Tufts Medicine
Tufts Medical Center

# Clinical Consequences of AMR

## The Impact on Health Care Systems and Patients

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November 11, 2025

# Objectives

- Describe the clinical consequences of antimicrobial resistance in different settings
- Recognize the economic and human burden of resistance

# Bad Moon Rising

| | Threat | Change in Rates or Number of Infections*** | | | |
|---|---|---|---|---|---|
| | | 2020 vs. 2019 | 2021 vs. 2020 | 2022 vs. 2021 | 2022 vs. 2019 |
| URGENT* | Hospital-onset CRE | ▲ Increase | ▲ Increase | — Stable | ▲ Increase |
| URGENT* | Hospital-onset Carbapenem-resistant *Acinetobacter* | — Stable | — Stable | — Stable | ▲ Increase** |
| URGENT* | Clinical Cases of *C. auris* | ▲ Increase | ▲ Increase | ▲ Increase | ▲ Increase |
| SERIOUS* | Hospital-onset MRSA | ▲ Increase | — Stable | ▼ Decrease | — Stable |
| SERIOUS* | Hospital-onset VRE | ▲ Increase | ▲ Increase | — Stable | ▲ Increase |
| SERIOUS* | Hospital-onset ESBL-producing Enterobacterales | ▲ Increase | — Stable | — Stable | ▲ Increase |
| SERIOUS* | Hospital-onset MDR *Pseudomonas aeruginosa* | ▲ Increase | ▲ Increase | — Stable | ▲ Increase |

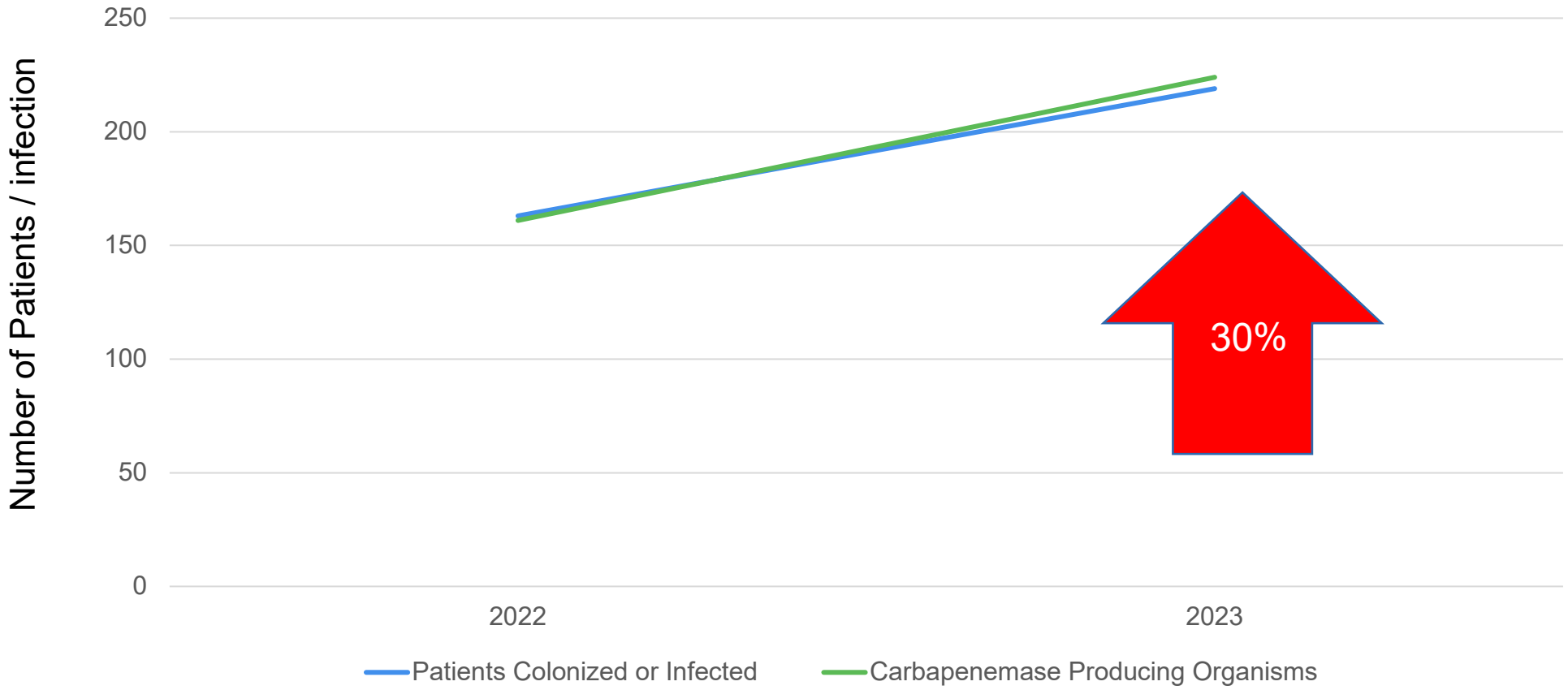
* Threat level for each pathogen, as categorized in CDC's *Antibiotic Resistance Threats in the United States, 2019*.
** There was no statistically significant difference in rate of hospital-onset carbapenem-resistant *Acinetobacter* in 2020, 2021, and 2022 when compared to the previous year. However, there was a statistically significant increase in rate of hospital-onset carbapenem-resistant *Acinetobacter* in 2022 when compared to 2019.
*** Hospital-onset rates were described using multivariable models for all threats except *C. auris*. Please note that in above table, stable indicates there was no statistically significant increase or decrease, decrease indicates a statistically significant decrease where $p<0.05$, and increase indicates a statistically significant increase where $p<0.05$, for all threats except for *C. auris*. Increases or decreases in *C. auris* were indicated by changes in the number of clinical cases reported nationally without hypothesis testing.

