ANTIMICROBIAL STEWARDSHIP IN GERIATRIC POPULATIONS

Kerry L. LaPlante, Pharm.D., FCCP, FIDSA, FIDP

Professor and Chairperson, Department of Pharmacy Practice
University of Rhode Island, College of Pharmacy

Adjunct Professor of Medicine,
The Warren Alpert Medical School of Brown University

Senior Director of the Rhode Island Infectious Diseases Research (RIID) Program
Co-Director of Antimicrobial Stewardship Program, and Infectious Diseases
Pharmacotherapy Specialist, Providence Veterans Medical Center

@Kerry_LaPlante

Disclosures

- Speaker Bureaus: None

- Grant Investigator: Merck, Pfizer, Shionogi,

- The information disseminated in this lecture is given in my personal capacity and not in my capacity as a VA employee nor does it necessarily reflect the views of the United States Department of Veterans Affairs or the Rhode Island Department of Health

This presentation <u>will not</u> include a discussion of unapproved or investigational uses of products or devices.
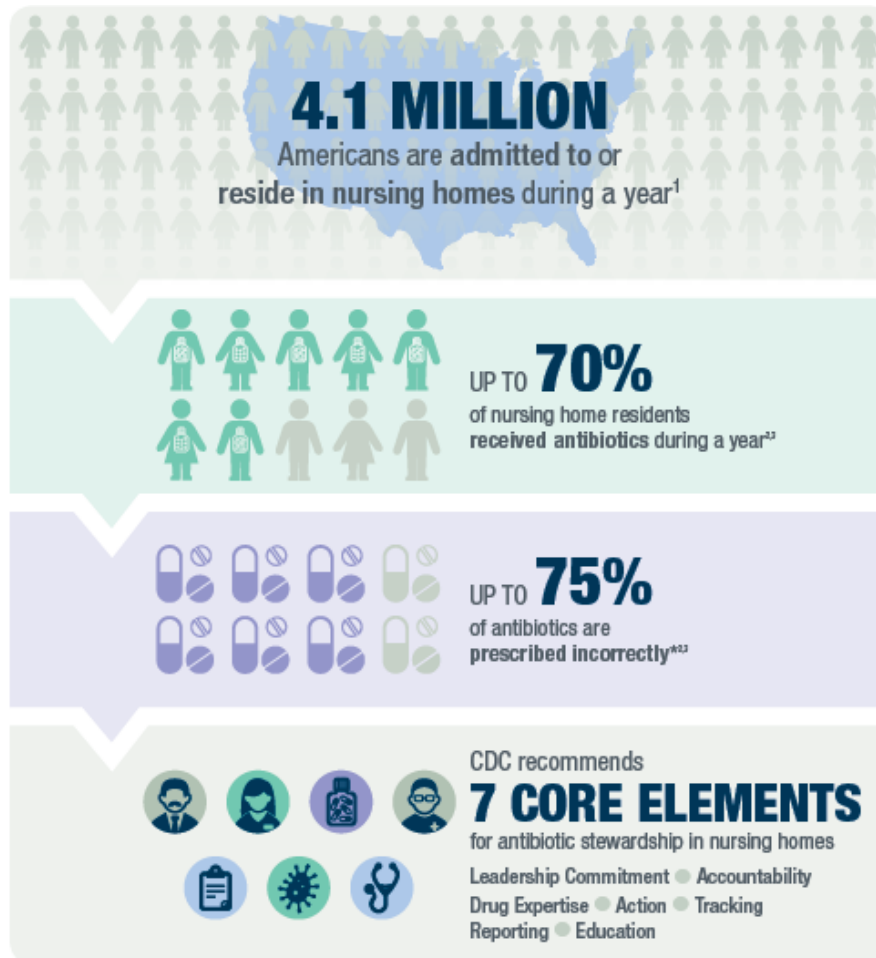
LEARNING OBJECTIVES

At the end of this session, the learner will be able to:

1. Describe the challenges related to the appropriate diagnosis of infections in older adults

2. Discuss optimal antimicrobial therapies for older adults based on pharmacokinetic and safety profiles

3. Demonstrate effective strategies to improve stewardship in older adults, including nursing homes
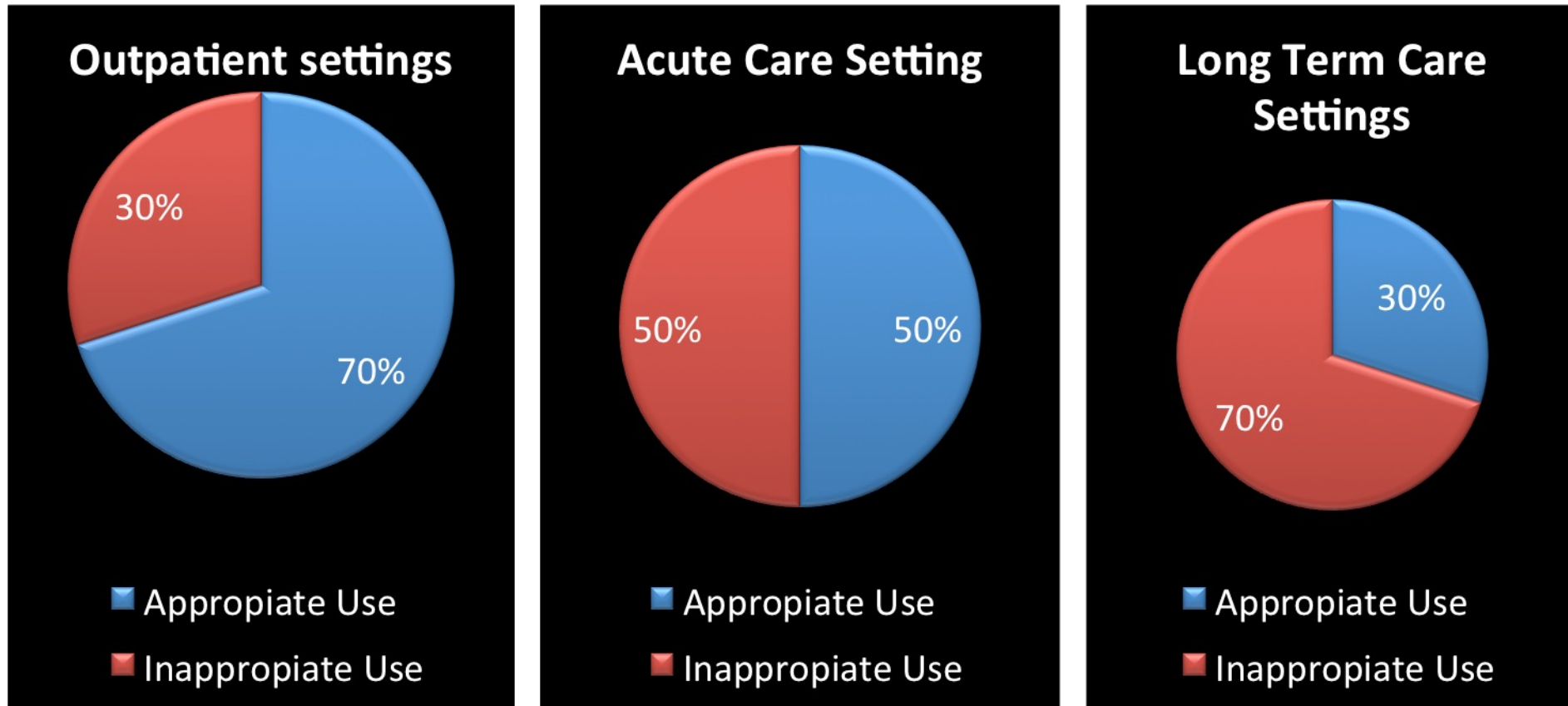
A Case Study

Overuse of Antibiotics in Nursing Homes

4.1 MILLION Americans are admitted to or reside in nursing homes during a year[1]

UP TO **70%** of nursing home residents received antibiotics during a year[2,3]

UP TO **75%** of antibiotics are prescribed incorrectly*[2,3]

