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# Study Shows That Inappropriate Antibiotic Prescribing for Children Leads to Increased Costs, Complications

Findings emphasize the importance of expanding outpatient antibiotic stewardship efforts

## 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 children diagnosed with seven common outpatient infections resulted in \$74 million in excess health care costs in the U.S. in 2017. The results also showed up to an eightfold 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>1</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>2</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 seven outpatient diagnoses. However, the estimated costs were likely higher, as only 55% of pediatric patients in the U.S. were privately insured (including employer-sponsored insurance and other private insurance) in 2017.<sup>3</sup>

According to the study:

- Inappropriate antibiotic selection for three common outpatient bacterial infections—middle ear infections, pharyngitis, and sinus infections—led to excess pediatric health care costs of about \$25.3 million, \$21.3 million, and \$7.1 million, respectively.
- Unnecessary antibiotic prescribing for two common viral diseases—upper respiratory tract infections (URIs), which are often referred to as the common cold, and influenza—increased health care costs by an estimated \$20.7 million.
- Unnecessary and inappropriate antibiotic prescribing for outpatient infections were associated with an increased risk of adverse events in patients. In particular, inappropriate antibiotic selection for middle ear, pharyngitis, and sinus infections was associated with a three-to-eight-times increased risk in the occurrence of *Clostridioides difficile*, formerly known as *Clostridium difficile*, infection (*C. diff*), a potentially life-threatening infection that can be associated with antibiotic use.

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 seven 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> *C. diff* is an ADE that can be caused by antibiotic exposure—particularly broad-spectrum antibiotics.<sup>5</sup>

### Diagnoses resulting in inappropriate antibiotic selection:

- Suppurative middle ear infection: An ear infection with discharge (pus).<sup>6</sup> Current pediatric prescribing guidelines recommend either treating the patient with antibiotics using amoxicillin as the first-line therapy or, in certain circumstances, waiting 48 to 72 hours to see whether symptoms improve without antibiotic treatment.<sup>7</sup>
- Pharyngitis: Inflammation of the throat, typically presenting as a sore throat.<sup>8</sup> The primary bacterial cause is group A *Streptococcus* (known as “strep throat”), which can be identified with a diagnostic test.<sup>9</sup> Amoxicillin or penicillin are the recommended first-line treatments for patients with strep throat.<sup>10</sup>
- Sinus infection: Sinus infections are one of the most common reasons antibiotics are prescribed in outpatient settings in the United States.<sup>11</sup> These infections can be caused by bacterial or viral pathogens, with antibiotics recommended only when a bacterial infection is suspected.<sup>12</sup> Amoxicillin or amoxicillin-clavulanate are the recommended first-line treatments for bacterial sinus infections.<sup>13</sup>

### Diagnoses resulting in unnecessary antibiotic prescribing:

- Nonsuppurative middle ear infection: A condition characterized by the presence of noninfected fluid in the middle ear.<sup>14</sup> Antibiotics are not recommended for this condition.<sup>15</sup>
- Bronchitis/Bronchiolitis: Types of infections that cause inflammation of the airways of the lungs.<sup>16</sup> Bronchiolitis is found only in young children and infants.<sup>17</sup> These infections are often caused by a virus, and current guidelines recommend against prescribing antibiotics.<sup>18</sup>
- Influenza: An illness caused by the influenza virus, commonly called the flu.<sup>19</sup> Because this is a viral infection, antibiotics are not recommended.<sup>20</sup>
- Viral URI: Often referred to as the common cold, this type of infection can cause symptoms such as cough, congestion, and sore throat.<sup>21</sup> Because this infection is caused by viruses, antibiotics are not recommended.<sup>22</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 seven conditions. All-cause costs included any health care expenditures regardless of the specific diagnosis or procedure (i.e., may not have been directly related to the original diagnosis). These costs included both those to the patient (via copayments, coinsurance, 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 children with bacterial infections?

Researchers found that inappropriate antibiotic selection for suppurative middle ear infections, pharyngitis, and sinus infections led to an increased risk of ADEs in patients as well as excess health care costs. Using non-first-line antibiotics to treat these three infections was associated with an increased risk of different ADEs. In particular, using an antibiotic other than penicillin or amoxicillin for treating pharyngitis was associated with an eightfold increased risk of *C. diff* occurrence in the pediatric 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 Pediatric Patients

	Excess cost per patient	Excess national costs (2017)	Adverse events
Suppurative middle ear infections	\$56	\$25.3 million	<i>C. difficile</i> infection, nausea/vomiting/abdominal pain, non- <i>C. difficile</i> diarrhea, anaphylaxis
Pharyngitis	\$42	\$21.3 million	<i>C. difficile</i> infection, nausea/vomiting/abdominal pain, non- <i>C. difficile</i> diarrhea
Sinus infections	\$21	\$7.1 million	<i>C. difficile</i> infection

When patients in this study received non-first-line antibiotics to treat these infections, they were often prescribed 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 use of broad-spectrum agents can increase the rate of ADEs.<sup>23</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 children with viral infections?

When assessing the impact of unnecessary antibiotic prescribing for viral infections in pediatric patients, the results were more mixed. There was an increased risk of some ADEs, including around a twofold increased risk of skin rash and around a threefold increased risk of unspecified allergic reaction with unnecessary prescribing for viral URIs and nonsuppurative middle ear infections.

Table 2

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

	Excess cost per patient	Excess national costs (2017)	Adverse events
<b>Influenza</b>	\$97	\$1.6 million	
<b>Viral URIs</b>	\$81	\$19.1 million	Skin rash, unspecified allergy
<b>Bronchiolitis</b>	No difference	N/A	
<b>Bronchitis</b>	No difference	N/A	
<b>Nonsuppurative middle ear infections</b>	-\$96	-\$15.4 million	Non- <i>C. difficile</i> diarrhea, skin rash, unspecified allergy

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Researchers found unnecessary prescribing for influenza and viral URIs to both be associated with excess health care spending. In contrast, unnecessary prescribing for nonsuppurative middle ear infections was actually associated with cost savings. The researchers posited that this may be due, in part, to errors in diagnostic coding, with some physicians possibly misclassifying patients who have suppurative middle ear infections (which may require an antibiotic prescription) as having nonsuppurative infections.

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

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 across outpatient health care facilities in the United States. 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 (CDC) recently published a toolkit for health care payers that outlines approaches for implementing these types of antibiotic stewardship activities.<sup>24</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>25</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 children ages 6 months to 17 years, researchers analyzed medical and pharmacy claims data from the IBM MarketScan Commercial Database for children diagnosed with seven common infections—suppurative middle ear infection, pharyngitis, sinus infection, bronchitis/bronchiolitis, influenza, viral URI, and nonsuppurative middle ear infection—from April 1, 2016, to Sept. 30, 2018. For bronchiolitis and bronchitis, only children ages 6 months to 3 years and ages 5 to 17 years, respectively, were included in the analysis. After inclusion/exclusion criteria were applied, a total of 2,804,245 children diagnosed with these infections were included in the study population. When estimating the 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 seven 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 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 three 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. Finally, the MarketScan database disproportionately includes residents from the South and underrepresents residents from the West, which may skew results.

A full description of the study methodology and additional limitations can be found in the article: “Association of Inappropriate Outpatient Pediatric Antibiotic Prescriptions With Adverse Drug Events and Health Care Expenditures,” *JAMA Network Open*.

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