

A large, dark-colored statue of a man in a suit, standing on a pedestal and pointing his right arm upwards with an arrow. The background shows a panoramic view of a city at sunset, with buildings and a hazy sky. The statue is positioned on the left side of the frame, and the cityscape extends to the horizon.

Outpatient Antibiotic Stewardship

A Review of Problems and Solutions

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Disclosures

I have no financial disclosures or conflicts of interest regarding the content of this presentation.

Presentation Overview

The purpose of this discussion is to review the importance of antibiotic stewardship in the outpatient setting, including primary care and speciality clinics, urgent cares, emergency departments.

Presentation Outline

- Case Study
- What is antibiotic stewardship and why is it important?
- In what ways could antibiotic prescribing practices be improved?
- How can we take steps in our own area of practice to intervene?

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Case Study

23 year old male with no significant past medical history presents to clinic complaining of a few small raised lesions on his forearm. He noticed them several days before. He reports no sick contacts, no insect bites, no history of allergic reactions. The only recent behavioral change is that he started working out at a local gym. He wanted to get it treated “before it got worse”.

On exam he has a few scattered small (<5mm) pustules to the forearm that are minimally painful.



1. Folliculitis: Symptoms, Causes, and Treatment. Georgia Dermatology Center.

<https://gadermctr.com/folliculitis-symptoms-causes-and-treatment/>. Published December 14, 2018. Accessed March 19, 2021.

The provider documentation includes folliculitis as the primary diagnosis of concern.

The patient was given a prescription for 300mg Clindamycin QID for 10 days.



Case continued

4 weeks later the patient presented back to the same clinic complaining of colicky abdominal and diarrhea. A few days ago he began to have 1-2 loose stools a day, and today it progressed to every 1-2 hours.

He has general malaise and fatigue but denies any fever, nausea, or vomiting. He does report good resolution of the rash that he was previously seen for.



- After a series of tests and stool studies, he was ultimately diagnosed with *Clostridium difficile* colitis.
- He was given metronidazole 500mg TID for 14 days.
- While there was some improvement on this treatment, he ultimately had recurrence a few months later.



How did this happen?

- Patient expectations that this problem must have a pharmaceutical solution.
- Provider wanted to meet patient expectations, and over-prescribed an inappropriate antibiotic for the diagnosis at hand.
- The provider under-appreciated the potential adverse effects of the antibiotic, even for the age group of the patient. There was a “well it can’t hurt” attitude.
- Busy clinic shift, little time to sit down and discuss treatment alternatives.



- This was a personal experience of mine as a patient
- Resulted in several rounds of *C. diff* treatment, including the threat of a stool transplant.
- It resulted in several months of a disrupted life alongside the constant gastrointestinal issue .
- I have already had once recurrence later down the road, and the threat of another is always looming.

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What is stewardship?

Being entrusted to protect and be responsible for the management of a limited resource



What is antibiotic stewardship?

- Broadly defined, it is the management of antibiotics use as a limited resource by improving prescribing practices so that:
 - Antibiotics are only prescribed when truly needed
 - And if needed, it ensures that the right drug, dose and duration are selected.²

Why the importance to manage
antibiotics in this way?

Resistance

Adverse Effects

Antibiotic Resistance

A brief historical overview

Penicillin 1941

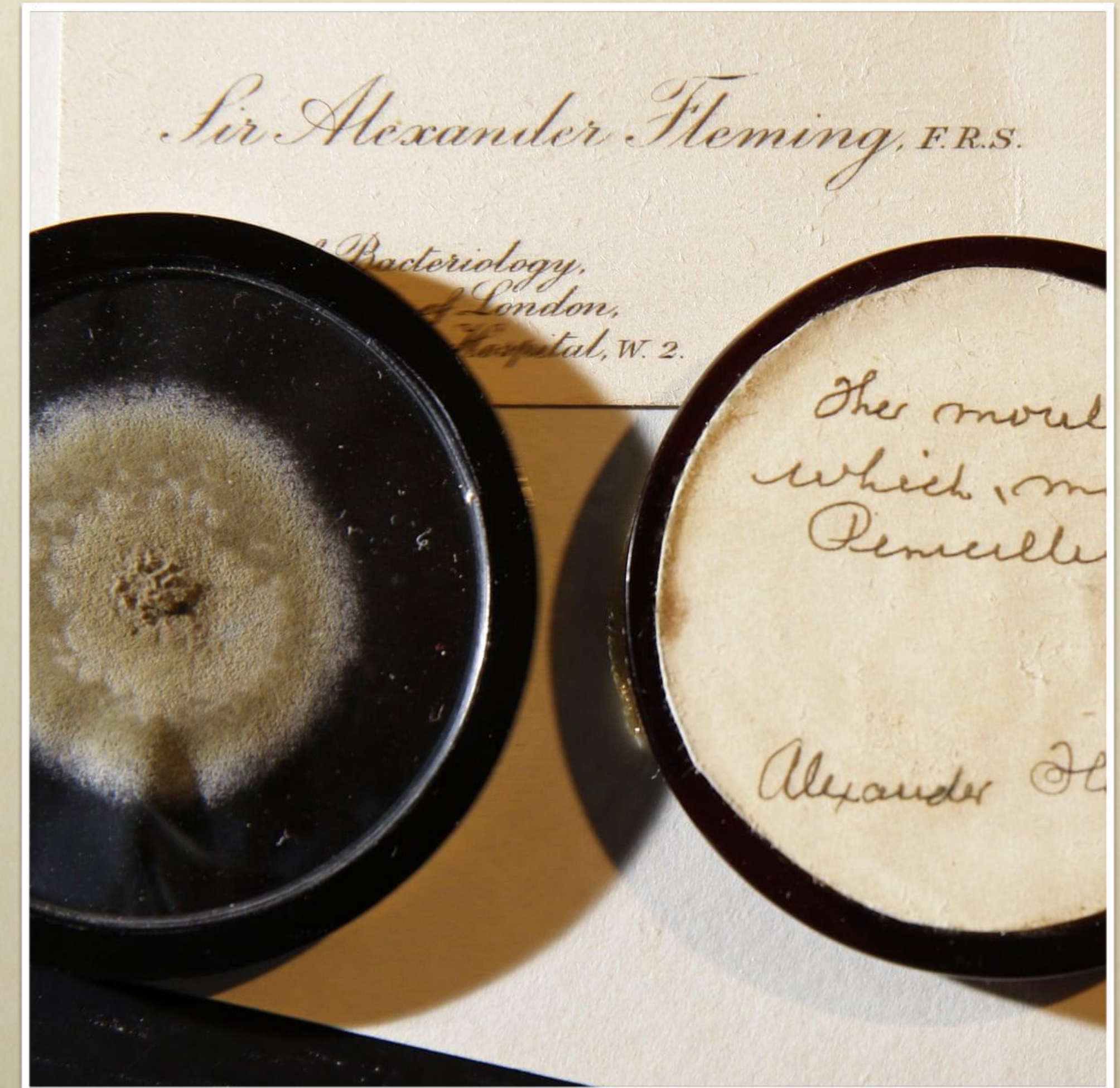
Penicillin resistant *Staphylococcus aureus* 1942