CDC recommends **7 CORE ELEMENTS** for antibiotic stewardship in nursing homes

Leadership Commitment • Accountability
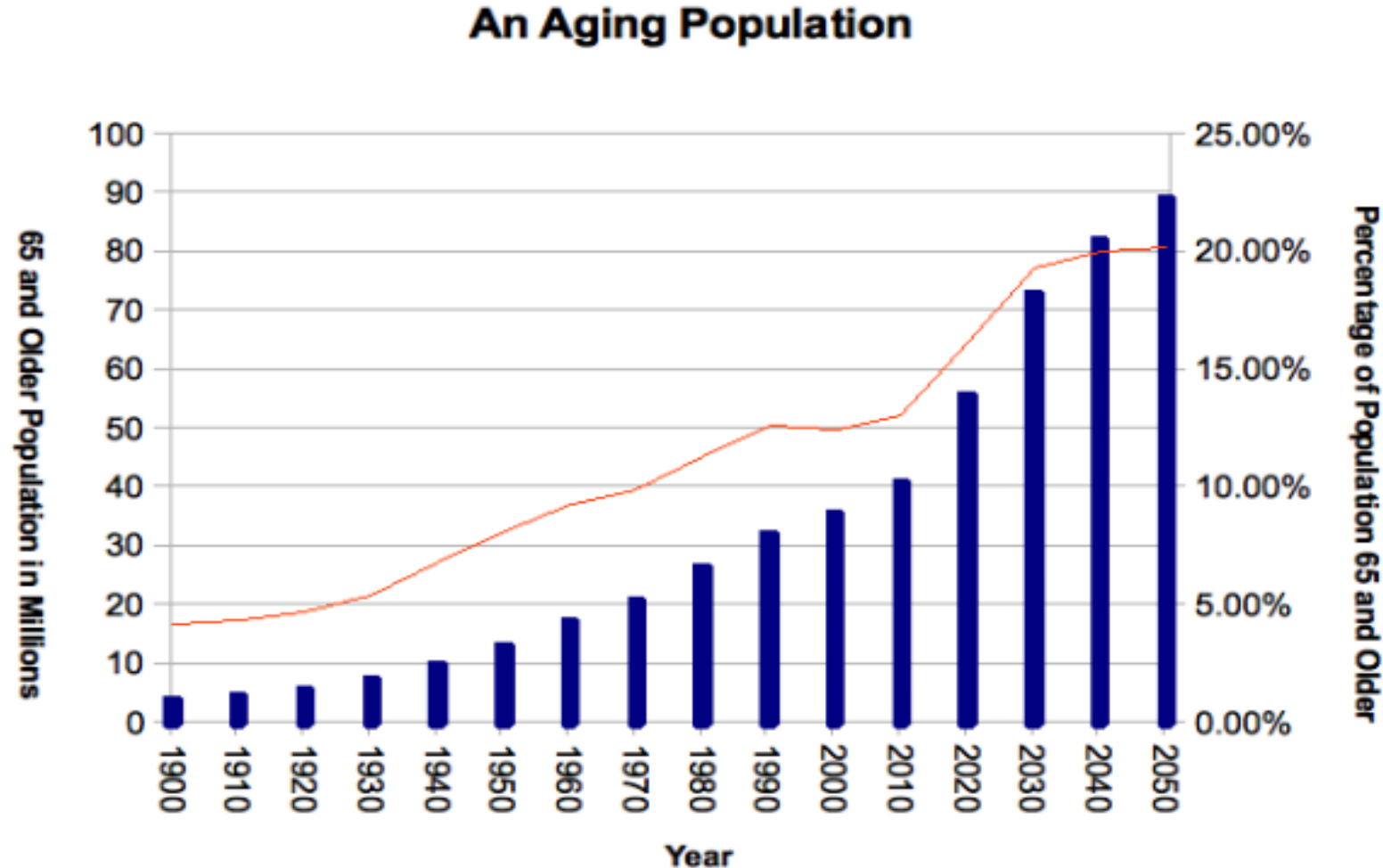Drug Expertise • Action • Tracking
Reporting • Education

- Antibiotics are some of the most commonly prescribed medications in nursing homes. Over the course of a year, up to 70% of nursing home residents get an antibiotic.

- Roughly 40% to 75% of antibiotics are prescribed incorrectly.

- In nursing homes, high rates of antibiotics are prescribed to prevent urinary tract infection (UTI) and respiratory tract infection (RTI). Prescribing antibiotics before there is an infection often contributes to misuse.

- Often residents are given antibiotics just because they are colonized with bacteria that are not making the person sick. Prescribing antibiotics for colonization contributes to antibiotic overuse.

Nursing Homes are encouraged to start with one or two of the Core elements and gradually add more activities over time

"Core Elements of Antibiotic Stewardship." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 7 Apr. 2021, https://www.cdc.gov/antibiotic-use/core-elements/index.html.

Antimicrobial "Misuse"

Fridkin S, et al. Morbidity and Mortality Weekly Report. United States Center for Disease Control and Prevention. 2014; 63(09):194-200. and http://www.cdc.gov Data accessed: August 2016

The United States is Aging

An Aging Population

The New York Times

BREAKING NEWS

Life expectancy in the U.S. fell precipitously in 2020 and 2021, the sharpest two-year decline in nearly 100 years, largely because of Covid.
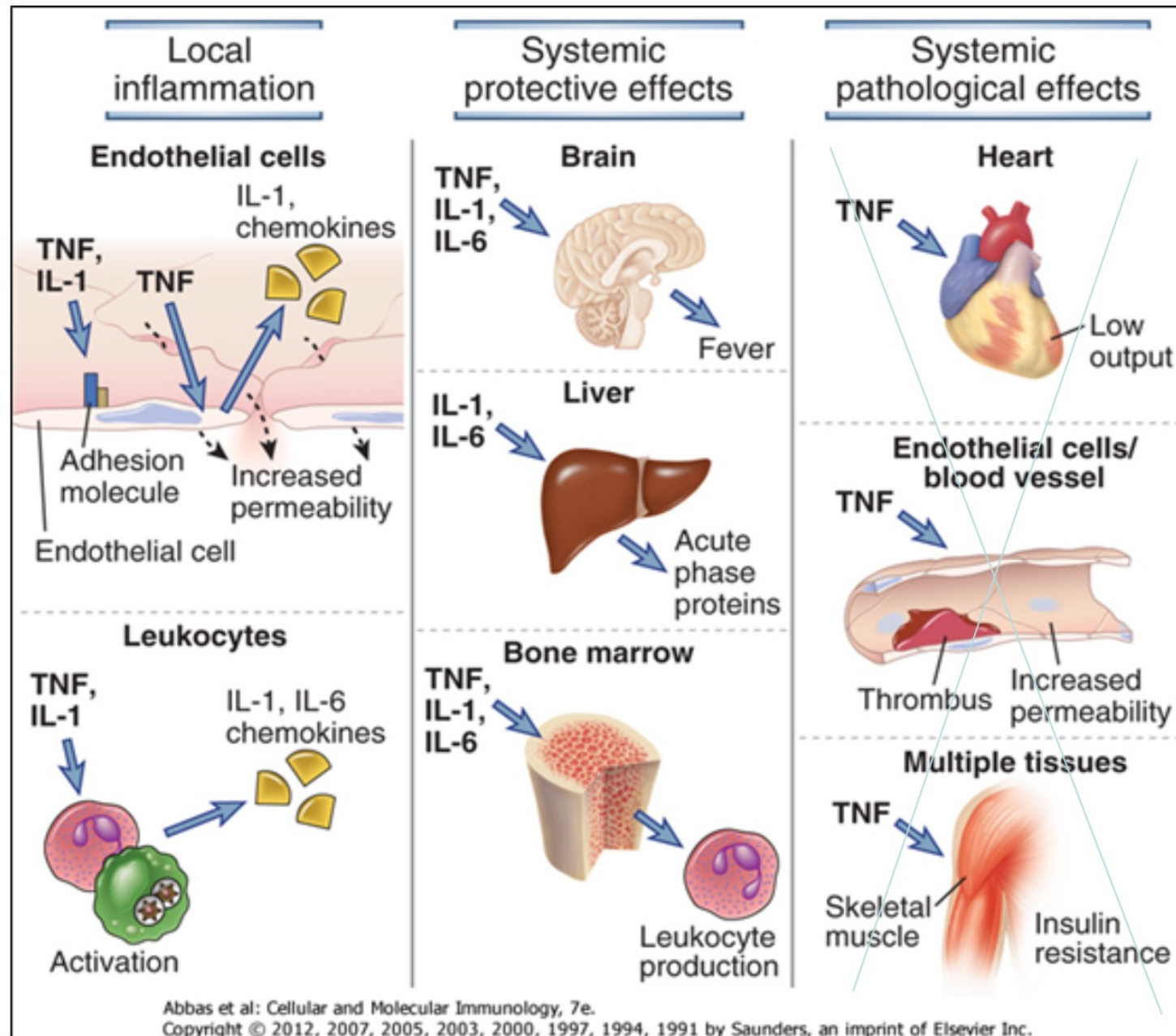
Wednesday, August 31, 2022 6:10 AM ET

In 2021, the average American could expect to live until the age of 76, federal health researchers reported. The figure represents a loss of almost three years since 2019.

[Read the latest](#)

Infections in the elderly

- Fever is absent or blunted 20%–30% of the time

- Diminished thermoregulatory responses, such as sudomotor and vasomotor responses

- Abnormalities in the production of and response to endogenous pyrogens such as IL-1, IL-6, and TNF

Local inflammation	Systemic protective effects	Systemic pathological effects

Local inflammation

Endothelial cells

TNF, IL-1

TNF

IL-1, chemokines

Adhesion molecule

Increased permeability

Endothelial cell

Leukocytes

TNF, IL-1

IL-1, IL-6 chemokines

Activation

Systemic protective effects

Brain

TNF, IL-1, IL-6

Fever

Liver

IL-1, IL-6

Acute phase proteins

Bone marrow

TNF, IL-1, IL-6

Leukocyte production

Systemic pathological effects

Heart

TNF

Low output

Endothelial cells/ blood vessel

TNF

Thrombus

Increased permeability

Multiple tissues

TNF

Skeletal muscle

Insulin resistance

Biologic Change With Age	Clinical Consequence
Reduced IL-2	Reduced T-cell help and symptoms
Reduced T-cell help	Reduced vaccine response (both antibody avidity and quantity)
Reduced IL-6, IFN-a response	Reduced fever
Reduced TNF-a	Reduced malaise and anorexia
Delayed increase and decline in inflammatory cytokines	Delayed symptom onset and resolution; prolonged prothrombotic state
Prothrombotic state	Increased risk from thrombotic outcomes (MI, CVA, etc.)
Increased IL-6 and 8 baseline	Increased delirium from cytokines

Also….chemokine levels elevated in subjects who developed delirium in the early postoperative period.

