

Antimicrobial resistance in foodborne pathogens: A One Health concern

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Antimicrobial resistance is a global health concern

Antibiotic Resistance Threats in the U.S., 2019

- Antimicrobials have been critical for treating infections in humans and animals
- Their use contributes to resistance
 - Resistant infections are difficult to treat
 - They contribute to longer hospital stays, greater medical costs, and are a leading cause of death

Each year, antibiotic-resistant bacteria and fungi cause at least an estimated:

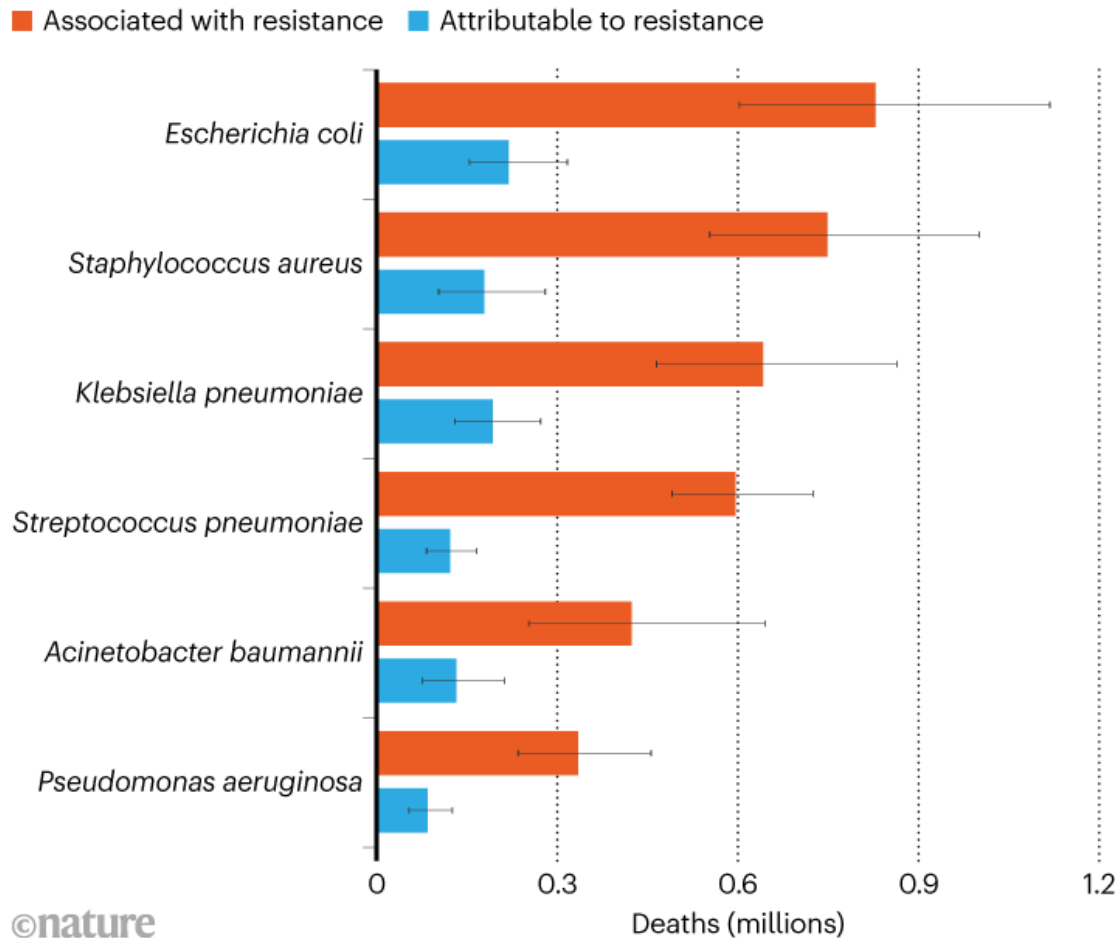


2,868,700
infections



35,900 deaths

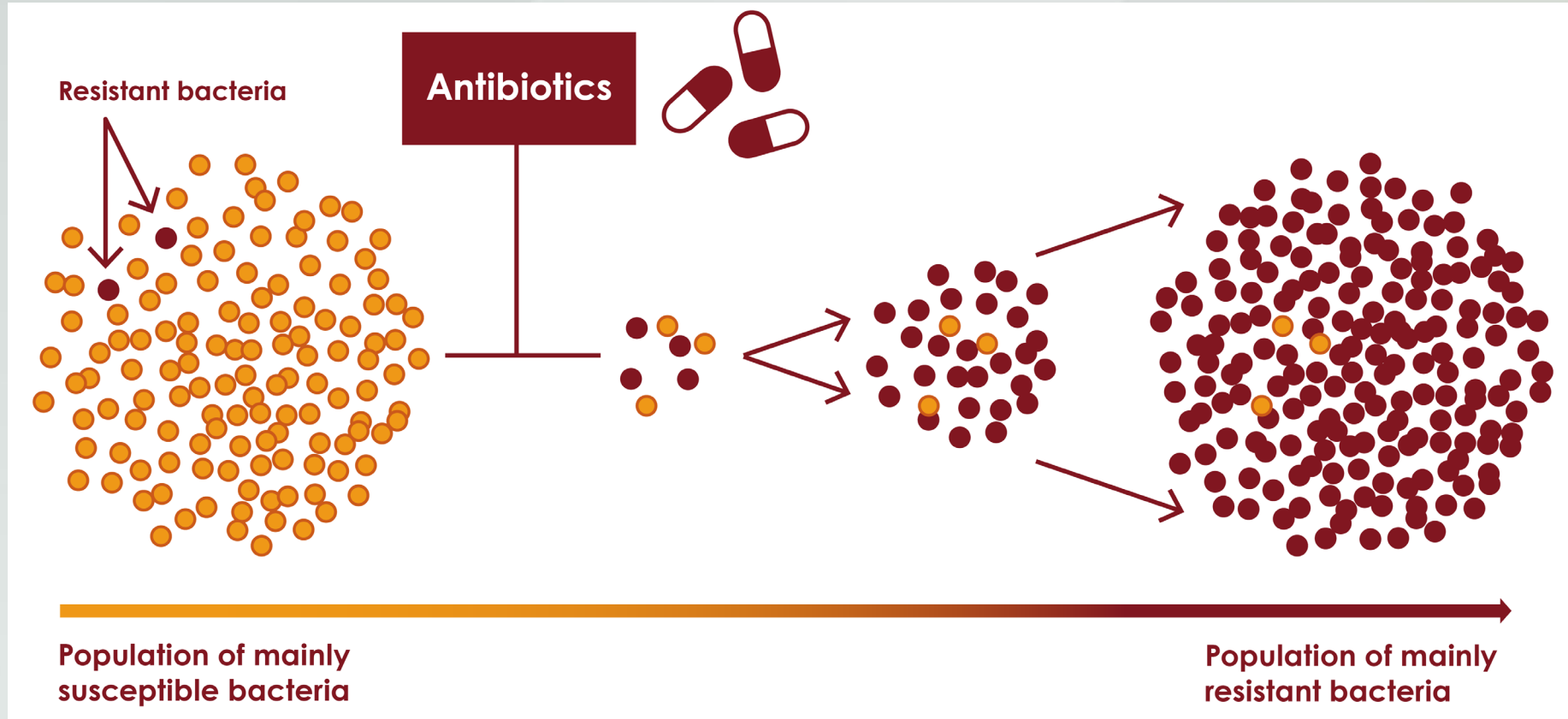
The number of resistant infections has increased steadily



