergies.

C. difficile

C. difficile causes diarrhea linked to at least 14,000 American deaths each year. When a person takes antibiotics, good bacteria that protect against infection are destroyed for several months. During this time, patients can get sick from *C. difficile* picked up from contaminated surfaces or spread from a healthcare provider's hands. Those most at risk are people, especially older adults, who take antibiotics and also get medical care. Take antibiotics exactly and only as prescribed.

Drug Interactions and Side Effects

Antibiotics can interact with other drugs patients take, making those drugs or the antibiotics less effective. Some drug combinations can worsen the side effects of the antibiotic or other drug. Common side effects of antibiotics include nausea, diarrhea, and stomach pain. Sometimes these symptoms can lead to dehydration and other problems. Patients should ask their doctors about drug interactions and the potential side effects of antibiotics. The doctor should be told immediately if a patient has any side effects from antibiotics.

GAPS IN KNOWLEDGE OF ANTIBIOTIC RESISTANCE

LIMITED NATIONAL, STATE, AND FEDERAL CAPACITY TO DETECT AND RESPOND TO URGENT AND EMERGING ANTIBIOTIC RESISTANCE THREATS

Even for critical pathogens of concern like carbapenem-resistant Enterobacteriaceae (CRE) and *Neisseria gonorrhoeae,* we do not have a complete picture of the domestic incidence, prevalence, mortality, and cost of resistance.

CURRENTLY, THERE IS NO SYSTEMATIC INTERNATIONAL SURVEILLANCE OF ANTIBIOTIC RESISTANCE THREATS

Today, the international identification of antibiotic resistance threats occurs through domestic importation of novel antibiotic resistance threats or through identification of overseas outbreaks.

DATA ON ANTIBIOTIC USE IN HUMAN HEALTHCARE AND IN AGRICULTURE ARE NOT SYSTEMATICALLY COLLECTED

Routine systems of reporting and benchmarking antibiotic use wherever it occurs need to be piloted and scaled nationwide.

PROGRAMS TO IMPROVE ANTIBIOTIC PRESCRIBING ARE NOT WIDELY USED IN THE UNITED STATES

These inpatient and outpatient programs hold great promise for reducing antibiotic resistance threats, improving patient outcomes, and saving healthcare dollars.

ADVANCED TECHNOLOGIES CAN IDENTIFY THREATS MUCH FASTER THAN CURRENT PRACTICE

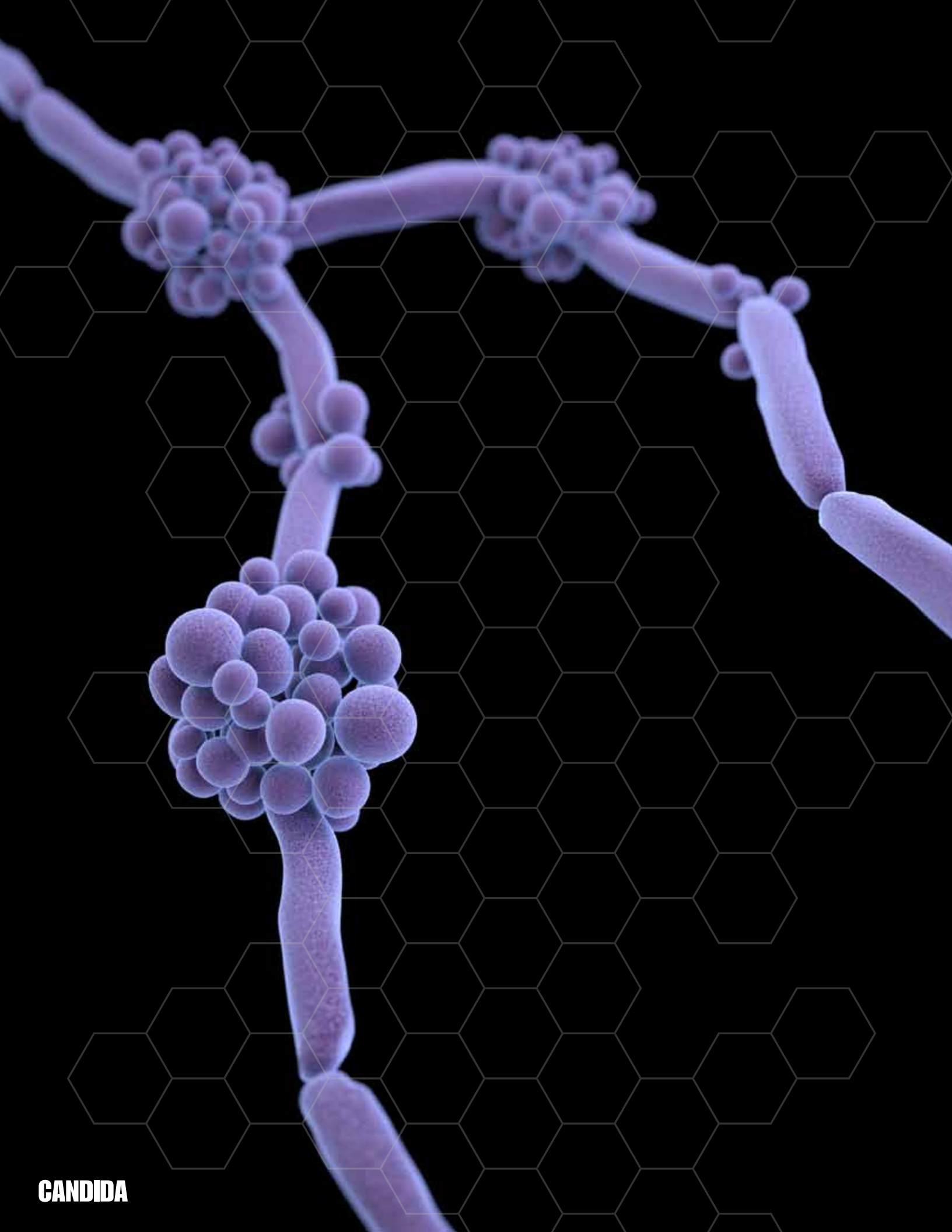
Advanced molecular detection (AMD) technologies, which can identify AR threats much faster than current practice, are not being used as widely as necessary in the United States.

Developing Resistance

Timeline of Key Antibiotic Resistance Events

Dates are based upon early reports of resistance in the literature. In the case of pan drug-resistant (PDR)-*Acinetobacter* and *Pseudomonas,* the date is based upon reports of healthcare transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.

ANTIBIOTIC RESISTANCE INDENTIFIED		ANTIBIOTIC INTRODUCED	
penicillin-R *Staphylococcus*	1940		
		1943	penicillin
		1950	tetracycline
		1953	erythromycin
tetracycline-R *Shigella*	1959		
		1960	methicillin
methicillin-R *Staphylococcus*	1962		
penicillin-R pneumococcus	1965		
erythromycin-R *Streptococcus*	1968	1967	gentamicin
		1972	vancomycin
gentamicin-R *Enterococcus*	1979		
		1985	imipenem and ceftazidime
ceftazidime-R Enterobacteriaceae	1987		
vancomycin-R *Enterococcus*	1988		
levofloxacin-R pneumococcus	1996	1996	levofloxacin
imipenem-R Enterobacteriaceae	1998		
XDR tuberculosis	2000	2000	linezolid
linezolid-R *Staphylococcus*	2001		
vancomycin-R *Staphylococcus*	2002		
PDR-*Acinetobacter and Pseudomonas*	2004/5	2003	daptomycin
ceftriaxone-R *Neisseria gonorrhoeae* PDR-Enterobacteriaceae	2009	2010	ceftaroline
ceftaroline-R *Staphylococcus*	2011		

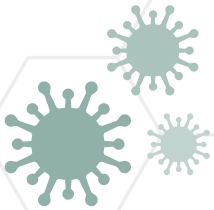


CANDIDA

FIGHTING BACK AGAINST ANTIBIOTIC RESISTANCE

Four Core Actions to Prevent Antibiotic Resistance

1 PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE



Avoiding infections in the first place reduces the amount of antibiotics that have to be used and reduces the likelihood that resistance will develop during therapy. There are many ways that drug-resistant infections can be prevented: immunization, safe food preparation, handwashing, and using antibiotics as directed and only when necessary. In addition, preventing infections also prevents the spread of resistant bacteria.

2 TRACKING

CDC gathers data on antibiotic-resistant infections, causes of infections and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts can develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

3 IMPROVING ANTIBIOTIC PRESCRIBING/STEWARDSHIP

Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic-resistant infections is to change the way antibiotics are used. Up to half of antibiotic use in humans and much of antibiotic use in animals is unnecessary and inappropriate and makes everyone less safe. Stopping even some of the inappropriate and unnecessary use of antibiotics in people and animals would help greatly in slowing down the spread of resistant bacteria. This commitment to always use antibiotics appropriately and safely—only when they are needed to treat disease, and to choose the right antibiotics and to administer them in the right way in every case—is known as antibiotic stewardship.

4 DEVELOPING NEW DRUGS AND DIAGNOSTIC TESTS

Because antibiotic resistance occurs as part of a natural process in which bacteria evolve, it can be slowed but not stopped. Therefore, we will always need new antibiotics to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

1. PREVENTING INFECTIONS, PREVENTING THE SPREAD OF RESISTANCE

FOUR CORE ACTIONS

PREVENTING INFECTIONS, PREVENTING SPREAD.

TRACKING RESISTANCE PATTERNS.

IMPROVING USE OF ANTIBIOTICS.

DEVELOPING NEW ANTIBIOTICS AND DIAGNOSTIC TESTS.

Preventing infections from developing reduces the amount of antibiotics used. This reduction in antibiotic use, in turn, slows the pace of antibiotic resistance. Preventing infections also prevents the spread of resistant bacteria. Antibiotic-resistant infections can be prevented in many ways. This section focuses on CDC's works to prevent antibiotic-resistant infections in healthcare settings, in the community, and in food.

CDC's Work to Prevent Infections and Antibiotic Resistance in Healthcare Settings

Antibiotic resistance in healthcare settings is a significant threat to public health. Because almost all Americans will receive care in a medical setting at some point, the problem can affect anyone. In addition, many times, patients in medical settings such as hospitals and long-term care facilities (e.g., skilled nursing facilities and nursing homes) are already vulnerable due to weak immune systems and underlying illness. For these patients, contracting an antibiotic-resistant infection is especially dangerous. By preventing antibiotic resistance in healthcare settings, patients' lives are better protected and their health can be better preserved. In addition, healthcare facilities, systems, insurers and patients can save dollars that otherwise would have been spent on more complex care and medications needed to manage antibiotic-resistant infections.

CDC works to prevent antibiotic resistance in healthcare settings by providing a system to track resistance and prescribing patterns at national, regional, and local levels; providing guidance to healthcare facilities interested in better antibiotic use; and working to prevent all patient infections through infection control guidelines, assistance implementing these guidelines, and laboratory expertise. Here are some examples of how CDC is working to prevent antibiotic resistance in healthcare settings:

Tracking

CDC's National Healthcare Safety Network (NHSN) is used by healthcare facilities to electronically report infections, antibiotic use, and resistance. Data currently submitted by hospitals to NHSN allow facilities, states, and regions the ability to track and benchmark antibiotic resistance in bacteria responsible for many healthcare-associated infections. As more hospitals submit data to the new NHSN Antibiotic Use and Resistance Module, they will be able to track and benchmark antibiotic resistance in all bacteria, as well as track antibiotic usage. This information will allow facilities to target areas of concern, to make needed improvements and to track the success of their efforts. In addition, NHSN allows CDC to perform and report national assessments of antibiotic resistance.

CDC's specialized, national reference laboratory tests bacteria samples from around the country to detect new and emerging resistance patterns that affect patient health. This

reference testing also provides an early warning of new resistance that has the potential to spread across the nation and that requires public health action.

Additionally, CDC recently conducted a survey in collaboration with its Emerging Infections Program to estimate the number of healthcare-associated infections and to better understand antibiotic use among inpatients in U.S. hospitals. The survey found that antibiotic use was frequent, that most antibiotic use was for treating active infections, and that vancomycin was the most commonly used antibiotic overall. Formal results are due to be published in late 2013 and 2014. CDC plans to conduct a repeat survey in 2014 that will include assessments of appropriate antibiotic prescribing.

Improving Antibiotic Prescribing

CDC manages the Get Smart program, a national campaign to improve antibiotic prescribing and use in both outpatient and inpatient settings. The program supports a variety of state-based programs modeled on the national effort. Each November, CDC publicizes its annual Get Smart About Antibiotics Week to raise awareness among patients, healthcare providers, hospital administrators, and policy makers about the threat of antibiotic resistance and the need to decrease inappropriate antibiotic use. CDC provides public health messages and resources for improving antibiotic use in healthcare settings and is now working with a variety of partners to improve the use of antibiotics in healthcare settings. One core activity is the development and implementation of the Antibiotic Stewardship Drivers and Change Package, a tool that provides healthcare facilities with a menu of interventions they can select from to improve antibiotic use. CDC developed and tested this tool with the Institute for Healthcare Improvement. Additional information about Get Smart About Antibiotics Week activities and messages can be found on CDC's website: http://www.cdc.gov/getsmart/. The Drivers and Change Package can be found at http://www.cdc.gov/getsmart/healthcare/improve-efforts/driver-diagram/index.html.

Protecting Patients from Infections

Preventing infections negates the need for antibiotic use in the first place, and scientific evidence shows that reducing antibiotic use in a single facility can reduce resistance in that facility. Taken on a national scale, infection prevention efforts can significantly decrease resistance. To help prevent infections, CDC conducts research to find new ways of preventing infections; provides the nation with infection prevention guidelines and tools to prevent infections; serves as the nation's reference laboratory to identify microorganisms; and offers the nation's largest healthcare-associated infection tracking system, NHSN, allowing facilities and states to identify and address problem areas.

CDC's Work to Prevent Antibiotic Resistance in the Community

Antibiotic-resistant infections outside of the hospital setting were rare until recently. Today, resistant infections that can be transmitted in the community include tuberculosis and respiratory infections caused by *Streptococcus pneumoniae*, skin infections caused by methicillin-resistant *Staphylococcus aureus,* and sexually transmitted infections such as gonorrhea.

CDC works to prevent antibiotic resistance in the community by providing systems to track infections and changes in resistance; improving prescribing at national, regional, and local levels; and limiting or interrupting the spread of infections. These activities are similar to the strategies used in medical settings, but the approach can differ because the population (potentially everyone) is large and the settings are different. Here are some examples of the strategies CDC uses to prevent antibiotic resistance in communities:

Tracking Community Infections and Resistance

These programs are examples of CDC's effort to identify critical infections in the community and monitor resistance trends.

- **Active Bacterial Core surveillance (ABCs):** Tracking infections caused by *Neisseria meningitidis, Streptococcus pneumoniae,* Groups A and B *Streptococcus,* and methicillin-resistant *Staphylococcus aureus*
- **Gonococcal Isolate Surveillance Project (GISP):** Collecting isolates from gonorrhea infections to monitor antibiotic resistance
- **National Tuberculosis Surveillance System (NTSS):** National Electronic Disease Surveillance System (NEDSS)-based reporting of tuberculosis cases including resistance data
- **Healthcare-Associated Infections-Community Interface (HAIC):** Tracking infections with *C. difficile* and with multidrug-resistant gram-negative microorganisms.

Improving Antibiotic Prescribing

Prescribing antibiotics when they are not needed or prescribing the wrong antibiotic in outpatient settings such as doctors' offices is common. In some cases, doctors might not order laboratory tests to confirm that bacteria are causing the infection, and therefore the antibiotic might be unnecessarily prescribed. In other cases, patients demand treatment for conditions such as a cold when antibiotics are not needed and will not help. Likewise, healthcare providers can be too willing to satisfy a patient's expectation for an antibiotic prescription. CDC manages the Get Smart program, a national campaign to improve antibiotic prescribing and use in both outpatient and inpatient settings, and supports a variety of state-based programs modeled on the national effort. CDC provides local public health authorities with messages and resources for improving antibiotic use in outpatient settings and is now working with a variety of partners to identify new approaches for improving antibiotic use.

Limiting and Interrupting the Spread of Antibiotic-Resistant Infections in the Community

Preventing the spread of infection in the community is a significant challenge, and many prevention interventions are used, depending on the type of infection and the route of transmission.

Here are some examples of CDC's activities to limit and interrupt the spread of antibiotic-resistant community infections:

- Contact Tracing: A prevention strategy that has proven successful is tracking cases (individuals who are infected) and tracing contacts (people who have had contact with a case that puts them at risk for infection as well). This process is used to ensure that all persons requiring an intervention such as treatment, prophylaxis, or temporary isolation from the general public are identified and managed appropriately. This approach is resource intensive, but it has successfully limited transmission of infections including tuberculosis, gonorrhea, and meningococcus.
- Vaccination: There are few vaccines for antibiotic-resistant bacteria, but the *S. pneumoniae* vaccine has proven that an effective vaccine can reduce antibiotic resistance rates. The vaccine targets certain types of the bacteria, even if it is a resistant type, and reduces the overall number of infections, including those that are caused by resistant strains. The first version of the vaccine was introduced in 2000 and reduced the frequency of antibiotic-resistant infections, but it did not protect against a particular strain of *S. pneumoniae* called serotype 19A. This strain became increasingly resistant to antibiotics and caused more infections because the vaccine did not offer protection. A new version of the vaccine, approved for use in 2010, protects against serotype 19A. As a result, the rate of resistant pneumococcal infections is decreasing.
- Treatment Guidelines: The spread of antibiotic resistance can be prevented if infections are effectively treated before the pathogen is spread to others. For some infections, laboratory tests for guiding treatment are not easily available or the turn-around time is slow or incomplete. This is the case for treating gonorrhea and tuberculosis. For these infections, healthcare providers rely on treatment guidelines for proper management of infections. CDC monitors resistance trends in *Neisseria gonorrhoeae* (the cause of gonorrhea) and *Mycobacterium tuberculosis* (the cause of tuberculosis) and publishes treatment guidelines to limit the progression of these diseases and the spread of bacteria.
- Promotion of Safe Sex: Increases in the spread of drug-resistant *Neisseria gonorrhoeae* poses unique challenges. To prevent transmission of this infection, CDC works to promote safer sexual behaviors such as abstinence, mutual monogamy, and correct and consistent condom use.

Preventing Infections: CDC's Work to Prevent Antibiotic Resistance in Food

Each year, millions of people in the United States become sick from foodborne and other enteric (gastrointestinal) infections. While many of these infections are mild and do not require treatment, antibiotics can be lifesaving in severe infections. Antibiotic resistance compromises our ability to treat these infections and is a serious threat to public health. Preventing resistant enteric infections requires a multifaceted approach and partnerships because bacteria that cause some infections, such as salmonellosis and campylobacteriosis, have animal reservoirs, while other bacteria, such as those that cause shigellosis and typhoid fever, have human reservoirs. To prevent antibiotic-resistant foodborne infections, CDC works closely with state and local health departments; with the U.S. Food and Drug Administration (FDA), which regulates antibiotics, many foods, animal feed, and other products; and with the U.S. Department of Agriculture (USDA), which regulates meat, poultry, and egg products.

Tracking Antibiotic Resistance

In 1996, the National Antimicrobial Resistance Monitoring System (NARMS) was established as a collaboration among CDC, FDA, USDA, and state and local public health departments. This national public health surveillance system tracks antibiotic resistance among *Salmonella, Campylobacter,* and other bacteria transmitted commonly through food. NARMS tests bacteria from humans (CDC), retail meats (FDA), and food-producing animals (USDA) in the United States. The primary objectives of the NARMS program are to:

- Monitor trends in antibiotic resistance among enteric bacteria from humans, retail meats, and food-producing animals.
- Disseminate information on antibiotic resistance to promote interventions that reduce antibiotic resistance among foodborne bacteria.
- Conduct research to better understand the emergence, persistence, and spread of antibiotic resistance.
- Provide data that assist the FDA in making decisions about approving safe and effective antibiotic drugs for animals.

The CDC reference laboratory conducts antibiotic susceptibility testing on isolates from sporadic cases and outbreaks of illness. The lab also confirms and studies bacteria that have new antibiotic resistance patterns. NARMS provides information about patterns of emerging resistance among enteric pathogens to stakeholders, including federal regulatory agencies, policymakers, consumer advocacy groups, industry, and the public, to guide public health prevention and policy efforts that protect people from resistant infections. For more information about NARMS: www.cdc.gov/narms.

Improving Antibiotic Use

Antibiotics are widely used in food-producing animals, and according to data published by FDA, there are more kilograms of antibiotics sold in the United States for food-producing animals than for people. (http://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM338170.pdf). This use contributes to the emergence of antibiotic-resistant bacteria in food-producing animals. Resistant bacteria in food-producing animals are of particular concern because these animals serve as carriers.

