



# Inappropriate Antibiotic Prescribing for Adults Comes With Increased Risks

Antibiotic stewardship efforts can minimize costs and complications

## Overview

A new study from Washington University in St. Louis and The Pew Charitable Trusts analyzing private health insurance claims data found that inappropriate antibiotic prescribing among adults diagnosed with common outpatient upper respiratory infections resulted in close to \$69 million in excess health care costs in the U.S. in 2017 (\$49.6 million for pharyngitis, and \$19.1 million for sinus infection).<sup>1</sup> The results also showed up to a nearly fourfold increased risk of individual adverse drug events (i.e., harmful effects from medications) among patients who received inappropriate antibiotics.

Antibiotic use drives the development of antibiotic-resistant bacteria, which cause more than 2.8 million infections and 35,000 deaths in the United States each year.<sup>2</sup> As a result, it is critical to improve antibiotic stewardship efforts, which help ensure that these drugs are prescribed appropriately. Oftentimes, however, health care providers in outpatient settings prescribe antibiotics inappropriately.<sup>3</sup>

Researchers quantified the health care costs and adverse events associated with the inappropriate selection of antibiotics for bacterial infections (i.e., prescribing antibiotics that are not the recommended, or first-line, drugs per treatment guidelines) and unnecessary antibiotic prescribing for viral infections (i.e., prescribing antibiotics when they don't work against viruses) for six outpatient diagnoses.

Improving antibiotic prescribing through the expansion of antibiotic stewardship efforts is critical to minimizing the threat of resistance, improving patient care, and reducing spending. Health care stakeholders—including payers and health care systems—all have a role to play in supporting stewardship efforts in outpatient practices.

## Adverse events and health care costs associated with inappropriate antibiotic prescribing

Researchers looked at the occurrence of adverse drug events (ADEs) from inappropriate antibiotic prescribing for six common outpatient diagnoses. An ADE is a harm from taking a medication and can include allergic reactions, nausea, vomiting, diarrhea, and rash.<sup>4</sup> *Clostridioides difficile* infection (*C. diff*), formerly known as *Clostridium difficile*, is a potentially life-threatening ADE that can be caused by antibiotic exposure—particularly from broad-spectrum antibiotics.<sup>5</sup>

### Diagnoses resulting in inappropriate antibiotic selection:

- Pharyngitis: Inflammation of the throat, typically presenting as a sore throat.<sup>6</sup> The primary bacterial cause is group A *Streptococcus* (known as “strep throat”), which can be identified with a diagnostic test.<sup>7</sup> Amoxicillin or penicillin are the recommended first-line treatments for patients with strep throat.<sup>8</sup>
- Sinus infection: Sinus infections are one of the most common reasons that antibiotics are prescribed in outpatient settings in the U.S.<sup>9</sup> These infections can be caused by bacterial or viral pathogens, with antibiotics recommended only when a bacterial infection is suspected.<sup>10</sup> Amoxicillin or amoxicillin-clavulanate are the recommended first-line treatments for bacterial sinus infections.

### Diagnoses resulting in unnecessary antibiotic prescribing:

- Nonsuppurative middle ear infection: A condition characterized by the presence of noninfected fluid in the middle ear.<sup>11</sup> Antibiotics are not recommended for this condition.<sup>12</sup>
- Bronchitis: An infection that causes inflammation of the airways of the lungs.<sup>13</sup> This infection is often caused by a virus, and current guidelines recommend against prescribing antibiotics.<sup>14</sup>
- Influenza: An illness caused by the influenza virus, commonly called the “flu.”<sup>15</sup> Because this is a viral infection, antibiotics are not recommended.<sup>16</sup>
- Viral upper respiratory infection (URI): Often referred to as the “common cold,” this type of infection can cause symptoms such as cough, congestion, and sore throat.<sup>17</sup> Because this infection is caused by viruses, antibiotics are not recommended.<sup>18</sup>

The researchers also evaluated the economic impact of inappropriate prescribing by assessing excess all-cause health care costs incurred by patients within 30 days of diagnosis with one of the six conditions. All-cause costs included any health care expenditures regardless of the specific diagnosis or procedure (i.e., they may not have been directly related to the original diagnosis). These costs included both those to the patient (via copayments, co-insurance, and deductibles paid to the health plan) and to health plans (via reimbursements for medical or pharmacy claims).