- In 2019, 6 pathogens caused ~80% of the 1.27 million deaths
- Resistant infections increased by 15% during the COVID-19 pandemic¹

Antibiotic use is a key contributor to the development of resistance

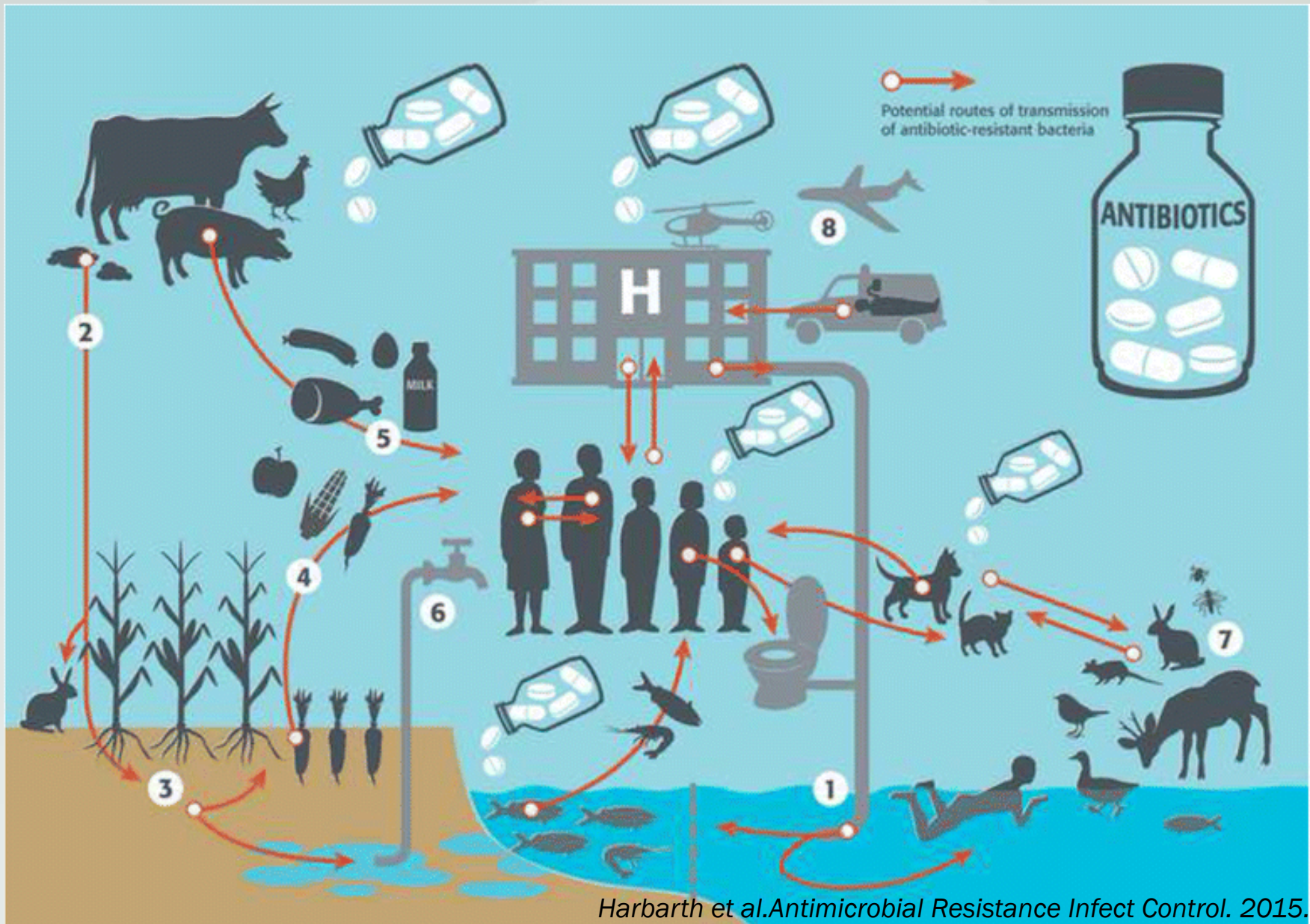
Global use of antibiotics has increased



<https://www.reactgroup.org/toolbox/understand/antibiotic-resistance/mutation-and-selection/>

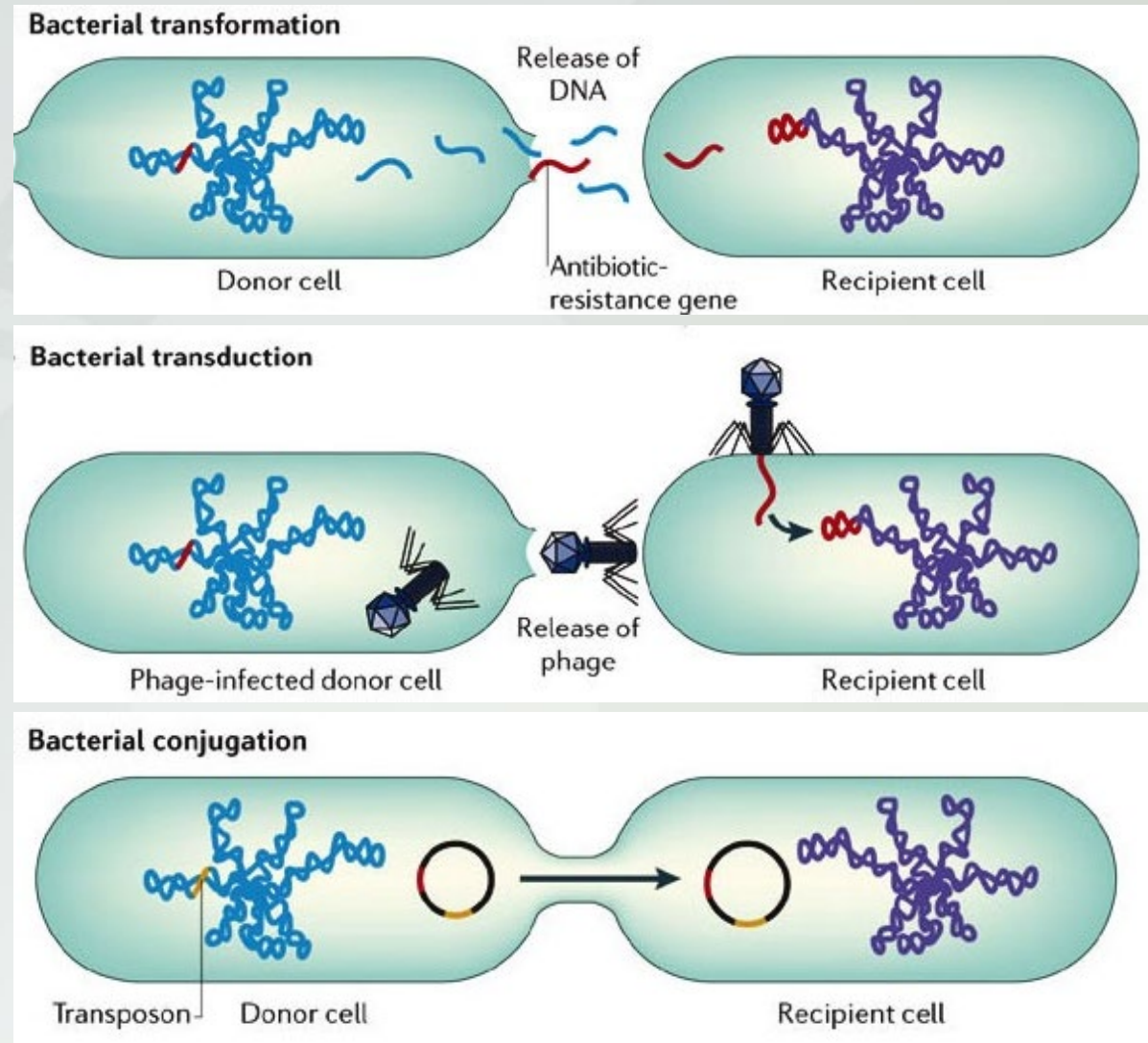
Antibiotic resistance is a One Health concern that can impact humans, animals, plants and the environment