Antimicrobial Resistance threats in the United States table shows change in rates and number of infections from 2019 to 2022.

CRE= carbapenem resistant enterobacterales MRSA= Methicillin resistant Staphylococcus aurues VRE= Vancomycin Resistant Enterococcus ESBL = extended spectrum beta-lactamase MDR= Multidrug resistant

Antimicrobial Resistance. CDC.gov Accessed 10/7/2024

# Carbapenemase Producing Organisms in Massachusetts




Candida auris and Carbapenemase-producing organism Surveillance Update. Commonwealth of Massachusetts: Department of Public Health. July 2, 2024.

# Use of antibiotics causes resistance

- The **use of antibiotics** is the most important modifiable risk factor for resistance.
- Unnecessarily longer courses of antibiotics can lead to resistance in individual patients and on a population level
- When prescribing antibiotics, make sure that they are necessary and always consider using the shortest duration




CDC. Be Antibiotics Aware Campaign 2023. Available from: https://www.cdc.gov/antibiotic-use/week/index.html. Minnesota Department of Public Health. 2022. Antibiotics Only When Needed. Available from: https://www.health.state.mn.us/diseases/antibioticresistance/own/index.html

# Mind blowing idea

- Stopping antibiotic treatment early **does not** cause resistance

- If the patient is clinically better, choosing shorter rather than longer courses of antibiotics is associated with fewer adverse events

# Clinical Consequences in Outpatient and Chronic Illness

# Poll Question

65 y/o female with **history of heart transplant** was seen in your outpatient clinic. When you evaluate the patient, she tells you her **urine smells funny** but she **denies** dysuria, urgency, frequency, abdominal pain or fever.

She said when this happened earlier in the year she received antibiotics and it helped with the urine smell.

What would you do next?

1. Send urine analysis with reflex to culture
2. Send urine culture alone given patient's symptoms
3. Start empiric antibiotics without delay since she is immunocompromised
4. Reassure the patient that she is not at risk of UTIs

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# Urine Odor

- Two research assistant used the "sniff" test to evaluate freshly voided urine for the presence of odor.
- The results of the “sniff” test were compared to urine analysis and culture results.
- Using urine odor to identify a UTI resulted in error in **one third** of cases

Midthun SJ, Paur R, Lindseth G. Urinary tract infections. Does the smell really tell? J Gerontol Nurs. 2004 Jun;30(6):4-9. doi: 10.3928/0098-9134-20040601-04. PMID: 15227931.