Methicillin 1960

Methicillin-resistant *Staphylococcus aureus* 1960

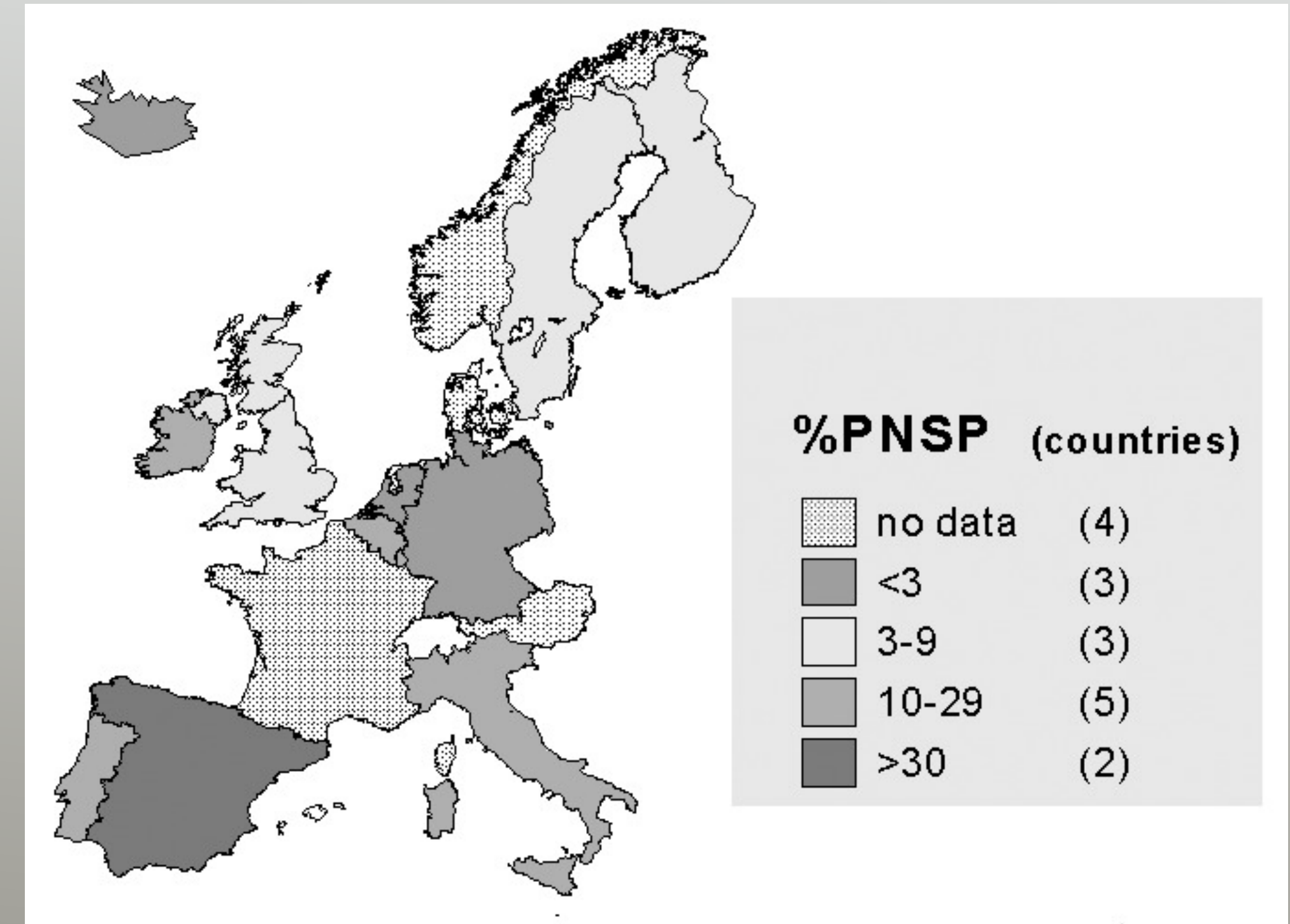
Extended-Spectrum cephalosporins 1980

Extended-spectrum beta-lactamase *E. coli* 1983



Resistance occurs at the population level

- European study that correlated resistance with antibiotic use.
- Countries with higher penicillin sales had higher rates of *Streptococcus pneumoniae* resistance to penicillin.⁴



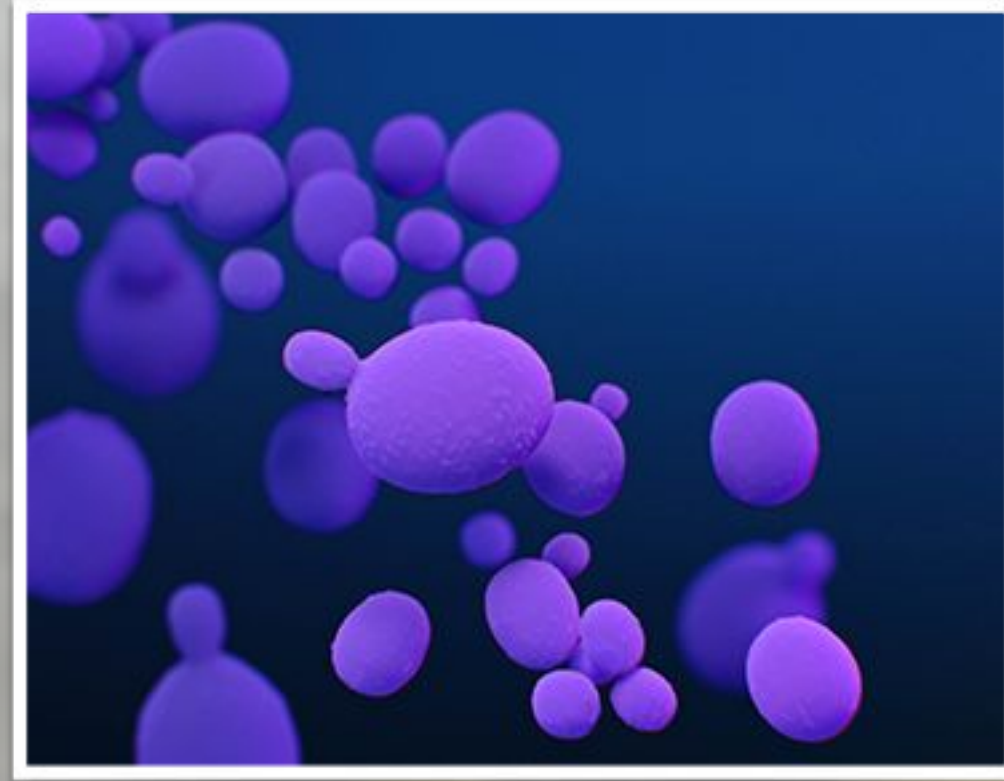
Resistance occurs at the individual level

Systematic Review in BMJ in 2010 reviewed 5 studies demonstrating increased odds of an individual having resistant *E. coli* following antibiotic treatment⁵

2 months OR - 2.5 (95% CI 2.1-2.9)

12 months OR - 1.3 (95% CI 1.2-1.5)