Antibiotic use is widespread



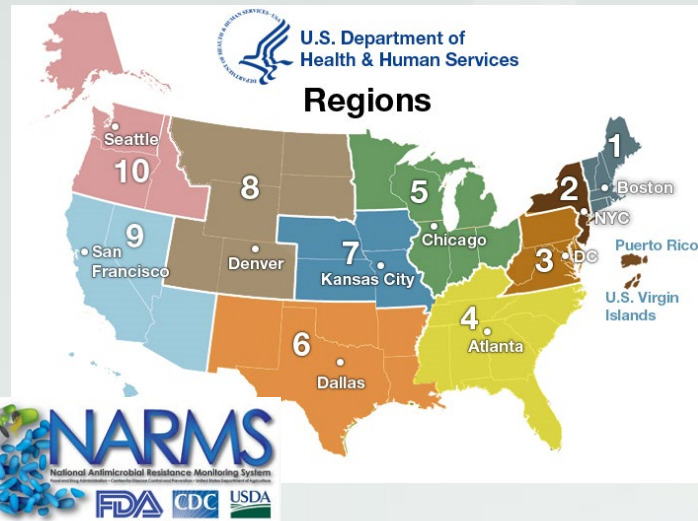
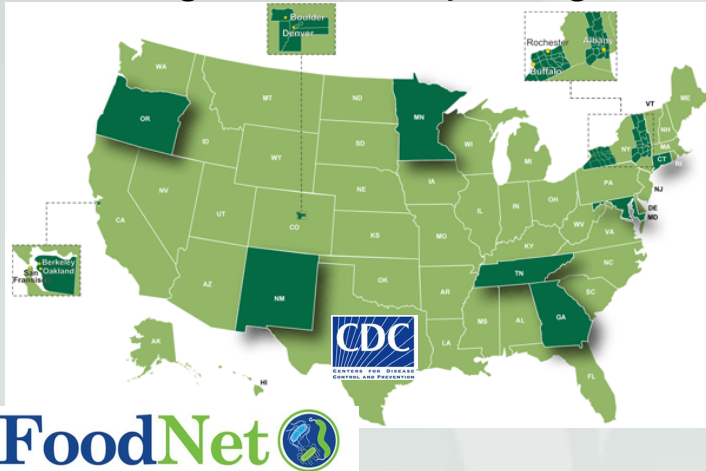
Evolution is critical for the emergence of antibiotic resistant bacterial pathogens

- Horizontal gene transfer (HGT) is a rapid process
 - Renders cells resistant to specific antibiotics by acquiring antibiotic resistance genes (ARGs)
- Resistance can also occur due to point mutations in some genes



Surveillance activities are important to define the problem

Monitoring foodborne pathogens...



Surveillance studies of patients in Michigan (2001-present)



- Campylobacter jejuni*
- Shiga toxin-producing *E. coli* (STEC)
- Salmonella*



- 1) Characterize the pathogens and identify risk factors for infection
- 2) Identify the impact of foodborne pathogens on the gut microbiome
- 3) Conduct comparative studies in food animals

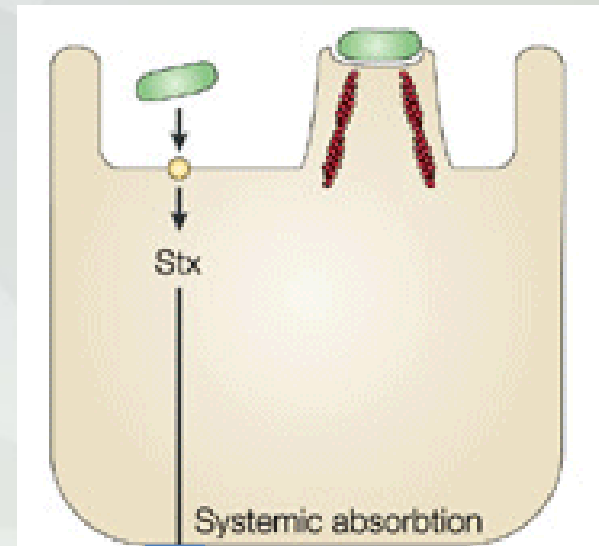
Source: ©EZUME IMAGES

A microscopic image showing several rod-shaped bacteria with numerous long, thin flagella (hairs) extending from their surfaces. The bacteria are reddish-brown in color and are set against a dark blue background with out-of-focus light spots. The text 'The evolution and emergence of STEC' is overlaid in white at the bottom of the image.

The evolution and emergence of STEC

Shiga toxin-producing *E. coli* (STEC) emerged in 1982

- Unusual illness reported in 47 people from MI and OR ¹
 - Grossly bloody diarrhea, severe abdominal cramping
 - Cases more likely to have eaten hamburgers at a specific restaurant
- Laboratory testing identified a rare *E. coli* serotype (O157:H7)
 - Had genes for the Shiga toxin (Stx) acquired by HGT via transduction