- chemokines are capable of disrupting blood-brain barrier integrity hence causing delirium

Evolution of the immune system in humans from infancy to old age
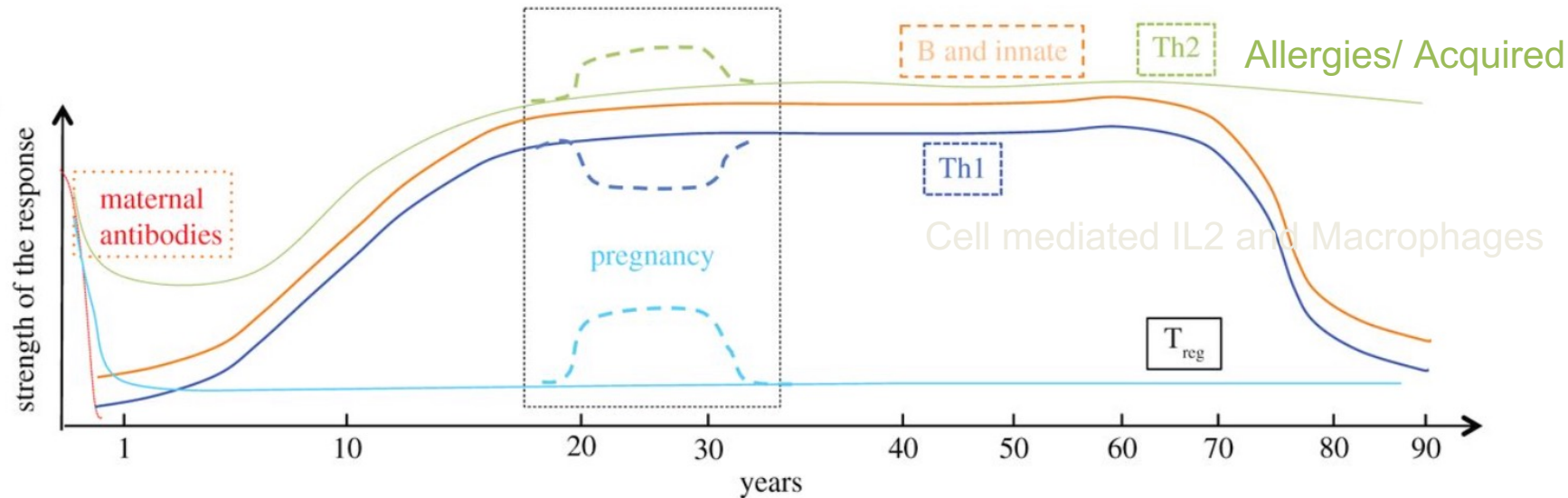
- **Innate immunity:** early first line of defense against invading pathogens (i.e., neutrophils, monocytes, macrophages, etc , which all interact with the adaptive immune system. (cytokine driven, generic in recognition and short lived)

- **Humoral / Acquired Immunity (more complex & memory): Specific T-cell responses hold microbes in check and B cells (memory and APC) If immunity is impaired through ageing, immunosuppressive therapy, infections, HIV-1 cancers and infections emerge**

Simon AK, Hollander GA, McMichael A. 2015 Proc. R. Soc. B

What defines a fever in older adults?

Fever	Or….	Source/Author
Persistent oral or TM: 99°F (≥37.2°C)	**Rectal**: Persistent temperature ≥37.5°C (99.5°F) **Increase**: over baseline temperature ≥1.3°C (2°F), independent of site measured or device used	Norman DC, et al Infect Dis Clin North Am. (1996) Norman DC. Clin Infect Dis (2000)
Fever (>37.9 C [100.2 F]	or a 1.5°C [2.4°F] increase above baseline temperature)	Lobe M, ICHE 2001
A single oral temperature >100°F (37.8°C) Repeated oral temperatures >99°F (37.2°C)	**Rectal** temperatures greater than 99.5°F (37.5°C) **Increase** in single temperature greater than 2°F (1.1°C) over baseline from any site.	High KP, IDSA 2008 Update **And** McGeer Criteria 2012 Update

Accuracy in taking temperature

Site	Comments
Rectal	• Gold Standard – most predictive of infection in elderly • Positively correlated with fever in 86% of pts vs. 66% by sublingual and 32% by axillary • Impractical in debilitated patients • Lack of cooperation
Oral (sublingual)	• Oral and axillary temperatures tended to be lower (0.66°C and 0.88°C, respectively) than rectal • Difficult in residents with disturbed behaviors of patients with dementia • Presence of tongue tremors, mouth-breathing, variations in the rate & depth of respiratory patterns, • Ingestion of hot and cold fluids
Tympanic membrane (TM) (infrared)	• Increased the popularity, Easier to obtain • Equivalent to or better than oral temperatures in correlating with rectal temperatures in a nursing home population. • High positive correlation between rectal and TM temperatures. • **Cerumen occlusion lowers infrared temperature measurement.**

Norman DC. Clin Infect Dis (2000) 31 (1): 148-151
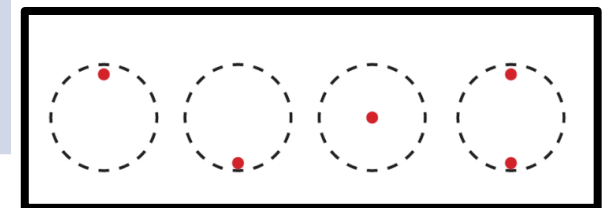
WHY are there mental status changes in older adults?

- Delirium versus Dementia

- UTI-induced delirium

- Dehydration

Characteristic	Delirium	Dementia
Onset	Rapid over a period of hours or days	Gradual over months and years
Course	Waxing and waning	Stable
Inattention	Present	* Absent
Altered of level of consciousness	Usually present	* Typically absent
Disorganized thinking present	May be present	* Typically absent
Sleep-wake cycle disturbance	Present	* Typically absent
Perceptual disturbances and hallucinations	May be present	* Typically absent
Is cognitive decline reversible?	Usually reversible	Rarely reversible

Pharmacokinetics in Aging

Absorption

- Reduce GI motility & blood flow
- Inc or dec. gastric acid secretion (reduced drug absorption), whereas reduced GI motility may result in more of the drug(s) being absorbed.
- Antacids and overuse of PPIs
- First-pass metabolism also may be increased

Distribution

- Muscle mass declines and the proportion of body fat increases

Metabolism

- ADR that requires hospitalization is approximately 10.7% for elderly patients as compared with 5.3% for the general population

Excretion

- T1/2 of drugs increases as renal function is reduced.
- Renal function declines – dec. in blood flow, dec. kidney mass, & dec. in the size and number of functioning nephrons.
- Renal changes are predictable (unlike liver)

Polypharmacy (and Adherence) in Ageing

- **Polypharmacy**: the number of medications (eg, using a large number of different medications prescribed by different providers), the necessity of the medications that are prescribed, or the complexity of a patient's problems
- One national survey showed that 50% of community-dwelling people older than 65 years use five or more prescription and over-the-counter medications per week, and 12% use ≥ 10.
- ADR that requires hospitalization is approximately 10.7% for elderly patients as compared with 5.3% for the general population

Drug	Adverse effect
Nonsteroidal anti-inflammatory drugs (eg, ibuprofen, naproxen)	Gastrointestinal bleeding, renal dysfunction
Diuretics (eg, hydrochlorothiazide, furosemide)	Hypotension, dehydration, electrolyte disturbance
Warfarin	Bleeding, many drug interactions
Angiotensin-converting enzyme inhibitors (eg, lisinopril)	Hypotension, renal dysfunction
Antidepressants (eg, amitriptyline)	Confusion, hypotension, constipation
Opiates (eg, morphine)	Confusion, disorientation, constipation
Prednisone	Osteoporosis, gastrointestinal problems, hyperglycemia
Benzodiazepines (eg, lorazepam)	Drowsiness, confusion

TREATMENT

Urinary tract infections: Most commonly treated infection in older adults

- Occurs in both community on long-term care settings
- Up to 40% of UTIs diagnosed in hospitalized older adults were diagnosed incorrectly
- Diagnosis often made without a clinical history and signs leading to over-diagnosis
- Accurate diagnosis of UTI and use of appropriate antibiotics can prevent:
  - *Clostridium difficile*, Gastroenteritis/diarrhea
  - Antibiotic resistant organisms
  - General medication adverse events
  - Antibiotic allergy

Asymptomatic bacteriuria (ASB) in Elderly

|	
Asymptomatic bacteriuria (ASB):	Dx based on cx of a urine specimen collected in a manner that minimizes contamination (A-II). Aacteriuria is define as clean catch voided urine in quantitative counts 10^5cfu/mL: •**Women**: Two consecutive isolation of the same bacterial strain •**Men**: A single specimen with 1 bacterial species isolated •Pyuria accompanying asymptomatic bacteriuria is NOT an indication to Tx w Abs.
Highest Risks (but do not screen)	• Premenopausal, nonpregnant women • Diabetic women • Elderly, institutionalized subject
Controversy	To treat ASB w antibiotics (when non- pregnant)?
	Nine studies, 1614 participants **Outcomes:** •Symptomatic UTI (RR 1.11, 95% CI 0.51 to 2.43) •Complications (RR 0.78, 95% CI 0. 35 to 1.74) •Mortality (RR 0.99, 95% CI 0.70 to 1.41) **Antibiotics were more effective for:** •Bacteriological cure (RR 2.67, 95% CI 1.85 to 3.85) •Adverse events (RR 3.77, 95% CI 1.40 to 10.15)
	Antibiotics were superior to no treatment for the bacteriological cure but with significantly more adverse events

Zalmanovici Trestioreanu A, Lador A, Sauerbrun-Cutler MT, Leibovici L. Antibiotics for asymptomatic bacteriuria. Cochrane Database of Systematic Reviews 2015
Hooton T, IDSA Guidelines for Diagnosis and Treatment of Asymptomatic Bacteriuria in Adults. CID 2005;40:643-54

Which guidance do we use?