Unfortunately, the patient went to a different clinic a few days later and received a course of antibiotics.

# Outpatient Antibiotic Use


**At least 28% of antibiotics prescribed in outpatient settings are considered unnecessary**

https://www.cdc.gov/antibiotic-use/hcp/data-research/antibiotic-prescribing.html

# Case

You are seeing her again 4 months late. She now has an urge to urinate every 30 minutes and burning sensation with urination.

She reports that she had received 4 courses of antibiotics this year for foul smelling urine.

You send a urine analysis with reflex to culture

Susceptibility

| | Escherichia coli ESBL MIC |
|---|---|
| $ Amoxicillin/Clavulanate | Resistant |
| $$ Ampicillin | Resistant |
| $$$ Ampicillin/Sulbactam | Resistant |
| $ Aztreonam | Susceptible |
| $ Cefazolin | Resistant |
| $$ Cefepime | Susceptible |
| Cefoxitin | Intermediate |
| $$ Cefpodoxime Proxetil | Resistant |
| $$ Ceftazidime | Susceptible |
| Ceftriaxone | Resistant |
| $ Ciprofloxacin | Resistant |
| $$$$ Ertapenem | Susceptible |
| $ Gentamicin | Susceptible |
| $$$ Levofloxacin | Resistant |
| $$$ Meropenem | Susceptible |
| $$ Piperacillin/Tazobactam | Susceptible |
| $ Tobramycin | Resistant |
| $ Trimethoprim/Sulfamethoxazole | Resistant |

The patient had to be admitted to receive IV antibiotics for simple cystitis

# Implications of Antibiotic Resistance for Common Infections

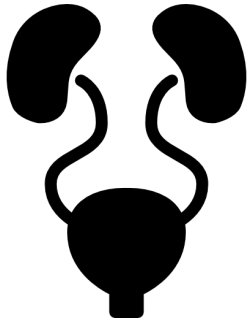
For outpatient UTIs, resistance rates among Enterobacterales isolates is approximately:

**20% for TMP-SMX, fluoroquinolones and nitrofurantoin**

**ESBL- producing isolates account for about 7–9%**

**Multidrug resistance (≥2 classes of oral agents) 16–18%**

Clinical failure was significantly higher in patients with antibiotic-resistant *E.coli* and *S. pneumoniae*

4 x 

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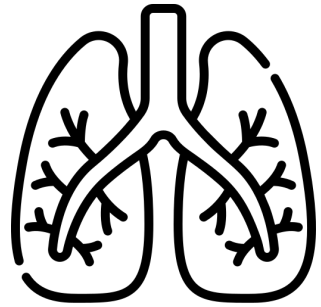
2 x 

The effect of antibiotics of the development of resistance is greatest in the month immediately after treatment but may persist **for up to 12 months.**

van Hecke O, Wang K, Lee JJ, Roberts NW, Butler CC. 2017. Clin Infect Dis.
Costelloe C et al., 2010, BMJ.
Aronin SI et al., 2022, Int J Infect Dis.

