

David C. Fiore, MD; Lacy P. Feticc, MD; Stephanie D. Wright, MD; Bonnie R. Ferrara, MD

Department of Family and Community Medicine, University of Nevada, Reno School of Medicine

dfiore@medicine.nevada.edu

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Antibiotic overprescribing: Still a major concern

Antibiotic overuse has far-reaching effects on patients' general health, as well as possible connections to HIV, diabetes, and obesity. Here's what we can do, now.

PRACTICE RECOMMENDATIONS

- › Explain to patients the rationale for not prescribing antibiotics when they are not indicated. **A**
- › Advocate for health care system electronic medical record systems designed to limit antibiotic prescribing to only appropriate cases. **A**
- › Provide patients and your community with educational materials to increase understanding of the risks of antibiotic overprescribing. **B**

Strength of recommendation (SOR)

- A** Good-quality patient-oriented evidence
- B** Inconsistent or limited-quality patient-oriented evidence
- C** Consensus, usual practice, opinion, disease-oriented evidence, case series

Despite universal agreement that antibiotic overprescribing is a problem, the practice continues to vex us. Antibiotic use—whether appropriate or not—has been linked to rising rates of antimicrobial resistance, disruption of the gut microbiome leading to *Clostridium difficile* infections, allergic reactions, and increased health care costs (TABLE 1¹⁻⁶). And yet, physicians continue to overprescribe this class of medication.

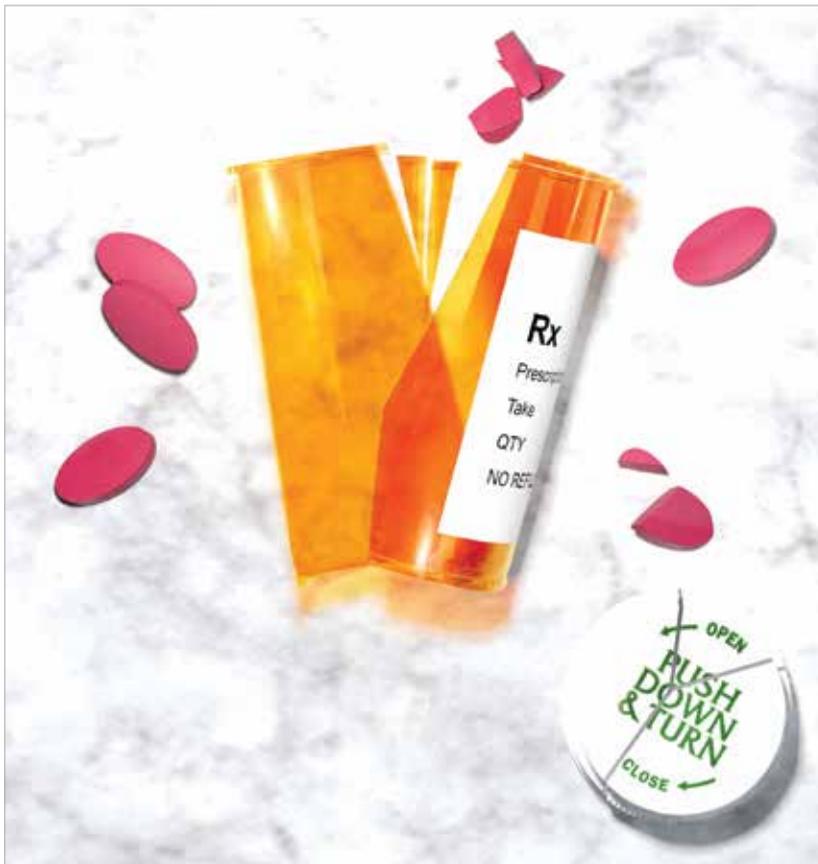
A 2016 Centers for Disease Control and Prevention (CDC) report estimates that at least 30% of antibiotics prescribed in US outpatient settings are unnecessary.⁷ Another report cites a slightly higher figure across a variety of health care settings.⁸ Pair these findings with the fact that there are currently few new drugs in development to target resistant bacteria, and you have the potential for a post-antibiotic era in which common infections could become lethal.⁷

In 2003, the CDC launched its “Get Smart: Know When Antibiotics Work” program, focused on decreasing inappropriate antibiotic use in the outpatient setting.⁹ In 2014, the White House released the National Action Plan for Combating Antibiotic-Resistant Bacteria with a goal of decreasing inappropriate outpatient antibiotic use by 50% and inappropriate inpatient use by 20% by 2020.¹⁰ And, on an international level, the World Health Organization (WHO) developed a 5-year strategic framework in 2015 for implementing its Global Action Plan on Antimicrobial Resistance.¹¹

Family practitioners are on the front lines of this battle. Here's what we can do now.