Resistant bacteria can contaminate the foods that come from those animals, and people who consume these foods can develop antibiotic-resistant infections. Antibiotics must be used judiciously in humans and animals because both uses contribute to not only the emergence, but also the persistence and spread of antibiotic-resistant bacteria.

Scientists around the world have provided strong evidence that antibiotic use in food-producing animals can harm public health through the following sequence of events:

- Use of antibiotics in food-producing animals allows antibiotic-resistant bacteria to thrive while susceptible bacteria are suppressed or die.
- Resistant bacteria can be transmitted from food-producing animals to humans through the food supply.
- Resistant bacteria can cause infections in humans.
- Infections caused by resistant bacteria can result in adverse health consequences for humans.

Because of the link between antibiotic use in food-producing animals and the occurrence of antibiotic-resistant infections in humans, antibiotics should be used in food-producing animals only under veterinary oversight and only to manage and treat infectious diseases, not to promote growth. CDC encourages and supports efforts to minimize inappropriate use of antibiotics in humans and animals, including FDA's strategy to promote the judicious use of antibiotics that are important in treating humans (http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/default.htm). CDC supports FDA's plan to implement draft guidance in 2013 that will operationalize this strategy (http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf). CDC has also contributed to a training curriculum for veterinarians on prudent antibiotic use in animals. CDC's efforts to improve antibiotic prescribing in humans are described in other sections of this report.

Preventing Infections

Efforts to prevent foodborne and other enteric infections help to reduce both antibiotic-resistant infections and antibiotic-susceptible infections (those that can be treated effectively with antibiotics). CDC activities that help prevent these infections include:

- Estimating how much foodborne illness occurs.
- Monitoring trends in foodborne infections.
- Investigating outbreaks and sporadic cases of foodborne illness to stop outbreaks and improve prevention.
- Attributing illnesses to specific foods and settings.
- Tracking and responding to changes in resistance.
- Determining the sources of antibiotic-resistant enteric infections.
- Educating consumers and food workers about safe food handling practices.
- Identifying and educating groups at high risk for infection.
- Promoting proper handwashing.

- Strengthening the capacity of state and local health departments to detect, respond to, and report foodborne infections.
- Developing better diagnostic tools to rapidly and accurately find sources of contamination.
- Providing recommendations for travelers on safe food and clean water.

2. TRACKING RESISTANCE PATTERNS

CDC gathers data on antibiotic-resistant infections, causes of infections, and whether there are particular reasons (risk factors) that caused some people to get a resistant infection. With that information, experts develop specific strategies to prevent those infections and prevent the resistant bacteria from spreading.

FOUR CORE ACTIONS

PREVENTING INFECTIONS, PREVENTING SPREAD.

TRACKING RESISTANCE PATTERNS.

IMPROVING USE OF ANTIBIOTICS.

DEVELOPING NEW ANTIBIOTICS AND DIAGNOSTIC TESTS.

CDC's Antibiotic Resistance and Antibiotic-Resistant Infections Tracking Platform

Tracking Networks	Data Collected	Resistant Bacteria/Fungus[3]
EIP Emerging Infections Program There are three main programs within the EIP: ■ **ABCs:** Active Bacterial Core surveillance ■ **HAIC:** Healthcare-Associated Infections-Community Interface ■ **FoodNet:** Foodborne Diseases Active Surveillance Network	A network of public health-academic-hospital collaborations in 10 states. It provides access to bacterial and fungal samples for testing and detailed clinical case data. The three main programs within EIP collect different types of resistance data: ■ ABCs provides clinical information and resistance data for bacteria that cause infections predominately in the community. ■ The HAIC provides clinical information and resistance data for bacteria and fungi that cause infections at the intersection of healthcare and the general community. ■ FoodNet supplies clinical and epidemiologic data on some human isolates in the National Antimicrobial Resistance Monitoring System (NARMS).	**ABCs:** *Streptococcus pneumoniae* Groups A and B *Streptococcus* Methicillin-resistant *Staphylococcus aureus* **HAIC:** *C. difficile* *Candida* (a fungus) Carbapenem-R Enterobacteriaceae MDR *Acinetobacter* FoodNet: (see NARMS list)
NARMS National Antimicrobial Resistance Monitoring System	A national public health surveillance system that tracks changes in the susceptibility of foodborne and other enteric bacteria to antibiotics of human and veterinary medical importance. NARMS is a collaboration among CDC, FDA, USDA, and state and local health departments. CDC tests bacterial isolates from humans, while FDA and USDA test isolates from retail meats and food animals.	*Salmonella* *Campylobacter* *Shigella*

Tracking Networks	Data Collected	Resistant Bacteria/Fungus[3]
NHSN National Healthcare Safety Network	A system that collects and provides data on infections and drug-resistance in healthcare settings. Since NHSN collects data directly from healthcare facilities, it can provide facility-level information on healthcare-associated infections and antibiotic resistance (and in the future, on antibiotic use).	*Staphylococcus aureus* *Enterococcus* Enterobacteriaceae *Acinetobacter* *Pseudomonas aeruginosa* *Candida* (a fungus)
GISP Gonococcal Isolate Surveillance Program	A program to track antibiotic resistance data for gonococcal isolates. Isolates are collected from sexually transmitted disease clinics in approximately 28 cities.	*Neisseria gonorrhoeae*
NTSS National Tuberculosis Surveillance System	National Electronic Disease Surveillance System (NEDSS)-based reporting of tuberculosis cases including resistance data. Public health departments from 50 states and the US territories contribute data.	*Mycobacterium tuberculosis*

[3]ABCs also includes surveillance for *Neisseria meningitidis* and *Haemophilus influenzae.* NARMS also includes surveillance for *E. coli O157* and *Vibrio* (non-*V. cholerae).*

3. ANTIBIOTIC STEWARDSHIP: IMPROVING PRESCRIBING AND USE

FOUR CORE ACTIONS

PREVENTING INFECTIONS, PREVENTING SPREAD.

TRACKING RESISTANCE PATTERNS.

IMPROVING USE OF ANTIBIOTICS.

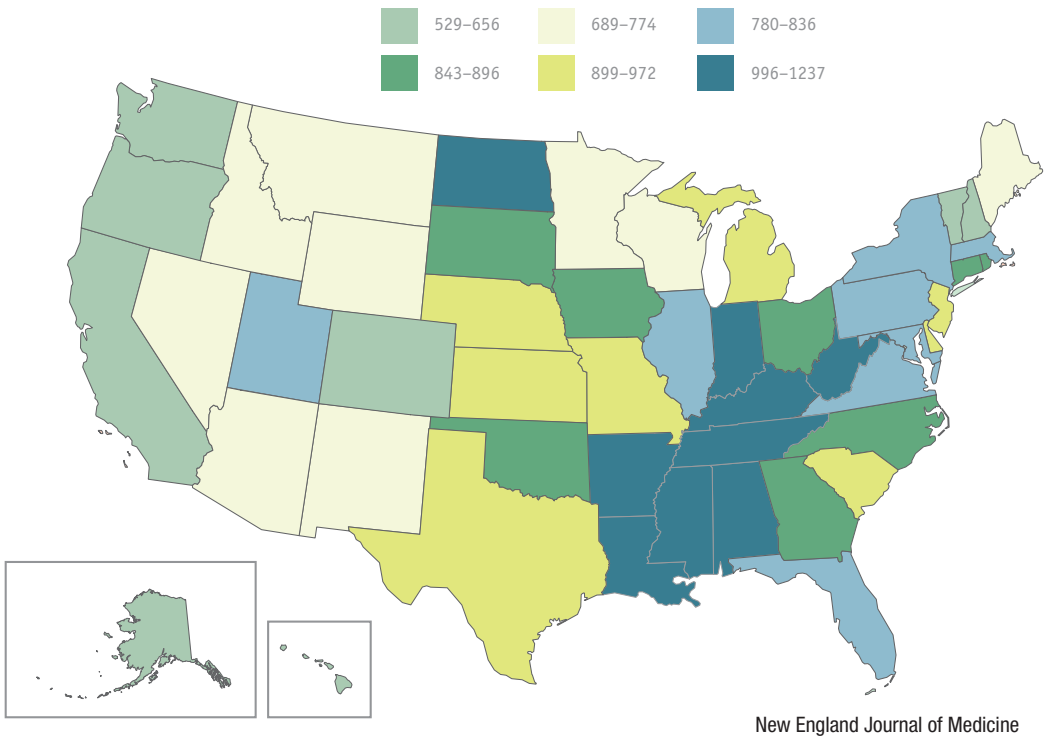
DEVELOPING NEW ANTIBIOTICS AND DIAGNOSTIC TESTS.

Antibiotics were first used to treat serious infections in the 1940s. Since then, antibiotics have saved millions of lives and transformed modern medicine. During the last 70 years, however, bacteria have shown the ability to become resistant to every antibiotic that has been developed. And the more antibiotics are used, the more quickly bacteria develop resistance *(see the Antibiotic Resistance Timeline in this report)*.

Anytime antibiotics are used, this puts biological pressure on bacteria that promotes the development of resistance. When antibiotics are needed to prevent or treat disease, they should always be used. But research has shown that as much as 50% of the time, antibiotics are prescribed when they are not needed or they are misused (for example, a patient is given the wrong dose). This not only fails to help patients; it might cause harm. Like every other drug, antibiotics have side effects and can also interact or interfere with the effects of other medicines. This inappropriate use of antibiotics unnecessarily promotes antibiotic resistance.

Antibiotics are a limited resource. The more that antibiotics are used today, the less likely they will still be effective in the future. Therefore, doctors and other health professionals around the world are increasingly adopting the principles of responsible antibiotic use, often called antibiotic stewardship. Stewardship is a commitment to always use antibiotics only when they are necessary to treat, and in some cases prevent, disease; to choose the right antibiotics; and to administer them in the right way in every case. Effective stewardship ensures that every patient gets the maximum benefit from the antibiotics, avoids unnecessary harm from allergic reactions and side effects, and helps preserve the life-saving potential of these drugs for the future. Efforts to improve the responsible use of antibiotics have not only demonstrated these benefits but have also been shown to improve outcomes and save healthcare facilities money in pharmacy costs.

Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010



The frequency with which doctors prescribe antibiotics varies greatly from state to state. The reasons for this variation are being studied and might suggest areas where improvements in antibiotic prescribing (fewer unnecessary prescriptions) would be most helpful.

ANTIBIOTIC STEWARDSHIP
IN YOUR FACILITY WILL

DECREASE

- ANTIBIOTIC RESISTANCE
- C. DIFFICILE INFECTIONS
- COSTS

INCREASE

- GOOD PATIENT OUTCOMES

PROMOTE ANTIBIOTIC BEST PRACTICES— A FIRST STEP IN ANTIBIOTIC STEWARDSHIP

- ENSURE ALL ORDERS HAVE DOSE, DURATION, AND INDICATIONS
- GET CULTURES BEFORE STARTING ANTIBIOTICS
- TAKE AN "ANTIBIOTIC TIMEOUT" REASSESSING ANTIBIOTICS AFTER 48–72 HOURS

ANTIBIOTIC STEWARDSHIP PROGRAMS ARE A "WIN-WIN" FOR ALL INVOLVED

A UNIVERSITY OF MARYLAND STUDY SHOWED ONE ANTIBIOTIC STEWARDSHIP PROGRAM **SAVED A TOTAL OF $17 MILLION** OVER EIGHT YEARS

ANTIBIOTIC STEWARDSHIP HELPS **IMPROVE PATIENT CARE AND SHORTEN HOSPTIAL STAYS,** THUS **BENEFITING PATIENTS AS WELL AS HOSPITALS**

4. DEVELOPING NEW ANTIBIOTICS AND DIAGNOSTIC TESTS

Because antibiotic resistance occurs as part of a natural evolution process, it can be significantly slowed but not stopped. Therefore, new antibiotics will always be needed to keep up with resistant bacteria as well as new diagnostic tests to track the development of resistance.

FOUR CORE ACTIONS

PREVENTING INFECTIONS, PREVENTING SPREAD.

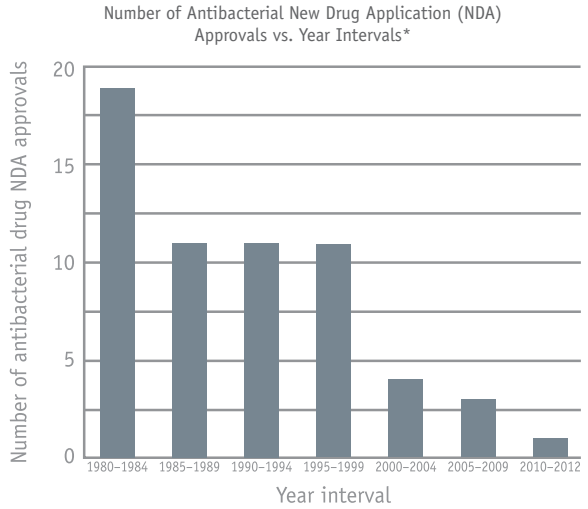
TRACKING RESISTANCE PATTERNS.

IMPROVING USE OF ANTIBIOTICS.

DEVELOPING NEW ANTIBIOTICS AND DIAGNOSTIC TESTS.

Tomorrow's Antibiotics: The Drug Pipeline

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.



*Intervals from 1980–2009 are 5-year intervals; 2010–2012 is a 3-year interval. Drugs are limited to systemic agents.
Data courtesy of FDA' s Center for Drug Evaluation and Research (CDER).

Examples of Recently Approved Drugs

Drug Name	Year Approved	Key Targeted Pathogens	Drug's Use and Resistance Trends
Quinupristin/ Dalfoprisitin	1999	*Staphylococcus* *Streptococcus*	This is a combination of two drugs that can be used to treat gram-positive infections. Because side effects are common, this drug is usually not a first choice for therapy. Resistance in target pathogens has been described, but the percentage in the United States is still low.
Moxifloxacin	1999	Enterobacteriaceae *Staphylococcus* *Streptococcus*	Moxifloxacin, like other fluoroquinolones, demonstrates broad spectrum activity, and it can be used to treat a range of infections. Unfortunately, there is cross-resistance among the fluoroquinolones, and resistance is increasing in all targeted pathogens, especially Enterobacteriaceae.
Linezolid	2000	*Staphylococcus* *Enterococcus*	Linezolid can be used to treat serious gram-positive infections. Resistance has occurred but it is still uncommon.
Ertapenem	2001	Enterobacteriaceae *Staphylococcus* *Streptococcus*	Ertapenem is a carbapenem that can be used to treat a wide range of infections. Dissemination of carbapenem-resistant Enterobacteriaceae (CRE) is impacting the drug's overall effectiveness.
Gemifloxacin	2003	Enterobacteriaceae *Streptococcus*	Gemifloxacin is a fluoroquinolone that can be used to treat mild to moderate community-associated respiratory disease. Like moxifloxacin, there is cross-resistance with other fluoroquinolone drugs so resistance is increasing.
Daptomycin	2003	*Staphylococcus* *Streptococcus* *Enterococcus*	Daptomycin is often used for treatment of serious gram-positive infections. Resistance is emerging in all of the targeted pathogens, but the resistance rates are currently low.
Tigecycline	2005	Enterobacteriaceae *Staphylococcus* *Streptococcus* *Enterococcus*	Tigecycline is often one of the only active agents for carbapenem-resistant gram-negative infections, and resistance is emerging. However, even in the absence of resistance, the effectiveness of this agent for treatment of the most serious infections is a concern.
Doripenem	2007	Enterobacteriaceae *Pseudomonas aeruginosa* *Acinetobacter spp.* *Streptococcus spp.*	Doripenem is a carbapenem drug most commonly used to treat serious gram-negative infections. Dissemination of carbapenem-resistant gram-negative pathogens like CRE is reducing the overall effectiveness of this drug.
Telavancin	2008	*Staphylococcus* *Streptococcus* *Enterococcus*	Telavancin is approved for treatment of gram-positive skin and soft tissue infections. Use is limited because it is administered intravenously and is therefore difficult to use in an outpatient setting. In addition, it should not be used in a woman of childbearing age without a pregnancy test.

Drug Name	Year Approved	Key Targeted Pathogens	Drug's Use and Resistance Trends
Ceftaroline	2010	Enterobacteriaceae *Staphylococcus* *Streptococcus*	Ceftaroline is a cephalosporin drug, but unlike other cephalosporins, this one can be used to treat MRSA infections. Resistance has been identified but is rare. Ceftaroline does not demonstrate any enhanced activity compared to other cephalosporins for Enterobacteriaceae. ESBL-producing isolates and CRE isolates are resistant to this drug as well. ESBL (extended-spectrum β-lactamase) is an enzyme that allows bacteria to become resistant to a wide variety of penicillins and cephalosporins .Bacteria that contain this enzyme are known as ESBLs or ESBL-producing bacteria.

CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE)

CURRENT ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES, BY MICROORGANISM

This section includes summaries for each microorganism, grouped by threat level: URGENT, SERIOUS, and CONCERNING.

THREAT LEVEL
URGENT

These bacteria are immediate public health threats that require urgent and aggressive action.

MICROORGANISMS WITH A THREAT LEVEL OF URGENT

Clostridium difficile

Carbapenem-resistant **Enterobacteriaceae**

Drug-resistant ***Neisseria gonorrhoeae***

CLOSTRIDIUM DIFFICILE

THREAT LEVEL
URGENT

This bacteria is an immediate public health threat that requires urgent and aggressive action.

250,000
INFECTIONS PER YEAR

14,000
DEATHS

$1,000,000,000
IN EXCESS MEDICAL COSTS PER YEAR

Clostridium difficile (C. difficile) causes life-threatening diarrhea. These infections mostly occur in people who have had both recent medical care and antibiotics. Often, *C. difficile* infections occur in hospitalized or recently hospitalized patients.

RESISTANCE OF CONCERN

- Although resistance to the antibiotics used to treat *C. difficile* infections is not yet a problem, the bacteria spreads rapidly because it is naturally resistant to many drugs used to treat other infections.
- In 2000, a stronger strain of the bacteria emerged. This strain is resistant to fluoroquinolone antibiotics, which are commonly used to treat other infections.
- This strain has spread throughout North America and Europe, infecting and killing more people wherever it spreads.

PUBLIC HEALTH THREAT

- 250,000 infections per year requiring hospitalization or affecting already hospitalized patients.
- 14,000 deaths per year.
- At least $1 billion in excess medical costs per year.
- Deaths related to *C. difficile* increased 400% between 2000 and 2007, in part because of a stronger bacteria strain that emerged.
- Almost half of infections occur in people younger than 65, but more than 90% of deaths occur in people 65 and older.
- About half of *C. difficile* infections first show symptoms in hospitalized or recently hospitalized patients, and half first show symptoms in nursing home patients or in people recently cared for in doctors' offices and clinics.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Tracking and reporting national progress toward preventing *C. difficile* infections.
- Promoting *C. difficile* prevention programs and providing gold-standard patient safety recommendations.
- Providing prevention expertise, as well as outbreak and laboratory assistance, to health departments and healthcare facilities.

WHAT YOU CAN DO

CEOs, Medical Officers, and other Healthcare Facility Leaders Can:

- Support better testing (nucleic acid amplification tests), tracking, and reporting of infections and prevention efforts.
- Ensure policies for rapid detection and isolation of patients with *C. difficile* are in place and followed.
- Assess hospital cleaning to be sure it is performed thoroughly, and augment this using an Environmental Protection Agency-approved, spore-killing disinfectant in rooms where *C. difficile* patients are treated.
- Notify other healthcare facilities about infectious diseases when patients transfer, especially between hospitals and nursing homes.
- Participate in a regional *C. difficile* prevention effort.

Healthcare Providers Can:

- Prescribe antibiotics carefully (see http://www.cdc.gov/getsmart/specific-groups/hcp/index.html). Once culture results are available, check whether the prescribed antibiotics are correct and necessary.
- Order a *C. difficile* test (preferably a nucleic acid amplification test) if the patient has had 3 or more unformed stools within 24 hours.
- Be aware of infection rates in your facility or practice, and follow infection control recommendations with every patient. This includes using contact precautions (gloves and gowns) and isolation for patients who are suspected to have *C. difficile,* and continuing those practices for those with positive test results.

Patients can:

- Take antibiotics only as prescribed by your doctor and complete the prescribed course of treatment. Antibiotics can be lifesaving medicines.
- Tell your doctor if you have been on antibiotics and get diarrhea within a few months.
- Wash your hands before eating and after using the bathroom.
- Try to use a separate bathroom if you have diarrhea, or be sure the bathroom is cleaned well if someone with diarrhea has used it.