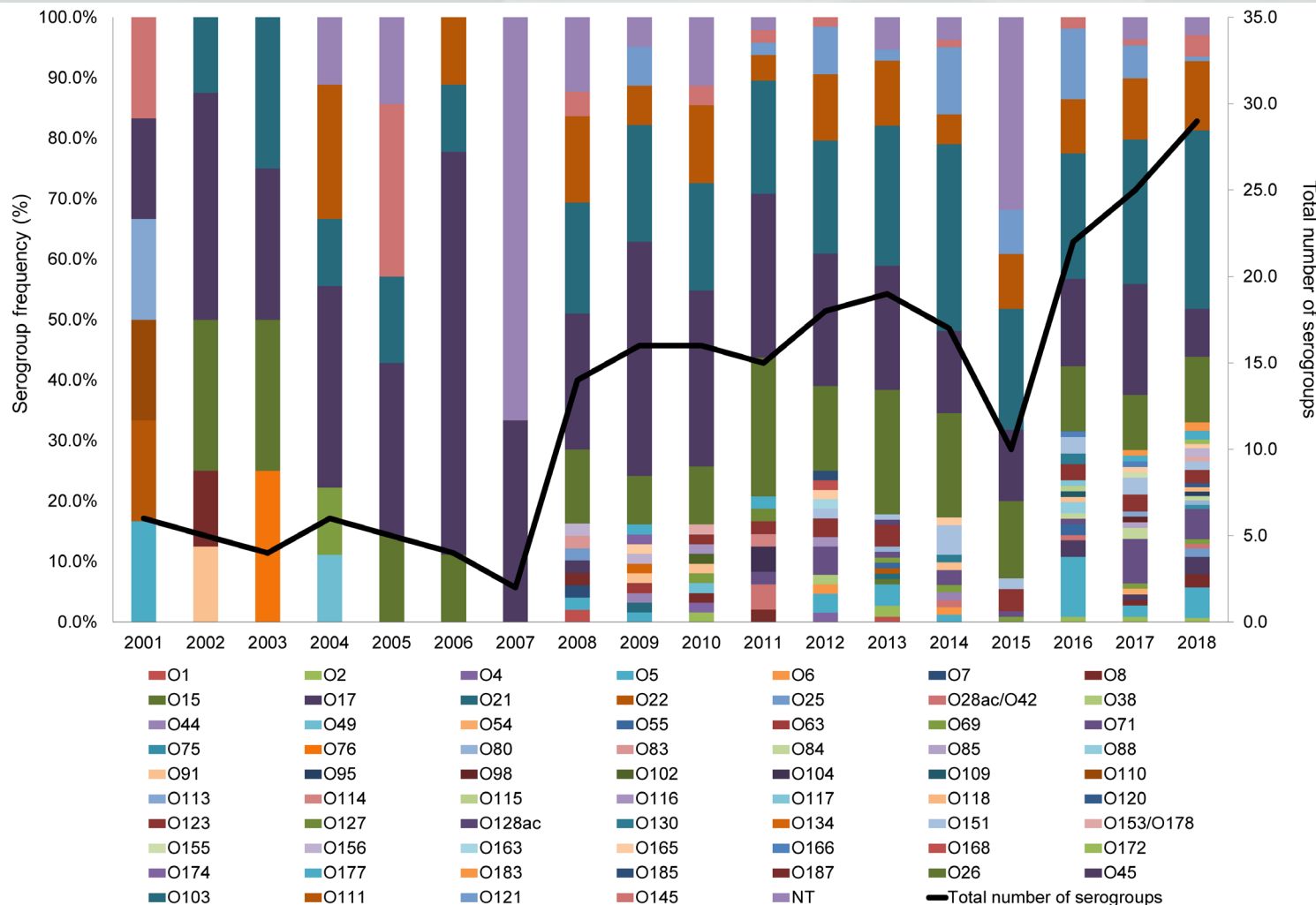


Kaper et al. Nat Rev 2004;2

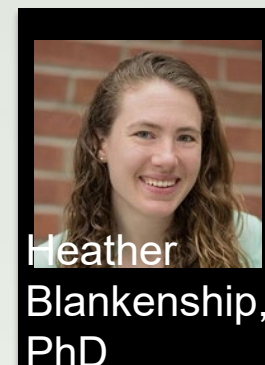
Life threatening complications like Hemolytic Uremic Syndrome (HUS)

¹Riley et al. N Engl J Med 1983; 308:681

The diversity of STEC serotypes has increased due to HGT of Stx genes



- Examined 894 isolates from patients with STEC infections
- Number of serogroups increased significantly over time



STEC diversity has also increased in the cattle reservoir

Sampled 1,096 cattle in 12 herds

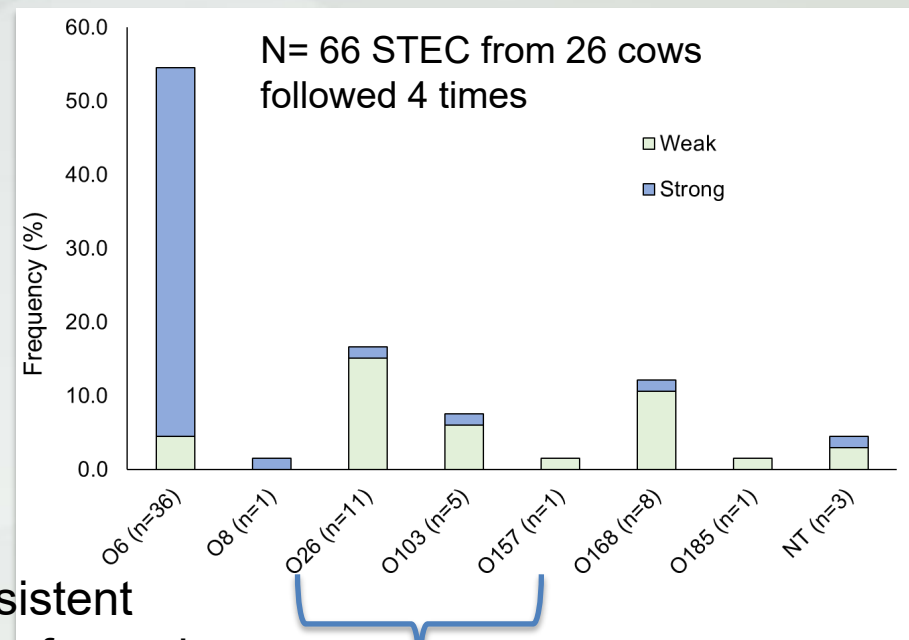
- 522 STEC isolates were recovered from 175 cattle
- O157 was found in only 19 (11%) animals



Transmission of STEC is common in a herd and many animals are persistent shedders



Evidence of STEC transmission between cattle and deer



Persistent isolates formed biofilms

New clinically important STEC strains emerged

Are STEC resistant to antibiotics?