Resistance: a real threat



Drug-resistant *Candida auris*



Carbapenm-resistant *Enterobacterales*



Carbapenm-resistant *Acinetobacter*

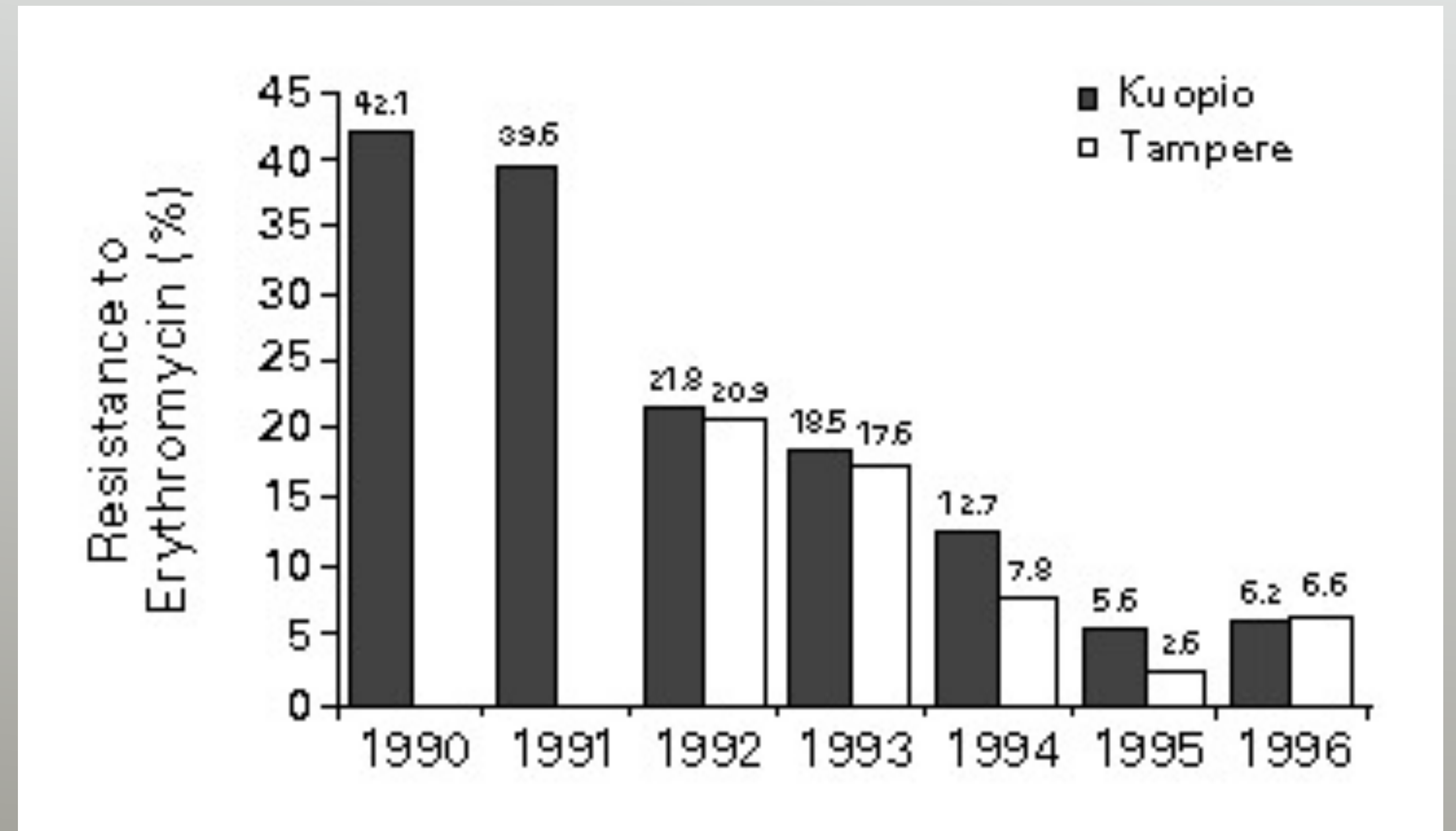


Drug-resistant *Neisseria gonorrhoeae*

Decreasing Antibiotic Use Reduces Resistance

Population Level

- Finland in early 1990s - growing group A Strep resistance to macrolides
- 1990 national health recommendation to reduce macrolide use.
- Decrease in macrolide use over 6 years resulted in steady decrease in GAS resistance to erythromycin.⁷



Decreasing Antibiotic Use Reduces Resistance

Hospital-Wide Level

- 731-bed tertiary care hospital in Greenville, NC
- Reduction in oral and IV ciprofloxacin use, driven by pharmacist who would suggest alternatives based on micro data.
- In 17 units, Cipro use decreased by 31%, and was associate with a reduction in MRSA infections.⁸



Why the importance to manage
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Resistance

Adverse Effects

Adverse Events from Antibiotic Use

- About 200,000 emergency department visits from adverse drug events each year attributable to antibiotic use.⁹
- Antibiotics are the second most common drug type leading to adverse events
- Amoxicillin and Sulfamethoxazole-trimethoprim account for over 25% of the ASE resulting in ED Visit



The antibiotic resulting in the most hospitalizations from adverse drug events?

Fluoroquinolones - hospitalization rate from an adverse drug event was higher than any other antibiotic (14.5%)¹⁰

Reducing fluoroquinolone use has been shown to have the greatest impact on *Clostridium difficile* reduction

Clostridium difficile infections

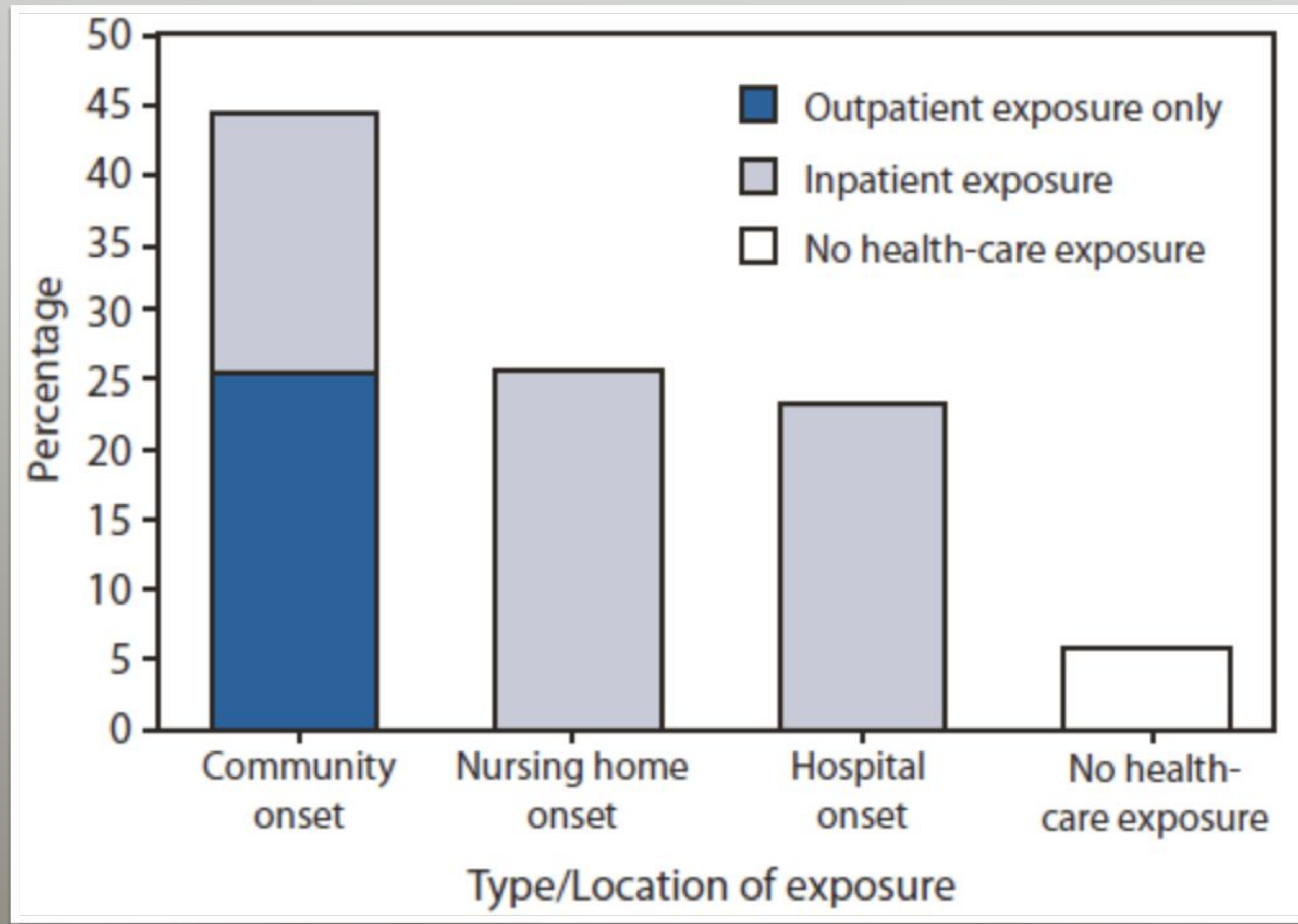
500,000 cases in the U.S. a year, 29,300 deaths¹¹

1 in 6 patients will have a recurrence in 4-6 weeks

10x more likely to get *C. diff* after taking an antibiotic

From 2000 to 2010, hospitalizations from *C. diff* infections doubled

Clostridium difficile infections: an outpatient problem



- Only 23% are hospital based¹²
- >30% are community associated

Reducing Outpatient Antibiotic Use Reduces Community *C. diff*

Strong correlation with outpatient prescribing practices and local rates of *C diff* infections.¹³

Reducing outpatient antibiotic prescribing by 10% (particularly amoxicillin-clavulanic acid) could reduce community *C diff* infections by 17%

13. Raymund Dantes, Yi Mu, Lauri A. Hicks, Jessica Cohen, Wendy Bamberg, Zintars G. Beldavs, Ghinwa Dumyati, Monica M. Farley, Stacy Holzbauer, James Meek, Erin Phipps, Lucy Wilson, Lisa G. Winston, L. Clifford McDonald, Fernanda C. Lessa, Association Between Outpatient Antibiotic Prescribing Practices and Community-Associated *Clostridium difficile* Infection, *Open Forum Infectious Diseases*, Volume 2, Issue 3, Summer 2015, ofv113, <https://doi.org/10.1093/ofid/ofv113>