ONLINE RESOURCES

Vital Signs, March 2012: Making Health Care Safer
http://www.cdc.gov/vitalsigns/hai/

Clostridium difficile Infection resources
http://www.cdc.gov/HAI/organisms/cdiff/Cdiff_infect.html

CS239559-B

CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

9,000 DRUG-RESISTANT INFECTIONS PER YEAR

600 DEATHS

CARBAPENEM-RESISTANT *KLEBSIELLA* SPP. **7,900**

1,400 CARBAPENEM-RESISTANT *E. COLI*

CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS

THREAT LEVEL
URGENT

This bacteria is an immediate public health threat that requires urgent and aggressive action.

Untreatable and hard-to-treat infections from carbapenem-resistant Enterobacteriaceae (CRE) bacteria are on the rise among patients in medical facilities. CRE have become resistant to all or nearly all the antibiotics we have today. Almost half of hospital patients who get bloodstream infections from CRE bacteria die from the infection.

RESISTANCE OF CONCERN

- Some Enterobacteriaceae are resistant to nearly all antibiotics, including carbapenems, which are often considered the antibiotics of last resort.
- More than 9,000 healthcare-associated infections are caused by CRE each year.
- CDC laboratories have confirmed at least one type of CRE in healthcare facilities in 44 states.
- About 4% of U.S. short-stay hospitals had at least one patient with a serious CRE infection during the first half of 2012. About 18% of long-term acute care hospitals had one.

PUBLIC HEALTH THREAT

An estimated 140,000 healthcare-associated Enterobacteriaceae infections occur in the United States each year; about 9,300 of these are caused by CRE. Up to half of all bloodstream infections caused by CRE result in death. Fortunately, bloodstream infections account for a minority of all healthcare-associated infections caused by Enterobacteriaceae. Each year, approximately 600 deaths result from infections caused by the two most common types of CRE, carbapenem-resistant *Klebsiella* spp. and carbapenem-resistant *E. coli*.

	Percentage of Enterobacteriaceae healthcare-associated infections resistant to carbapenems	Estimated number of infections	Estimated number of deaths attributed
Carbapenem-Resistant *Klebsiella* spp.	11%	7,900	520
Carbapenem-resistant *E. coli*	2%	1,400	90

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Tracking illness and identifying risk factors for CRE infections using two systems, the National Healthcare Safety Network and the Emerging Infections Program.
- Providing CRE outbreak support, such as staff expertise, prevention guidelines, tools, and lab assistance, to states and facilities.
- Developing tests and prevention programs to identify and control CRE. CDC's "Detect and Protect" effort (http://www.cdc.gov/hai/pdfs/cre/CDC_DetectProtect.pdf) supports regional CRE programs.
- Helping medical facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities Can:

- Know CRE trends in your region.
- Coordinate regional CRE tracking and control efforts in areas with CRE. Areas not yet or rarely affected by CRE infections can be proactive in CRE prevention efforts.
- Require facilities to alert each other when transferring patients with any infection.
- Consider including CRE infections on your state's Notifiable Diseases list.

Healthcare CEOs, Medical Officers, and Other Healthcare Facility Leaders Can:

- Require and strictly enforce CDC guidance for CRE detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify CRE and alert clinical and infection prevention staff when these bacteria are present.
- Know CRE trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about infections, including CRE.
- Join or start regional CRE prevention efforts, and promote wise antibiotic use.

Health Care Providers Can:

- Know if patients with CRE are hospitalized at your facility, and stay aware of CRE infection risks. Ask if your patients have received medical care somewhere else, including another country.
- Follow infection control recommendations with every patient, using contact precautions for patients with CRE. Whenever possible, dedicate rooms, equipment, and staff to CRE patients.
- Prescribe antibiotics wisely (http://www.cdc.gov/getsmart/healthcare). Use culture results to modify prescriptions if needed.
- Remove temporary medical devices as soon as possible.

Patients Can:

- Tell your doctor if you have been hospitalized in another facility or country.
- Take antibiotics only as prescribed.
- Insist that everyone wash their hands before touching you.

ONLINE RESOURCES

Vital Signs, March 2013: Making Health Care Safer

2012 CRE Toolkit
http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html

MMWR, March 2013
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6209a3.htm?s_cid=mm6209a3_w

Get Smart for Healthcare
http://www.cdc.gov/getsmart/healthcare

Carbapenem-resistant Enterobacteriaceae (CRE) Resources
http://www.cdc.gov/HAI/organisms/cre/index.html

CS239559-B

DRUG-RESISTANT NEISSERIA GONORRHOEAE

THREAT LEVEL
URGENT

This bacteria is an immediate public health threat that requires urgent and aggressive action.

246,000 DRUG-RESISTANT GONORRHEA INFECTIONS

188,600 RESISTANCE TO TETRACYCLINE

11,480 REDUCED SUSCEPTIBILITY TO CEFIXIME

3,280 REDUCED SUSCEPTIBILITY TO CEFTRIAXONE

2,460 REDUCED SUSCEPTIBILITY TO AZITHROMYCIN

820,000 GONOCOCCAL INFECTIONS PER YEAR

Neisseria gonorrhoeae causes gonorrhea, a sexually transmitted disease that can result in discharge and inflammation at the urethra, cervix, pharynx, or rectum.

RESISTANCE OF CONCERN

N. gonorrhoeae is showing resistance to antibiotics usually used to treat it. These drugs include:

- cefixime (an oral cephalosporin)
- ceftriaxone (an injectable cephalosporin)
- azithromycin
- tetracycline

PUBLIC HEALTH THREAT

Gonorrhea is the second most commonly reported notifiable infection in the United States and is easily transmitted. It causes severe reproductive complications and disproportionately affects sexual, racial, and ethnic minorities. Gonorrhea control relies on prompt identification and treatment of infected persons and their sex partners. Because some drugs are less effective in treating gonorrhea, CDC recently updated its treatment guidelines to slow the emergence of drug resistance. CDC now recommends only ceftriaxone plus either azithromycin or doxycycline as first-line treatment for gonorrhea. The emergence of cephalosporin resistance, especially ceftriaxone resistance, would greatly limit treatment options and could cripple gonorrhea control efforts.

In 2011, 321,849 cases of gonorrhea were reported to CDC, but CDC estimates that more than 800,000 cases occur annually in the United States.

	Percentage	Estimated number of cases
Gonorrhea		820,000
Resistance to any antibiotic	30%	246,000
Reduced susceptibility to cefixime	<1%	11,480
Reduced susceptibility to ceftriaxone	<1%	3,280
Reduced susceptibility to azithromycin	<1%	2,460
Resistance to tetracycline	23%	188,600

Source: The Gonococcal Isolate Surveillance Project (GISP)–5,900 isolates tested for susceptibility in 2011.
For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

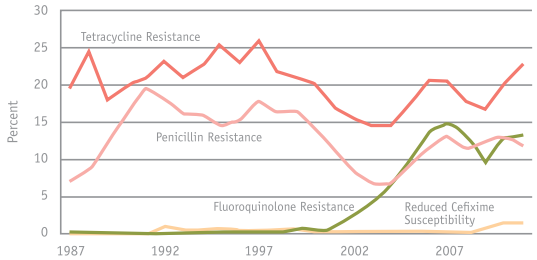
DRUG-RESISTANT NEISSERIA GONORRHOEAE

FIGHTING THE SPREAD OF RESISTANCE

Cephalosporin-resistant *N. gonorrhoeae* is often resistant to multiple classes of other antibiotics and as a result, infections caused by these bacteria will likely fail empiric treatment regimens. If cephalosporin-resistant *N. gonorrhoeae* becomes widespread, the public health impact during a 10-year period is estimated to be 75,000 additional cases of pelvic inflammatory disease (a major cause of infertility), 15,000 cases of epididymitis, and 222 additional HIV infections because HIV is transmitted more readily when someone is co-infected with gonorrhea. In addition, the estimated direct medical costs would total $235 million. Additional costs are anticipated to be incurred as a result of increased susceptibility monitoring, provider education, case management, and the need for additional courses of antibiotics and follow-up.

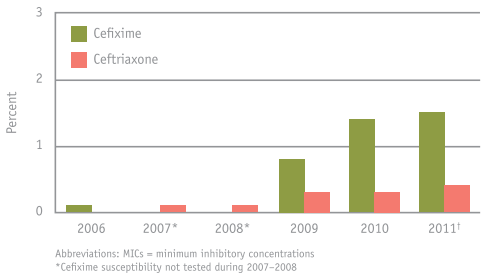
Gonorrhea is a global problem, requiring a global approach. Action in the United States alone is unlikely to prevent resistance from developing, but rapid detection and effective treatment of patients and their partners might slow the spread of resistance. Preventing gonorrhea is critical. Screening, rapid detection, prompt treatment, and partner services are the foundations of gonorrhea control in the United States. Effectively addressing the heavy burden of gonorrhea and anticipated arrival of cephalosporin resistance requires continued use of these strategies as well as the use of expedited partner therapy, promotion of safer sexual behaviors such as abstinence, mutual monogamy, and correct and consistent condom use, and activities designed to rapidly detect and respond to antibiotic-resistant infections

New resistance patterns have developed over time. Resistance to previously used antibiotics, such as penicillin, remains common.



Source: The Gonococcal Isolate Surveillance Project (GISP).

These trends are an early warning of cephalosporin resistance.



Source: The Gonococcal Isolate Surveillance Project (GISP).

WHAT CDC IS DOING

CDC is closely monitoring resistance in *N. gonorrhoeae* in the United States and actively collaborating with the World Health Organization to enhance global surveillance. In the United States, CDC recently released a national response plan and is working closely with local and state STD programs to enhance preparedness. CDC recently updated its gonorrhea treatment recommendations to stay a step ahead of this rapidly evolving bacterium, and is collaborating with the NIH National Institute of Allergy and Infectious Diseases to find new treatment options.

ONLINE RESOURCES

CDC's gonorrhea website
http://www.cdc.gov/std/gonorrhea/default.htm

CDC's Antibiotic-Resistant Gonorrhea website:
http://www.cdc.gov/std/Gonorrhea/arg/default.htm

New Treatment Guidelines for Gonorrhea: Antibiotic Change. MedScape CDC Expert Commentary, 2012. http://www.medscape.com/viewarticle/768883

Kirkcaldy RD, Bolan GA, Wasserheit JN. Cephalosporin-Resistant Gonorrhea in North America. JAMA 2013;209(2):185-187.
http://jama.jamanetwork.com/article.aspx?articleid=1556135

CDC. Update to CDC's Sexually Transmitted Diseases Treatment Guidelines, 2010: Oral cephalosporins no longer a recommended treatment for gonococcal infections. MMWR 2012;61(31):590-594.
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?

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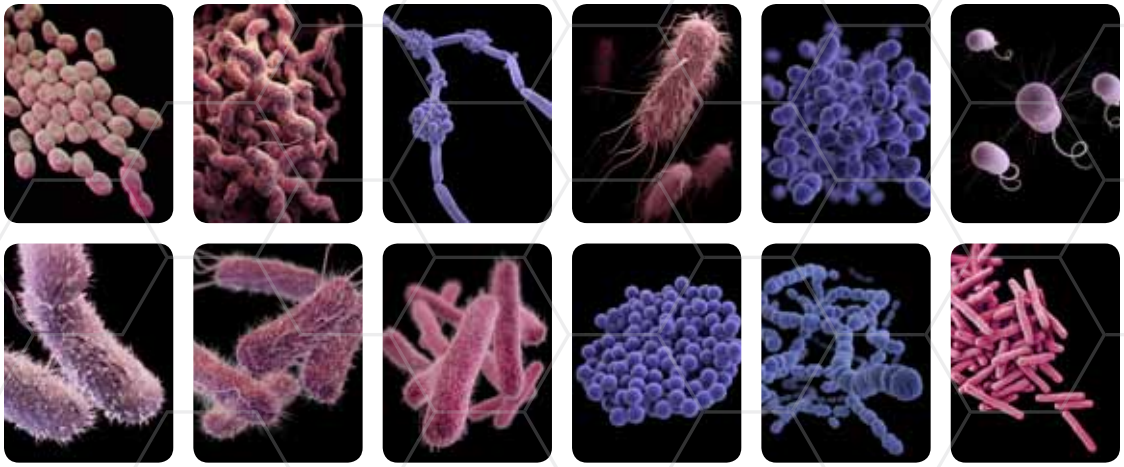

THREAT LEVEL
SERIOUS

These bacteria are a serious concern and require prompt and sustained action to ensure the problem does not grow.

MICROORGANISMS WITH A THREAT LEVEL OF SERIOUS

Multidrug-resistant ***Acinetobacter***

Drug-resistant ***Campylobacter***

Fluconazole-resistant ***Candida*** (a fungus)

Extended spectrum β-lactamase producing **Enterobacteriaceae (ESBLs)**

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

Multidrug-resistant ***Pseudomonas aeruginosa***

Drug-resistant **non-typhoidal *Salmonella***

Drug-resistant ***Salmonella*** **Typhi**

Drug-resistant ***Shigella***

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

Drug-resistant ***Streptococcus pneumoniae***

Drug-resistant **tuberculosis**

MULTIDRUG-RESISTANT ACINETOBACTER

7,300 MULTIDRUG-RESISTANT *ACINETOBACTER* INFECTIONS

500 DEATHS FROM MULTIDRUG-RESISTANT INFECTIONS

12,000 *ACINETOBACTER* INFECTIONS PER YEAR

AT LEAST THREE DIFFERENT CLASSES OF ANTIBIOTICS
NO LONGER CURE RESISTANT ACINETOBACTER INFECTIONS

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Acinetobacter is a type of gram-negative bacteria that is a cause of pneumonia or bloodstream infections among critically ill patients. Many of these bacteria have become very resistant to antibiotics.

RESISTANCE OF CONCERN

Some *Acinetobacter* strains are resistant to nearly all or all antibiotics including carbapenems, often considered antibiotics of last resort.

- About 63% of *Acinetobacter* is considered multidrug-resistant, meaning at least three different classes of antibiotics no longer cure *Acinetobacter* infections.
- Approximately 2% of healthcare-associated infections reported to CDC's National Healthcare Safety Network are caused by *Acinetobacter,* but the proportion is higher among critically ill patients on mechanical ventilators (about 7%).

PUBLIC HEALTH THREAT

An estimated 12,000 healthcare-associated *Acinetobacter* infections occur in the United States each year. Nearly 7,000 (or 63%) of these are multidrug-resistant, and about 500 deaths are attributed to these infections.

	Percentage of all *Acinetobacter* healthcare-associated infections that are multidrug-resistant	Estimated number of infections	Estimated number of deaths attributed
Multidrug-resistant *Acinetobacter*	63%	7,300	500

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

MULTIDRUG-RESISTANT ACINETOBACTER

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Tracking illness and identifying risk factors for drug-resistant infections using two systems, the National Healthcare Safety Network and the Emerging Infections Program.
- Providing outbreak support such as staff expertise, prevention guidelines, tools, and lab assistance, to states and facilities.
- Developing tests and prevention recommendations to control drug-resistant infections.
- Helping medical facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities Can:

- Know resistance trends in your region.
- Coordinate local and regional infection tracking and control efforts.
- Require facilities to alert each other when transferring patients with any infection.

Healthcare CEOs, Medical Officers, and other Healthcare Facility Leaders Can:

- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections and alert clinical and infection prevention staff when these bacteria are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.

Healthcare Providers Can:

- Know the type of drug-resistant infections that are present in your facility and patients.
  - Request immediate alerts when the lab identifies drug-resistant infections in your patients.
  - Alert the other facility when you transfer a patient with a drug-resistant infection.
- Protect patients from drug-resistant infections.
  - Follow relevant guidelines and precautions at every patient encounter.
  - Prescribe antibiotics wisely.
  - Remove temporary medical devices such as catheters and ventilators as soon as no longer needed.

Patients and Their Loved Ones Can:

- Ask everyone including doctors, nurses, other medical staff, and visitors, to wash their hands before touching the patient.
- Take antibiotics exactly as prescribed.

ONLINE RESOURCES

***Acinetobacter* in Healthcare Settings**
http://www.cdc.gov/HAI/organisms/acinetobacter.html

Healthcare-associated Infections, Guidelines and Recommendations
http://www.cdc.gov/HAI/prevent/prevent_pubs.html

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DRUG-RESISTANT CAMPYLOBACTER

310,000 DRUG-RESISTANT *CAMPYLOBACTER* INFECTIONS PER YEAR

1,300,000 *CAMPYLOBACTER* INFECTIONS PER YEAR

13,000 HOSPITALIZATIONS

120 DEATHS

THREAT LEVEL **SERIOUS**

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Campylobacter usually causes diarrhea (often bloody), fever, and abdominal cramps, and sometimes causes serious complications such as temporary paralysis.

RESISTANCE OF CONCERN

Physicians rely on drugs like ciprofloxacin and azithromycin for treating patients with severe disease. Resistant infections sometimes last longer. *Campylobacter* is showing resistance to:

- ciprofloxacin
- azithromycin

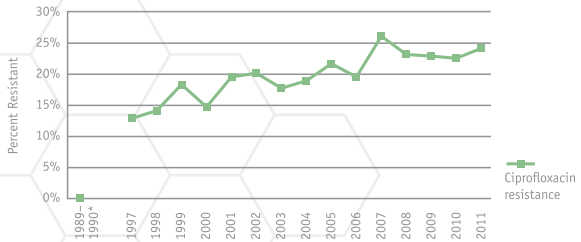
PUBLIC HEALTH THREAT

Campylobacter is estimated to cause approximately 1.3 million infections, 13,000 hospitalizations, and 120 deaths each year in the United States. CDC is seeing resistance to ciprofloxacin in almost 25% of *Campylobacter* tested and resistance to azithromycin in about 2%. Costs are expected to be higher for resistant infections because antibiotic-resistant *Campylobacter* infections sometimes last longer.

	Percentage of all *Campylobacter**	Estimated number of illnesses per year	Estimated illnesses per 100,000 U.S. population	Estimated number of deaths per year
Resistance to ciprofloxacin	23%	310,000	102.3	28
Resistance to azithromycin	2%	22,000	7.4	<5
Resistance to azithromycin or ciprofloxacin	24%	310,000	103.9	28

Campylobacter drug resistance increased from 13% in 1997 to almost 25% in 2011.

Increasing Resistance to Ciprofloxacin in *Campylobacter*, 1989–2011



*3-year average (2009–2011)

*Data for 1989–1990 were from a sentinel county survey. Annual testing began in 1997.

For more information about data methods and references, please see appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

FIGHTING THE SPREAD OF RESISTANCE

Campylobacter spreads from animals to people through contaminated food, particularly raw or undercooked chicken and unpasteurized milk. Infections may also be acquired through contact with animals and by drinking contaminated water. Antibiotic use in food animals can result in resistant *Campylobacter* that can spread to humans. Resistant *Campylobacter* are common in many countries and cause illness in travelers. Key measures to prevent resistant infections include:

- Avoiding inappropriate antibiotic use in food animals.
- Tracking antibiotic use in different types of food animals.
- Stopping spread of *Campylobacter* among animals on farms.
- Improving food production and processing to reduce contamination.
- Educating consumers and food workers about safe food handling practices.

WHAT CDC IS DOING

- Tracking changes in antibiotic resistance through ongoing surveillance.
- Promoting initiatives that measure and improve antibiotic use in food animals.
- Determining foods responsible for outbreaks of *Campylobacter* infections.
- Supporting and improving local, state, and federal public health surveillance.
- Guiding prevention efforts by estimating how much illness occurs and identifying the sources of infection.
- Educating people about how to avoid *Campylobacter* infections.

WHAT YOU CAN DO

- **Clean.** Wash hands, cutting boards, utensils, sinks, and countertops.
- **Separate.** Keep raw meat, poultry, and seafood separate from ready-to-eat foods.
- **Cook.** Use a food thermometer to ensure that foods are cooked to a safe internal temperature.
- **Chill.** Keep your refrigerator below 40°F and refrigerate food that will spoil.
- Avoid drinking raw milk and untreated water.
- Report suspected illness from food to your local health department.
- Don't prepare food for others if you have diarrhea or vomiting.
- Be especially careful preparing food for children, pregnant women, those in poor health, and older adults.
- Consume safe food and water when traveling abroad.