- Antibiotics are not recommended to treat patients with STEC

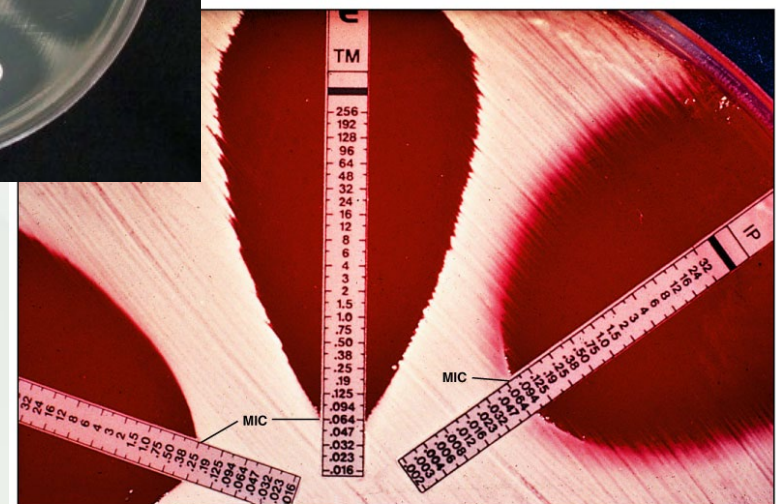


Antibiotics can increase Shiga toxin production

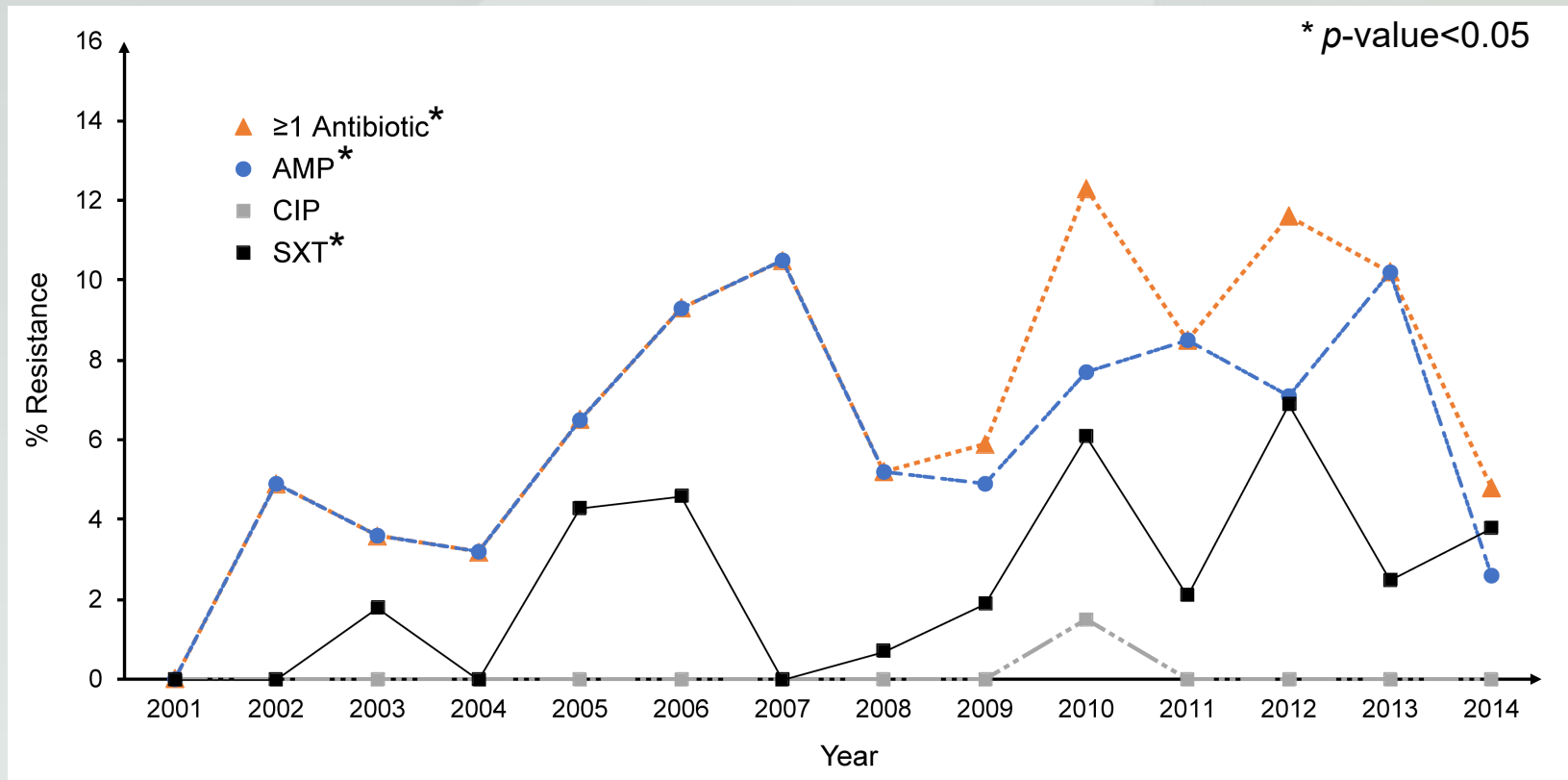


Detecting resistance phenotypes:

- Disk diffusion
- Minimum inhibitory concentration (MIC) is the concentration that completely inhibits bacterial growth



Antibiotic resistance has emerged in STEC and increased in frequency



Non-O157 STEC isolates were significantly more likely to be resistant than O157 isolates

Mukherjee et al. Emerg Infect Dis. 2017; 23(9);

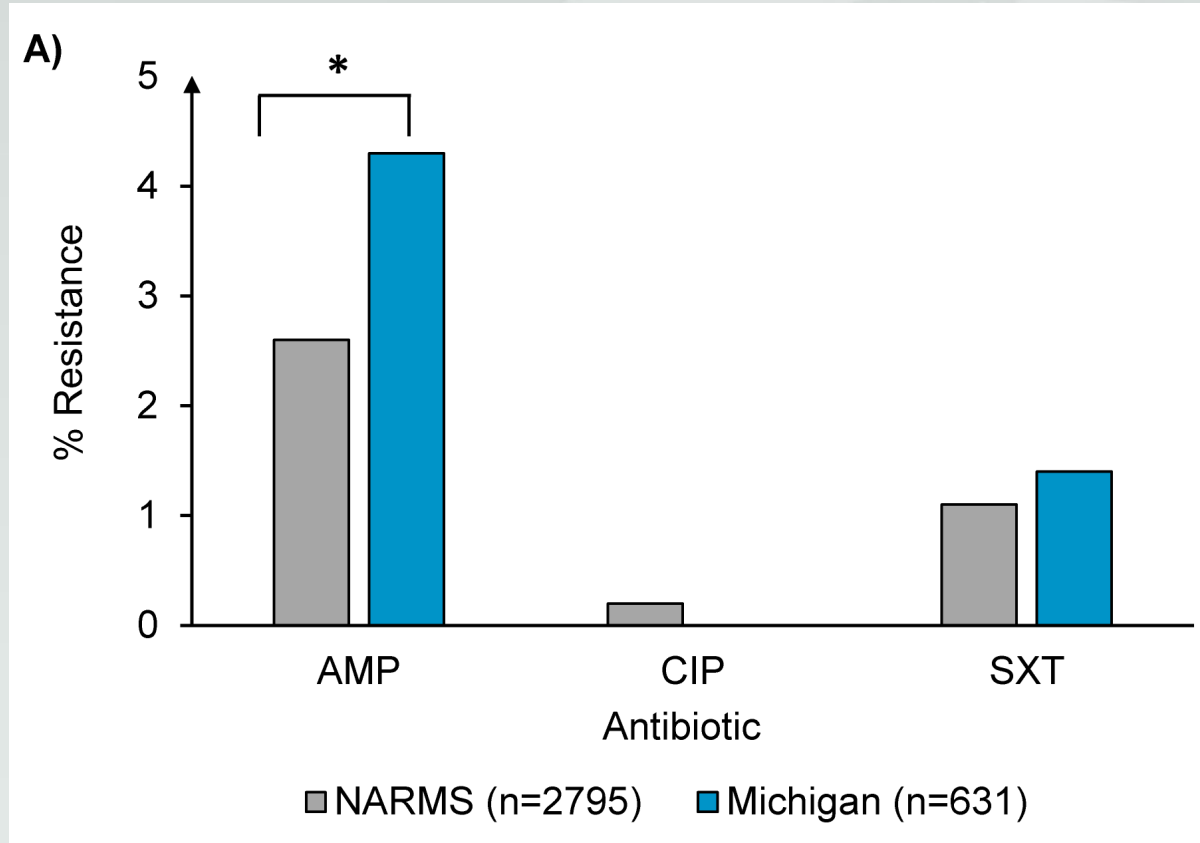
Mukherjee et al. Antimicrob Agents Chemother. 2021;65: e01189