Presentation Overview

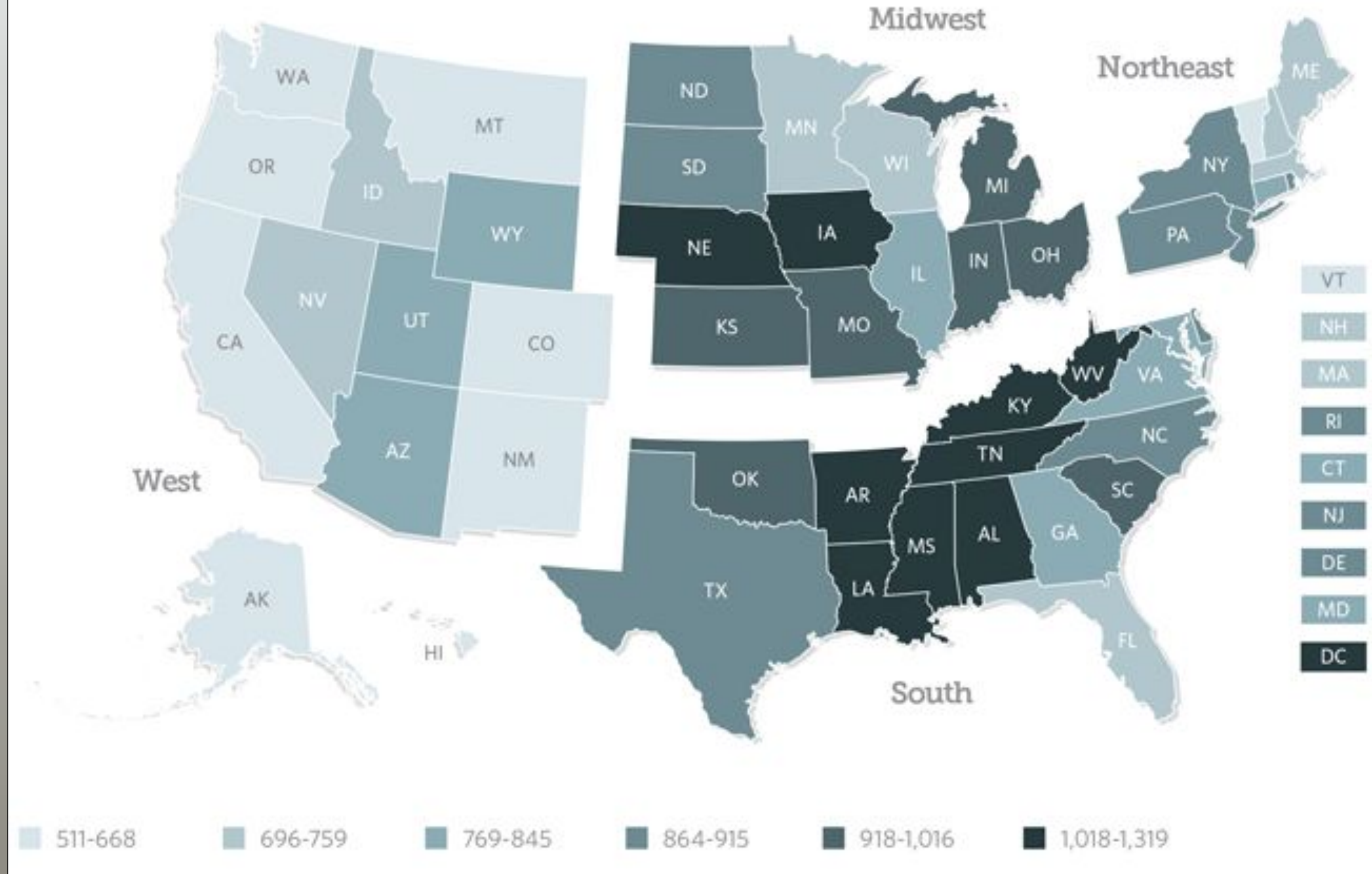
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Outpatient Antibiotic Use

- More than 60% of antibiotic expenditure in the U.S. comes from outpatient antibiotic use.¹⁴
- In the U.S., there were 838 antibiotic prescriptions dispensed per 1000 persons in 2015 (double the rate of Sweden



Antibiotic prescriptions per 1,000 people



Outpatient Antibiotic Use

- The majority of human antibiotics are prescribed in the outpatient setting
- To make a large impact on antibiotic use and address antibiotic stewardship, much of the effort needs to be focused on outpatient clinics.



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4 types of inappropriate antibiotic use

Unnecessary
Antibiotic Use

Errors in Dosing

Improper
Selection

Errors in
Duration

Unnecessary Antibiotic Use

1/3 of antibiotic prescriptions given in the outpatient setting can be considered unnecessary¹⁵

Rhinosinusitis

Otitis Media

Pharyngitis

Skin/Cutaneous Infections

Urinary Tract Infections

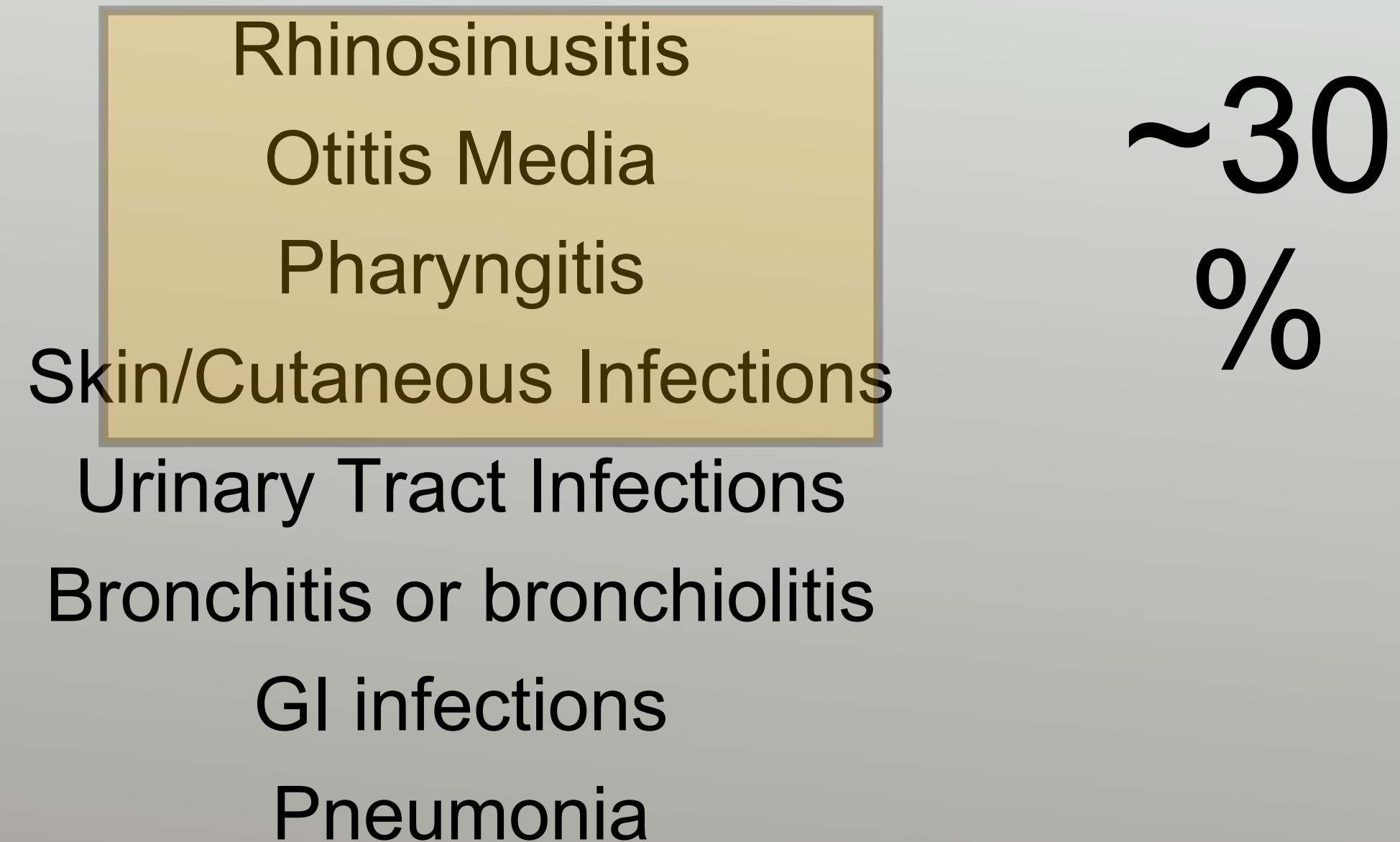
Bronchitis or bronchiolitis

GI infections

Pneumonia

Unnecessary Antibiotic Use

1/3 of antibiotic prescriptions given in the outpatient setting can be considered unnecessary¹⁵