When and where are antibiotics most often inappropriately prescribed?

The diagnosis leading to the most frequent inappropriate prescribing of antibiotics is acute respiratory tract infection (ARTI), which includes bronchitis, otitis media, pharyngitis,



Up to 40% of antibiotic prescriptions for acute respiratory tract infections are unnecessary.

sinusitis, tonsillitis, the common cold, and pneumonia. Up to 40% of antibiotic prescriptions for these conditions are unnecessary.^{8,12} Bronchitis is the most common ARTI diagnosis associated with inappropriate antibiotic prescriptions, while sinusitis, suppurative otitis media, and pharyngitis are the diagnoses associated with the lion's share of all (appropriate and inappropriate) antibiotic prescriptions within the ARTI category.^{8,9,12,13} There are national clinical guidelines delineating when antibiotic treatment is appropriate for these conditions.¹⁴⁻¹⁶

■ **With respect to setting**, studies have presented conflicting results as to whether there is a difference between antibiotic prescribing in office-based vs emergency department (ED) settings. Here is a sample of some of the literature to date:

- One study found a higher rate of antibiotic prescribing during ED visits (21%) than office visits (9%), despite the fact that between 2007 and 2009, more antibiotic prescriptions were written for adults in primary care offices than in either outpatient hospital clinics or EDs.¹⁷

- A cross-sectional study focused on the frequency with which antibiotics were prescribed for uncomplicated acute rhinosinusitis. Researchers analyzed data from 2005 to 2010 National Ambulatory Medical Care Surveys (NAMCS) and National Hospital Ambulatory Medical Care Surveys (NHAMCS) and found that more than half of the patients received prescriptions for antibiotics, but that there was no overall difference in antibiotic prescriptions between primary care and ED presentation.¹⁸
- A retrospective analysis that examined antibiotic prescribing found that between 2006 and 2010, outpatient hospital practices (56%) and community-practice offices (60%) prescribed more antibiotics for ARTIs than EDs (51%).¹²

Stick to narrow-spectrum agents when possible

Using broad-spectrum antibiotics, such



INSTANT POLL

What most often leads you to prescribe antibiotics outside of professional guideline recommendations?

- Patient demand
- Fear of losing the patient
- Doubt about whether an infection is viral or bacterial
- Disagreement with professional guidelines

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TABLE 1

Known and potential harms of antibiotic overprescribing¹⁻⁶

Known harms	Potential harms
Antibiotic-associated diarrhea	Increased asthma
<i>Clostridium difficile</i> colitis	Increased obesity
Tendon rupture (quinolones)	Impaired immune system
Long QT syndrome (macrolides and others)	Mental health effects
Renal compromise	
Allergic reactions	

> We should pause before prescribing drugs that can alter our microbiome in complex and only partially understood ways.

as quinolones or imipenem, first line, contributes more to the problem of antibiotic resistance than does prescribing narrow-spectrum antibiotics such as amoxicillin, cephalexin, or trimethoprim-sulfamethoxazole.⁷ Yet between 2007 and 2009, broad-spectrum agents were prescribed for 61% of outpatient adult visits in which patients received an antibiotic prescription.¹⁷ Quinolones (25%), macrolides (20%), and aminopenicillins (12%) were most commonly prescribed, and antibiotic prescriptions were most often written for respiratory conditions, such as bronchitis, for which we now know antibiotics are rarely indicated.¹⁷

Between 2006 and 2008, pediatric patients who received antibiotic prescriptions were given broad-spectrum agents 50% of the time, of which macrolides were the class most commonly prescribed.¹³

More recently, researchers examined the frequency with which physicians prescribe narrow-spectrum, first-line antibiotics for otitis media, sinusitis, and pharyngitis using 2010 to 2011 NAMCS/NHAMCS data. They found that physicians used first-line agents recommended by professional guidelines 52% of the time, although it was estimated that they would have been appropriate in 80% of cases; pediatric patients were more likely to receive appropriate first-line antibiotics than adult patients.¹⁹ Macrolides, especially azithromycin, were the most common non-first-line antibiotics prescribed.^{19,20} The bottom line is that when antibiotics are indicated for upper respiratory infections (otitis media, sinusitis, and pharyngitis), physicians should prescribe a narrow-spectrum antibiotic first.