ONLINE RESOURCES

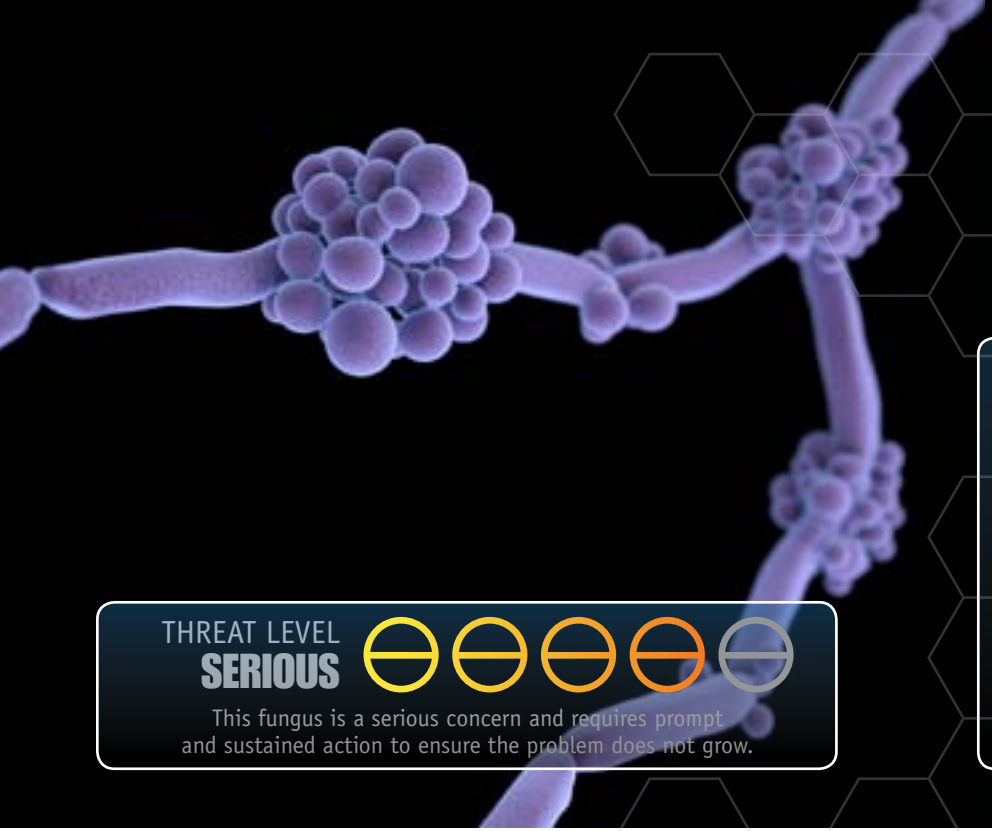
National Antimicrobial Resistance Monitoring System
http://www.cdc.gov/narms

***Campylobacter* Information**
http://www.cdc.gov/nczved/divisions/dfbmd/diseases/campylobacter/

Traveler's Health
http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-2-the-pre-travel-consultation/travelers-diarrhea.htm

Vital Signs, June 2011: Making Food Safer to Eat
http://www.cdc.gov/VitalSigns/FoodSafety/

FLUCONAZOLE-RESISTANT CANDIDA



THREAT LEVEL
SERIOUS

This fungus is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

3,400
FLUCONAZOLE-RESISTANT *CANDIDA* INFECTIONS

220
DEATHS

46,000
CANDIDA INFECTIONS PER YEAR

Candidiasis is a fungal infection caused by yeasts of the genus *Candida*. There are more than 20 species of *Candida* yeasts that can cause infection in humans, the most common of which is *Candida albicans*. *Candida* yeasts normally live on the skin and mucous membranes without causing infection. However, overgrowth of these microorganisms can cause symptoms to develop. Symptoms of candidiasis vary depending on the area of the body that is infected.

Candida is the fourth most common cause of healthcare-associated bloodstream infections in the United States. In some hospitals it is the most common cause. These infections tend to occur in the sickest of patients.

RESISTANCE OF CONCERN

- Some *Candida* strains are increasingly resistant to first-line and second-line antifungal treatment agents. Recent data demonstrate a marked shift among infections towards *Candida* species with increased resistance to antifungal drugs including azoles and echinocandins.
- CDC conducts multicenter surveillance for antifungal resistance in the United States, candidal infections, their economic impact, and possible areas where prevention and control strategies can be focused.

PUBLIC HEALTH THREAT

An estimated 46,000 healthcare-associated *Candida* infections occur among hospitalized patients in the United States each year. Roughly 30% of patients with bloodstream infections (candidemia) with drug-resistant *Candida* die during their hospitalization. CDC estimates that each case of *Candida* infection results in 3–13 days of additional hospitalization, and a total of $6,000–$29,000 in direct healthcare costs. Based on these estimates, we calculate resistant *Candida* infections may add millions of dollars in excess costs to U.S. healthcare expenditures each year.

	Percentage of Candida bloodstream isolates testing resistant	Estimated number of infections per year	Estimated number of deaths
Fluconazole-resistant *Candida* species	7%	3,400	220

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

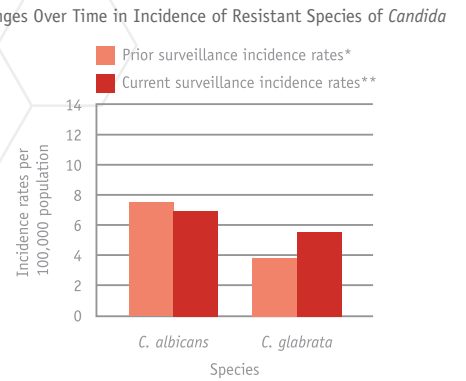
FIGHTING THE SPREAD OF RESISTANCE

Prevention strategies for candidemia are not well defined. Most infectious are thought to be caused by *Candida* that the patient carries on his or her own body. Therapy to prevent infections (antifungal prophylaxis) may be appropriate for some groups at high risk of developing *Candida* bloodstream infection, such as low-birth-weight infants. CDC recommendations for catheter care and handwashing can be helpful in reducing transmission in healthcare institutions.

WHAT CDC IS DOING

Prevention of significant morbidity and mortality from candidemia remains a challenge. Although antifungal prophylaxis has been shown to be effective in selected patient populations, there is still debate on the application of risk prevention tools and other prevention strategies. There is a continued need for surveillance of candidemia to develop and evaluate prevention strategies and to monitor for changes in incidence and resistance.

There is increasing incidence of *Candida* infections due to azole- and echinocandin-resistant strains.



*This accounts for data collected from Atlanta, GA from 1992-1993 and from Baltimore, MD from 1998–2000.
**This accounts for data collected from 2008–present.

ONLINE RESOURCES

CDC's candidiasis website
http://www.cdc.gov/fungal/candidiasis/

EXTENDED SPECTRUM β-LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE

26,000 DRUG-RESISTANT INFECTIONS

1,700 DEATHS

140,000 ENTEROBACTERIACEAE INFECTIONS PER YEAR

$40,000 IN EXCESS MEDICAL COSTS PER YEAR FOR EACH INFECTION

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Extended-spectrum β-lactamase is an enzyme that allows bacteria to become resistant to a wide variety of penicillins and cephalosporins. Bacteria that contain this enzyme are known as ESBLs or ESBL-producing bacteria. ESBL-producing Enterobacteriaceae are resistant to strong antibiotics including extended spectrum cephalosporins.

RESISTANCE OF CONCERN

Some Enterobacteriaceae are resistant to nearly all:

- penicillins
- cephalosporins

In these cases, the remaining treatment option is an antibiotic from the carbapenem family. These are drugs of last resort, and use of them is also contributing to resistance (see CRE fact sheet).

- Nearly 26,000 (or 19%) healthcare-associated Enterobacteriaceae infections are caused by ESBL-producing Enterobacteriaceae.
- Patients with bloodstream infections caused by ESBL-producing Enterobacteriaceae are about 57% more likely to die than those with bloodstream infections caused by a non ESBL-producing strain.

PUBLIC HEALTH THREAT

An estimated 140,000 healthcare-associated Enterobacteriaceae infections occur in the United States each year. CDC estimates that bloodstream infections caused by ESBL-containing Enterobacteriaceae result in upwards of $40,000 in excess hospital charges per occurrence. Approximately 26,000 infections and 1,700 deaths are attributable to ESBLs.

	Percentage of Enterobacteriaceae healthcare-associated infections resistant to extended spectrum cephalosporins	Estimated number of infections	Estimated number of deaths attributed
ESBL-producing *Klebsiella* spp.	23%	17,000	1,100
ESBL-producing *E. coli*	14%	9,000	600
Totals		26,000	1,700

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

EXTENDED SPECTRUM β-LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Tracking illness and identifying risk factors for drug-resistant infections using two systems, the National Healthcare Safety Network and the Emerging Infections Program.
- Providing outbreak support, such as staff expertise, prevention guidelines, tools, and lab assistance, to states and facilities.
- Developing tests and prevention recommendations to control drug-resistant infections.
- Helping medical facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities Can:

- Know resistance trends in your region.
- Coordinate local and regional infection tracking and control efforts.
- Require facilities to alert each other when transferring patients with any infection.

Health Care CEOs, Medical Officers, and Other Healthcare Facility Leaders Can:

- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections and alert clinical and infection prevention staff when these bacteria are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.

Healthcare Providers Can:

- Know when and what types of drug-resistant infections are present in your facility and patients.
- Request immediate alerts when the lab identifies drug-resistant infections in your patients.
- Alert the other facility when you transfer a patient with a drug-resistant infection.
- Protect patients from drug-resistant infections.
- Follow relevant guidelines and precautions at every patient encounter.
- Prescribe antibiotics wisely.
- Remove temporary medical devices such as catheters and ventilators as soon as no longer needed.

Patients and Their Loved Ones Can:

- Ask everyone including doctors, nurses, other medical staff, and visitors, to wash their hands before touching the patient.
- Take antibiotics only and exactly as prescribed.

ONLINE RESOURCES

CDC's Heathcare-associated Infections(HAI) website
www.cdc.gov/hai

Healthcare-associated Infections (HAIs), Guidelines and Recommendations
www.cdc.gov/hicpac/pubs.html

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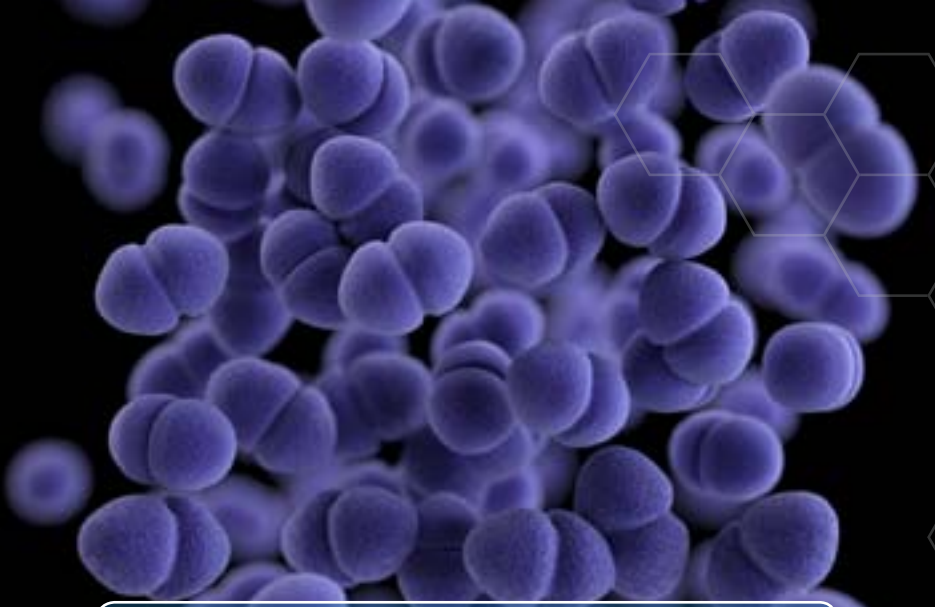

VANCOMYCIN-RESISTANT ENTEROCOCCUS (VRE)

20,000 DRUG-RESISTANT *ENTEROCOCCUS* INFECTIONS

1,300 DEATHS FROM DRUG-RESISTANT *ENTEROCOCCUS* INFECTIONS

66,000 *ENTEROCOCCUS* INFECTIONS PER YEAR

SOME *ENTEROCOCCUS* STRAINS ARE RESISTANT TO VANCOMYCIN

LEAVING FEW OR NO TREATMENT OPTIONS

THREAT LEVEL **SERIOUS**

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Enterococci cause a range of illnesses, mostly among patients receiving healthcare, but include bloodstream infections, surgical site infections, and urinary tract infections.

RESISTANCE OF CONCERN

- *Enterococcus* often cause infections among very sick patients in hospitals and other healthcare-settings.
- Some *Enterococcus* strains are resistant to vancomycin, an antibiotic of last resort, leaving few or no treatment options.
- About 20,000 (or 30%) of *Enterococcus* healthcare-associated infections are vancomycin resistant.

PUBLIC HEALTH THREAT

An estimated 66,000 healthcare-associated *Enterococcus* infections occur in the United States each year. The proportion of infections that occur with a vancomycin resistant strain differs by the species of *Enterococcus;* overall 20,000 vancomycin-resistant infections occurred among hospitalized patients each year, with approximately 1,300 deaths attributed to these infections.

	Percent of all *Enterococcus* healthcare-associated infections resistant to vancomycin	Estimated number of infections	Estimated number of deaths attributed
Vancomycin-resistant *Enterococcus faecium*	77%	10,000	650
Vancomycin-resistant *Enterococcus faecalis*	9%	3,100	200
Vancomycin-resistant *Enterococcus* (species not determined)	40%	6,900	450
Totals		20,000	1,300

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

VANCOMYCIN-RESISTANT ENTEROCOCCUS (VRE)

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Tracking illness and identifying risk factors for drug-resistant infections using two systems, the National Healthcare Safety Network and the Emerging Infections Program.
- Providing outbreak support such as staff expertise, prevention guidelines, tools, and lab assistance, to states and facilities.
- Developing tests and prevention recommendations to control drug-resistant infections.
- Helping medical facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities can:

- Know resistance trends in your region.
- Coordinate local and regional infection tracking and control efforts.
- Require facilities to alert each other when transferring patients with any infection.

Healthcare CEOs, Medical Officers, and other Healthcare Facility Leaders can:

- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections and alert clinical and infection prevention staff when these germs are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.

Doctors and Nurses can:

- Know when and what types of drug-resistant infections are present in your facility and patients Request immediate alerts when the lab identifies drug-resistant infections in your patients.
- Alert the other facility when you transfer a patient with a drug-resistant infection.
- Protect patients from drug-resistant infections.
- Follow relevant guidelines and precautions at every patient encounter.
- Prescribe antibiotics wisely.
- Remove temporary medical devices such as catheters and ventilators as soon as no longer needed.

Patients and their loved ones can:

- Ask everyone including doctors, nurses, other medical staff, and visitors, to wash their hands before touching the patient.
- Take antibiotics only and exactly as prescribed.

ONLINE RESOURCES

Vancomycin-resistant Enterococci (VRE) in Healthcare Settings
http://www.cdc.gov/HAI/organisms/vre/vre.html

Healthcare-associated Infections (HAIs), Guidelines and Recommendations
www.cdc.gov/hicpac/pubs.html

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MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA

6,700 MULTIDRUG-RESISTANT *PSEUDOMONAS* INFECTIONS

440 DEATHS

51,000 *PSEUDOMONAS* INFECTIONS PER YEAR

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Pseudomonas aeruginosa is a common cause of healthcare-associated infections including pneumonia, bloodstream infections, urinary tract infections, and surgical site infections.

RESISTANCE OF CONCERN

- Some strains of *Pseudomonas aeruginosa* have been found to be resistant to nearly all or all antibiotics including aminoglycosides, cephalosporins, fluoroquinolones, and carbapenems.
- Approximately 8% of all healthcare-associated infections reported to CDC's National Healthcare Safety Network are caused by *Pseudomonas aeruginosa*.
- About 13% of severe healthcare-associated infections caused by *Pseudomonas aeruginosa* are multidrug resistant, meaning several classes of antibiotics no longer cure these infections.

PUBLIC HEALTH THREAT

An estimated 51,000 healthcare-associated *Pseudomonas aeruginosa* infections occur in the United States each year. More than 6,000 (or 13%) of these are multidrug-resistant, with roughly 400 deaths per year attributed to these infections.

	Percentage of all *Pseudomonas aeruginosa* healthcare-associated infections that are multidrug-resistant	Estimated number of infections	Estimated number of deaths attributed
Multi-drug resistant *Pseudomonas aeruginosa*	13%	6,700	440

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Identifying and tracking risk factors for drug-resistant infections using two systems, the National Healthcare Safety Network and the Emerging Infections Program.
- Providing outbreak support such as staff expertise, prevention guidelines, tools, and lab assistance, to states and facilities.
- Developing tests and prevention recommendations to control drug-resistant infections.
- Helping medical facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities Can:

- Know resistance trends in your region.
- Coordinate local and regional infection tracking and control efforts.
- Require facilities to alert each other when transferring patients with any infection.

Health Care CEOs, Medical Officers, and Other Healthcare Facility Leaders Can:

- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections and alert clinical and infection prevention staff when these bacteria are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.

Healthcare Providers Can:

- Know when and what types of drug-resistant infections that are present in your facility and patients.
- Request immediate alerts when the lab identifies drug-resistant infections in your patients.
- Alert the other facility when you transfer a patient with a drug-resistant infection.
- Protect patients from drug-resistant infections.
- Follow relevant guidelines and precautions at every patient encounter.
- Prescribe antibiotics wisely.
- Remove temporary medical devices such as catheters and ventilators as soon as no longer needed.

Patients and Their Loved Ones Can:

- Ask everyone including doctors, nurses, other medical staff, and visitors, to wash their hands before touching the patient.
- Take antibiotics only and exactly as prescribed.

ONLINE RESOURCES

Healthcare-associated Infections (HAI)
www.cdc.gov/hai

Healthcare-associated Infections (HAIs), Guidelines and Recommendations
www.cdc.gov/hicpac/pubs.html

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DRUG-RESISTANT NON-TYPHOIDAL SALMONELLA

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

100,000
DRUG-RESISTANT *SALMONELLA* INFECTIONS PER YEAR

1,200,000
SALMONELLA INFECTIONS PER YEAR

$365,000,000
IN MEDICAL COSTS PER YEAR

Non-typhoidal *Salmonella* (serotypes other than Typhi, Paratyphi A, Paratyphi B, and Paratyphi C) usually causes diarrhea (sometimes bloody), fever, and abdominal cramps. Some infections spread to the blood and can have life-threatening complications.

RESISTANCE OF CONCERN

Physicians rely on drugs, such as ceftriaxone and ciprofloxacin, for treating patients with complicated *Salmonella* infections. Resistant infections are more severe and have higher hospitalization rates. Non-typhoidal *Salmonella* is showing resistance to:

- ceftriaxone
- ciprofloxacin
- multiple classes of drugs

PUBLIC HEALTH THREAT

Non-typhoidal *Salmonella* causes approximately 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths each year in the United States. Direct medical costs are estimated to be $365 million annually. CDC is seeing resistance to ceftriaxone in about 3% of non-typhoidal *Salmonella* tested, and some level of resistance to ciprofloxacin in about 3%. About 5% of non-typhoidal *Salmonella* tested by CDC are resistant to five or more types of drugs. Costs are expected to be higher for resistant than for susceptible infections because resistant infections are more severe, those patients are more likely to be hospitalized, and treatment is less effective.

	Percentage of all non-typhoidal *Salmonella**	Estimated number of illnesses per year	Estimated illnesses per 100,000 U.S. population	Estimated number of deaths per year
Ceftriaxone resistance	3%	36,000	12.0	13
Ciprofloxacin resistance or partial resistance	3%	33,000	10.9	12
Resistance to 5 or more antibiotic classes	5%	66,000	21.9	24
Any resistance pattern above	8%	100,000	34.1	38

*3-year average (2009–2011)
For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

DRUG-RESISTANT NON-TYPHOIDAL SALMONELLA

FIGHTING THE SPREAD OF RESISTANCE

Salmonella spreads from animals to people mostly through food. Antibiotic use in food animals can result in resistant *Salmonella*, and people get sick when they eat foods contaminated with *Salmonella*. Key measures to prevent resistant infections include:

- Avoiding inappropriate antibiotic use in food animals.
- Tracking antibiotic use in different types of food animals.
- Stopping spread of *Salmonella* among animals on farms.
- Improving food production and processing to reduce contamination.
- Educating consumers and food workers about safe food handling practices.

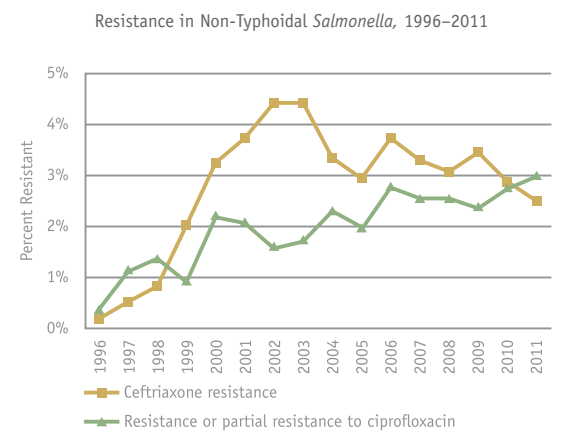
WHAT CDC IS DOING

- Tracking changes in antibiotic resistance through ongoing surveillance.
- Promoting initiatives that measure and improve antibiotic use in food animals.
- Determining foods responsible for outbreaks of *Salmonella* infections.
- Supporting and improving local, state, and federal public health surveillance.
- Guiding prevention efforts by estimating how much illness occurs and identifying the sources of infection.
- Educating people about how to avoid *Salmonella* infections.