# “I want to give patients antibiotics just to be on the safe side”

# Treatment of asymptomatic bacteruria

673 women with asymptomatic bacteruria

361 treated

312 NOT treated

**6 months**

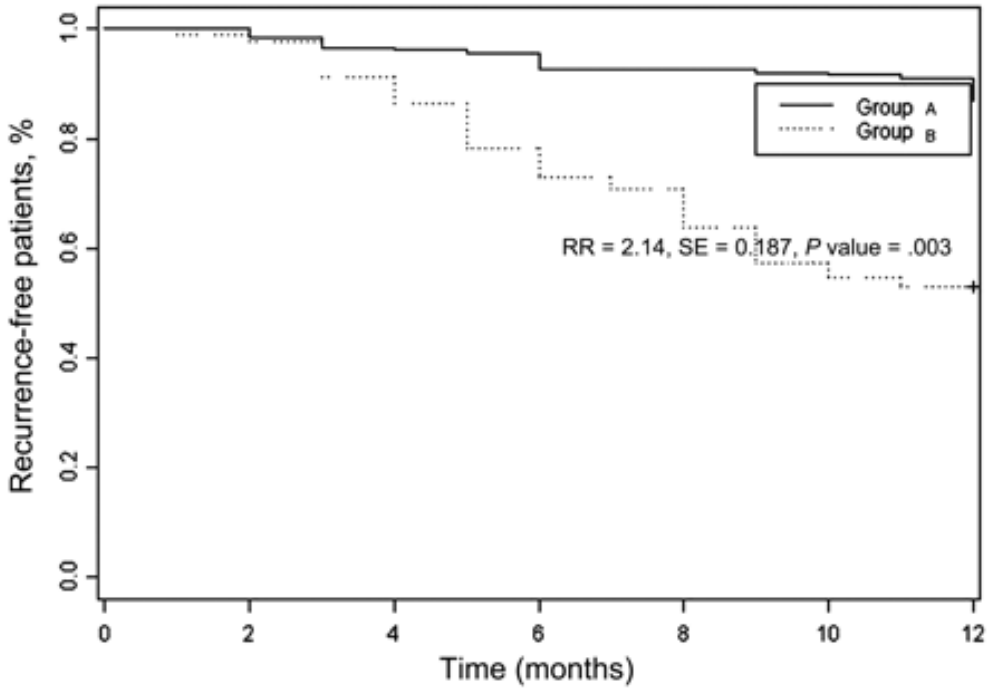
98 (29.7%) symptomatic UTI

23 (7.6%) symptomatic UTI

**12 months**

169 (46.8%) symptomatic UTI

41 (13.1%) symptomatic UTI




Tommaso Cai, Sandra Mazzoli, Nicola Mondaini, Francesca Meacci, Gabriella Nesi, Carolina D'Elia, Gianni Malossini, Vieri Boddi, Riccardo Bartoletti, The Role of Asymptomatic Bacteriuria in Young Women With Recurrent Urinary Tract Infections: To Treat or Not to Treat?, *Clinical Infectious Diseases*, Volume 55, Issue 6, 15 September 2012, Pages 771–777, https://doi-org.ezproxy.library.tufts.edu/10.1093/cid/cis534

# Treatment of asymptomatic bacteruria

## Resistance >> in treatment group

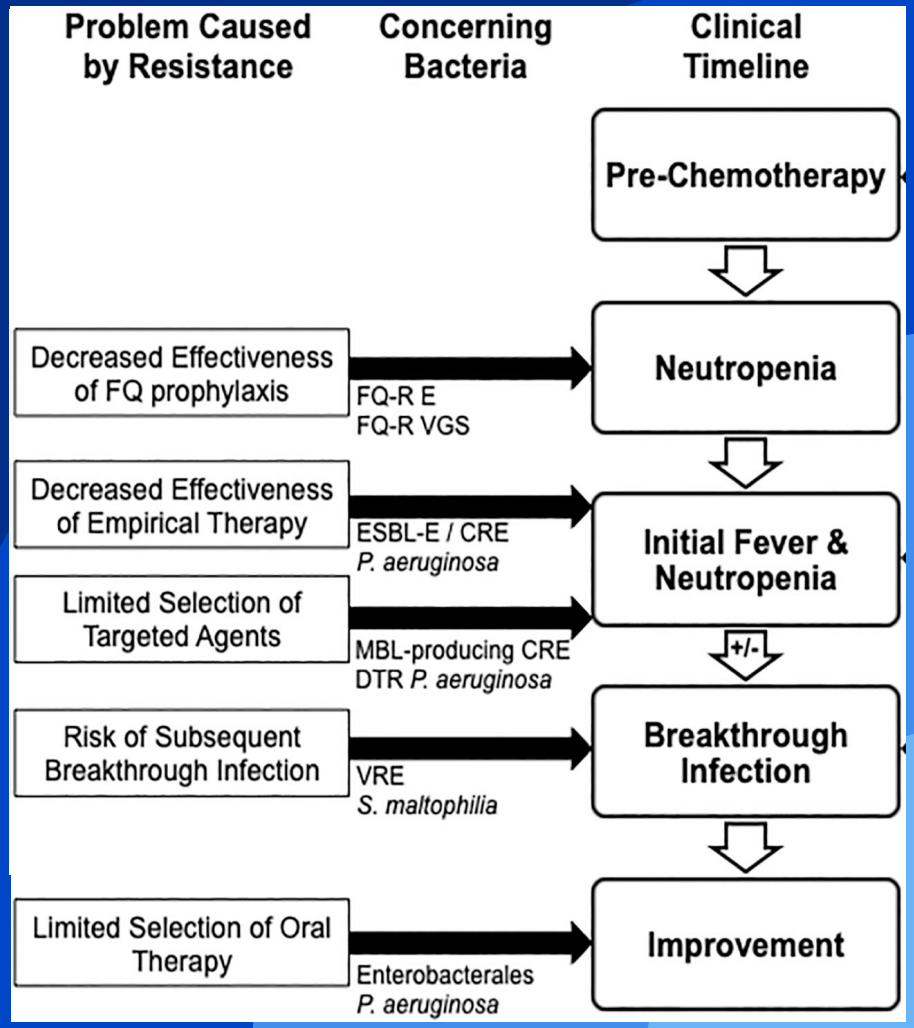
| | Group A (n = 257) | Group B (n = 293) | |
|---|---|---|---|
| Antibiotics tested on *E. coli*[b] | | | |
| Amoxicillin–clavulanic acid | 1/26 (3.8) | 23/93 (24.7) | .03 (4.2/1) |
| Trimethoprim-sulfamethoxazole | 3/26 (11.5) | 32/93 (34.4) | .01 (5.8/1) |
| Ciprofloxacin | 5/26 (19.2) | 41/93 (44.0) | .03 (4.3/1) |