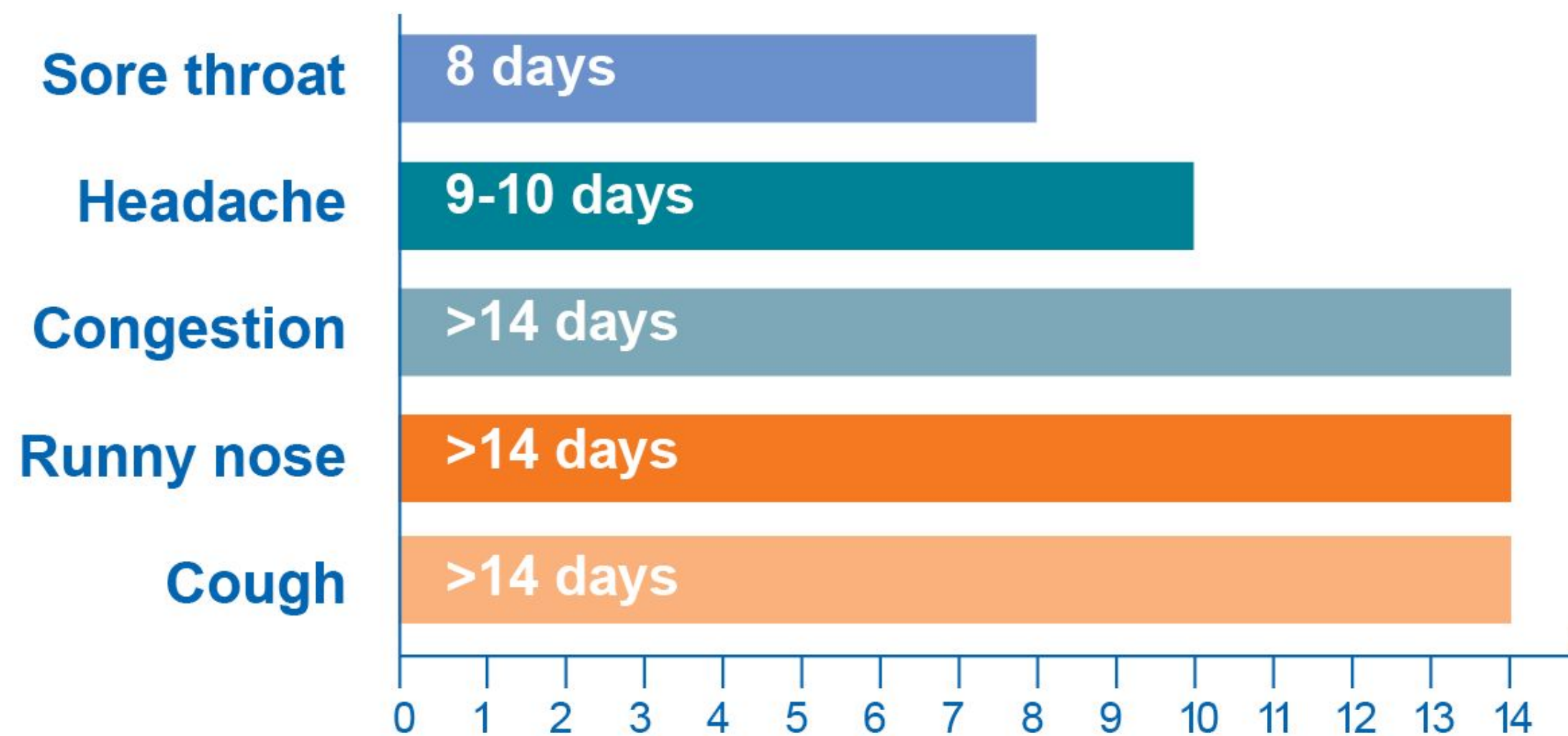
Rhinosinusitis

- Defined:
 - Rhinitis - inflammation of nasal mucosa
 - Sinusitis - inflammation of paranasal sinuses
- Usually caused by a viral upper respiratory infection (common cold)
 - Rhinovirus (up to 50%), Coronavirus (15%), influenza (15%)¹⁶
- <2% progress to acute bacterial sinusitis



Viral vs. Bacterial Sinusitis

How long can symptoms linger with a typical cold?



- Bacterial sinusitis is not as common as viral, and is a clinical diagnosis, with no specific laboratory test to confirm
- Persistent symptoms (>10 days), worsening symptoms after initial improvement, or severe symptoms (fever >102.2 with purulent nasal discharge and facial pain) meet the criteria for bacterial sinusitis

Do Antibiotics Help in Acute Sinusitis?

- RCT in 2012 compared 10 days of amoxicillin with placebo for those diagnosed with acute sinusitis.
- At 10 days - no difference in days missed from work, disease recurrence, satisfaction with care, or serious adverse events.¹⁸



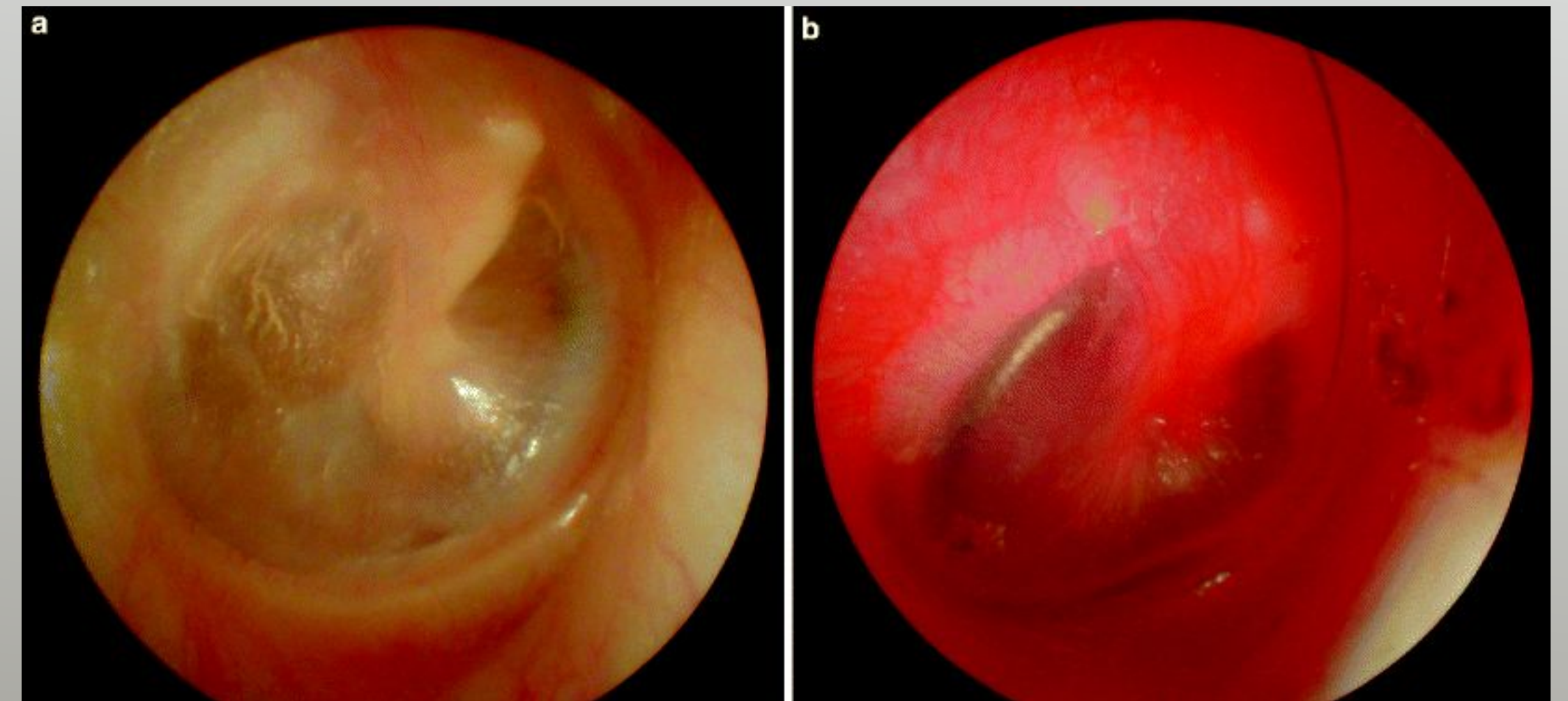
Do Antibiotics Help in Acute Sinusitis?