WHAT YOU CAN DO

- **Clean.** Wash hands, cutting boards, utensils, and countertops.
- **Separate.** Keep raw meat, poultry, and seafood separate from ready-to-eat foods.
- **Cook.** Use a food thermometer to ensure that foods are cooked to a safe internal temperature.
- **Chill.** Keep your refrigerator below 40°F and refrigerate food that will spoil.
- Avoid drinking raw milk.
- Report suspected illness from food to your local health department.
- Don't prepare food for others if you have diarrhea or vomiting.
- Be especially careful preparing food for children, pregnant women, those in poor health, and older adults.

Drug resistance in non-typhoidal *Salmonella* continues to climb from 1996 levels.



For more information about data methods and references, please see appendix.

ONLINE RESOURCES

National Antimicrobial Resistance Monitoring System
http://www.cdc.gov/narms

Salmonella
http://www.cdc.gov/salmonella/index.html

Vital Signs, June 2011: Making Food Safer to Eat
http://www.cdc.gov/VitalSigns/FoodSafety/?pkw=vs_fs009

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DRUG-RESISTANT SALMONELLA SEROTYPE TYPHI

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

3,800
DRUG-RESISTANT *SALMONELLA* TYPHI INFECTIONS PER YEAR IN THE U.S.

67%
OF *SALMONELLA* TYPHI INFECTIONS ARE DRUG RESISTANT

620
HOSPITALIZATIONS DUE TO *SALMONELLA* TYPHI PER YEAR IN THE U.S.

21,700,000 *SALMONELLA* TYPHI INFECTIONS WORLDWIDE

Salmonella serotype Typhi causes typhoid fever, a potentially life-threatening disease. People with typhoid fever usually have a high fever, abdominal pain, and headache. Typhoid fever can lead to bowel perforation, shock, and death.

RESISTANCE OF CONCERN

Physicians rely on drugs such as ceftriaxone, azithromycin, and ciprofloxacin for treating patients with typhoid fever. *Salmonella* serotype Typhi is showing resistance to:

- ceftriaxone
- azithromycin
- ciprofloxacin (resistance is so common that it cannot be routinely used)

PUBLIC HEALTH THREAT

Salmonella Typhi causes approximately 21.7 million illnesses worldwide. In the United States, it causes approximately 5,700 illnesses and 620 hospitalizations each year. Most illnesses occur in people who travel to some parts of the developing world where the disease is common. Travel-associated infections are more likely to be antibiotic resistant. CDC is seeing some level of resistance to ciprofloxacin in two-thirds of *Salmonella* Typhi tested. CDC has not yet seen resistance to ceftriaxone or azithromycin in the United States, but this has been seen in other parts of the world. Resistant infections are likely to cost more than susceptible infections because illness may last longer. Deaths in the United States are rare now, but before there were antibiotics, 10% to 20% of patients died.

	Percentage of all *Salmonella* Typhi*	Estimated number of illnesses per year	Estimated illnesses per 100,000 U.S. population	Estimated number of deaths per year
Resistance or partial resistance to ciprofloxacin	67%	3,800	1.3	<5

*3-year average (2009–2011)
For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

DRUG-RESISTANT SALMONELLA SEROTYPE TYPHI

FIGHTING THE SPREAD OF RESISTANCE

Salmonella serotype Typhi spreads from one person to another through food or water contaminated with feces. Typhoid fever is common in developing countries lacking safe water and adequate sanitation. Most U.S. cases are associated with travel to those countries. Sometimes the source is a carrier who is no longer ill, but is still infected. Key measures to prevent the spread of resistant infections include:

- Vaccinating people traveling to countries where typhoid fever is common.
- Consuming safe food and water when traveling in those countries.
- Improving access to clean water and sanitation for people living in those countries.
- Reporting changes in resistance to people who diagnose and treat patients with typhoid fever.
- Investigating cases of typhoid fever to identify and treat carriers.

WHAT CDC IS DOING

- Providing recommendations for travelers on vaccination, safe food, and clean water.
- Tracking and reporting changes in antibiotic resistance through ongoing surveillance.
- Determining settings and high-risk groups for resistant infections in the U.S. and other countries.
- Educating healthcare providers about specific resistance problems and the need to vaccinate travelers.
- Promoting safer water and sanitation in countries where typhoid fever is common.
- Building public health capacity in other countries to diagnose, track, and control typhoid fever.

ONLINE RESOURCES

National Antimicrobial Resistance Monitoring System
http://www.cdc.gov/narms

Typhoid Fever
http://www.cdc.gov/nczved/divisions/dfbmd/diseases/typhoid_fever/

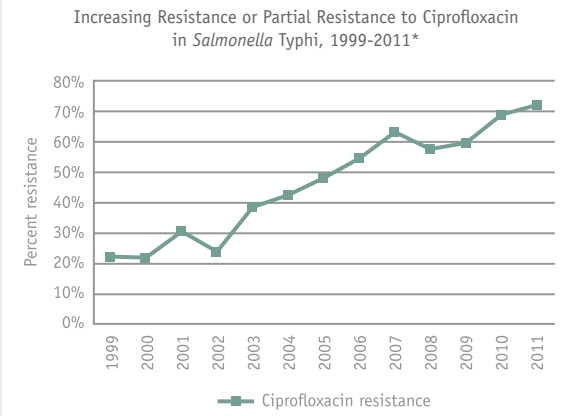
Traveler's Health "Traveler's Diarrhea"
http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-2-the-pre-travel-consultation/travelers-diarrhea.htm

WHAT YOU CAN DO

If you're traveling to a country where typhoid fever is common:

- Get vaccinated against typhoid fever before you depart.
- Choose foods and drinks carefully while traveling even if you are vaccinated. That means: boil it, cook it, peel it, or forget it.
  - Boil or treat water yourself.
  - Eat foods that are hot and steaming.
  - Avoid raw fruits and vegetables unless you peel them yourself.
  - Avoid cold food and beverages from street vendors.
- If you get sick with high fever and a headache during or after travel, seek medical care at once and tell the healthcare provider where you have traveled.

Drug resistance in *Salmonella* Typhi has jumped significantly—from about 20% in 1999 to more than 70% in 2011.



DRUG-RESISTANT SHIGELLA

27,000 DRUG-RESISTANT *SHIGELLA* INFECTIONS PER YEAR

500,000 *SHIGELLA* INFECTIONS PER YEAR

40 DEATHS PER YEAR

THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Shigella usually causes diarrhea (sometimes bloody), fever, and abdominal pain. Sometimes it causes serious complications such as reactive arthritis. High-risk groups include young children, people with inadequate handwashing and hygiene habits, and men who have sex with men.

RESISTANCE OF CONCERN

Resistance to traditional first-line drugs such as ampicillin and trimethoprim-sulfamethoxazole has become so high that physicians must now rely on alternative drugs like ciprofloxacin and azithromycin to treat infections. Resistant infections can last longer than infections with susceptible bacteria (bacteria that can be treated effectively with antibiotics). *Shigella* is showing resistance to:

- ciprofloxacin
- azithromycin

	Percentage of all *Shigella**	Estimated number of illnesses per year	Estimated illnesses per 100,000 U.S. population	Estimated number of deaths per year
Ciprofloxacin resistance	2%	12,000	4.0	<5
Azithromycin resistance	3%	15,000	5.1	<5
Azithromycin or ciprofloxacin resistance	6%	27,000	9.1	<5

*Percentage of all isolates that were resistant in 2011.
For more information about data methods and references, please see technical appendix.

PUBLIC HEALTH THREAT

Shigella causes approximately 500,000 diarrheal illnesses, 5,500 hospitalizations, and 40 deaths each year in the United States. CDC is seeing resistance to ciprofloxacin in 1.6% of the *Shigella* cases tested and resistance to azithromycin in approximately 3%. Because initial treatment can fail, costs are expected to be higher for resistant infections.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

FIGHTING THE SPREAD OF RESISTANCE

Shigella spreads from one person to another in feces through direct contact, or through contaminated surfaces, food, or water. Antibiotic use in humans can result in resistant *Shigella* and hasten further spread. Key measures to prevent resistant infections include:

- Promoting thorough and frequent hand washing with soap, especially in child care centers, elementary schools, restaurants, and homes with small children.
- Using antibiotics to treat more severe *Shigella* infections and managing milder infections with fluids and rest.
- Reporting changes in resistance to healthcare providers.
- Detecting and controlling outbreaks of *Shigella* infections.
- Educating consumers and food workers about safe food handling practices.

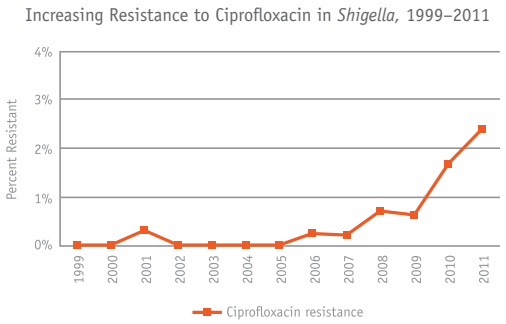
WHAT CDC IS DOING

- Tracking changes in antibiotic resistance through ongoing surveillance.
- Determining settings and high-risk groups for outbreaks of resistant infections.
- Educating healthcare providers about specific resistance problems.
- Promoting prudent antibiotic use and handwashing.

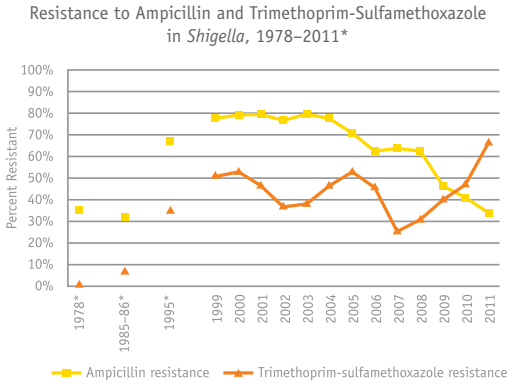
WHAT YOU CAN DO

- Don't prepare food for others if you have diarrhea or vomiting.
- Keep children who have diarrhea and who are in diapers out of child care settings and swimming pools.
- Avoid sexual behavior that is likely to transmit infection when you have diarrhea.
- Consume safe food and water when traveling abroad.

Drug-resistant *Shigella* has been making steady increases since 2006.



While resistance to ampicillin has decreased, *Shigella* continues to become more resistant to trimethoprim-sulfamethoxazole.



*Data for 1978-1995 were from three sentinel county surveys. Annual testing began in 1999.

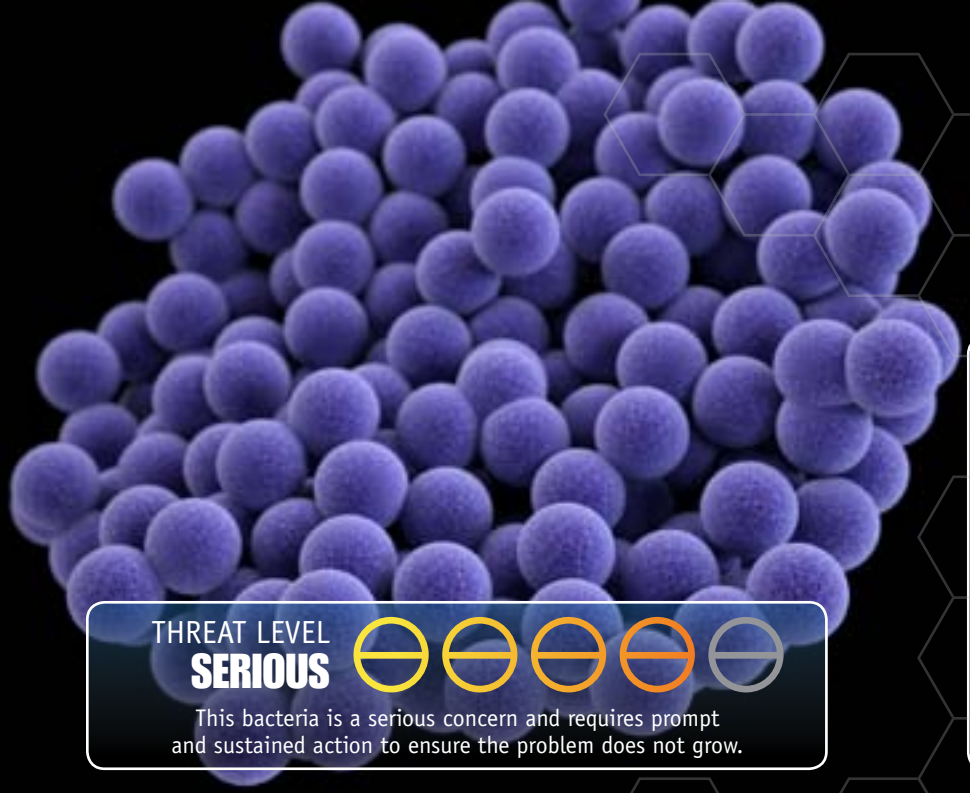
ONLINE RESOURCES

National Antimicrobial Resistance Monitoring System
http://www.cdc.gov/narms

Shigellosis
http://www.cdc.gov/nczved/divisions/dfbmd/diseases/shigellosis/

Traveler's Health "Traveler's Diarrhea"
http://wwwnc.cdc.gov/travel/yellowbook/2012/chapter-2-the-pre-travel-consultation/travelers-diarrhea.htm

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)



THREAT LEVEL
SERIOUS

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

80,461
SEVERE MRSA INFECTIONS PER YEAR

11,285
DEATHS FROM MRSA PER YEAR

STAPH BACTERIA ARE A LEADING CAUSE OF
HEALTHCARE-ASSOCIATED INFECTIONS

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes a range of illnesses, from skin and wound infections to pneumonia and bloodstream infections that can cause sepsis and death. Staph bacteria, including MRSA, are one of the most common causes of healthcare-associated infections.

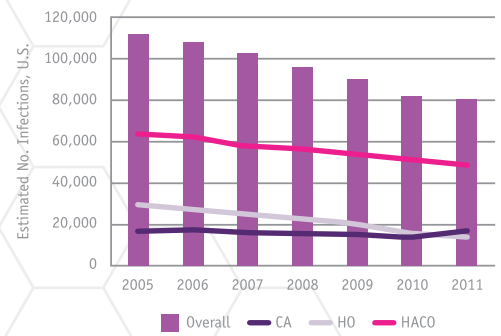
RESISTANCE OF CONCERN

Resistance to methicillin and related antibiotics (e.g., nafcillin, oxacillin) and resistance to cephalosporins are of concern.

PUBLIC HEALTH THREAT

CDC estimates 80,461 invasive MRSA infections and 11,285 related deaths occurred in 2011. An unknown but much higher number of less severe infections occurred in both the community and in healthcare settings.

Severe MRSA infections mostly occur during or soon after inpatient medical care.



For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

FIGHTING THE SPREAD OF RESISTANCE

Although still a common and severe threat to patients, invasive MRSA infections in healthcare settings appear to be declining. Between 2005 and 2011 overall rates of invasive MRSA dropped 31%; the largest declines (54%) were observed among infections occurring during hospitalization. Success began with preventing central-line associated bloodstream infections with MRSA, where rates fell nearly 50% from 1997 to 2007.

During the past decade, rates of MRSA infections have increased rapidly among the general population (people who have not recently received care in a healthcare setting). There is some evidence that these increases are slowing, but they are not following the same downward trends as healthcare-associated MRSA.

WHAT CDC IS DOING

- Tracking illness and identifying risk factors for drug-resistant infections using two systems, the National Healthcare Safety Network and the Emerging Infections Program.
- Providing states and facilities with outbreak support such as staff expertise, prevention guidelines, tools, and lab assistance.
- Developing tests and prevention recommendations to control drug-resistant infections.
- Helping healthcare facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities Can:

- Know resistance trends in your region.
- Coordinate local and regional infection tracking and control efforts.
- Require facilities to alert each other when transferring patients with any infection.

Healthcare CEOs, Medical Officers, and Other Healthcare Facility Leaders Can:

- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections and alert clinical and infection prevention staff when these bacteria are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.

Healthcare Providers Can:

- Know when and types of drug-resistant infections are present in your facility and patients.
- Request immediate alerts when the lab identifies drug-resistant infections in your patients.
- Alert the other facility when you transfer a patient with a drug-resistant infection.
- Protect patients from drug-resistant infections.
- Follow relevant guidelines and precautions at every patient encounter.
- Prescribe antibiotics wisely.
- Remove temporary medical devices such as catheters and ventilators as soon as no longer needed.

Patients and Their Loved Ones Can:

- Ask everyone, including doctors, nurses, other medical staff, and visitors, to wash their hands before touching the patient.
- Take antibiotics only and exactly as prescribed.

ONLINE RESOURCES

Resources CDC's MRSA website
www.cdc.gov/hai/mrsa

Prevention Guidelines for MRSA
www.cdc.gov/hicpac/pubs.html

Medscape/CDC Expert Commentaries about MRSA
http://www.medscape.com/partners/cdc/public/cdc-commentary

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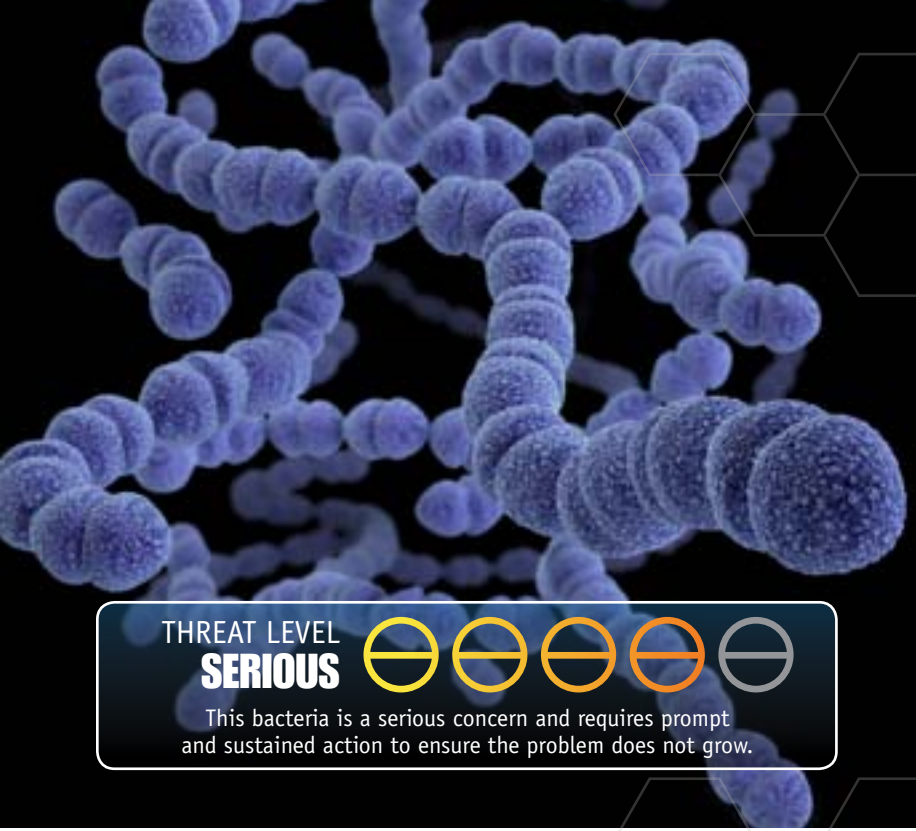


DRUG-RESISTANT STREPTOCOCCUS PNEUMONIAE

1,200,000 DRUG-RESISTANT INFECTIONS PER YEAR

19,000 EXCESS HOSPITALIZATIONS

7,000 DEATHS

$96,000,000 IN EXCESS MEDICAL COSTS PER YEAR

THREAT LEVEL **SERIOUS**

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Streptococcus pneumoniae (S. pneumoniae, or pneumococcus) is the leading cause of bacterial pneumonia and meningitis in the United States. It also is a major cause of bloodstream infections and ear and sinus infections.

RESISTANCE OF CONCERN

S. pneumoniae has developed resistance to drugs in the penicillin and erythromycin groups. Examples of these drugs include amoxicillin and azithromycin (Zithromax, Z-Pak). *S. pneumoniae* has also developed resistance to less commonly used drugs.

PUBLIC HEALTH THREAT

Pneumococcal disease, whether or not resistant to antibiotics, is a major public health problem. Pneumococcal disease causes 4 million disease episodes and 22,000 deaths annually. Pneumococcal ear infections (otitis media) are the most common type of pneumococcal disease among children, causing 1.5 million infections that often result in antibiotic use. Pneumococcal pneumonia is another important form of pneumococcal disease. Each year, nearly 160,000 children younger than 5 years old see a doctor or are admitted to the hospital with pneumococcal pneumonia. Among adults, over 600,000 seek care for or are hospitalized with pneumococcal pneumonia. Pneumococcal pneumonia accounts for 72% of all direct medical costs for treatment of pneumococcal disease.