Tommaso Cai, Gabriella Nesi, Sandra Mazzoli, Francesca Meacci, Paolo Lanzafame, Patrizio Caciagli, Liliana Mereu, Saverio Tateo, Gianni Malossini, Cesare Selli, Riccardo Bartoletti, Asymptomatic Bacteriuria Treatment Is Associated With a Higher Prevalence of Antibiotic Resistant Strains in Women With Urinary Tract Infections, *Clinical Infectious Diseases*, Volume 61, Issue 11, 1 December 2015, Pages 1655–1661, https://doi.org/10.1093/cid/civ696

# Clinical Consequences in Cancer Patients

# Timeline of issues caused by antibiotic resistance in patients with hematologic malignancies




## Indirect impact on patients

**Infections can lead to delays in chemotherapy and cancer directed treatments**

Gottesdiener LS et al., 2023, Transpl Infect Dis.

# Clinical and Economic burdens

# Impact of AMR on Patients With Resistant Infections

## Increased Morbidity and Mortality

- All cause mortality
- Hospital length of stay
- Need for ICU care
- Time on ventilator
- Excess surgery
- Functional decline and need for post acute care

## Economic Impact

- Loss of work
- Increased Healthcare Costs

# Impact of AMR on the Health Care System

**Impact of AMR on the Heath Care System**

Increased resource utilization and cost

- Healthcare costs ~4.6 billion/year due to AMR
- Need for ICU beds
- Readmissions
- Need for isolation and infection control measures
- Diagnostic testing

**Impact of AMR on Patients Without Resistant Infections**

- Exposure to MDR organisms during routine care
  - i.e. elective surgeries
- Exposure to broader antibiotics
  - Overuse of broad spectrum agents in high resistance settings
- Caregiver fatigue



Nelson RE et al., 2021, Clin Infect Dis.
Merrick B et al., 2021, J Hosp Infect.

# The human face of resistance


CredThis image was generated with the assistance of OpenAI's DALL-E 2

## Antimicrobial resistance: *Patient stories*

Many patients and their families have suffered the debilitating effects of antimicrobial-resistant infections. Many have even lost their lives due to these infections. Their compelling and heart-wrenching stories highlight the urgent need to address drug-resistant infections and the lack of new antimicrobial development. If you would like to share your story, please **contact us**.

https://www.idsociety.org/public-health/patient-stories2

Rump B *et al.*, 2019. *Clinical Microbiology and Infection.*
Hamilton RA *et al.*, 2024. *Scientific Reports.*

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