- Cochrane review concluded that the risks of antibiotics in adults with acute uncomplicated sinusitis likely outweighs the benefit:
 - NNT for 1 patients to have benefit from antibiotics 18
 - NNT for 1 patients to have harm from antibiotics (nausea, abdominal pain, rash) was 8



Acute Otitis Media

- The most common infection in childhood that results in an antibiotic prescriptions.¹⁹
- 66% of cases will have both bacteria and viruses detected



AAP Guidelines for Acute Otitis Media

Immediate antibiotics

Tympanic membrane perforation
<2 years of age with bilateral AOM
Severe AOM (fever >102.2,
symptoms > 48 hours, severe pain)

Observation/Delay for 72 hours

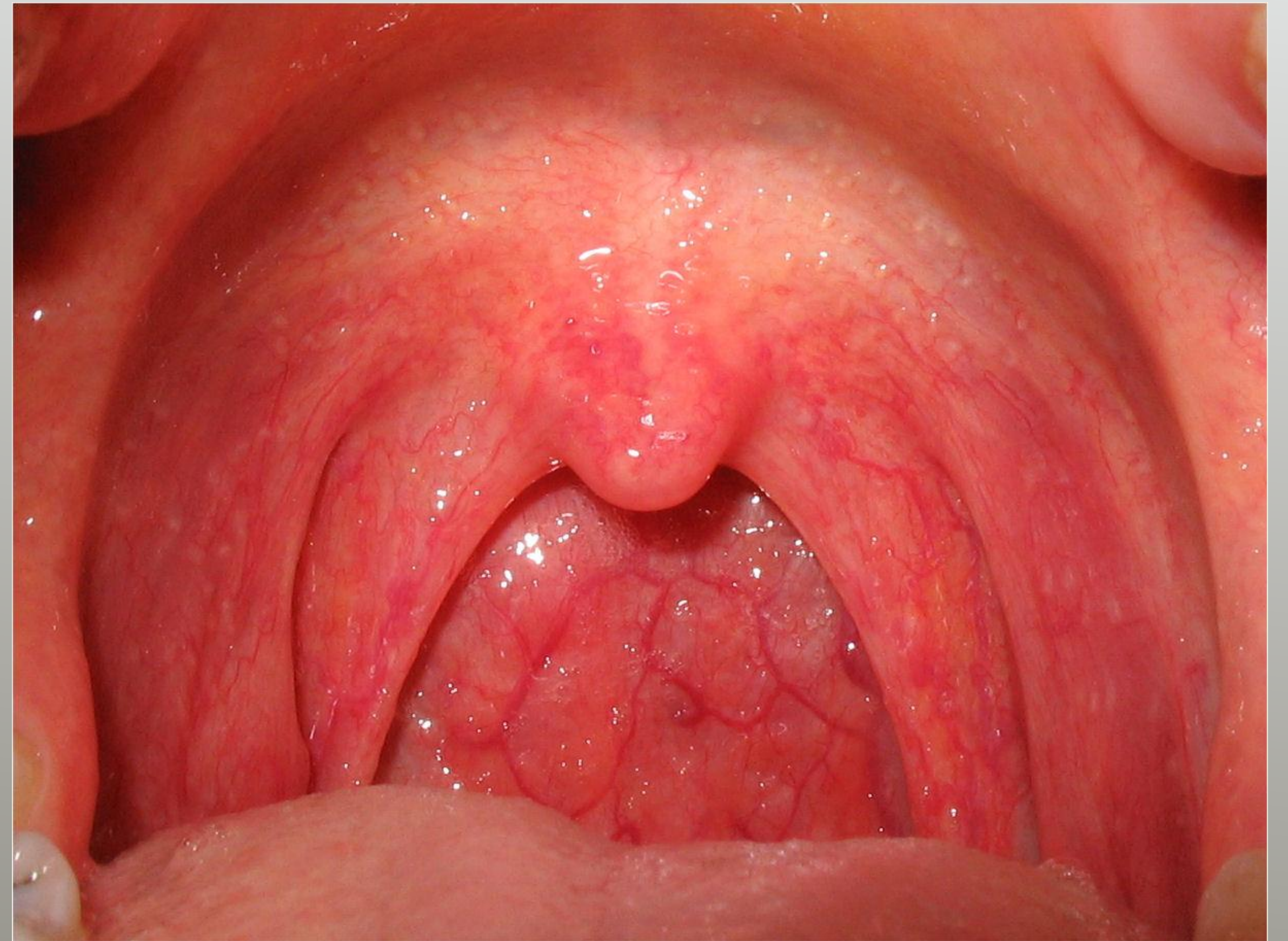
<2yo with unilateral non-severe
AOM
>2yo with non-severe AOM)

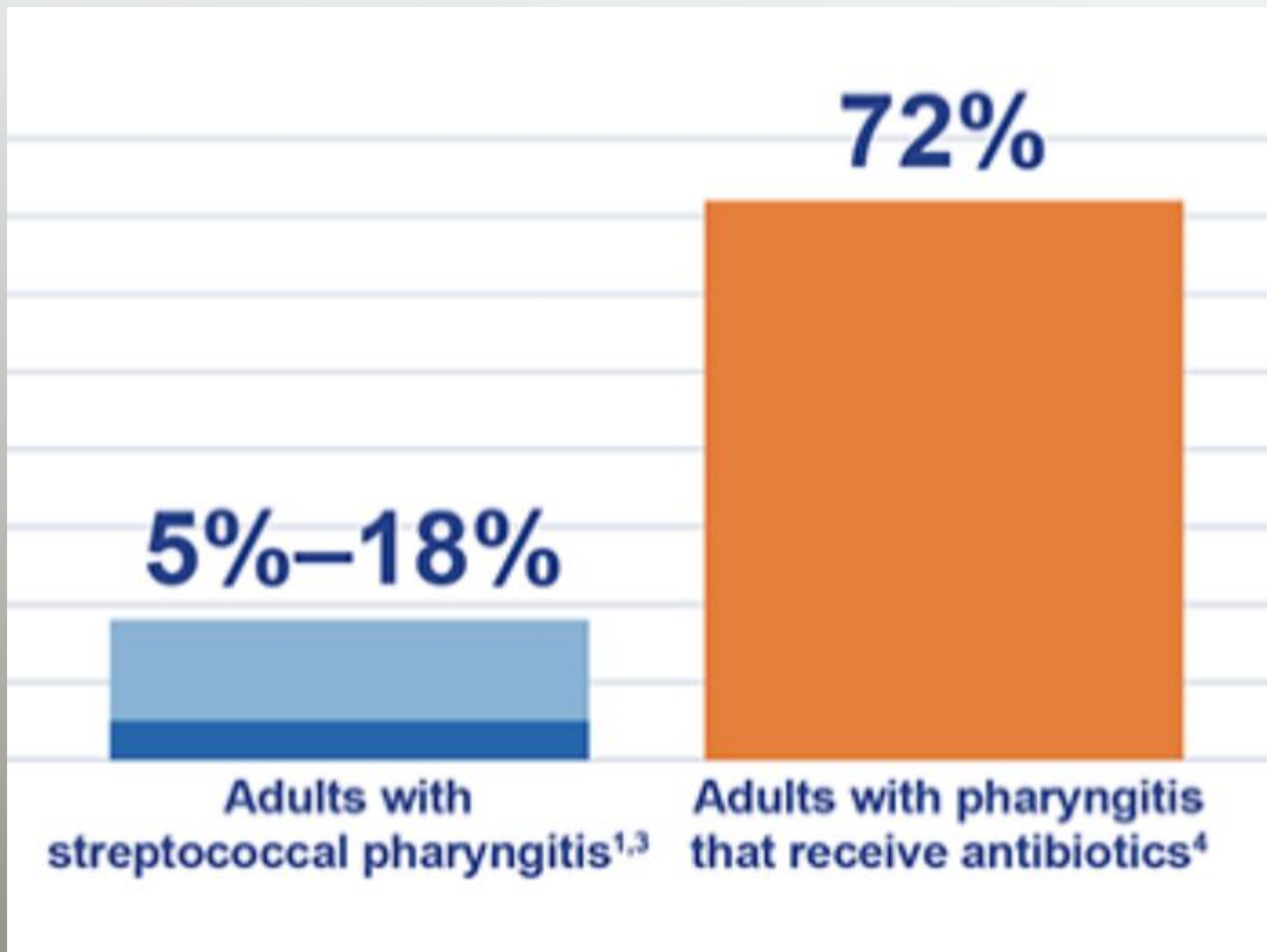
Is there a reason to delay?

- RCT enrolled 283 pediatric patients with AOM received either immediate or delayed antibiotics²¹
 - 62% - patients who received a delayed antibiotic did not fill the prescription
 - 13% - immediate antibiotic group that did not fill prescriptions
- No difference in resolution of AOM and no serious ASE or follow up visits.