- Many Consensus guidelines / recommendations to facilitate decisions on empiric antibiotics but no Gold Standard
  - Loeb Criteria (1991)- General
  - McGeer criteria (1991, 2012 update)
  - Society of Healthcare Epidemiology of America (SHEA/CDC) Criteria
  - IDSA Criteria for infection - Residents in LTCF

No Symptoms = **No Antibiotics**
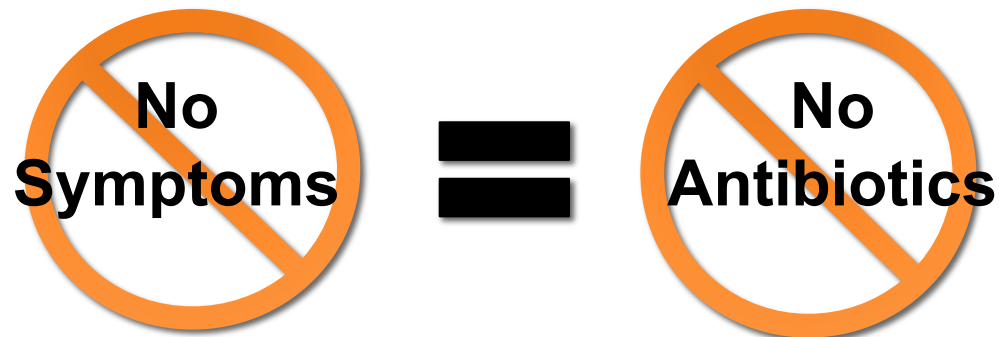
McGeer Criteria – Surveillance 1991

- Three of the following criteria:
  - Fever ≥ 37.8◦C (oral)
  - New or increased burning, pain on urination, frequency or urgency
  - New flank or suprapubic pain or tenderness
  - Change in character of urine (e.g. foul smell, bloody urine, increased sediment)
  - Worsening mental or functional status

- Surveillance
- Never validated
- Low frequency of urinary symptoms—particularly in those with dementia who comprise the majority of NH patients.
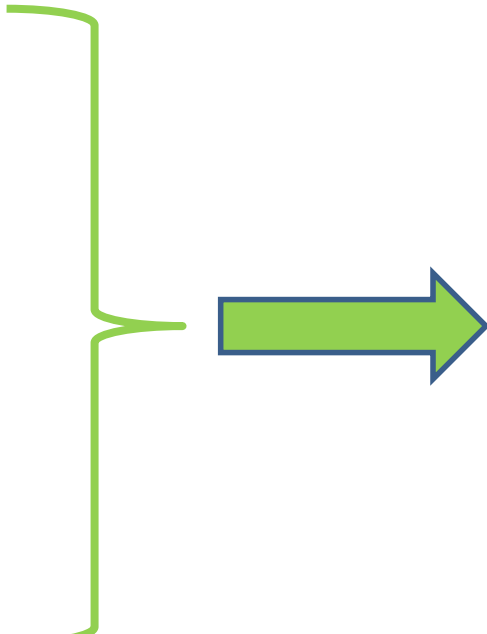
McGeer A, Campbell B, Emori TG, et al. Definitions of infection surveillance in long-term care facilities. Am J Infect Control. 1991;19:1–7

Loeb Criteria Development of Minimum Criteria for the Initiation of Antibiotics in LTCF

- Acute dysuria alone or Fever (>37.9°C / 100°F) plus one of the following:
  - New or worsening urgency
  - Frequency
  - Suprapubic Pain
  - Gross hematuria
  - Costovertebral angle tenderness
  - Urinary Incontinence

- Practical and commonly accepted
- Low adherence to the Loeb criteria (0%–38.9%, mean 10.2%)
- 75% of residents who did not meet the minimum criteria for antibiotic initiation still received antibiotics
- Not particularly helpful clinically—particularly in NH
  - PPV ~57% for bacteruria plus pyuria

M. Lobe *Infect Control Hosp Epidemiol* 2001; 22:120-124

IDSA: Clinical practice guideline for the evaluation of fever and infection in older adult residents of LTCF: 2008

Non- Catheterized

- Acute onset of UTI Sx:
- Fever
- Dysuria
- Gross hematuria
- New or worsening urinary incontinence
- Suspected bacteremia (A-II)

→ Take clean catch Urine and send for a UA:
if Pyuria AND positive leucocyte esterase OR nitrate positive then C&S

UA and Ucx should not be performed for asymptomatic residents (A-1 recommendation)

High KP, Clinical practice guideline for the evaluation of fever and infection in older adult residents of LTCF: 2008 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009

SHEA/CDC 2012 criteria –
Criteria for Defining UTI Events in NHSN LTCF

Without indwelling catheter

- Swelling testis/epididymis/prostate or
- Fever/Leukocytosis plus one criteria:
  - Acute CVA tenderness
  - Suprapubic Pain
  - Gross Hematuria
  - New or increased incontinence
  - New urgency or frequency
- or Positive Urine Cx (10^5 CFU) plus 2 of above

Stone ND, et al. Surveillance definitions in long-term care facilities: Revisiting the McGeer criteria. *Infect Control Hosp Epidemiol* 2012;33(10):965-977.

Antibiotic Selection: Empiric

2010 International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women

- Beta-lactams (eg. cephalexin, amoxicillin, amoxicillin/ clavulanate) are not listed first-line since they require longer durations (outpatient compliance) slightly and may not always be susceptible (eg. amoxicillin)
  - In a LTCF setting compliance is not an issue and cultures are followed
  - **Cephalexin** susceptibilities in urine can be determined from antibiograms
    - Dose: 500 mg Q6hr; *CrCl <30 mL/min* →   500 mg BID x 5-7 days

- Fluoroquinolones (cipro preferred): option for patients who cannot take any previously mentioned antibiotics
  - Preserves the efficacy for these patients or for pyelonephritis
    - Dose: 500mg PO BID x 3 days

Gupta et al, CID 2011;52:e103-e120

Urinary Tract Infection (UTI) Pathway to Assist with Antibiotic Use for Sub-Acute Care, Long-Term Care & Nursing Home Facilities

START: Suspected UTI. What are the patient's symptoms?

STOP

Mental Status Changes (residents seems "off"), Foul Smelling Urine, *OR* Urine Color Changes (dark or cloudy)

Antibiotics and Urine Culture NOT INDICATED, further monitoring required

WAIT

Seek alternative causes changes (i.e. dehydration, medications, environmental changes, metabolic problems, bleeding, cardiovascular, stroke, etc.)

PLACE RESIDENT ON CLOSE MONITORING PROTOCOL
Provide increased fluid intake (unless contraindicated)
Monitor & document input / output and vital signs every shift for next 24 hours.

GO

Acute Dysuria (pain or discomfort when urinating) *OR*
FEVER (single temp. >100°F (37.8°C) or repeated temps >99°F (37.2°C) or
Increase in single temperature greater than 2°F (1.1°C) over baseline

AND

At least *ONE* of the following symptoms to indicate urine as source of infection: Urgency, frequency, subrapubic pain, gross hematuria, costovertebral angle tenderness, urinary incontinence

Take Clean Catch Urine (pre protocol) and send for culture and susceptibility

LaPlante KL

Average Susceptibilities of UTI Causing Organisms* Across 13 Long Term Care Facilities in Rhode Island

Medication	% Susceptibility
Ampicillin/Sulbactam	61%
Cefazolin	**81%**
Ciprofloxacin	49%
Ceftriaxone	**88%**
Ertapenem	100%
Cefepime	89%
Cefoxitin	93%
Gentamicin	81%
Imipenem	100%
Levofloxacin	50%
Nitrofurantoin	53%
Sulfamethoxazole/ Trimethoprim	62%
Ceftazidime	88%
Tobramycin	85%
Piperacillin/Tazobactam	92%
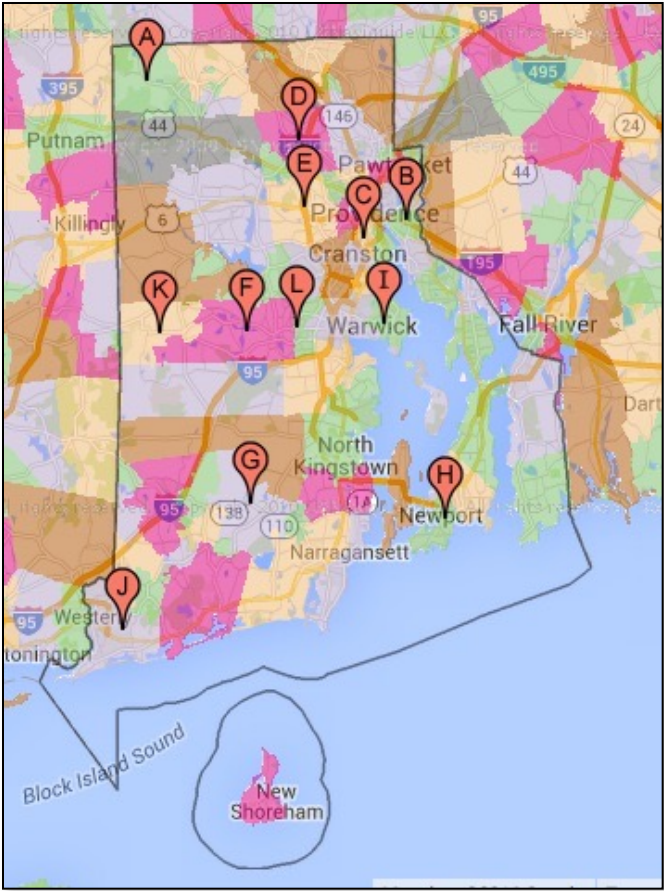
*Each letter denote the center of the zipcode

*Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Providencia spp. (n=513)

~ *Clostridium difficile* ~
Designated an **URGENT** Global Threat by the CDC

"**THREAT LEVEL URGENT**: immediate public health threat that requires urgent and aggressive action"

- ✓ **Spans all Health Care (ACF, LTCF, AmCF, Urgent Care)**
- ✓ **HAC (Costs 1% of CMS)**
- ✓ **Preventable (Patient Focused)**

CDC=Centers for Disease Control and Prevention.