Antibiotic overprescribing affects the gut and beyond

The human intestinal microbiome is composed of a diverse array of bacteria, viruses, and parasites.²¹ The main functions of the gut microbiome include interacting with the immune system and participating in biochemical reactions in the gut, such as absorption of fat-soluble vitamins and the production of vitamin K.

As we know, antibiotics decrease the diversity of gut bacteria, which, in turn, can cause less efficient nutrient extraction, as well as a vulnerability to enteric infections.²¹ It is well known, for example, that the bacterial gut microbiome can either inhibit or promote diarrheal illnesses such as those caused by *C. difficile*. *C. difficile* infection (CDI) is now the most common health care-related infection, accounting for approximately a half million health care facility infections a year.²² CDI extends hospital stays an average of almost 10 days and is estimated to cost the health care system \$6.3 billion annually.²³

Antibiotics can also eliminate antibiotic-susceptible organisms, allowing resistant organisms to proliferate.⁴ They also promote the transmission of genes for antibiotic resistance between gut bacteria.⁴

Beyond the gut

Less well known is that gut bacteria can promote or inhibit extraintestinal infections.

■ **Gut bacteria and HIV.** In early human immunodeficiency virus (HIV) infections, for example, gut populations of *Lactobacillus* and *Bifidobacteria* are reduced, and the gut barrier becomes compromised.²⁴ Increasing translocation of bacterial products is associ-

TABLE 2

3 practice- and system-level interventions that can decrease antibiotic prescribing³⁴⁻³⁶

1. Monthly e-mails to physicians that compare their antibiotic prescribing to set goals or “top performers” within the organization.
2. Electronic medical record “prompts” that require physicians to provide an “antibiotic justification note” when a potentially inappropriate antibiotic is prescribed for a particular diagnosis.
3. Distribution of patient information that explains the limitations and potential harms of overprescribing antibiotics to patients.

ated with HIV disease progression. Preservation of *Lactobacillus* populations in the gut is associated with markers predictive of better HIV outcomes, including a higher CD4 count, a lower viral load, and less evidence of gut microbial translocation.²⁴ This underscores the importance of maintaining a healthy gut flora in patients with HIV, using such steps as avoiding unnecessary antibiotics.

■ Gut bacteria and stress, depression.

Antibiotics directly induce the expression of key genes that affect the stress response.²⁵ While causative studies are lacking, there is a growing body of evidence suggesting that the gut microbiome is involved in 2-way communication with the brain and can affect, and be affected by, stress and depression.^{21,26-30} Diseases and conditions that seem to have a putative connection to a disordered microbiome (dysbiosis) include depression, anxiety, Crohn’s disease, type 2 diabetes, and obesity.

■ Gut bacteria and childhood obesity.

Repeated use of broader-spectrum antibiotics in children <24 months of age increases the risk of developing childhood obesity.^{1,6} One theory for the association is that the effects of broad-spectrum antibiotics on the intestinal flora of young children may alter long-term energy homeostasis resulting in a higher risk for obesity.¹

■ Gut bacteria and asthma.

Studies demonstrate differences in the gut microbiome of asthmatic and nonasthmatic patients. These differences affect the activities of helper T-cell subsets (Th1 and Th2), which in turn affect the development of immune tolerance.³¹

Although additional studies are needed to confirm these findings, the evidence collected thus far should make us all pause

before prescribing drugs that can alter our microbiome in complex and only partially understood ways.

What can we do right now?

The issues created by the inappropriate prescribing of antibiotics have been known for decades, and multiple attempts have been made to find solutions and implement change. Although some small successes have occurred, little overall progress has been made in reducing antibiotic prescribing in the general population. A historical review of why physicians prescribe antibiotics inappropriately and the interventions that have successfully reduced this prescribing may prove valuable as we continue to look for new, effective answers.

■ Why do we overprescribe antibiotics?

A 2015 systematic literature review found that patient demand, pharmaceutical company marketing activities, limited up-to-date information sources, and physician fear of losing their patients are major reasons physicians cite for prescribing antibiotics.³²

In a separate study that explored antibiotic prescribing habits for acute bronchitis,³³ clinicians cited “patient demand” as the major reason for prescribing antibiotics. Respondents also reported that “other physicians were responsible for inappropriate antibiotic prescribing.”³³

Strategies that work

Some early intervention programs directed at reducing antibiotic prescribing demonstrated success (TABLE 2).³⁴⁻³⁶ One example comes from a 1996 to 1998 study of 4 primary care practices.³⁴ Researchers evaluated the



Monthly emails to physicians comparing their prescribing habits to peers and top performers reduced inappropriate antibiotic prescribing for acute respiratory tract infections.