In 30% of severe *S. pneumoniae* cases, the bacteria are fully resistant to one or more clinically relevant antibiotics. Resistant infections complicate treatment and can result in almost 1,200,000 illnesses and 7,000 deaths per year. Cases of resistant pneumococcal pneumonia result in about 32,000 additional doctor visits and about 19,000 additional hospitalizations each year. The excess costs associated with these cases are approximately $96 million.

Invasive pneumococcal disease means that bacteria invade parts of the body that are normally sterile, and when this happens, disease is usually severe, causing hospitalization or even death. The majority of cases and deaths occur among adults 50 years or older, with the highest rates among those 65 years or older. Almost everyone who gets invasive pneumococcal disease needs treatment in the hospital.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

DRUG-RESISTANT STREPTOCOCCUS PNEUMONIAE

FIGHTING THE SPREAD OF RESISTANCE

Pneumococcal conjugate vaccine (PCV) is an effective tool to prevent infections. Vaccine use has not only reduced the burden of invasive pneumococcal disease, but it has also reduced antibiotic resistance by blocking the transmission of resistant *S. pneumoniae* strains. From 2000–2009, PCV7 provided protection against seven pneumococcal strains, and beginning in 2010 use of PCV13 expanded that protection to 13 strains. Achieving high vaccination coverage and encouraging appropriate antibiotic use will slow the spread of pneumococcal resistance. Using the right antibiotic at the right time is crucial.

WHAT CDC IS DOING

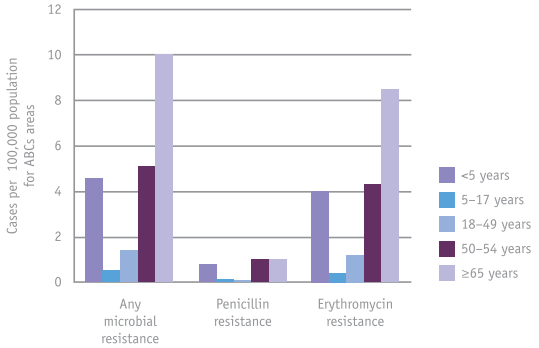
Through partnerships between CDC, state health departments, and universities, CDC is tracking *S. pneumoniae* through its Active Bacterial Core surveillance (ABCs). CDC is promoting appropriate antibiotic use among outpatient health care providers and the public through its Get Smart: Know When Antibiotics Work program. As part of this program, CDC hosts Get Smart About Antibiotic Week, an annual one week observance of the importance of appropriate antibiotic use and its impact on antibiotic resistance. CDC is also working with many partners in the U.S. to ensure that pneumococcal vaccines are available for children and that uptake is high.

WHAT YOU CAN DO

- Prevent infections by getting recommended vaccines and practicing good hand hygiene.
- Take antibiotics exactly as the doctor prescribes. Do not skip doses. Complete the prescribed course of treatment, even when you start feeling better.
- Only take antibiotics prescribed for you; do not share or use leftover antibiotics.
- Do not save antibiotics for the next illness. Discard any leftover medication once the prescribed course of treatment is completed.
- Do not ask for antibiotics when your doctor thinks you do not need them.

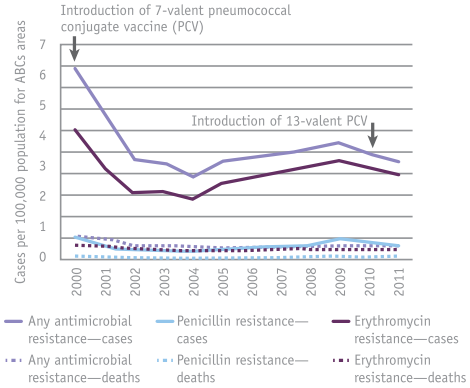
The very young and senior adults are most at risk for drug-resistant pneumococcal disease.

Cases of antibiotic-resistant invasive disease per 100,000 persons, by age group and resistance profile — Active Bacterial Core surveillance



Vaccination prevents spread of drug-resistant *S. pneumoniae* infections.

Cases and deaths per 100,000 population by resistance profile — ABCs areas, 2000–2011



In 2010, 13-valent pneumococcal conjugate vaccine (PCV13) replaced 7-valent pneumococcal conjugate vaccine (PCV7).

ONLINE RESOURCES

Pneumococcal Disease
www.cdc.gov/pneumococcal

Pneumococcal Vaccine Recommendations
http://www.cdc.gov/vaccines/vpd-vac/pneumo/in-short-both.htm#who

Get Smart: Know When Antibiotics Work Program
http://www.cdc.gov/getsmart/

Active Bacterial Core surveillance (ABCs)
http://www.cdc.gov/abcs/index.html

Drug-Resistant *Streptococcus pneumoniae* (DRSP) Surveillance Toolkit
http://www.cdc.gov/abcs/reports-findings/surv-manual.html

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DRUG-RESISTANT TUBERCULOSIS

1,042 DRUG-RESISTANT TUBERCULOSIS CASES IN 2011 (U.S.)

10,528 TUBERCULOSIS CASES IN 2011 (U.S.)

TUBERCULOSIS IS AMONG THE MOST COMMON INFECTIOUS DISEASES AND **FREQUENT CAUSES OF DEATH WORLDWIDE**

THREAT LEVEL **SERIOUS**

This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.

Tuberculosis (TB) is among the most common infectious diseases and a frequent cause of death worldwide. TB is caused by the bacteria *Mycobacterium tuberculosis (M. tuberculosis)* and is spread most commonly through the air. *M. tuberculosis* can affect any part of the body, but disease is found most often in the lungs. In most cases, TB is treatable and curable with the available first-line TB drugs; however, in some cases, *M. tuberculosis* can be resistant to one or more of the drugs used to treat it. Drug-resistant TB is more challenging to treat — it can be complex and requires more time and more expensive drugs that often have more side effects. Extensively Drug-Resistant TB (XDR TB) is resistant to most TB drugs; therefore, patients are left with treatment options that are much less effective. The major factors driving TB drug resistance are incomplete or wrong treatment, short drug supply, and lack of new drugs. In the United States most drug-resistant TB is found among persons born outside of the country.

RESISTANCE OF CONCERN

- Resistance to antibiotics used for standard therapy
- Resistance to isoniazid (INH)
- Some TB is multidrug-resistant (MDR), showing resistance to at least INH and rifampicin (RMP), two essential first-line drugs
- Some TB is XDR TB, defined as MDR TB plus resistance to any fluoroquinolone and to any of the three second-line injectable drugs (i.e., amikacin, kanamycin, capreomycin)

	Number of cases	Cases per 100,000 U.S. population	Percent of all TB cases in U.S.
Any first-line resistance	1,042	0.33	10%
INH resistance	740	0.24	7%
MDR TB	124	0.04	1%
XDR TB	6	0.0019	<1%
Deaths caused by antibiotic-resistant TB	50		

For more information about data methods and references, please see technical appendix.

PUBLIC HEALTH THREAT

Of a total of 10,528 cases of TB in the United States reported in 2011, antibiotic resistance was identified in 1,042, or 9.90%, of all TB cases.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

FIGHTING THE SPREAD OF RESISTANCE

Health care providers can help prevent drug-resistant TB by quickly suspecting and diagnosing cases, following recommended treatment guidelines, monitoring patients' response to treatment, and ensuring therapy is completed. Additional drug-resistant TB prevention measures include implementing effective infection control procedures that help limit exposure to known drug-resistant TB patients in settings such as hospitals, prisons, or homeless shelters.

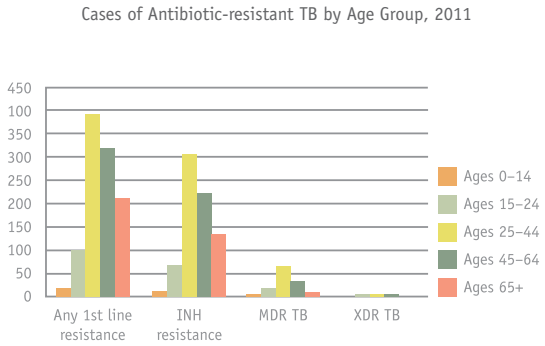
WHAT CDC IS DOING

CDC conducts ongoing surveillance for drug-resistant TB in all 50 states and the District of Columbia using the National Tuberculosis Surveillance System (NTSS). The TB Genotyping Information Management System (TBGIMS), a Web-based system designed to improve access and dissemination of genotyping information nationwide, complements the ongoing surveillance for drug- resistant TB by linking genotyping results to surveillance data. In 2009, CDC implemented the Molecular Detection of Drug Resistance Service (MDDR), a national clinical referral service which provides rapid confirmation of MDR and XDR TB. Molecular drug-resistant testing enhances but does not replace culture or conventional drug-susceptibility testing.

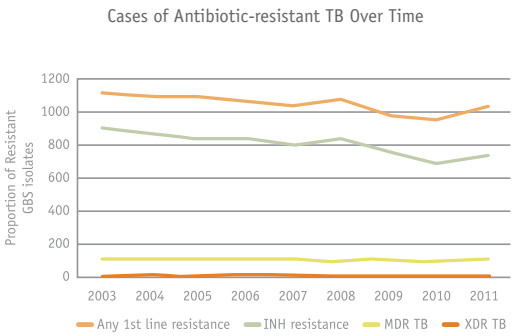
Other CDC activities directed at preventing spread of drug-resistant TB include funding of five TB Regional Training and Medical Consultation Centers (RTMCCs) from 2013–2017. The RTMCCs are regionally assigned to cover all 50 states and the U.S. territories. One of the primary purposes of each RTMCC is to provide medical consultation to TB programs and medical providers, particularly for complex, drug-resistant cases. Additionally, the RTMCCs offer trainings that provide information on diagnosing and treating drug-resistant TB.

Additionally, CDC international activities include studies to improve first and second line antibiotic use in patients with drug-resistant TB.

Antibiotic resistance occurs most often among those aged 25-44.



The number of TB cases with isoniazid resistance or any first-line antibiotic resistance declined from 2003 through 2011. However, both types of resistance had increases in cases in 2011. Multidrug-resistant TB has been fairly consistent over this same time period



ONLINE RESOURCES

http://www.cdc.gov/tb/

http://www.cdc.gov/tb/topic/drtb/default.htm

http://www.cdc.gov/tb/publications/factsheets/drtb/mdrtb.htm

http://www.cdc.gov/tb/topic/drtb/xdrtb.htm

http://www.cdc.gov/tb/statistics/reports/2011/default.htm

http://www.cdc.gov/tb/topic/Laboratory/mddr.htm

http://www.aphl.org/aphlprograms/infectious/tuberculosis/Pages/default.aspx

http://www.tbcontrollers.org/

http://www.who.int/tb/publications/mdr_surveillance/en/index.html

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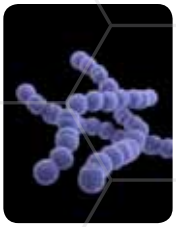


THREAT LEVEL
CONCERNING

These bacteria are concerning, and careful monitoring and prevention action are needed.

MICROORGANISMS WITH A THREAT LEVEL OF CONCERNING

Vancomycin-resistant ***Staphylococcus aureus*** **(VRSA)**

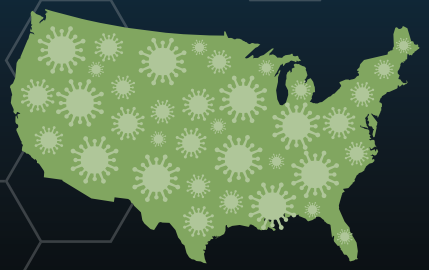
Erythromycin-resistant **Group A *Streptococcus***

Clindamycin-resistant **Group B *Streptococcus***

VANCOMYCIN-RESISTANT STAPHYLOCOCCUS AUREUS

13 CASES

IN **4** STATES SINCE 2002



SOME STAPHYLOCOCCUS STRAINS ARE RESISTANT TO VANCOMYCIN

LEAVING FEW OR NO TREATMENT OPTIONS

THREAT LEVEL

CONCERNING

This bacteria is concerning, and careful monitoring and prevention action are needed.

Staphylococcus aureus is a common type of bacteria that is found on the skin. During medical procedures when patients require catheters or ventilators or undergo surgical procedures, *Staphylococcus aureus* can enter the body and cause infections. When *Staphylococcus aureus* becomes resistant to vancomycin, there are few treatment options available because vancomycin-resistant *S. aureus* bacteria identified to date were also resistant to methicillin and other classes of antibiotics.

RESISTANCE OF CONCERN

In rare cases, CDC has identified *Staphylococcus aureus* that is resistant to vancomycin, the antibiotic most frequently used to treat serious *S. aureus* infections.

PUBLIC HEALTH THREAT

A total of 13 cases of vancomycin-resistant *Staphylococcus aureus* (VRSA) have been identified in the United States since 2002.

VRSA infection continues to be a rare occurrence. A few existing factors seem to predispose case patients to VRSA infection, including:

- Prior MRSA and enterococcal infections or colonization
- Underlying conditions (such as chronic skin ulcers and diabetes)
- Previous treatment with vancomycin

	Number of cases	Cases per 100,000 U.S. population	Percentage of all *Genus species* cases in U.S.	Number of deaths	Deaths per 100,000 U.S. population
Vancomycin-resistant *Staphylococcus aureus*	13	N/A	N/A	0	N/A

For more information about data methods and references, please see technical appendix.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

VANCOMYCIN-RESISTANT STAPHYLOCOCCUS AUREUS

FIGHTING THE SPREAD OF RESISTANCE

WHAT CDC IS DOING

- Confirming cases after being notified by local public health authorities.
- Providing states and facilities with outbreak support such as staff expertise, prevention guidelines, tools, and lab assistance.
- Developing tests and prevention recommendations to control drug-resistant infections.
- Helping medical facilities improve antibiotic prescribing practices.

WHAT YOU CAN DO

States and Communities Can:

- Know resistance trends in your region.
- Coordinate local and regional infection tracking and control efforts.
- Require facilities to alert each other when transferring patients with any infection.

Healthcare CEOs, Medical Officers, and Other Healthcare Facility Leaders Can:

- Require and strictly enforce CDC guidance for infection detection, prevention, tracking, and reporting.
- Make sure your lab can accurately identify infections, and alert clinical and infection prevention staff when these bacteria are present.
- Know infection and resistance trends in your facility and in the facilities around you.
- When transferring a patient, require staff to notify the other facility about all infections.
- Join or start regional infection prevention efforts.
- Promote wise antibiotic use.

Healthcare Providers Can:

- Know when and what types of drug-resistant infections are present in your facility and patients.
- Request immediate alerts when the lab identifies drug-resistant infections in your patients.
- Alert the other facility when you transfer a patient with a drug-resistant infection.
- Treat wounds aggressively.
- Use vancomycin responsibly.
- Protect patients from drug-resistant infections.
  - Follow relevant guidelines and precautions at every patient encounter.
  - Prescribe antibiotics wisely.
  - Remove temporary medical devices such as catheters and ventilators as soon as no longer needed.

Patients and Their Loved Ones Can:

- Ask everyone, including doctors, nurses, other medical staff, and visitors, to wash their hands before touching the patient.
- Take antibiotics only and exactly as prescribed.

ONLINE RESOURCES

Vancomycin-Intermediate/Resistant Staphylococcus (VISA/VRSA) in Healthcare Settings
http://www.cdc.gov/HAI/organisms/visa_vrsa/visa_vrsa.html

Healthcare-associated Infections (HAIs), Guidelines and Recommendations
www.cdc.gov/hicpac/pubs.html

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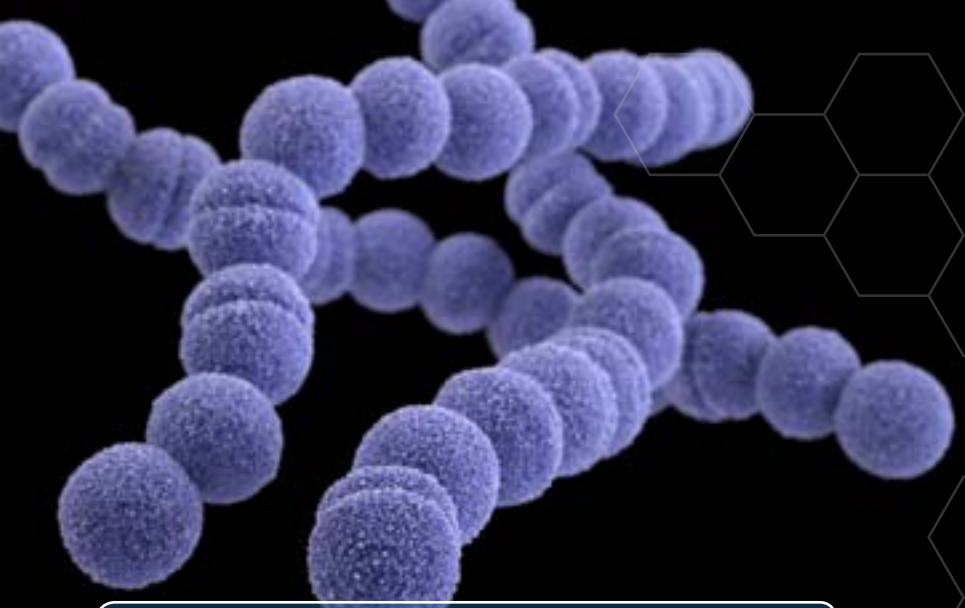


ERYTHROMYCIN-RESISTANT GROUP A STREPTOCOCCUS

1,300 DRUG-RESISTANT GROUP A STREP INFECTIONS PER YEAR

160 DEATHS

1–2.6 MILLION STREP THROAT INFECTIONS PER YEAR

GROUP A STREP IS THE LEADING CAUSE OF **NECROTIZING FASCIITIS ("FLESH-EATING" DISEASE)**

THREAT LEVEL **CONCERNING**

This bacteria is concerning, and careful monitoring and prevention action are needed.

Group A *Streptococcus* (GAS) causes many illnesses, including pharyngitis (strep throat), streptococcal toxic shock syndrome, necrotizing fasciitis ("flesh-eating" disease), scarlet fever, rheumatic fever, and skin infections such as impetigo.

RESISTANCE OF CONCERN

GAS has developed resistance to clindamycin and a category of drugs called macrolides. Macrolides include erythromycin, azithromycin and clarithromycin. GAS has also developed resistance to a less commonly used drug—tetracycline. Of these, resistance to erythromycin and the other macrolide antibiotics is of the most immediate concern.

PUBLIC HEALTH THREAT

Each year in the United States, erythromycin-resistant, invasive GAS causes 1,300 illnesses and 160 deaths.

GAS is a leading cause of upper respiratory tract infections such as strep throat. There are 1-2.6 million cases of strep throat in the U.S. each year. These bacteria are also the leading cause of necrotizing fasciitis, an invasive disease that can be fatal in 25%–35% of cases. Invasive disease means that bacteria invade parts of the body that are normally sterile. When this happens, disease is usually very severe, causing hospitalization or even death. Those at highest risk for invasive disease are the elderly, those with skin lesions, young children, people in group living situations such as nursing homes, and those with underlying medical conditions, such as diabetes.

Penicillin is the recommended first-line treatment for GAS infections. Amoxicillin is a type of penicillin that is often used to treat strep throat. Currently, GAS is not resistant to treatment with penicillin. If resistance to penicillin emerges, it would severely compromise treatment of invasive GAS infections. For people who are allergic to penicillin, two of the alternative antibiotics, azithromycin and clarithromycin, can be used to treat strep throat. In fact, azithromycin is prescribed more commonly than penicillin. Of GAS bacterial samples tested at CDC from 2010 and 2011, 10% were erythromycin-resistant (and therefore resistant to other macrolides such as azithromycin and clarithromycin), while 3.4% were clindamycin-resistant. Increasing resistance to erythromycin will complicate treatment of strep throat, particularly for those who cannot tolerate penicillin.

A more current concern is the increase in bacteria that show the genetic potential for becoming resistant to clindamycin. Clindamycin has a unique role in treatment of severe GAS infections. For severe, life-threatening infections, like necrotizing fasciitis and toxic shock syndrome, a combination of penicillin and clindamycin is recommended for treatment.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

ERYTHROMYCIN-RESISTANT GROUP A STREPTOCOCCUS

FIGHTING THE SPREAD OF RESISTANCE

Encouraging appropriate antibiotic use, including using the right antibiotic at the right time, and for the right amount of time, is crucial to preventing the spread of drug-resistant GAS. Doctors should adhere to the recommended antibiotics for treating GAS infections, including using penicillin or amoxicillin whenever possible.