Pharyngitis

- Most Cases of pharyngitis are caused by viruses
- For uncomplicated acute pharyngitis - the IDSA recommendation are that only confirmed cases of streptococcal pharyngitis require antibiotics²²





IDSA Testing Guidelines

- Only test those who
 - At least 3 years of age
 - Signs and symptoms of group A pharyngitis, without signs of viral URI
- 20% of asymptomatic children will have colonization of group A strep that do not necessitate treatment
- Centor criteria can be used in adults to determine who meets eligibility for RADT (2 or more should be tested)
- Only treat those
 - Who meet clinically criteria for strep pharyngitis and who test positive on RADT (or throat culture in children)

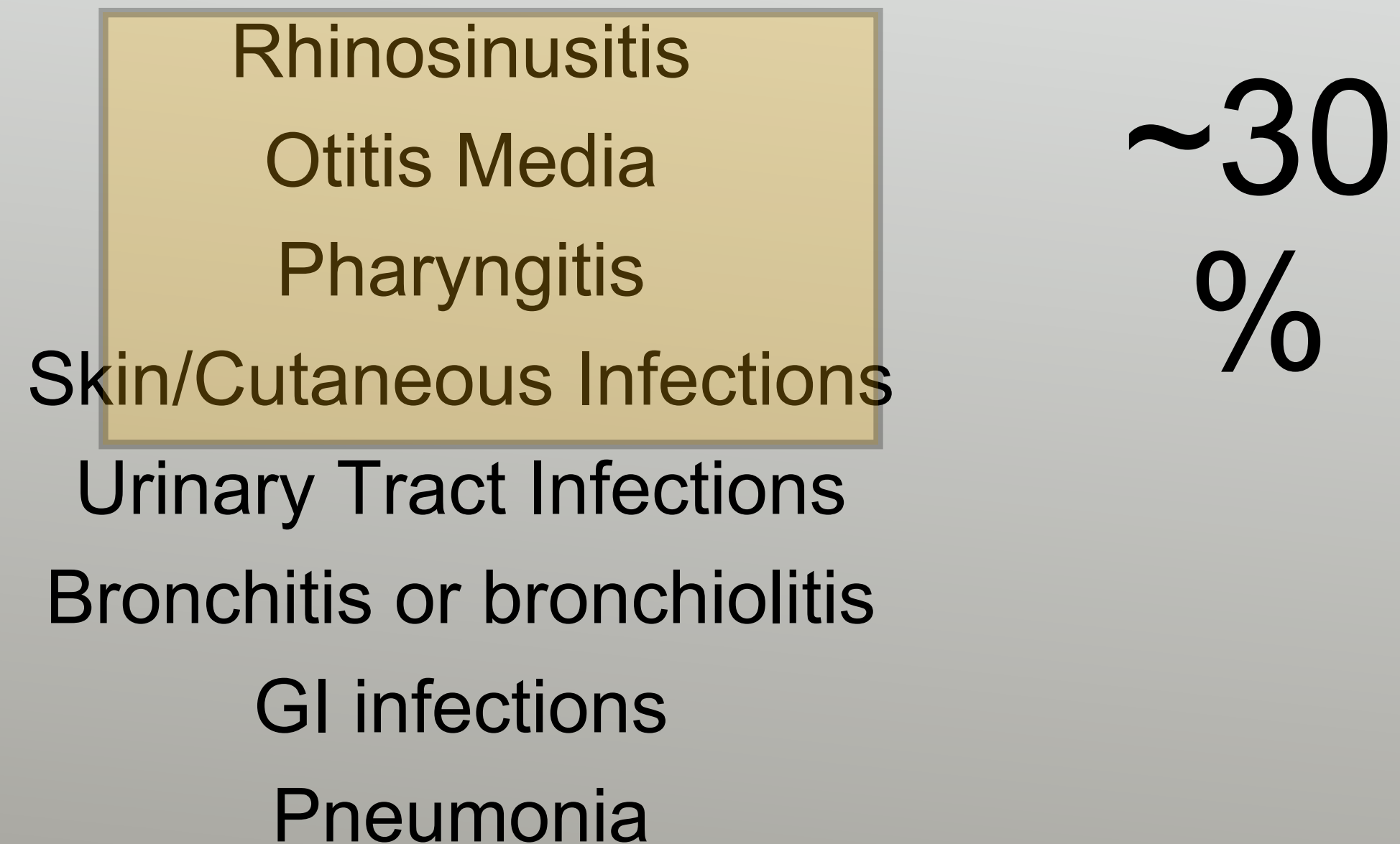


Are These Followed?

- 18% of adults with sore throat and 2 or more center criteria were found to have a positive strep test
- 72% of adults with pharyngitis in one study between 2010-2011 received antibiotics²³

Unnecessary Antibiotic Use

1/3 of antibiotic prescriptions given in the outpatient setting can be considered unnecessary¹⁵



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Improper Antibiotic Selection

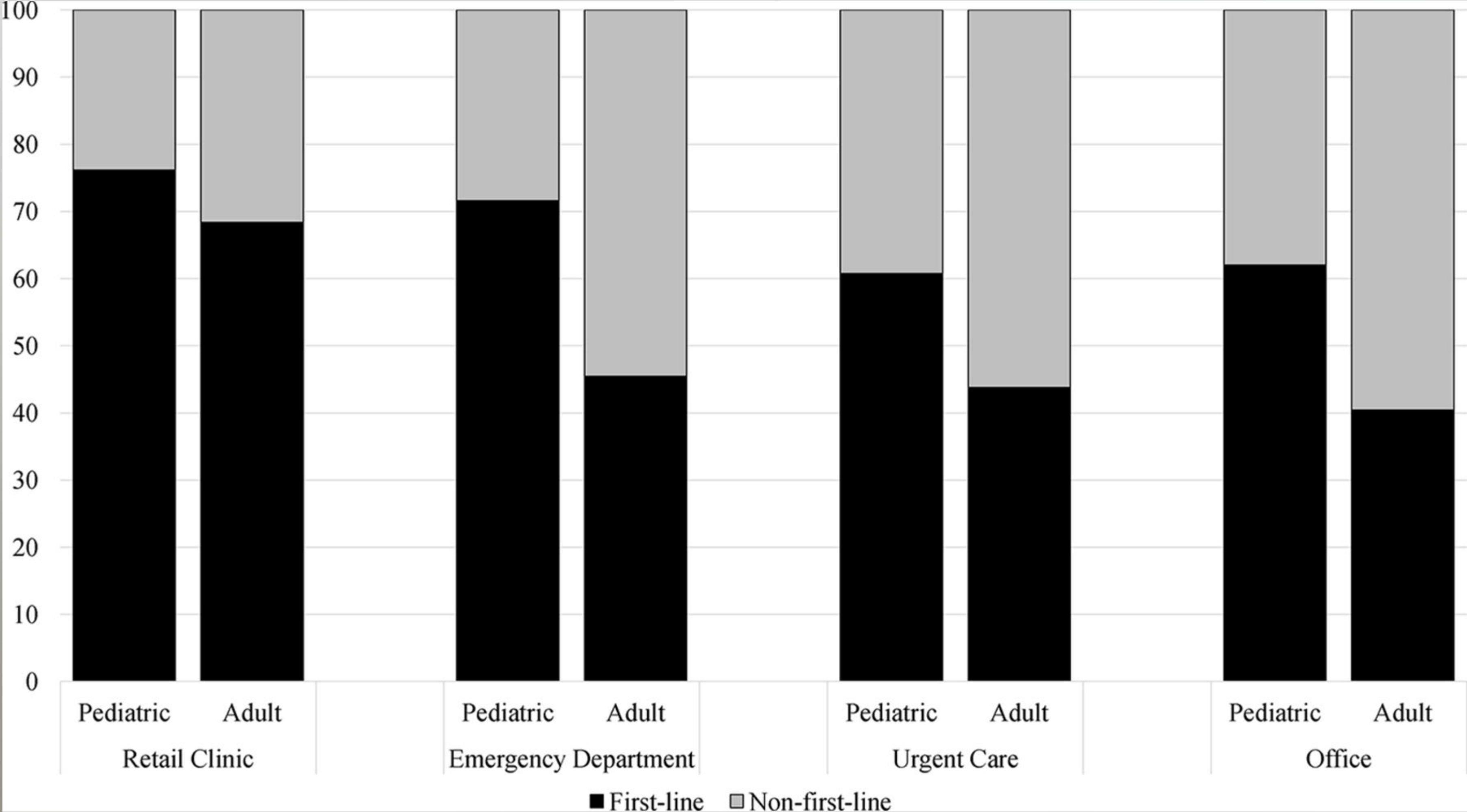
- Patients with uncomplicated disease with no allergies should receive first line agents for treatment of their infection

Acute otitis media - Penicillin or Amoxicillin

Sinusitis - Amoxicillin or Amoxicillin-Clavulanate

Pharyngitis - Penicillin or Amoxicillin

First Line Agent Selection



24 Palms, D., Hicks, L., Bartoces, M., Hersh, A., Zetts, R., Hyun, D. and Fleming-Dutra, K., 2019. First-Line Antibiotic Selection in Outpatient Settings. *Antimicrobial Agents and Chemotherapy*, 63(11)..

Do first line agents matter?