CDC. Antibiotic resistance threats in the United States, 2013. ONLINE Sept 16, 2013. Available:
    http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf.
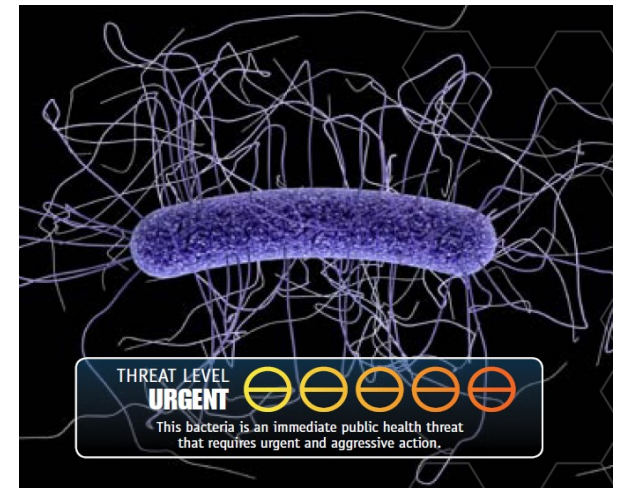
The CDC has designated *Clostridioides difficile* as an urgent global threat, calling it an "*immediate public health threat that requires urgent and aggressive action*."
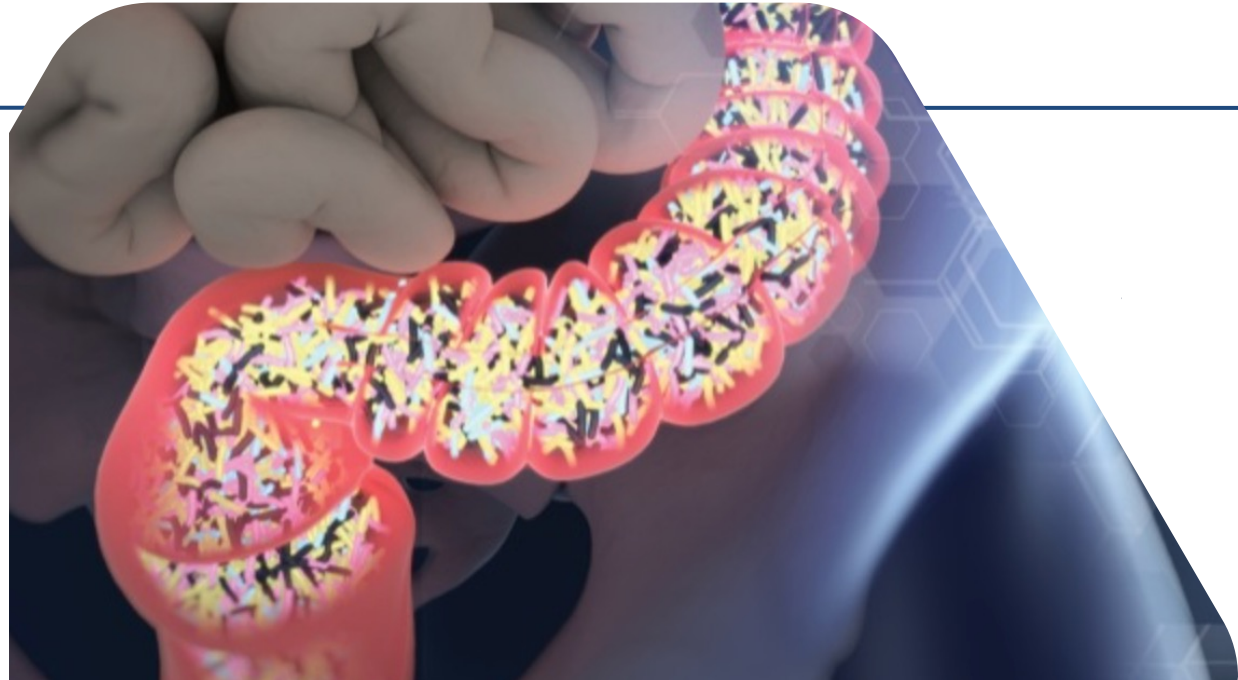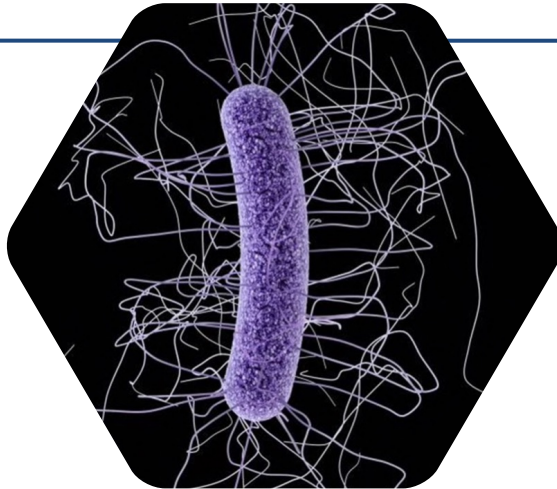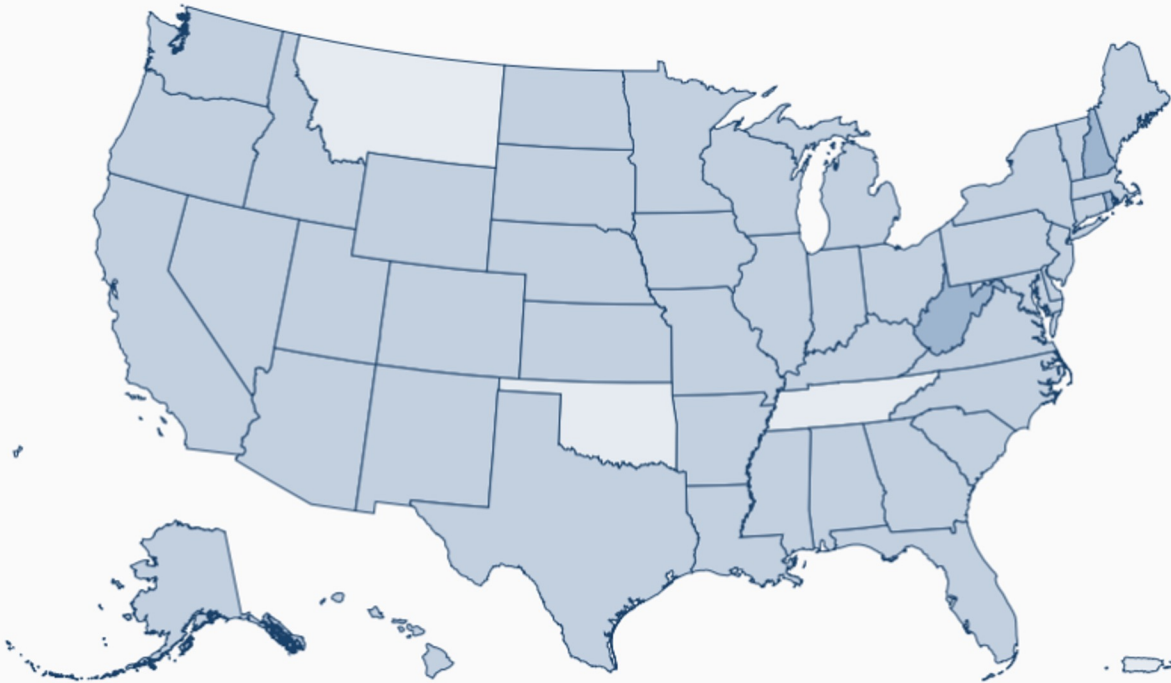
- *CDC. Antibiotic Resistance Threats in the United States, 2019.*
- *US Department of Health and Human Services, CDC; 2019.*
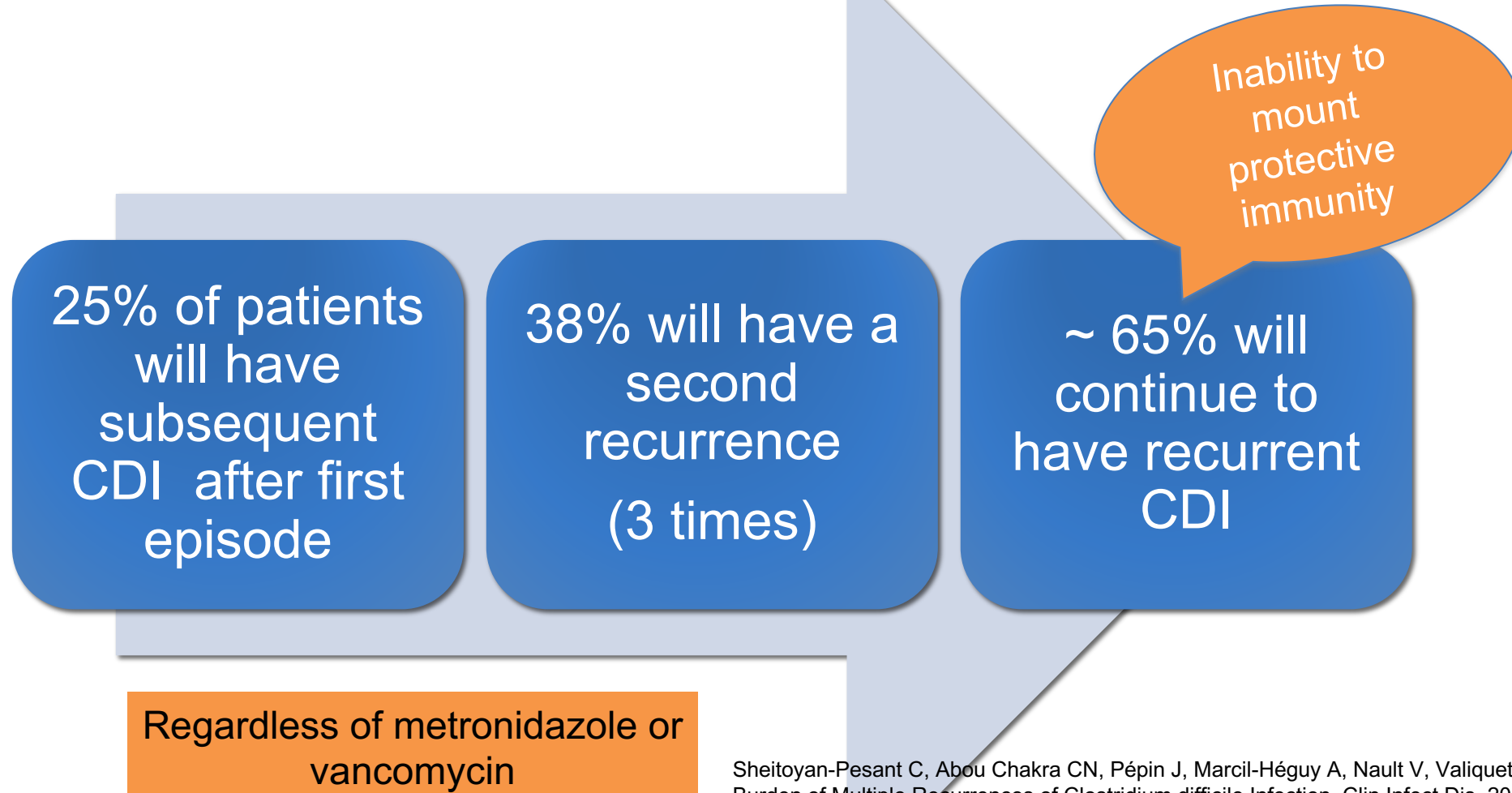
C. Difficile Standardized Infection Ratio (SIR), HNSN 2020