WHAT CDC IS DOING

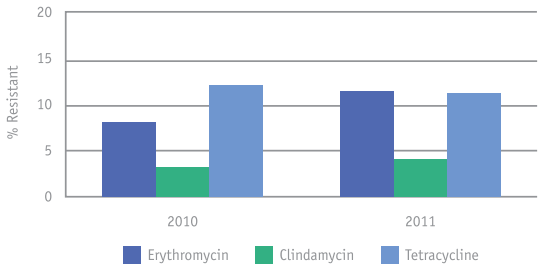
CDC has collaborated with the Infectious Diseases Society of America to update guidance on diagnosing strep throat and selecting antibiotics to treat it. These guidelines reinforce appropriate use of antibiotics for this common illness. CDC is also promoting appropriate antibiotic use among outpatient healthcare providers and the public through its Get Smart: Know When Antibiotics Work program. As part of this program, CDC hosts Get Smart About Antibiotics Week, an annual one-week observance of the importance of appropriate antibiotic use and its impact on antibiotic resistance. Through partnerships between CDC, state health departments, and universities, CDC is tracking GAS through Active Bacterial Core surveillance (ABCs).

WHAT YOU CAN DO

- Prevent infections by practicing good hand hygiene.
- Take antibiotics exactly as the doctor prescribes. Do not skip doses. Complete the prescribed course of treatment, even when you start feeling better.
- Only take antibiotics prescribed for you. Do not share or use leftover antibiotics.
- Do not save antibiotics for the next illness. Discard any leftover medication once the prescribed course of treatment is completed.
- Do not ask for antibiotics when your doctor thinks you do not need them.

Rates of resistance to two core antibiotics continue to increase for group A strep.

Prevalence of erythromycin, clindamycin and tetracycline resistance among group A streptococcal isolates, CDC's Active Bacterial Core surveillance (ABCs), 2010–2011



ONLINE RESOURCES

Active Bacterial Core surveillance (ABCs)
http://www.cdc.gov/abcs/index.html

Get Smart: Know When Antibiotics Work Program
http://www.cdc.gov/getsmart/

Group A Strep
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/groupastreptococcal_g.htm

Necrotizing Fasciitis
http://www.cdc.gov/features/necrotizingfasciitis/

Strep Throat
http://www.cdc.gov/features/strepthroat/

Scarlet Fever
http://www.cdc.gov/features/scarletfever/

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CLINDAMYCIN-RESISTANT GROUP B STREPTOCOCCUS

THREAT LEVEL
CONCERNING

This bacteria is concerning, and careful monitoring and prevention action are needed.

7,600 DRUG-RESISTANT GROUP B STREP INFECTIONS

440 DEATHS

27,000 SEVERE CASES OF GBS IN 2011

GROUP B STREP IS THE LEADING CAUSE OF
SERIOUS BACTERIAL INFECTIONS IN NEWBORNS

Group B *Streptococcus* (GBS) is a type of bacteria that can cause severe illnesses in people of all ages, ranging from bloodstream infections (sepsis) and pneumonia to meningitis and skin infections.

RESISTANCE OF CONCERN

GBS has developed resistance to clindamycin and erythromycin. GBS that are resistant to erythromycin will also be resistant to azithromycin. Recently, the very first cases with resistance to vancomycin have been detected among adults. These cases are extremely rare and also very concerning since vancomycin is the most commonly used drug for treatment of potentially resistant gram-positive infections in adults. Strains with decreasing responsiveness to treatment with penicillin drugs have been described but remain very rare. Resistance to clindamycin is of the most immediate clinical concern, although the other forms of resistance are worrisome.

PUBLIC HEALTH THREAT

Each year in the United States, clindamycin-resistant Group B Strep causes an estimated 7,600 illnesses and 440 deaths.

In the United States, GBS is the leading cause of serious bacterial infections in newborns, including bloodstream infections, meningitis, and pneumonia. When these GBS infections occur in the first 7 days of life, they are known as early-onset disease. To prevent early-onset disease in newborns, antibiotics are given during labor and delivery to mothers who test positive for GBS (tested at 35–37 weeks of pregnancy with a vaginal/rectal swab) and to those who have other risk factors for passing GBS to their newborns.

GBS also is one of the most common causes of meningitis and other severe infections in infants from 7 days to 3 months old (late-onset disease). GBS is also an increasing cause of bloodstream infections, pneumonia, skin and soft tissue infections, and bone and joint infections in adults, especially among pregnant women, the elderly, and people with certain medical conditions such as diabetes.

CDC estimates from preliminary data that 27,000 cases of severe GBS disease, such as blood infections or meningitis, occurred in 2011, causing 1,575 deaths. Forty-nine percent of GBS isolates (samples) tested were erythromycin-resistant, and 28% were clindamycin-resistant. Although the incidence of early-onset disease has been decreasing, the proportion of GBS infections resistant to erythromycin and clindamycin has increased steadily since 2000.

Resistance to the penicillin drug class could threaten the success of strategies to prevent early-onset disease and lead to treatment failures since penicillin drugs are the top choice for treating GBS. Additionally, the increasing resistance to recommended second-line drugs, clindamycin and erythromycin, limits prevention and treatment for patients with GBS who are allergic to penicillin.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CLINDAMYCIN-RESISTANT GROUP B STREPTOCOCCUS

FIGHTING THE SPREAD OF RESISTANCE

Doctors should test all pregnant women for GBS at 35–37 weeks of pregnancy and adhere to the recommended antibiotics during labor and delivery for prevention of early-onset disease. Broad efforts to promote appropriate use of antibiotics in outpatient and inpatient settings will also help minimize the spread of resistance among GBS bacteria.

WHAT CDC IS DOING

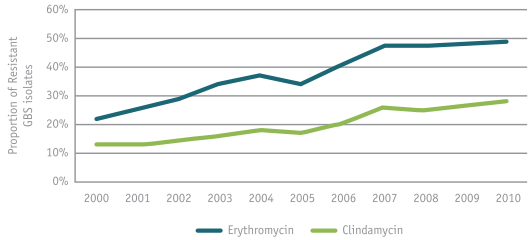
CDC, in collaboration with professional associations, has developed evidence-based Guidelines for the Prevention of Perinatal Group B Streptococcal Disease. These guidelines discuss diagnosis and management, and recommendations are provided regarding antibiotic choices and dosing. They also support GBS screening for all pregnant women at 35–37 weeks of pregnancy and use of antibiotics during labor and delivery to prevent newborn infection. Through partnerships between CDC, state health departments, and universities, CDC is tracking GBS through its Active Bacterial Core surveillance (ABCs). This program monitors antibiotic resistance and has contributed to the detection of the very first cases in the U.S. of vancomycin-resistant GBS, as well as tracking of susceptibility trends of other antibiotics important for treatment of GBS. CDC is promoting appropriate antibiotic use among outpatient health care providers and the public through its Get Smart: Know When Antibiotics Work program.

WHAT YOU CAN DO

- Pregnant women should talk to their doctor or nurse about their GBS status and let them know of any medication allergies during a checkup.
- When women get to the hospital or birthing center for delivery, they should remind their doctor or nurse if they have GBS and if they are allergic to any medications.
- Practice appropriate antibiotic use whenever you see a doctor or are prescribed an antibiotic for any condition:
  - Take antibiotics exactly as the doctor prescribes. Do not skip doses. Complete the prescribed course of treatment, even when you start feeling better.
  - Only take antibiotics prescribed for you. Do not share or use leftover antibiotics.
  - Do not save antibiotics for the next illness. Discard any leftover medication once the prescribed course of treatment is completed.
  - Do not ask for antibiotics when your doctor thinks you do not need them.

Group B strep continues to become more resistant to two major antibiotics, leaving those allergic to first line drugs in jeopardy.

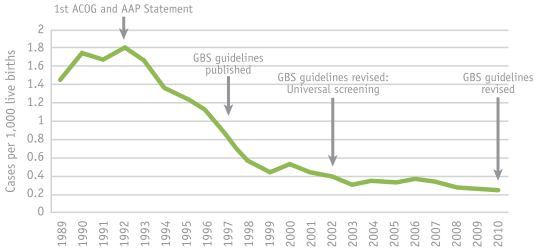
Proportion of Group B *Streptococcus* isolates resistant to erythromycin and clindamycin—
Active Bacterial Core surveillance (ABCs), 2000-2010*



*Most recent data available.

Early-onset group B strep disease has declined by 80% since the introduction of evidence-based prevention strategies.

Incidence of Early-Onset Disease Caused by Group B *Streptococcus*—
Active Bacterial Core surveillance (ABCs), 1989–2010



ACOG = American College of Obstetricians and Gynecologists, AAP = American Academy of Pediatrics

ONLINE RESOURCES

Group B Strep (GBS)
http://www.cdc.gov/groupbstrep/about/index.html

Active Bacterial Core surveillance (ABCs)
http://www.cdc.gov/abcs/index.html

EXTENDED SPECTRUM β-LACTAMASE PRODUCING ENTEROBACTERIACEAE

TECHNICAL APPENDIX

Technical Appendix

Clostridium difficile

Methods

National estimates of the number of *Clostridium difficile (C. difficile)* infections (CDI) requiring hospitalization or in already hospitalized patients were obtained from the data submitted through the Emerging Infections Program's *C. difficile* surveillance in 2011, of 34 counties in 10 U.S. states (http://www.cdc.gov/hai/eip/cdiff_techinfo.html). During 2011, a total of 15,452 CDI cases were identified across the participating sites. Data on hospitalization following CDI or at the time of infection were obtained for all cases from 8 of 10 U.S. states and from a random sample of 33% from cases from the other 2 states. The sampled cases were used to estimate total number of hospitalizations in the 2 states where sampling was performed. The national estimates were made using 2011 population estimates from U.S. Census Bureau adjusting for age, gender and race distribution of the American population.[1] Approximately 18% of cases were reported without a race value. Multiple imputation was used to estimate the missing race based on the data that are available and the results were summarized. The *C. difficile* attributable mortality was estimated from death certificate data.[2] Trends on deaths related to *C. difficile* were obtained from the CDC's National Center for Health Statistics.[3] Estimates were rounded to two significant digits.

References

1 Lessa FC, Mu, Y, Cohen J, Dumyati G, Farley MM, Winston L, Kast K, Holzbauer S, Meek J, Beldavs S, McDonald LC, Fridkin SK. Presented at the IDWeek 2012, Annual Meeting of the Infectious Disease Society of America, Society for Healthcare Epidemiology, Pediatric Infectious Disease Society, and HIV Medical Association; San Diego, October 2012.

2 Hall AJ, Curns AT, McDonald LC, Parashar UD, Lopman BA. The Roles of *Clostridium difficile* and Norovirus Among Gastroenteritis-Associated Deaths in the United States, 1999-2007. Clin Infect Dis. 2012 Jul;55(2):216–23.

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Technical Appendix

Carbapenem-Resistant Enterobacteriaceae

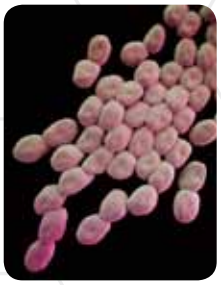
Multidrug-Resistant *Acinetobacter*

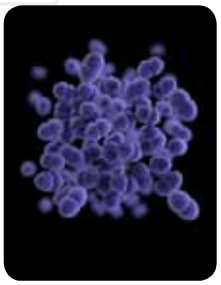
Fluconazole-Resistant *Candida*

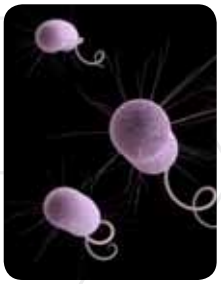
Extended Spectrum B-lactamase producing Enterobacteriaceae (ESBLs)

Vancomycin-Resistant *Enterococcus* (VRE)

Multidrug-Resistant *Pseudomonas aeruginosa*







Methods

National estimates of the number of healthcare-associated infections (HAIs) with Enterobacteriaceae, *Pseudomonas aeruginosa, Candida*, *Acinetobacter,* or Enterococci were obtained from a 2011 survey of 11,282 patients in 183 hospitals in 10 different states, among whom 452 were identified with at least one HAI for a total of 504 HAIs (some patients had >1 HAI).

Many assumptions were made in deriving national estimates, using these 452 patients, and adjusting for age and length of stay using the 2010 Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality. For 2011, an estimated 647,985 patients had at least one HAI, resulting in an estimated 721,854 HAIs.[1] 481 pathogens were reported among the 504 HAIs detected; 50 *K. pneumonia* or *K. oxytoca* (9.9%), 47 *E. coli* (9.3%), 46 *Enterococci spp.* (9.1%), 36 *P. aeruginosa* (7.1%), 34 *Candida spp.* (6.7%), 8 *Acinetobacter spp.* (1.6%). For each pathogen, the pathogen-specific annual estimate was obtained by multiplying this proportion (of all HAIs) by the national HAI estimate (721,854). Next, the estimated no. of resistant infections was obtained by multiplying the respective pathogen-specific national estimate by the proportion of pathogens reported as non-susceptible to the antimicrobial of interest from other CDC data systems. For Enterobacteriaceae, *Pseudomonas aeruginosa, Acinetobacter,* and Enterococci this was CDC's National Healthcare Safety Network and includes the mean percent non-susceptible across the device and procedure-associated HAIs reported during 2009–2010[2]; see individual fact sheets in this report for percent resistance for each pathogen.

For *Candida* by the proportion of *Candida* species testing non-susceptible to fluconazole that were submitted to CDC for confirmatory testing as part of the Emerging Infections Program Surveillance of *Candida* bloodstream infections during 2008-2011.[3] In this program a total of 2,675 *Candida* species isolates associated with bloodstream infections were submitted as part of the EIP population-based surveillance in 2 US cities, azole resistance was identified in 165 cases, or 7%.

The number of deaths attributable to the antimicrobial-resistant healthcare-associated infection was determined by multiplying the estimated number of resistant infections by 6.5%, an overall estimate of attributable mortality from antibiotic-resistant hospital-onset infections previously determined.[4] This estimate accounts for the overall distribution of the different types of infections commonly caused by antibiotic-resistant pathogens in hospitalized patients and is generally much lower than the crude mortality observed in many of these patients owing to their severe underlying disease status. Definitions of multidrug resistance used in this analysis are published elsewhere.[2] The proportion of U.S. hospitals reporting carbapenem-resistant Enterobacteriaceae was derived as reported elsewhere.[5] Estimates were rounded to two significant digits.

References

1 Magill SS, Edwards JR, Bamberg W, Beldavs Z, Dumyati G, Kainer M, Lynfield R, Maloney M, McAllister-Hollod L, Nadle J, Ray SR, Thompson DL, Wilson LE, Fridkin SK. Presented at the IDWeek 2012, Annual Meeting of the Infectious Disease Society of America, Society for Healthcare Epidemiology, Pediatric Infectious Disease Society, and HIV Medical Association; San Diego, October 2012.

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Technical Appendix

Neisseria gonorrhoeae

Methods

Estimates of the number of gonococcal infections with any resistance pattern, reduced susceptibility to cephalosporins or azithromycin, or resistance to tetracycline are reported. They are derived by multiplying an estimate of the annual number of gonococcal infections in the United States[1] by the prevalence of reduced susceptibility or resistance among urethral *Neisseria gonorrhoeae* isolates collected and tested by the Gonococcal Isolate Surveillance Project (GISP) during 2011.[2]

Many assumptions were made in deriving the estimates. Data from the National Health and Nutrition Examination Survey (NHANES) provided accurate gonorrhea prevalence estimates, although NHANES only measures urogenital infections and does not include oropharyngeal or rectal infections. The average duration of infection, used to calculate incidence, was based on expert opinion, due to an absence of published data. Also, estimates of resistance in GISP are nationally representative. However, compared to the regional distribution of reported gonococcal infections, GISP relatively over-samples patients from the West Coast, where resistance has traditionally first emerged in the United States. The Clinical Laboratory Standards Institute categorizes susceptibility to cefixime and ceftriaxone as minimum inhibitory concentrations (MICs) ≤0.25 µg/ml.[3] For this analysis, isolates with cefixime MICs ≥0.25 µg/ml were considered to have reduced cefixime susceptibility, and isolates with ceftriaxone MICs ≥0.125 µg/ml were considered to have reduced ceftriaxone susceptibility. An azithromycin MIC ≥2.0 µg/ml was considered to have reduced azithromycin susceptibility, and a tetracycline MIC ≥2.0 µg/ml was considered resistant. Resistance to any antimicrobial includes resistance to penicillin (MIC ≥ 2 µg/ml), tetracycline, ciprofloxacin (MIC ≥ 1µg/ml), or spectinomycin (MIC ≥ 128 µg/ml), or reduced susceptibility to the cephalosporins or azithromycin.

GISP, established in 1986, is a sentinel surveillance system with partners that include CDC, sexually transmitted disease clinics at 25–30 sentinel sites, and 5 regional laboratories in the United States.[4] Gonococcal isolates are collected from up to the first 25 men diagnosed with gonococcal urethritis at each sentinel site each month. Antimicrobial susceptibility testing is performed using agar dilution for a panel of antimicrobials that includes penicillin, tetracycline, ciprofloxacin, spectinomycin, cefixime, ceftriaxone, and azithromycin.

References

1 Satterwhite CL et al. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. Sex Transm Dis 2013;40(3):187–93.

2 CDC. Sexually transmitted diseases surveillance 2011. Atlanta: U.S. Department of Health and Human Services; 2012.

3 Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Third Informational Supplement. CLSI document M100-S23. Wayne, PA; Clinical and Laboratory Standards Institute; 2013; 33(1):100–102.

4 CDC GISP website: http://www.cdc.gov/std/GISP.

Technical Appendix

Drug-Resistant *Campylobacter*

Methods

Estimates of the number of illnesses and deaths from infections with *Campylobacter* resistant to ciprofloxacin or azithromycin are reported. They were derived by multiplying an estimate of the annual number of *Campylobacter* illnesses or deaths in the United States[1] by the average prevalence of resistance among *Campylobacter* tested by the National Antimicrobial Resistance Monitoring System (NARMS) during the years 2009–2011. Resistance breakpoints from the NARMS 2011 Human Isolates Report were used.[2]

Many assumptions were made in deriving the estimates. The estimated number of illnesses from resistant *Campylobacter* was divided by the U.S. population and multiplied by 100,000 to calculate the estimated number of illnesses from resistant infections per 100,000 people. The U.S. population in 2006 (approximately 299 million people) was used for the calculations because the estimated number of *Campylobacter* illnesses in the United States was based on this population.[1] The sentinel county survey data displayed in Figure 1 was previously reported.[3]

References

1 Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. Emerg Infect Dis 2011;17:7–15.

2 CDC. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report, 2011. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2013.

3 Gupta A, Nelson JM, Barrett TJ, et al. Antimicrobial Resistance among *Campylobacter* Strains, United States, 1997–2001. Emerg Infect Dis 2004;10:1102-9.

Technical Appendix

Drug-Resistant Non-Typhoidal *Salmonella*

Methods

Estimates of the number of illnesses and deaths from infections with non-typhoidal *Salmonella* resistant to ceftriaxone, resistant or partially resistant to ciprofloxacin, or resistant to five or more antibiotic classes are reported. They were derived by multiplying an estimate of the annual number of non-typhoidal *Salmonella* illnesses or deaths in the United States[1] by the average prevalence of resistance among non-typhoidal *Salmonella* isolates tested by the National Antimicrobial Resistance Monitoring System (NARMS) during the years 2009–2011. Resistance breakpoints from the NARMS 2011 Human Isolates Report were used.[3] For ciprofloxacin, isolates with intermediate susceptibility results (minimum inhibitory concentration of 0.12–0.5 µg/ml) were considered partially resistant.

Many assumptions were made in deriving the estimates. The estimated number of illnesses from resistant *Salmonella* was divided by the U.S. population and multiplied by 100,000 to calculate the estimated number of illnesses from resistant *Salmonella* per 100,000 population. The U.S. population in 2006 (approximately 299 million people) was used for the calculations because the estimated number of non-typhoidal *Salmonella* illnesses in the United States was based on this population.[1] The methods used to estimate the direct medical costs for *Salmonella* infections were previously reported.[2]

References

1 Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. Emerg Infect Dis. 2011;17:7–15.

2 CDC. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report, 2011. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2013.

3 CDC. Vital Signs: Incidence and Trends of Infection with Pathogens Transmitted Commonly Through Food—Foodborne Diseases Active Surveillance Network, 10 U.S. Sites, 1996–2010. MMWR 2011;60:749–55.