Resistance frequencies differ in Michigan relative to national frequencies

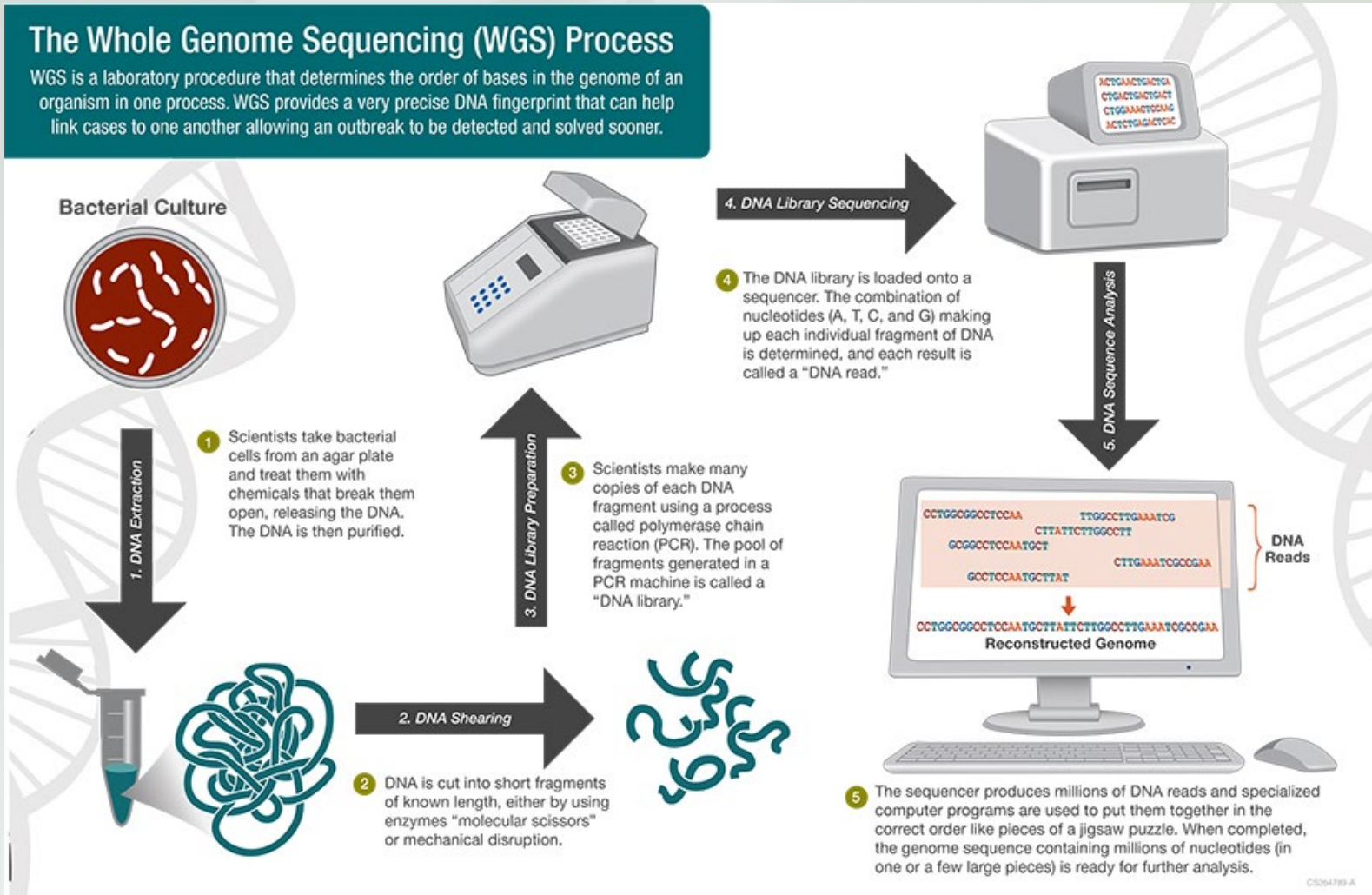


Unique features in different geographic locations likely select for different resistance phenotypes



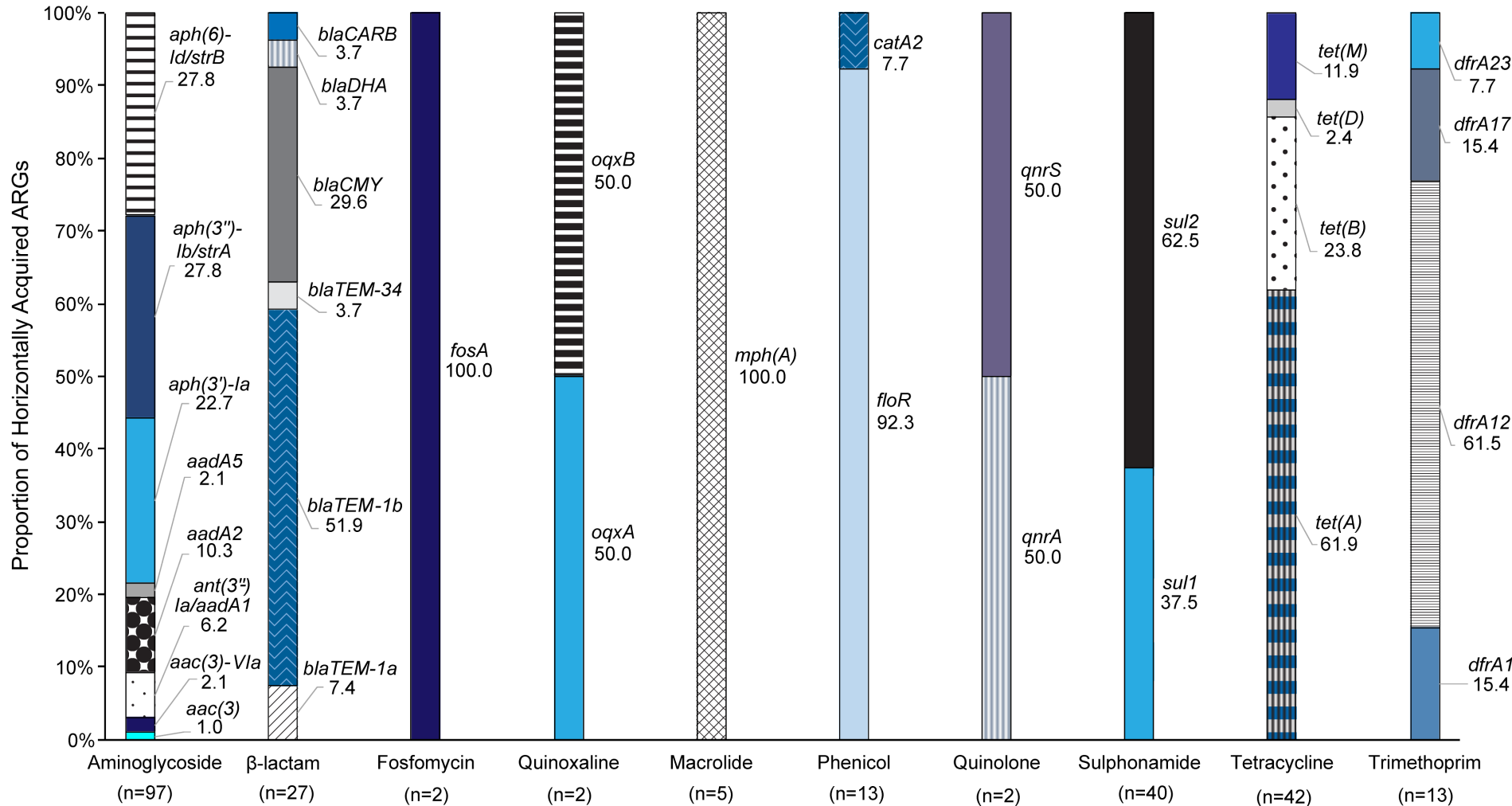
Detecting resistance genotypes

- Molecular methods can detect antibiotic resistance genes and gene variation



Used sequencing to identify resistance genes

- Examined 208 non-O157 genomes
 - Identified 33 unique horizontally acquired resistance genes