Five states with highest laboratory-diagnosed CDI cases, by SIR:
- New Hampshire: 0.82
- West Virginia: 0.75
- Rhode Island: 0.71
- North Dakota: 0.66
- Massachusetts: 0.66

Standardized Infection Ratio
☐ 0.00 - 0.49 ☐ 0.49 - 0.75 ☐ 0.75 - 0.96 ☐ 0.96 - 1.19 ☐ 1.20 - 1.56 ☐ 1.57+

The SIR for *C. difficile* infections across US, general acute-care hospitals in 2020 was **0.52**.

CDC. C. difficile Infections, 2020. Atlanta, GA: US Department of Health and Human Services, CDC; 2020.

Multiple Recurrent *C. Difficile* Infection

25% of patients will have subsequent CDI after first episode

38% will have a second recurrence (3 times)

~ 65% will continue to have recurrent CDI

Inability to mount protective immunity

Regardless of metronidazole or vancomycin

Aslam S, et al, Lancet Infectious Diseases 2005
McFarland LV et al, Am J Gastroenterol. 2002
McFarland LV et al, JAMA, 1994

Sheitoyan-Pesant C, Abou Chakra CN, Pépin J, Marcil-Héguy A, Nault V, Valiquette L. Clinical and Healthcare Burden of Multiple Recurrences of Clostridium difficile Infection. Clin Infect Dis. 2016 Mar 1;62(5):574-580. doi: 10.1093/cid/civ958. Epub 2015 Nov 17. PMID: 26582748.

Singh T, Bedi P, Bumrah K, Singh J, Rai M, Seelam S. Updates in Treatment of Recurrent *Clostridium difficile* Infection. J Clin Med Res. 2019 Jul;11(7):465-471. doi: 10.14740/jocmr3854. Epub 2019 Jun 11. PMID: 31236163; PMCID: PMC6575119.

Diarrhea Differential: Other Causes

- Antibiotics (10–20% of cases)

- Lactose intolerance

- Laxatives

- Traveler's diarrhea

- Pancreatic insufficiency

- Alcohol intoxication

- Irritable Bowel Syndrome (IBS)

- Inflammatory Bowel Disease (IBD)

- Celiac disease

- Other bacterial, viral, or parasitic infections and toxins (Norovirus, Shigella, Salmonella)

What symptoms make CDI less likely?
- No response to oral vancomycin
- Long duration of symptoms prior to testing/diagnosis
- Diarrhea that resolves in 24-48 hours

When to Suspect an Active CDI

- Acute onset diarrhea **(three or more loose stools in past 24 hours)**
  - No recent laxative or enema use
  - No recent lactulose, tube feedings, or IV contrast
  - Consider other causes of diarrhea based on the patient's clinical presentation.

- Risk Factors for CDI

- Signs and Symptoms
  - Elevated white blood cell count
  - Abdominal pain
  - Temperature higher than 38º C

- No recent history of a positive *C. diff* test result (see Colonization)

Risk Factors for *C. difficile*

65 or older
Antibiotic use in the past 60 days
Recent hospital or nursing home stay
Immunocompromised host (likely to be colonized)
Previous *C. difficile* infection (Most recurrences happen within two to four weeks of completing course of anti-CDI therapy.)

CDC. Your Risk of C. diff, 2021. Atlanta, GA: US Department of Health and Human Services, CDC; 2021.

Considerations for CDI Testing

Clinical Considerations

- Assess for appropriateness of testing: implement diagnostic stewardship program that is either staffed in real time or automated in the EHR

- Discontinue laxatives, wait at least 48 hours before testing if still symptomatic.

- Once a patient has a positive CDI test result, do not repeat testing to detect cure as tests may remain positive for six or more weeks.

Laboratory Considerations

- Implement laboratory procedures to ensure testing of only appropriate specimens (e.g., **unformed stool that take the shape of the container**) for *C. difficile* or its toxins.

- Report test results IMMEDIATELY to clinical care providers and infection control personnel through reliable means (e.g., a laboratory alert system).

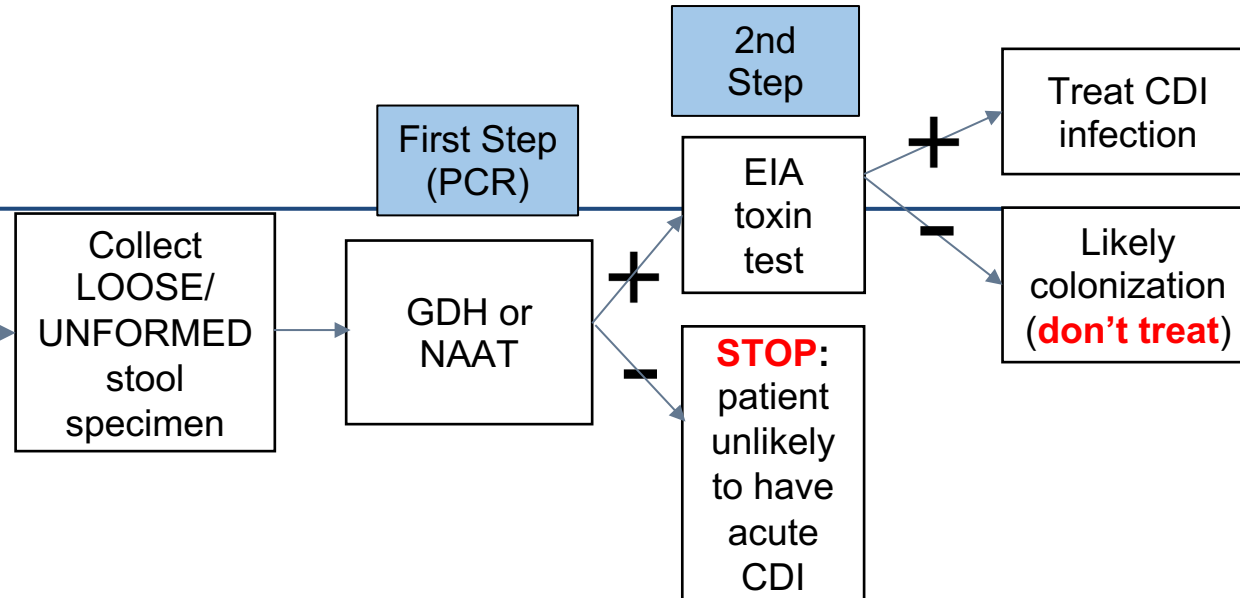# Statewide Strategy: Consider Two-Step Testing

Critical step in testing

Laboratory should report results one step at a time, but note "IN PROGRESS" once first step of test is complete.
See following slide for examples.

MUST have clinical suspicion for CDI
- Acute onset diarrhea (≥3 loose stools in past 24 hours)
- Risk factors for CDI (e.g., antibiotic use in past 60 days, hospitalization, advanced age)
- Signs &Symptoms: elevated WBC, abdominal pain, T > 38°C
- No recent history of a (+) *C. diff* test
- No recent laxative use

Place patient on Infection Control Precautions and start treatment.

Collect LOOSE/ UNFORMED stool specimen

First Step (PCR)

GDH or NAAT

+

2nd Step

EIA toxin test

−

STOP: patient unlikely to have acute CDI

+ Treat CDI infection

− Likely colonization (**don't treat**)

Complete two-step testing in 24 hours (Per CDC/NHSN)

Note: If PCR result is positive, put patient on infection control precautions.