Technical Appendix

Drug-Resistant *Salmonella* Serotype Typhi

Methods

An estimate of the number of illnesses and deaths from *Salmonella* serotype Typhi resistant or partially resistant to ciprofloxacin was derived by multiplying an estimate of the annual number of illnesses or deaths from typhoid fever in the United States[1] by the average prevalence of ciprofloxacin resistance or partial resistance among *Salmonella* Typhi isolates tested by the National Antimicrobial Resistance Monitoring System (NARMS) during 2009–2011. Resistance breakpoints from the NARMS 2011 Human Isolates Report were used.[2] For ciprofloxacin, isolates with intermediate susceptibility results (minimum inhibitory concentration of 0.12–0.5 µg/ml) were considered partially resistant.

Many assumptions were made in deriving the estimates. The estimated number of illnesses from ciprofloxacin resistant or partially resistant *Salmonella* Typhi was divided by the U.S. population and multiplied by 100,000 to calculate the estimated number of illnesses from resistant or partially resistant infections per 100,000 people. The U.S. population in 2006 (approximately 299 million people) was used for the calculations because the estimated number of typhoid fever illnesses in the United States was based on this population. Worldwide case estimates[3] and pre-antibiotic era mortality[4] are from published sources.

References

1 Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. Emerg Infect Dis 2011;17(1):7–15.

2 CDC. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report, 2011. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2013.

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4 Heymann DL, editor. Control of Communicable Diseases Manual. 19th ed. Washington DC: American Public Health Association; 2008.

Technical Appendix

Drug-Resistant *Shigella*

Methods

Estimates of the number of illnesses and deaths from infections with *Shigella* resistant to azithromycin or ciprofloxacin are reported. They were derived by multiplying an estimate of the annual number of *Shigella* illnesses or deaths in the United States[1] by the prevalence of resistance among *Shigella* tested by the National Antimicrobial Resistance Monitoring System (NARMS) in 2011, the year azithromycin testing began. Resistance breakpoints from the NARMS 2011 Human Isolates Report were used.[2] As clinical azithromycin breakpoints have not been established for *Shigella,* the values used here were based on epidemiological cut-off values used in the NARMS report. Isolates with azithromycin minimal inhibitory concentrations of ≥32 µg/ml were considered resistant.

Many assumptions were made in deriving these estimates. The estimated number of illnesses from resistant *Shigella* was divided by the U.S. population and multiplied by 100,000 to calculate the estimated number of illnesses from resistant infections per 100,000 people. The U.S. population in 2006 (approximately 299 million people) was used for the calculations because the estimated number of *Shigella* illnesses in the United States was based on this population.[1] The sentinel county survey data displayed were previously reported.[3,4,5]

References

1 Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. Emerg Infect Dis 2011;17:7–15.

2 CDC. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report, 2011. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2013.

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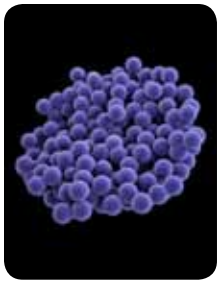

Technical Appendix

Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Methods

National estimates of the number of invasive MRSA healthcare-associated infections (HAIs) were derived from the Emerging Infection Program/Active Bacterial Core Surveillance[1] for Invasive MRSA using data reported for infections occurring during 2011 (http://www.cdc.gov/abcs/reports-findings/surv-reports.html). During 2011, 4,872 reports of invasive MRSA (isolates of MRSA cultured from a normally sterile site and identified by a participating clinical laboratory) were received from the 9 participating program sites (population of 19,393,677). Reports include both healthcare-associated infections and community-associated infections, but are limited to invasive infections (approximately 85% are bloodstream infections).

Estimates were made using National Center for Health Statistics bridged-race vintage 2011 post-censal file and U.S. renal data systems, adjusting for race, age, gender, and receipt of dialysis. Mortality includes all-cause mortality during hospitalization, and estimates were adjusted in similar fashion as infection estimates. Approximately 18% of cases were reported without a race value, multiple imputation was used to estimate the missing race based on the data that are available and the results were summarized. Regarding device and procedure-associated infections with MRSA, the proportion of facilities reporting at least one *S. aureus* HAI reported as MRSA for each HAI type was obtained from CDC's National Healthcare Safety Network Antimicrobial Resistance Report 2009–2010.[2] Estimates were rounded to two significant digits.

References

1 Kallen AJ, Mu Y, Bulens S, Reingold A, Petit S, Gershman K, Ray SM, Harrison LH, Lynfield R, Dumyati G, Townes JM, Schaffner W, Patel PR, Fridkin SK; Active Bacterial Core surveillance (ABCs) MRSA Investigators of the Emerging Infections Program. Health care-associated invasive MRSA infections, 2005–2008. JAMA. 2010

2 Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, Kallen A, Limbago B, Fridkin S; National Healthcare Safety Network (NHSN) Team and Participating NHSN Facilities. Antimicrobial-resistant pathogens associated with healthcare-associated infections: summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009–2010. Infect Control Hosp Epidemiol. 2013 Jan;34(1):1–14

Technical Appendix

Vancomycin-Resistant *Staphylococcus aureus*

Methods

Vancomycin resistant *S. aureus* (VRSA) have been a nationally notifiable condition since 2004.[1] The national estimate of the number of VRSA cases is derived from individual case reports and confirmation at the Centers for Disease Control and Prevention (CDC). All reported VRSA are submitted to CDC for confirmatory antimicrobial susceptibility with reference broth microdilution.[2] Vancomycin resistance in *S. aureus* is defined as an MIC ≥ 16 ug/ ml. All isolates meeting this criterion are further characterized with PCR to detect known resistance mechanisms. All 13 U.S. VRSA identified to date have carried the *vanA* resistance determinant.[3]

References

1 http://wwwn.cdc.gov/nndss/document/nndss_event_code_list_2013.pdf

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3 http://www.cdc.gov/HAI/settings/lab/vrsa_lab_search_containment.html

Technical Appendix

Drug-Resistant *Streptococcus pneumoniae*

Methods

Trends in the incidence of antibiotic-resistant invasive pneumococcal disease per 100,000 persons 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 *Streptococcus pneumoniae*, at 10 sites located throughout the United States representing a population of approximately 30 million persons. Isolates are collected on ≥90% of all cases (approximately 3200 isolates per year) and sent to reference laboratories for susceptibility testing to eighteen different antibiotics using Clinical and Laboratory Standards Institute (CLSI) methods. Estimates of invasive pneumococcal disease are also from ABCs.[2]

Estimates of the burden of antibiotic resistant pneumococcal disease are derived from three sources. First, numbers of cases were estimated by applying the rate for full resistance to clinically relevant drugs (i.e. penicillin, ceftriaxone, cefotaxime, erythromycin, levofloxacin, tetracycline, trimethoprim/sulfamethoxazole) in 2011 (30%) to estimates of cases of all *S. pneumoniae* infections (4 million) as estimated by Huang and colleagues.[3] Numbers of deaths were estimated by applying the rate of full resistance to a clinically relevant drug (33%) to the total number of deaths from pneumococcal disease.[3] Excess pneumococcal pneumonia visits, hospitalizations, and costs were estimated using the previous overall burden estimates[3] but consideration of the burden of disease that would have occurred in the absence of resistance to penicillin, erythromycin, and levofloxacin.[4]

References

1 CDC. Active Bacterial Core Surveillance Methodology (2012). http://www.cdc.gov/abcs/index.html [Accessed 5/23/2013].

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Technical Appendix

Erythromycin-Resistant Group A *Streptococcus*

Methods

Estimates of the proportion of GAS isolates resistant to erythromycin, clindamycin and tetracycline 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 representing a population of approximately 32 million people. Isolates are collected on ~80% of all cases (approximately ~1000 isolates per year) and sent to reference laboratories for susceptibility testing to twelve different antibiotics using Clinical and Laboratory Standards Institute (CLSI) methods.

Cases and deaths were estimated by applying 2011 resistant rate to erythromycin (10%, see Strep Group A *Streptococcus* pathogen page) to total cases (13300) and total deaths (1,550) reported in the 2011 report of the Active Bacteria Core surveillance (ABCs).[2]

References

1 CDC, Active Bacterial Core Surveillance Methodology (2012). http://www.cdc.gov/abcs/index.html [Accessed 5/23/2013].

2 http://www.cdc.gov/abcs/reports-findings/survreports/gas11.html

Technical Appendix

Clindamycin-Resistant Group B *Streptococcus*

Methods

Estimates of the proportion of GBS 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 GBS, at 10 sites located throughout the United States representing a population of approximately 32 million persons. Isolates are collected currently from 7 of these states, from ~85% of the cases in these states (approximately ~1500 isolates per year) and sent to reference laboratories for susceptibility testing to twelve different antibiotics using Clinical and Laboratory Standards Institute (CLSI) methods. Estimates of severe disease are also from ABCs.[2]

Cases and deaths were estimated by applying the 2010 overall resistant rate to clindamycin (28%) from the ABCs antimicrobial susceptibilities report[3] to total cases (27,000) and total deaths (1,575) reported in the 2011 ABCs GBS surveillance report.[2]

References

1 CDC. Active Bacterial Core Surveillance Methodology (2012). http://www.cdc.gov/abcs/index.html [Accessed 5/23/2013].

2 CDC. Active Bacterial Core Surveillance (ABCs) Report, Emerging Infections Program network, Group B *Streptococcus* (2011). http://www.cdc.gov/abcs/reports-findings/survreports/gbs11.pdf [Accessed 7/23/2013].

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GLOSSARY

Active Bacterial Core surveillance (ABCs): A core component of CDC's Emerging Infections Programs network (EIP), a collaboration between CDC, state health departments, and universities. ABCs is an active laboratory- and population-based surveillance system that tracks invasive bacterial pathogens of public health importance. It currently operates among 10 EIP sites across the United States, representing a population of approximately 41 million persons. At this time, ABCs conducts surveillance for six pathogens: group A and group B *Streptococcus* (GAS, GBS), *Haemophilus influenzae, Neisseria meningitidis, Streptococcus pneumoniae,* and methicillin-resistant *Staphylococcus aureus* (MRSA).

Adverse drug event: When therapeutic drugs (example, antibiotics) have harmful effects; when someone has been harmed by a medication.

Aminoglycoside: A type of antibiotic that destroys the functioning of gram-negative bacteria. Increased resistance to aminoglycosides has made them less useful.

Antibiotic: Type of medicine made from mold or bacteria that kills or slows the growth of other bacteria. Examples include penicillin and streptomycin.

Antibiotic class: A grouping of antibiotics that are similar in how they work and how they are made.

Antibiotic growth promotion: Giving farm animals antibiotics to increase their size in order to produce and sell more meat.

Antibiotic resistance: The result of bacteria changing in ways that reduce or eliminate the effectiveness of antibiotics. Antibiotic resistance is one type of antimicrobial resistance.

Antibiotic stewardship: Coordinated efforts and programs to improve the use of antimicrobials. For example, facilities with antibiotic stewardship programs have made a commitment to always use antibiotics appropriately and safely—only when they are needed to prevent or treat disease, and to choose the right antibiotics and to administer them in the right way in every case.

Antimicrobial: A general term for the drugs, chemicals, or other substances that either kill or slow the growth of microorganisms. Among the antimicrobial agents in use today are antibacterial drugs (which kill bacteria), antiviral agents (which kill viruses), antifungal agents (which kill fungi), and antiparisitic drugs (which kill parasites).

Antimicrobial resistance: The result of microorganisms changing in ways that reduce or eliminate the effectiveness of drugs, chemicals, or other agents used to cure or prevent infections. In this report, the focus is on antibiotic resistance, which is one type of antimicrobial resistance.

Azithromycin: A macrolide antibiotic used to treat infections caused by gram-positive bacteria and infections such as respiratory tract and soft-tissue infections.

Azoles: A large class of drugs developed to treat fungal infections.

Bacteria: Single-celled organisms that live in and around us. Bacteria can be helpful, but in certain conditions can cause illnesses such as strep throat, ear infections, and bacterial pneumonia.

Bacteriology: The study of bacteria.

Beta (β)-lactamase enzyme: A chemical produced by certain bacteria that can destroy some kinds of antibiotics.

Broad-spectrum antibiotic: An antibiotic that is effective against a wide range of bacteria.

Carbapenem: A type of antibiotic that is resistant to the destructive beta-lactamase enzyme of many bacteria. Carbapenems are used as a last line of defense for many bacteria, but increased resistance to carbapenems has made them less useful.

Cefixime: A cephalosporin antibiotic that is resistant to the destructive beta-lactamase enzyme of many bacteria.

Ceftriaxone: A cephalosporin antibiotic that is resistant to the destructive beta-lactamase enzyme of many bacteria.

Cephalosporin: Cephalosporins are a class of antibiotics containing a large number of drugs. Some more recently developed cephalosporins are resistant to the destructive beta-lactamase enzyme produced by many bacteria.

Ciprofloxacin: A broad-spectum fluoroquinolone antibiotic that is important in treating serious bacterial infections, especially when resistance to older antibiotic classes is suspected.

Clindamycin: An antibiotic used to treat certain types of bacterial infections, including infections of the lungs, skin, blood, female reproductive organs, and internal organs.

Conjugate vaccine: A vaccine in which an antigen is attached to a carrier protein from the same microorganism. This approach enhances the immunological response to the vaccine and thereby enhances the overall effectiveness of the vaccine.

Echinocandins: A class of drugs developed to treat fungal infections.

EIP: The Emerging Infections Program network is a national resource for surveillance, prevention, and control of emerging infectious diseases. It was established in 1995. The EIP is a network of 10 state health departments and their collaborators in local health departments, academic institutions, other federal agencies, and public health and clinical laboratories; infection preventionists; and healthcare providers.

Endogenous flora: Bacteria that naturally reside in or on the body.

Epidemiology: The study of diseases to find out who is affected, how disease is spread, trends in illnesses and deaths, what behaviors or other risk factors might put a person at risk, and other information that can be used to develop prevention strategies. Epidemiologists use surveys and surveillance systems to track illnesses, and they often investigate disease outbreaks.

Erythromycin: An antibiotic used to treat certain infections caused by bacteria, such as bronchitis, diphtheria, Legionnaires' disease, pertussis (whooping cough), pneumonia, rheumatic fever, sexually transmitted diseases, and infections of the ear, intestine, lung, urinary tract, and skin. It is also used before some surgery or dental work to prevent infection.

Extended-spectrum antibiotic: An antibiotic that has been chemically modified to attack additional types of bacteria, usually those that are gram-negative.

Extensively drug-resistant (XDR): Resistance to nearly all drugs that would be considered for treatment. Exact definitions for XDR differ for each type of bacteria.

Fluconazole: An antifungal drug in the azole class.

Fluoroquinolones: Broad-spectrum antibiotics that play an important role in treatment of serious bacterial infections, especially hospital-acquired infections and others in which resistance to older antibacterial classes is suspected. Increasing resistant to fluoroquinolones is making them less effective.

Fungus: A single-celled or multicellular organism. Fungi can be opportunistic pathogens (such as aspergillosis, candidiasis, and cryptococcosis) that cause infections in people with compromised immune systems, such as cancer patients, transplant recipients, and people with HIV/AIDS. Fungi can also be or pathogens (such as the endemic mycoses, histoplasmosis and coccidioidomycosis, and superficial mycoses) that cause infections in healthy people. Fungi are used to develop antibiotics, antitoxins, and other drugs used to treat various diseases.

GISP: The Gonococcal Isolate Surveillance Project was established in 1986 to monitor U.S. trends in antimicrobial susceptibilities of strains of *Neisseria gonorrhoeae,* the type of bacteria that causes gonorrhea. The goal of GISP is to establish a rational basis for the selection of drugs used to treat gonorrhea. GISP is a collaborative project between selected sexually transmitted disease clinics, five regional laboratories, and CDC.

HAIs: Healthcare-associated infections are those that occur in hospitals, outpatient clinics, nursing homes, and other facilities where people receive care.

Hand hygiene: The practice of cleaning hands. This practice protects against infection and illness.

Hypervirulent: Increased ability to cause severe disease, relapse rates, and death.

Invasive disease: A disease that can spread within the body to healthy tissue.

Isolate/bacterial isolate: A pure culture or sample of bacteria used to study their properties.

Isoniazid (INH): A first-line drug used to treat tuberculosis. Strains of tuberculosis resistant to INH and rifampin are considered to be multidrug resistant.

Macrolide: A type of antibiotic used to treat infections caused by gram-positive bacteria and infections such as respiratory tract and soft-tissue infections. Macrolides are often used

in people allergic to penicillin, but resistance to macrolides is increasing and has made them less useful.

Methicillin: An antibiotic derived from penicillin. It was previously used to treat bacteria such as *Staphylococcus aureus.*

Microbiology: The study of microorganisms.

Microorganism: Organisms so small that a microscope is required to see them. This term includes bacteria, fungi, parasites, and viruses.

Morbidity: The number of people who are infected with a specified illness in a given time period.

Mortality: The number of people who die in a given time from a specified illness.

MRSA: Methicillin-resistant *Staphylococcus aureus* is used to describe any strain of *S. aureus* that is resistant to all types of penicillin (not just methicillin) as well as cephalosporin.

Multidrug-resistant (MDR): Microorganisms that are resistant to multiple classes of antimicrobials. The exact number of drugs that a microorganism is resistant to varies depending on the infection or pathogen.

NARMS: The National Antimicrobial Resistance Monitoring System monitors antimicrobial resistance in foodborne and other enteric bacteria, including *Salmonella, Campylobacter, Shigella, Escherichia coli* O157, and *Vibrio* (non-*V. cholerae*). NARMS is a collaboration among CDC, the U.S. Food and Drug Administration (FDA), the U.S. Department of Agriculture (USDA), and state and local health departments.

Narrow-spectrum antibiotic: An antibiotic that is active against a limited range of bacteria.

NHSN: CDC's National Healthcare Safety Network is the nation's most widely used healthcare-associated infection tracking system. NHSN provides facilities, states, regions, and the nation with data needed to identify problem areas, measure progress of prevention efforts, and ultimately eliminate healthcare-associated infections. In addition, NHSN allows healthcare facilities to track blood safety errors and important healthcare process measures such as healthcare personnel influenza vaccine status and infection control adherence rates.

Outbreak: When a group of people develop the same illness around the same time, and the number of people affected is higher than normal. Outbreak investigations are conducted to identify what exposure the affected people had in common.

Pan drug-resistance (PDR): Resistance to all drugs that would be considered for treatment. Exact definitions for PDR differ for each bacteria.

Penicillins: A class of antibiotics including amoxicillin, methicillin, piperacillin and other drugs based on the first true antibiotic discovered in 1928 by Dr. Alexander Fleming. Increased resistance has made many types of penicillins less useful.

Pneumonia: An inflammatory condition of the lungs affecting primarily the microscopic air

sacs known as alveoli. It is usually caused by infection with viruses or bacteria, and typical symptoms include a cough, chest pain, fever, and difficulty breathing.

Reservoir: A person, animal, insect, plant, or other host that is carrying a pathogen (for example, bacteria or fungi) that causes infectious diseases. Some pathogens have animal reservoirs (to survive, they need animal hosts). Others pathogens have human reservoirs (to survive, they need human hosts).

Resistant bacteria: Microorganisms that have changed in ways that reduce or eliminate the effectiveness of drugs, chemicals, or other agents to cure or prevent infections.

Rifampin: A first-line drug used to treat tuberculosis. Strains of tuberculosis resistant to isoniazid (INH) and rifampin (RMP) are considered to be multidrug resistant.

Strain/bacterial strain: A strain is a genetic variant or subtype of a microorganism (for example, a flu strain is a subtype of the flu virus). Some strains of bacteria are resistant to antibiotics, and others are not. When bacteria become resistant to antibiotics, they can share their resistance with other bacteria to create new resistant bacterial strains.

Superinfection: An infection following a previous infection, especially when caused by microorganisms that are resistant or have become resistant to the antibiotics used earlier.

Surveillance: The ongoing systematic collection and analysis of data. Surveillance systems that monitor infectious diseases provide data that can be used to develop actions to prevent infectious diseases.

Susceptible bacteria: When antibiotics are effective at killing or stopping the growth of a certain bacteria, the bacteria is known as susceptible to antibiotics. Susceptible infections are infections that can be treated effectively with antibiotics.

Systemic agents: Drugs that travel through the bloodstream and reach cells throughout the body.

Tetracyclines: A class of broad-spectrum antibiotics including tetracycline, doxycycline, minocycline, and other drugs. Increased resistance has made many types of tetracyclines less useful.

Vaccine: A product that produces immunity in a person's body and therefore protects them from an infectious disease. Vaccines are administered through shots, by mouth, and by aerosol mist.

Vancomycin: A drug that is frequently used to treat methicillin-resistant *Staphylococcus aureus* infections and that is also effective against other bacteria.

Virus: A strand of DNA or RNA in a protein coat that must get inside a living cell to grow and reproduce. Viruses cause many types of illness. For example, varicella virus causes chickenpox, and the human immunodeficiency virus (HIV) causes acquired immune deficiency syndrome (AIDS).

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