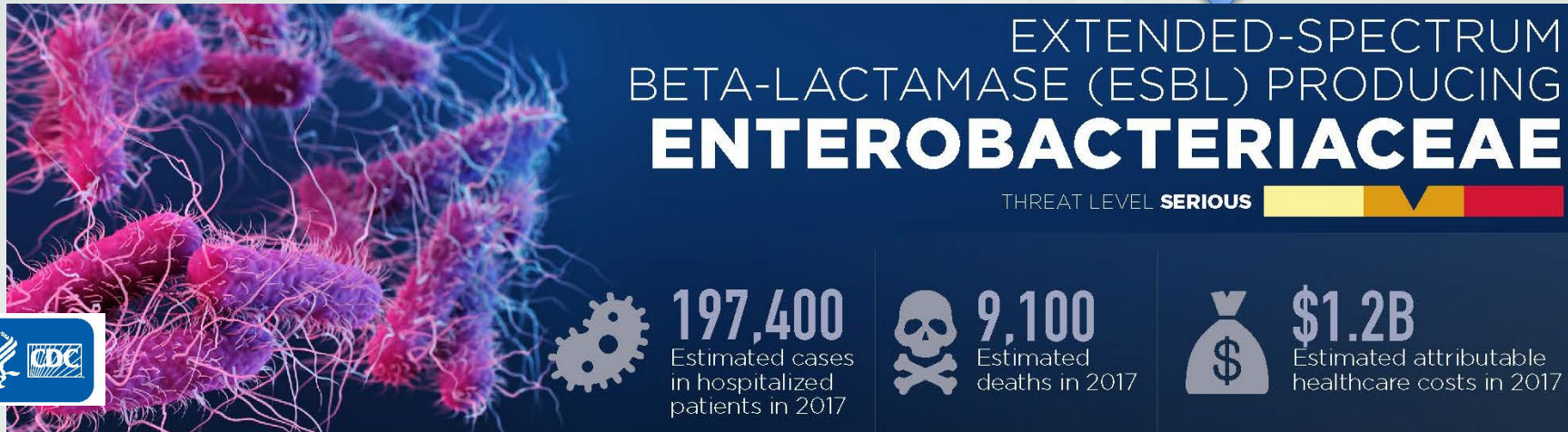
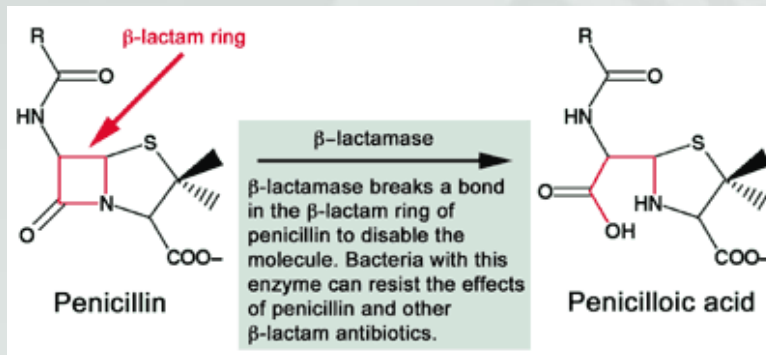


Why is resistance in STEC relevant?

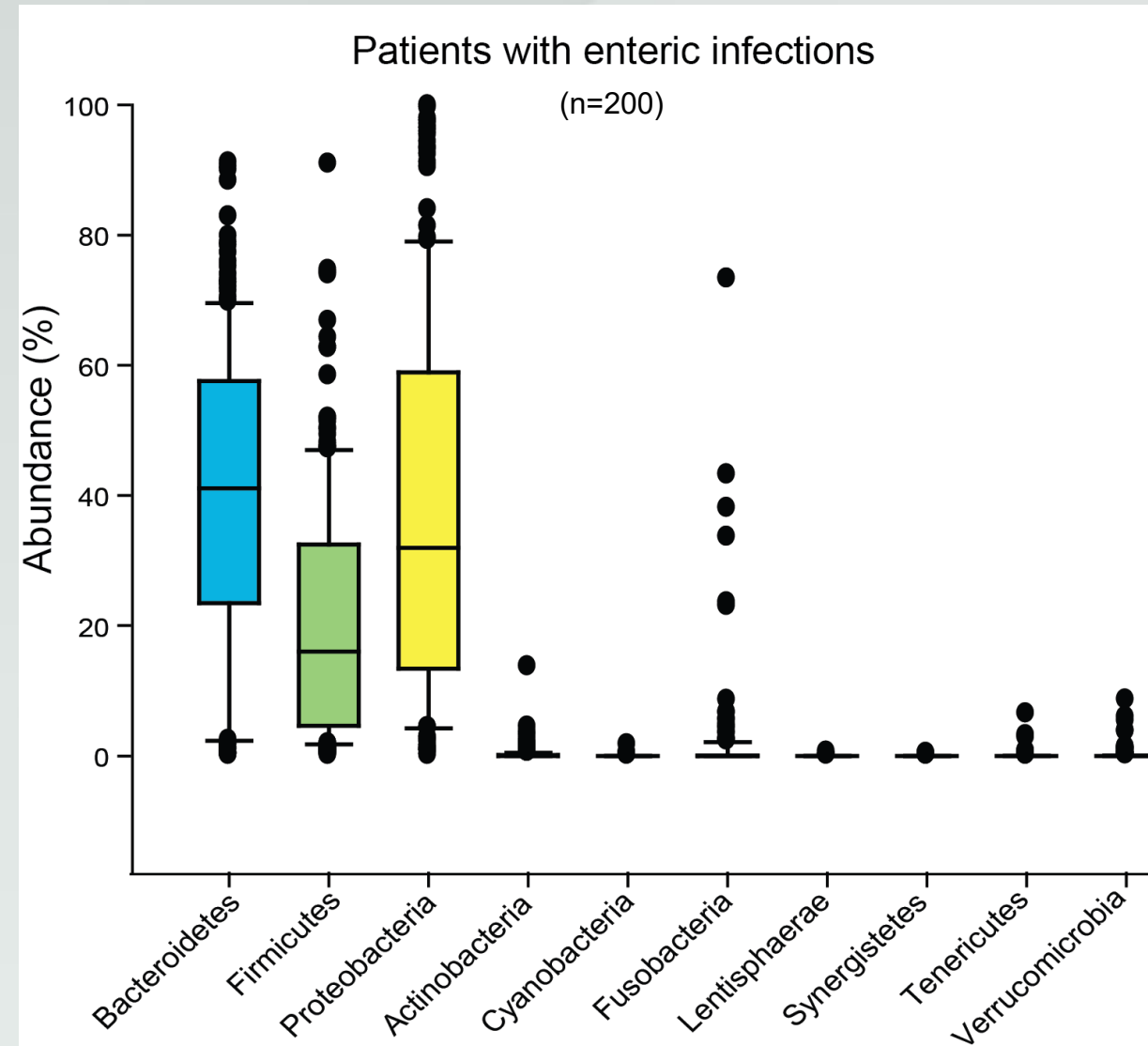
- The pathogens can bring genes into the gut microbiome
 - β -lactamase genes were detected that could be transferred to *E. coli*