AMSEC Suggested Approach

Sample lab results (Lifespan)

PCR

EIA

C Difficile Toxin PCR   **DETECTED** ❗

Comment: C. difficile toxin gene has been detected, refer to C. difficile toxin EIA for additional information,

Value: Not Detected

Comment: No free toxin detected. These results may suggest C. difficile colonization or the level of toxin is below the level of detection by EIA. The significance of these results must be interpreted in the context of the patient's clinical presentation, treat only if clinically indicated. Continue contact precautions.

Why are there two testing steps?
- PCR tests are specific for toxigenic strains but do not test for active toxin production. PCR tests cannot differentiate between actively infected and colonized patients, which may result in unnecessary treatment.
- The EIA toxin test detects the presence of free toxins in the body and, in combination with a positive PCR test, confirms an active CDI.
- No test can stand alone. Consideration of clinical judgment is important.

Clinical Definition	IDSA/SHEA Guidelines June 2021 (Strength of Recommendation/ Quality of Evidence)	ACG Guidelines May 2021 (Strength of Recommendation/ Quality of Evidence)
Initial episode, non-severe	Preferred: Fidaxomicin 200 mg orally twice daily for 10 days (Conditional/Moderate) Alternative: Vancomycin 125 mg orally four times daily for 10 days (Strong/High) Alternative if above regimen unavailable: Metronidazole 500 mg orally three times daily for 10-14 days (Weak/High)	Vancomycin 125 mg orally four times daily for 10 days (Strong/Low) OR Fidaxomicin 200 mg orally twice daily for 10 days (Strong/Moderate) OR Metronidazole for low-risk patients: 500 mg orally three times daily for 10 days (Strong/Moderate)

Clinical Definition	IDSA/SHEA Guidelines June 2021 (Strength of Recommendation/ Quality of Evidence)	ACG Guidelines May 2021 (Strength of Recommendation/Quality of Evidence)
Initial episode, severe	Preferred: Fidaxomicin 200 mg orally twice daily for 10 days (Conditional/Moderate) Alternative: Vancomycin 125 mg orally four times daily for 10 days (Strong/High)	Vancomycin 125 mg orally four times daily for 10 days (Strong/Low) OR Fidaxomicin 200 mg orally twice daily for 10 days (Conditional/Very Low) Note: Limited data in patients with fulminant CDI and life-threatening illness

Clinical Definition	IDSA/SHEA Guidelines June 2021 (Strength of Recommendation/Quality of Evidence)	ACG Guidelines May 2021 (Strength of Recommendation/Quality of Evidence)
First Recurrence	**Preferred: Fidaxomicin 200 mg orally twice daily for 10 days OR twice daily for 5 days followed by every other day for 20 days** *(Conditional/Moderate)* **Alternative: Vancomycin in a tapered and pulsed regimen OR if metronidazole was used for the initial episode: 125 mg orally four times daily for 10 days** *(Conditional/Low)*	**Vancomycin a tapered and pulsed regimen** after an initial course of fidaxomicin, vancomycin, or metronidazole *(Strong/Very Low)* OR **Fidaxomicin** after an initial course of vancomycin or metronidazole *(Conditional/Moderate)*
Second or Subsequent Recurrence	**Fidaxomicin 200 mg twice daily for 10 days, OR twice daily for 5 days, followed by once every other day for 20 days** *(Weak/Low)* OR **Vancomycin in a tapered and pulsed regimen** *(Weak/Low)* OR **Vancomycin** 125 mg orally four times daily for 10 days followed by **rifaximin** 400 mg three times daily for 20 days *(Weak/Low)* OR **FMT** if appropriate antibiotic treatment for 2 prior recurrences *(Conditional/Low)*	**FMT** to prevent further recurrences in patients experiencing their second or further recurrence *(Strong/Moderate)* **Vancomycin prophylaxis (Suggested dose: 125 mg orally daily) for patients who are not candidates for FMT or who relapsed after FMT** *(Conditional/Very Low)***, or who require ongoing or frequent courses of antibiotics** *(Conditional/Low)*

Clinical Definition	IDSA/SHEA Guidelines June 2021 *(Strength of Recommendation/ Quality of Evidence)*	ACG Guidelines May 2021 *(Strength of Recommendation/ Quality of Evidence)*
Fulminant CDI	**Vancomycin** 500 mg orally or by nasogastric tube four times daily (***Strong/Moderate***) **Consider adding rectal vancomycin** 500 mg four times daily if ileus present (***Weak/Low***) **Consider adding metronidazole** 500 mg IV every 8 hours, particularly if ileus is present (***Strong/Moderate***)	**Adequate volume resuscitation** **AND** **Vancomycin** 500 mg orally every 6 hours for the first 48-72 hours *(Strong/Very Low)* **Consider adding rectal vancomycin** 500 mg every 6 hours if ileus present *(Conditional/Very Low)* **Consider adding metronidazole** 500 mg IV every 8 hours, **particularly in cases of paralytic ileus** *(Conditional/Very Low)* **FMT for patients refractory to antibiotics, particularly if poor surgical candidates**

| Clinical Definition	IDSA/SHEA Guidelines June 2021 *(Strength of Recommendation/ Quality of Evidence)*	ACG Guidelines May 2021 *(Strength of Recommendation/ Quality of Evidence)*
Use of Bezlotoxumab for prevention of CDI recurrence Dose: 10 mg/kg IV once during administration of standard of care antibiotics	Recommended in patients with **CDI recurrence within the last 6 months** (*Conditional/Very Low*) **In settings where logistics are not an issue, patients with primary CDI and risk factors for CDI recurrence (age ≥ 65 years, immunocompromised, severe CDI) may benefit.** *Data in combination with idaxomicin are limited.* *Caution for use in patients with congestive heart failure.*	**Recommended in patients age 65 or older <u>and</u> with at least one risk factor of recurrence:** · Severe CDI · Second CDI episode within past 6 months · Immunocompromised (*Conditional/Moderate*) *Caution in patients with a history of heart failure or severe underlying cardiovascular comorbidities.*

Probiotics

- **Proposed Mechanism:** colonization/normalization of intestinal microbiota, competitive exclusion of pathogens, immune and metabolic modulation

- Although high-quality evidence is lacking, the idea of probiotics is appealing to patients. As dietary supplements, probiotics are not strictly regulated by the FDA.

- **ACG Guidelines:** Recommend **AGAINST** the use of probiotics for both primary and secondary prevention of CDI.
  - Primary Prevention: *Conditional recommendation against use, moderate quality of evidence*
  - Secondary Prevention: *Strong recommendation against use, very low quality of evidence*
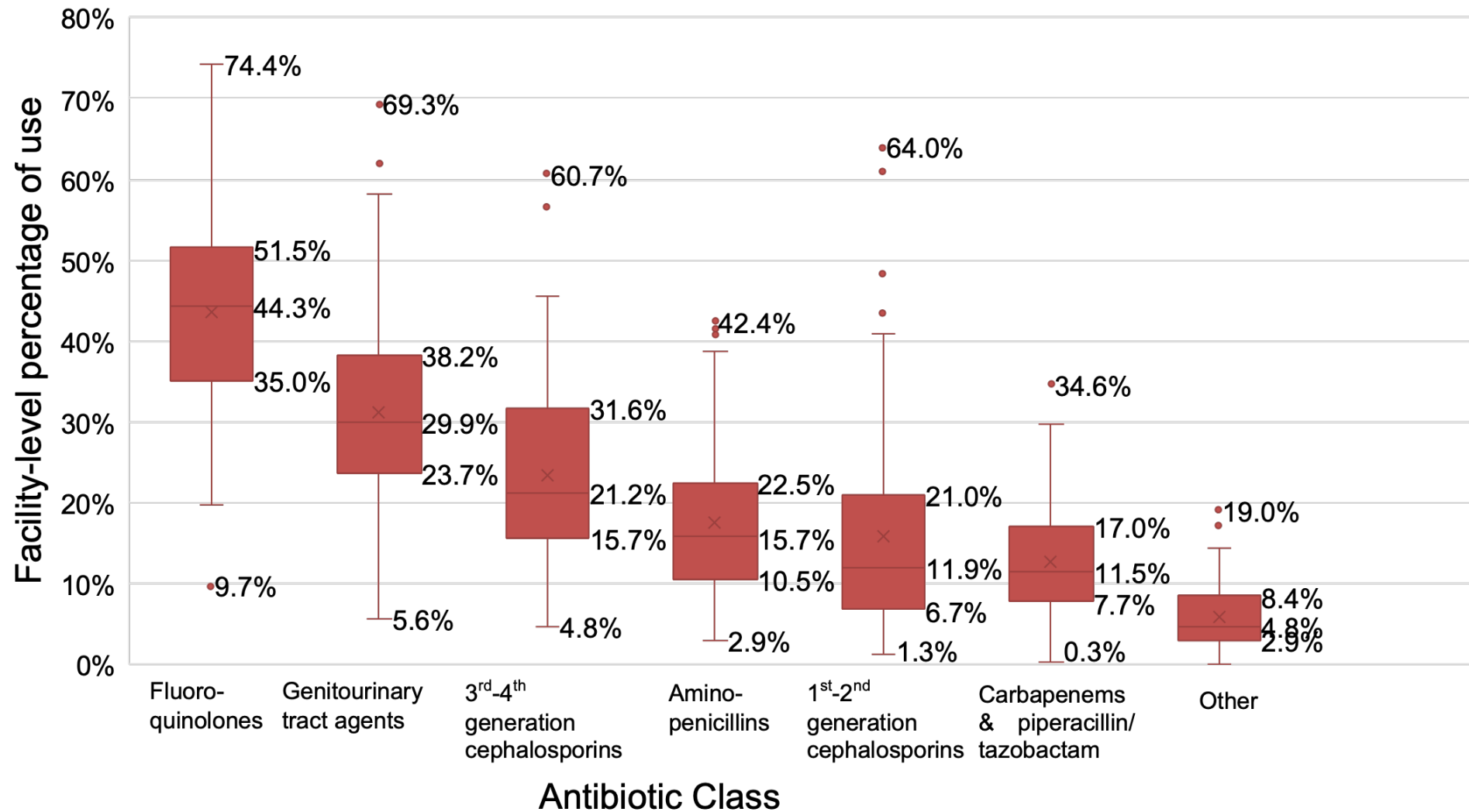
Note: Some studies have found that probiotics impede normal recolonization of the colon after antibiotic use