- First line agents (like amoxicillin) are more likely to cure AOM or sinusitis
- Overall broad antibiotics promote resistance and ASE
- Non-first line agents can be less effective
 - Macrolides (“Z-pack”) are not recommended for sinusitis or AOM but are often over-prescribed in the outpatient setting²⁰
 - Streptococcal resistance to macrolides significantly higher than penicillins

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Errors in Duration

- The minimum effective duration is an important concept in antimicrobial stewardship
 - A shorter duration is as effective as a longer one in some conditions and minimizes harm
 - Community acquired pneumonia, 3-5 days is as effective as 7-10 days
 - Pyelonephritis - 5-7 days is as effective as 10-14 days.

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Stepwise Approach to Improving Antibiotic Prescribing

Step 1: Identify high priority conditions that warrant improvement

Step 2: Identify barriers that lead to deviation from best practices

Step 3: Establish standards for antibiotics prescribing.

Identify High Priority Conditions

- Those conditions that are seen in the your practice and may commonly result in antibiotic prescriptions, especially those mentioned earlier
 - Pharyngitis
 - Sinusitis
 - Otitis Media
 - Bronchitis
 - URI

Identify Barriers to Best Practices

- Clinician knowledge gaps
- Pressure to see patients quickly
- Perception of patient expectations and patient satisfaction



Identify Standards for Prescribing

- Standards based on evidence based practice and societal guidelines
- IDSA and CDC publish guidelines on numerous conditions requiring antibiotic use

Promote Commitment to Stewardship

“As your doctors, we promise to treat your illness in the best way possible. We are also dedicated to avoid prescribing antibiotics when they are likely to do more harm than good.”

Promote Commitment to Stewardship

- Commitment poster reduced inappropriate prescribing for URIs by 20%²⁸

A Commitment to Our Patients About Antibiotics

Antibiotics only fight infections caused by bacteria. Like all drugs, they can be harmful and should only be used when necessary. Taking antibiotics when you have a virus can do more harm than good: you will still feel sick and the antibiotic could give you a skin rash, diarrhea, a yeast infection, or worse.

Antibiotics also give bacteria a chance to become more resistant to them. This can make future infections harder to treat. It means that antibiotics might not work when you really do need them. Because of this, it is important that you only use an antibiotic when it is necessary to treat your illness.

How can you help? When you have a cough, sore throat, or other illness, tell your doctor you only want an antibiotic if it is really necessary. If you are not prescribed an antibiotic, ask what you can do to feel better and get relief from your symptoms.

Your health is important to us. As your healthcare providers, we promise to provide the best possible treatment for your condition. If an antibiotic is not needed, we will explain this to you and will offer a treatment plan that will help. We are **dedicated** to prescribing antibiotics **only** when they are needed, and we will avoid giving you antibiotics when they might do more harm than good.

If you have any questions, please feel free to ask us.

Sincerely,

To learn more
about antibiotic
prescribing and use, visit
www.cdc.gov/antibiotic-use.



Improve Clinical Decision Making

- Clinical support tools - via outside EMR or integrated into EMR to provide guidance on appropriate antibiotic use
- Provider education, lectures, CME on evidence based diagnostic criteria and treatment recommendations
- Provide timely access to persons of expertise - pharmacy, infectious disease

Improve Patient Understanding of Decision Making

Why does taking antibiotics lead to antibiotic resistance?

Any time antibiotics are used, they can cause side effects and lead to antibiotic resistance. Antibiotic resistance is one of the most urgent threats to the public's health. Always remember:

1. Antibiotic resistance does not mean the body is becoming resistant to antibiotics; it is that bacteria have become resistant to the antibiotics designed to kill them.
2. When bacteria become resistant, antibiotics cannot fight them, and the bacteria multiply.
3. Some resistant bacteria can be harder to treat and can spread to other people.

More than 2.8 million antibiotic-resistant infections occur in the United States each year, and more than 35,000 people die as a result.

What is the right way to take antibiotics?

If you need antibiotics, take them exactly as prescribed.

Improving the way healthcare professionals prescribe antibiotics, and the way we take antibiotics, helps keep us healthy now, helps fight antibiotic resistance, and ensures that these life-saving drugs will be available for future generations.

Talk with your doctor if you have any questions about your antibiotics, or if you develop any side effects, especially diarrhea, since that could be *Clostridioides difficile* infection (also called *C. difficile* or *C. diff*), which needs to be treated. *C. diff* can lead to severe colon damage and death.

What are the side effects?

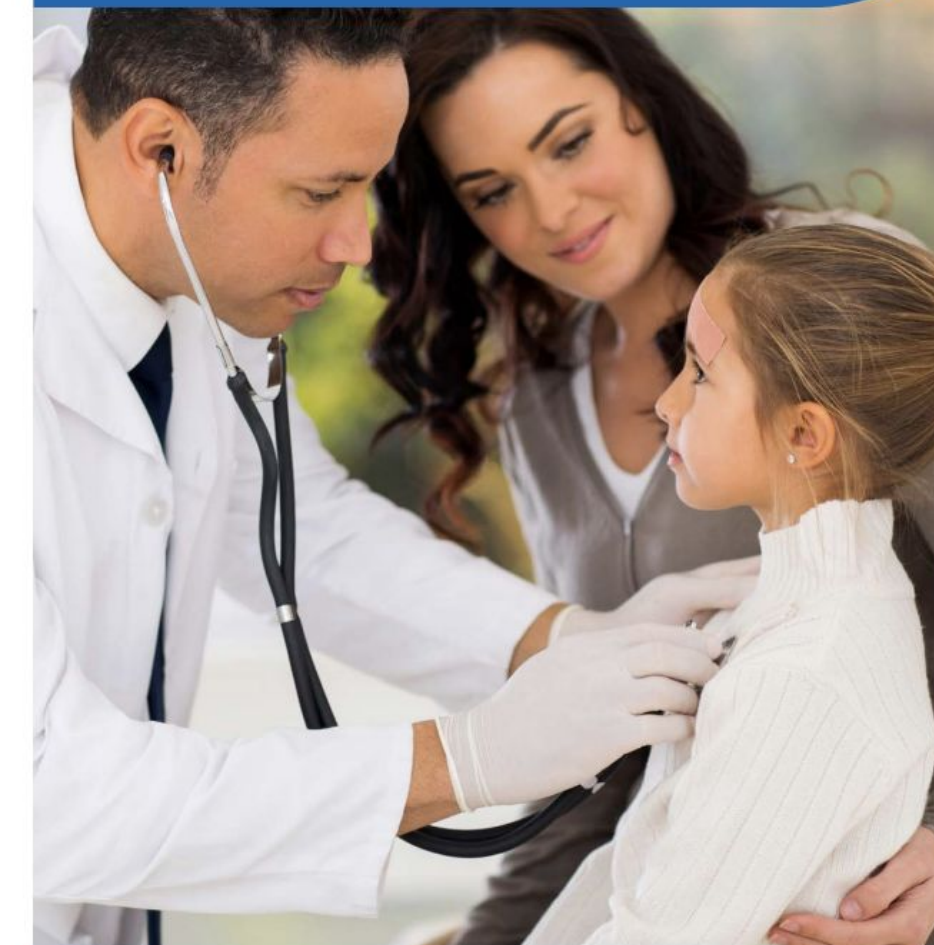
Common side effects range from minor to very severe health problems and can include:

- Rash
- Dizziness
- Nausea
- Diarrhea
- Yeast infections

More serious side effects can include:

- *Clostridioides difficile* infection
- Severe and life-threatening allergic reactions

Antibiotics Aren't Always the Answer.



Can I feel better without antibiotics?



**BE
ANTIBIOTICS
AWARE**
SMART USE, BEST CARE

Respiratory viruses usually go away in a week or two without treatment. To stay healthy and keep others healthy, you can:



Clean Hands



Cover Coughs



Stay Home
When Sick



Get
Recommended
Vaccines

To learn more about antibiotic prescribing and use, visit www.cdc.gov/antibiotic-use



Improve Patient Understanding of Decision Making

- Leverage social media to promote antibiotic stewardship
- U.S. Antibiotic Awareness Week November 18-24, 2021.
- Twitter #BeAntibioticsAware



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Take-Aways

- Over-prescribing antibiotics is a public health crisis in the U.S. and worldwide, and is resulting in real complications and dangers to patients and healthcare practices
- Resistance and Adverse Side Effects can be reduced by reducing the number of inappropriate antibiotics that are prescribed
- The problem is solved at the front-lines, with providers improving their own practices and using evidence based guidelines when treating an acute infection
- Self-education and awareness is the first step to improving decision making.

Thank you!

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