## What happens when the wrong antibiotics are prescribed for adults with bacterial infections?

Researchers found that inappropriate antibiotic selection for pharyngitis and sinus infections resulted in an increased risk of some ADEs among adults. Using non-first-line antibiotics to treat these two infections was associated with an increased risk of ADEs. In particular, using an antibiotic other than penicillin or amoxicillin for treating pharyngitis was associated with an almost threefold increased risk of *C. diff* occurrence among the adult patients in this study. Improving antibiotic prescribing for these diagnoses could help minimize negative impacts on patients.

Table 1

### Increased Health Care Costs and Adverse Drug Events Associated With Inappropriate Antibiotic Selection in Privately Insured Adult Patients

	Excess cost per patient	Excess national costs (2017)	Adverse events
Pharyngitis	\$67	\$49.6 million	Nausea/vomiting/abdominal pain, <i>C. difficile</i> infection, non- <i>C. difficile</i> diarrhea
Sinus infections	\$18	\$19.1 million	Nausea/vomiting/abdominal pain

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When patients in this study received non-first-line antibiotics to treat these infections, they were often given broad-spectrum antibiotics, such as azithromycin and cefdinir, which may have contributed to the increased occurrence of ADEs. Broad-spectrum antibiotics target a wide variety of bacteria and are an important tool when combating serious infections. However, a previous study showed that using broad-spectrum agents among pediatric patients with respiratory tract infections can increase the rate of ADEs.<sup>19</sup> One example of this effect is that the use of azithromycin—which is not a first-line treatment for either bacterial infection in this study but is often used inappropriately—has been associated with incidences of nausea, vomiting, abdominal pain, and diarrhea.<sup>20</sup> Additionally, using broad-spectrum antibiotics for bacterial infections that can be treated with drugs that target a narrower spectrum of bacteria is not recommended in order to minimize the development of antibiotic resistance.

## What happens when antibiotics are prescribed needlessly for adults with viral infections?

When assessing the impact of unnecessary antibiotic prescribing for viral infections in adult patients, the results were more mixed. There was an increased risk of some ADEs, including up to an almost fourfold increased risk of having a general allergic reaction with unnecessary prescribing for viral URIs, bronchitis, and nonsuppurative middle ear infections.

Table 2

### Increased Health Care Costs and Adverse Drug Events Associated With Unnecessary Antibiotic Prescribing in Privately Insured Adult Patients

	Excess cost per patient	Excess national costs (2017)	Adverse events
<b>Influenza</b>	No difference	N/A	N/A
<b>Viral URIs</b>	No difference	N/A	General allergic reaction, vulvovaginal candidiasis or vaginitis
<b>Bronchitis</b>	-\$53	-\$28.7 million	Non- <i>C. difficile</i> diarrhea, general allergic reaction
<b>Nonsuppurative middle ear infections</b>	No difference	N/A	General allergic reaction, vulvovaginal candidiasis or vaginitis

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Researchers found that unnecessary prescribing for influenza, viral URIs, and nonsuppurative middle ear infections was not associated with a measurable amount of excess health care spending. The researchers posited that these findings may have been affected by the study population being restricted to healthy, commercially insured adults. In addition, unnecessary prescribing for bronchitis was actually associated with cost savings. The researchers suggested that individuals with bronchitis who appropriately did not receive antibiotics may have been more likely to seek additional care through follow-up outpatient and emergency department encounters due to symptoms of persistent bronchitis, which likely increased health care costs. These results indicate that further patient education—including that bronchitis symptoms can last for weeks and that antibiotics do not alter duration of illness—is needed to minimize follow-up visits.

## Key targets, actions to reduce excess costs and risks

This research is the second study published by researchers at Washington University in St. Louis quantifying the health care costs and adverse drug events associated with inappropriate antibiotic prescribing. The first study, which focused on privately insured patients under 18 years of age, also found evidence that inappropriate prescribing leads to increased costs and complications.<sup>21</sup> This research demonstrates the impact that inappropriate antibiotic prescribing has on both individual patients and the health care system, but additional work is needed to increase antibiotic stewardship throughout outpatient health care facilities in the U.S. Stewardship efforts aim to ensure that antibiotics are prescribed only for bacterial infections and that, when needed, the correct antibiotic is used at the proper dose and duration. Health care stakeholders—including health care payers and health systems—have a key role to play in increasing stewardship efforts and improving antibiotic prescribing practices.