TABLE 3

Tips for maintaining patient/parent satisfaction without prescribing antibiotics^{9,37,38}

Explain to patients/parents the difference between a viral and bacterial infection and why antibiotics are not appropriate for viral infections. Let them know that if the condition worsens, you will see them again quickly.
Describe an acute respiratory tract infection as a “chest cold” rather than an upper respiratory infection or—even worse—bronchitis.
Use a “symptom treatment prescription pad” that lists such things as salt water gargles, nasal rinses, sucking on hard candies, and taking acetaminophen or a nonsteroidal anti-inflammatory drug, so that patients have something tangible with which to leave the office.
Consider providing a “delayed prescription” for antibiotics if you are uncertain about the need to prescribe one. Advise the patient to have it filled only if symptoms don’t improve in a few days.

>
Patients and parents reported higher satisfaction with physicians who explained why antibiotics were not indicated vs physicians who simply prescribed them.

impact of a multidimensional intervention effort targeted at clinicians and patients and aimed at lowering the use of antimicrobial agents for acute uncomplicated bronchitis in adults. It incorporated a number of elements, including office-based and household patient educational materials, and a clinician intervention involving education, practice profiling, and academic detailing. Physicians in this program reduced their rates of antibiotic prescribing for uncomplicated bronchitis from 74% to 48%.³⁴

■ **Employing EMRs.** A more recent study focused on using electronic medical records (EMRs) and communications to modify physician antibiotic prescribing.³⁵ By sending physicians monthly emails comparing their prescribing patterns to peers and “typical top performers,” inappropriate antibiotic prescriptions for ARTIs went from 19.9% to 3.7%.³⁵

In another effort, the same researchers modified physicians’ EMRs to detect when potentially inappropriate antibiotics were prescribed. The system then prompted the physician to provide an “antibiotic justification note,” which remained visible in the patient’s chart. This approach, which encouraged physicians to follow prescribing guidelines by taking advantage of their concerns about their reputations, produced a 77% reduction in antibiotic prescribing.³⁵

■ **Focusing on the public.** Studies have also examined the effectiveness of educating the public about when antibiotics are not likely to be helpful and of the harms of

unnecessary antibiotics. Studies conducted in Tennessee and Wisconsin that combined prescriber and community education about unnecessary antibiotics for children found that the intervention reduced antibiotic prescribing in both locations by about 19% compared with about a 9% reduction in the control groups.^{36,37}

Does prescribing antibiotics affect patient satisfaction?

The results are mixed as to whether prescribing antibiotics affects patient satisfaction. Two studies in the early 2000s found that both patients and parents reported higher satisfaction with physicians who explained why antibiotics were not indicated vs physicians who simply prescribed them, and that such explanations do not need to take a lot of time.^{37,38} (See TABLE 3^{9,37,38} for patient care tips.)

A more recent study found that higher antibiotic prescribing practices in Britain were associated with modestly higher patient satisfaction ratings.³⁹ The authors of this study noted, however, that reduced antibiotic prescribing may be a proxy for other practice patterns that affected satisfaction ratings.

Reducing antibiotic prescribing reduces resistance

There is also strong evidence that when physicians decrease antibiotic prescribing, antimicrobial resistance follows suit. One of the earlier landmark studies to demonstrate this

was a Finnish study published in 1997.⁴⁰ The authors found that a reduction of macrolide antibiotic consumption in Finland led to a reduction in streptococci macrolide resistance from 16.5% to 8.6%.⁴⁰

Since then, multiple studies have demonstrated similar results for both respiratory and urinary tract infections.^{41,42} A 2017 meta-analysis analyzing 32 studies found that antibiotic stewardship programs reduced the incidence of infections and colonization with multidrug-resistant Gram-negative bacteria (51% reduction), extended-spectrum beta-lactamase-producing Gram-negative bacteria (48%), and methicillin-resistant *Staphylococcus aureus* (37%). There was also a reduction in the incidence of *C. difficile* infections (32%).⁴³

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CORRESPONDENCE

David C. Fiore, MD, Department of Family and Community Medicine, University of Nevada, Reno School of Medicine, Brigham Bldg, MS 316, Reno, NV 89557; dfiore@medicine.nevada.edu.

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