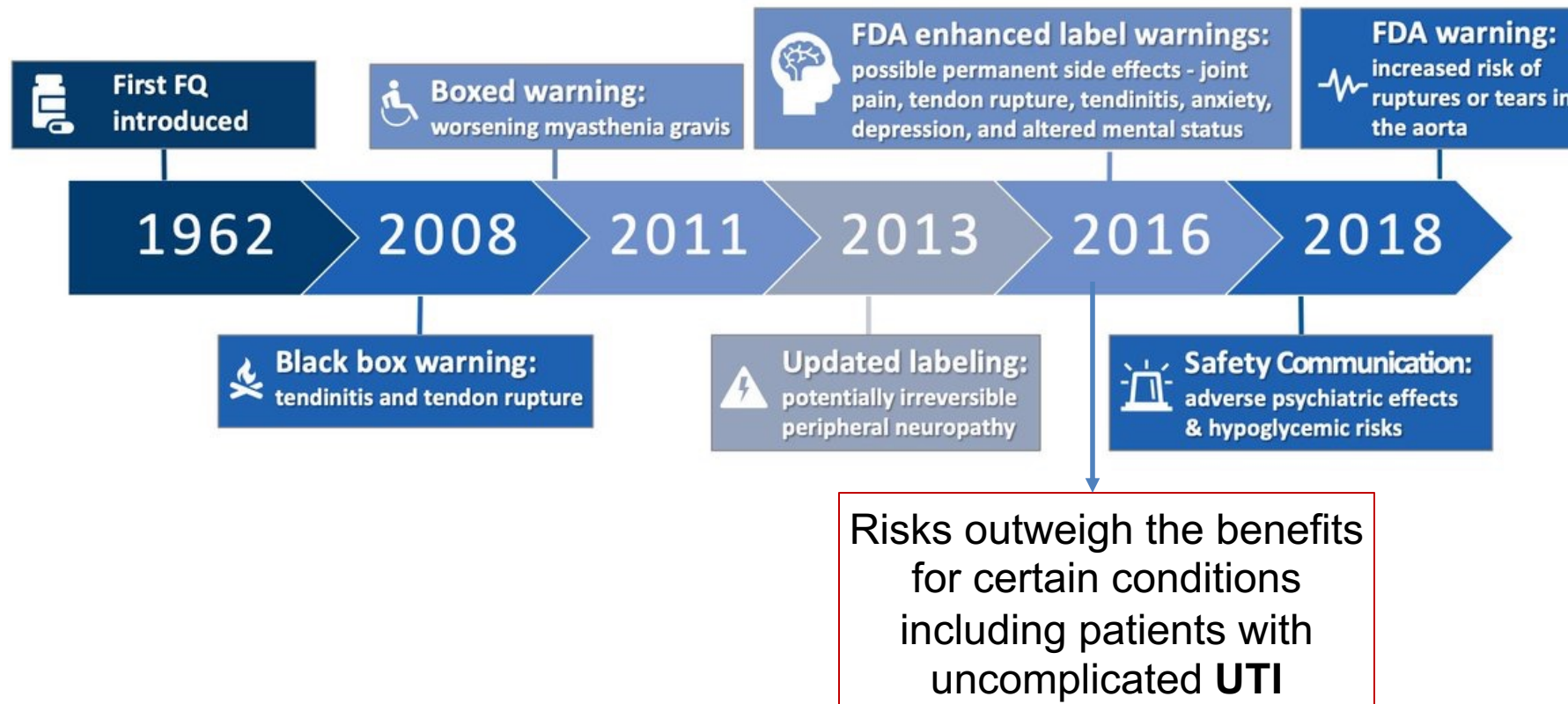# Antibiotic Stewardship: Linear Association Between Antibiotic Risk Index and CDI
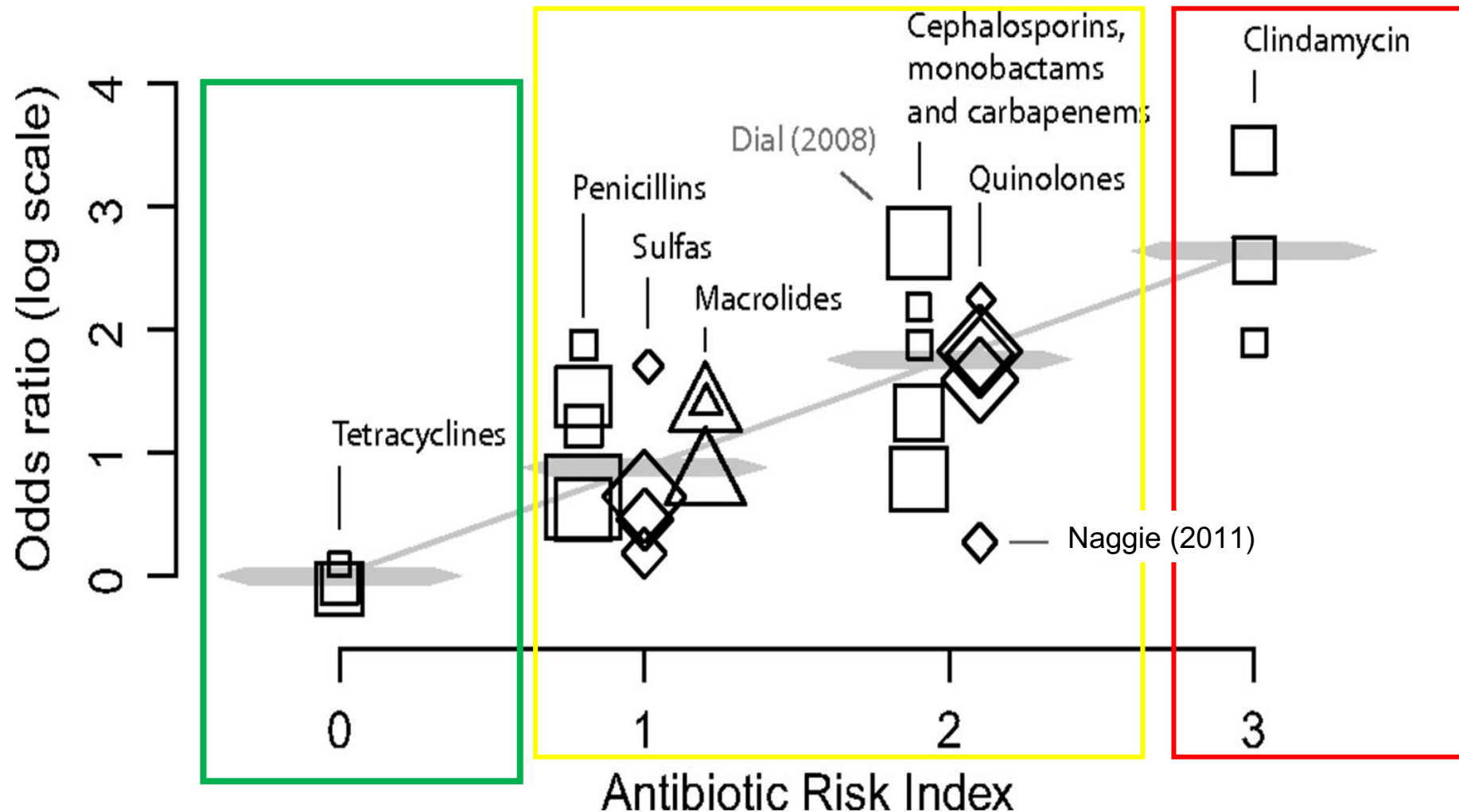
Brown KA, Khanafer N, Daneman N, Fisman DN. *Meta-analysis of antibiotics and the risk of community-associated Clostridium difficile infection. Antimicrob Agents Chemother. 2013 May;57(5):2326-32.*

VA Nursing Homes UTIs Facility-Level: Frequency of Antibiotic Use by Class

The History of Fluoroquinolones

First FQ introduced

Boxed warning: worsening myasthenia gravis

FDA enhanced label warnings: possible permanent side effects - joint pain, tendon rupture, tendinitis, anxiety, depression, and altered mental status

FDA warning: increased risk of ruptures or tears in the aorta

1962 2008 2011 2013 2016 2018

Black box warning: tendinitis and tendon rupture

Updated labeling: potentially irreversible peripheral neuropathy

Safety Communication: adverse psychiatric effects & hypoglycemic risks

Risks outweigh the benefits for certain conditions including patients with uncomplicated **UTI**

https://www.fda.gov/Drugs/DrugSafety/ucm628753.htm
https://www.fda.gov/Drugs/DrugSafety/ucm511530.htm

Take Home Message

- The US population is aging
- Thermoregulatory responses and immunity is waning in elderly
- Antibiotic overuse and resistance is highest in older adults
- UTI and CDI are the greatest concern for older adults

"TODAY IS THE OLDEST YOU'VE EVER BEEN, AND THE YOUNGEST YOU'LL EVER BE AGAIN."

-ELEANOR ROOSEVELT