Health care payers—such as private health insurance companies, Medicare, and Medicaid—can support antibiotic stewardship by:

- Using their medical and pharmacy claims data to assess the antibiotic prescribing practices of providers within their network and offering personalized feedback aimed at improving prescribing.
- Educating patients and providers on antibiotic resistance and the need for antibiotic stewardship.
- Incentivizing expanded antibiotic stewardship efforts by incorporating stewardship into health care quality improvement efforts. The Centers for Disease Control and Prevention recently published a toolkit for health care payers that outlines approaches for implementing these types of antibiotic stewardship activities.<sup>22</sup>

Health systems can improve outpatient antibiotic prescribing by:

- Providing resources and support to outpatient facilities within their networks, as doctors are more likely to trust information that comes from their own health system.<sup>23</sup>
- Leveraging shared data resources to analyze prescribing practices and provide ongoing feedback to their affiliated facilities.
- Including outpatient facilities in antibiotic stewardship programs.

## Appendix: Methodology

In order to assess the impact of inappropriate antibiotic prescribing in outpatient settings for adults ages 18 to 64 years, researchers analyzed medical and pharmacy claims data from the Merative™ MarketScan® Commercial Database for adults diagnosed with six common infections—pharyngitis, sinus infection, bronchitis, influenza, viral URI, and nonsuppurative middle ear infection—from April 1, 2016, to Sept. 30, 2018. After inclusion/exclusion criteria were applied, a total of 3,294,598 adults diagnosed with these infections were included in the study population. When estimating the annual total excess national health care costs, the researchers used data only from 2017 in order to have a full calendar year. All other data analysis included data from the entire study period.

Researchers identified adverse drug events in this study population by looking for the occurrence of these events within a patient's medical claims from two to 90 days (depending on type of adverse drug event) after being diagnosed with one of the six infections. To estimate excess health care costs, researchers looked at: 1) all-cause health care expenditures (irrespective of diagnosis or procedure) and, 2) adverse drug event-associated health care expenditures, both within the 30 days after the patient received a diagnosis. Differences in costs between appropriate and inappropriate treatment groups were then estimated to identify excess health care costs

because of inappropriate prescribing. The all-cause health care expenditures are presented in this fact sheet and represent an “upper bound” of health care costs associated with inappropriate antibiotic prescribing because this approach included all health care costs regardless of direct relationship with the initial diagnosis. Expenditures were adjusted to 2018 U.S. dollars, the most recent year of data, based on the medical care component of the consumer price index.

This study was subject to several limitations. For example, it relied on diagnostic coding within medical claims data to identify patients with the infections of interest. Patients may have been misclassified with a given infection because of differences in diagnostic coding practices by health care providers or a misdiagnosis. This may have led to patients with viral infections being misclassified as having a bacterial infection or vice versa. Additionally, for this study, “appropriate” therapy for the two bacterial infections was limited to include only patients who received recommended first-line antibiotics. However, there are situations—such as patient allergy—in which it is appropriate to receive a non-first-line agent.

A full description of the study methodology and additional limitations can be found in the article: “Comparative Safety and Attributable Health Care Expenditures Following Inappropriate Versus Appropriate Outpatient Antibiotic Prescriptions Among Adults with Upper Respiratory Infections,” *Clinical Infectious Diseases*.

## Acknowledgments

The Pew Charitable Trusts’ antibiotic resistance project team—David Hyun, Rachel Zetts, and Kyra Fryling — would like to thank Heather Cable, Demetra Asposporos, Matt Moser, Aesah Lew, and Ned Drummond for their assistance in developing this fact sheet. The team would also like to thank Anne Butler, Derek Brown, Michael Durkin, John Sahrman, Katelin Nickel, Caroline O’Neil, Margaret Olsen, and Jason Newland for their contributions to the research reported in this fact sheet. Neither they nor their organizations may necessarily agree with the findings.

## Endnotes

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