Emergence of extended spectrum β -lactamase-producing Enterobacteriaceae (now Enterobacterales)



Expansion of Enterobacterales occurs during foodborne bacterial infection

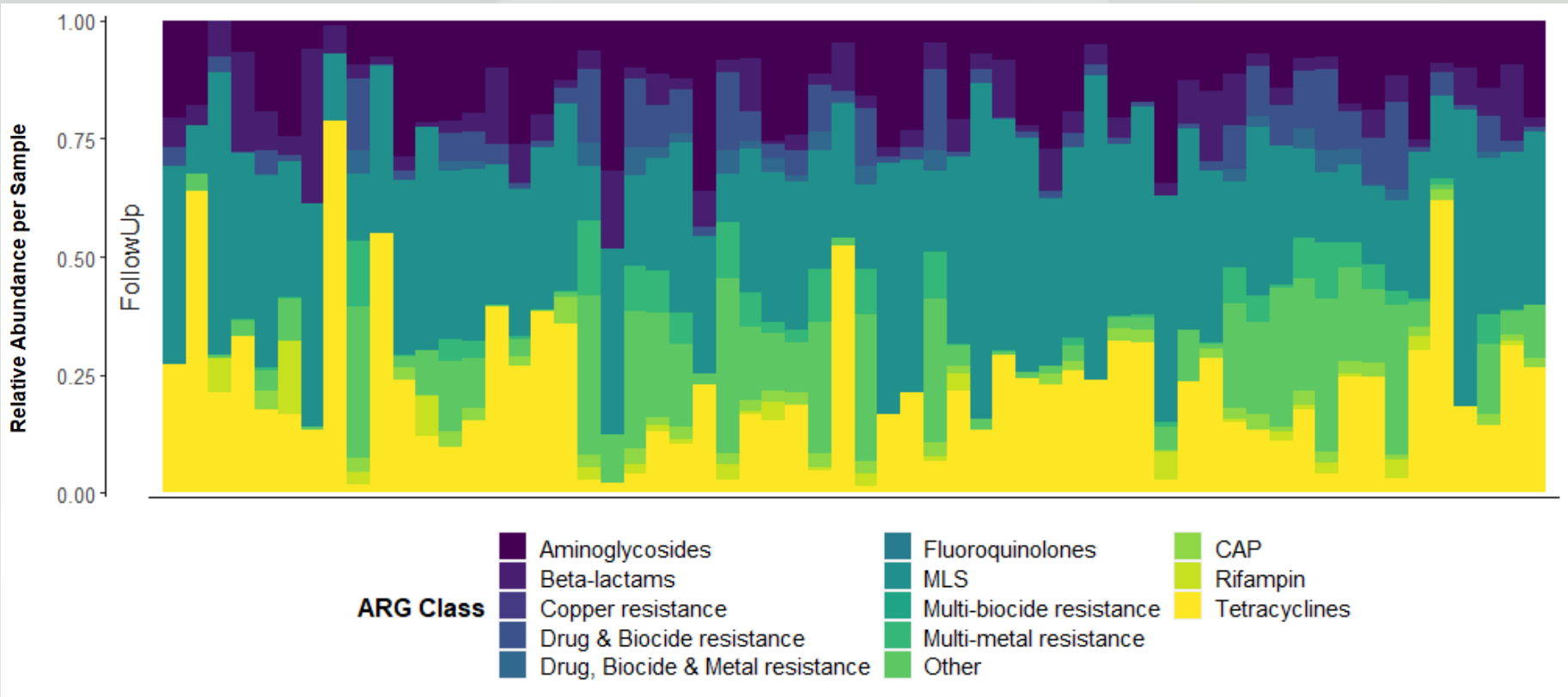


Patients had a greater abundance of Proteobacteria than healthy family members

Singh et al. Microbiome 2015



β -lactamase genes persist in the gut following recovery from infection



β -lactamase genes persisted in the gut microbiome of dairy cattle given antibiotics to prevent mastitis



Zoe Hansen

Summary

- Antibiotic resistance is a global concern
 - Resistant foodborne pathogens have emerged because of the ease of transfer of resistance genes and selection by antibiotics
- Surveillance is critical for monitoring new pathogen traits such as virulence and resistance
 - In Michigan, the STEC population has diversified, and antibiotic resistance frequencies have increased
- Persistence of resistance genes in the gut microbiome can lead to the emergence of new resistant opportunistic pathogens

Combating foodborne infections and antimicrobial resistance requires a One Health approach

One Health



People who protect human, animal, and environmental health, and other partners

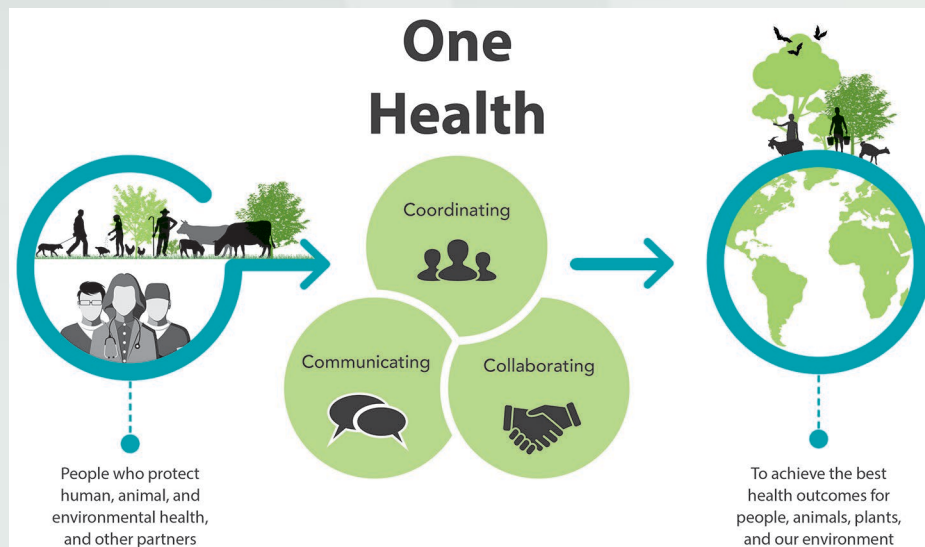


Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

To achieve the best health outcomes for people, animals, plants, and our environment

Possible solutions

- Enhanced surveillance
- Improved education and awareness
- Judicious use to prevent selection and spread
- Limit use of specific antibiotics that are critically important in human health



Centers for Disease
Control and Prevention
National Center for Emerging and
Zoonotic Infectious Diseases

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