# Antimicrobial Stewardship: Surgery-focused Review

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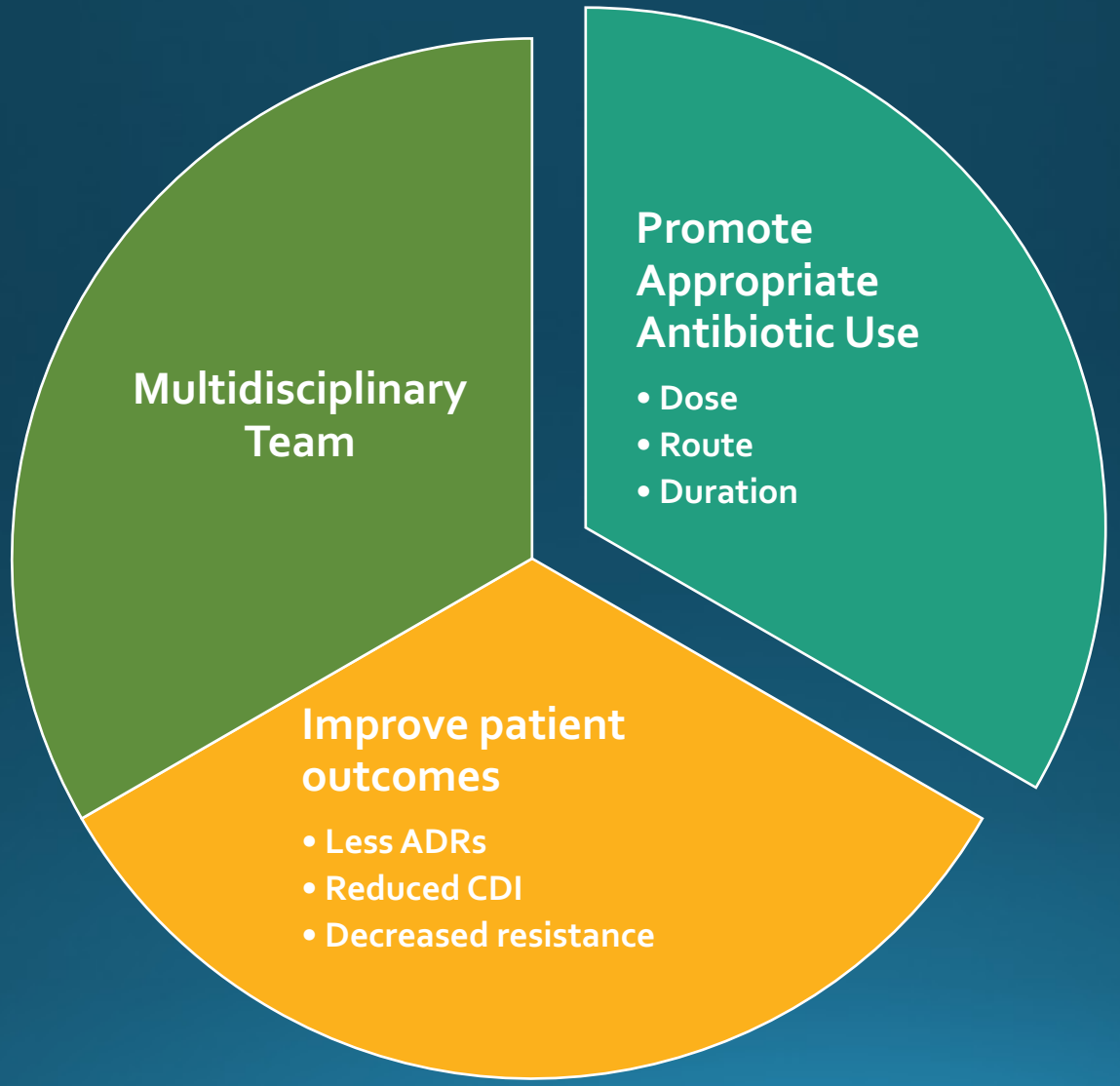
# Objectives

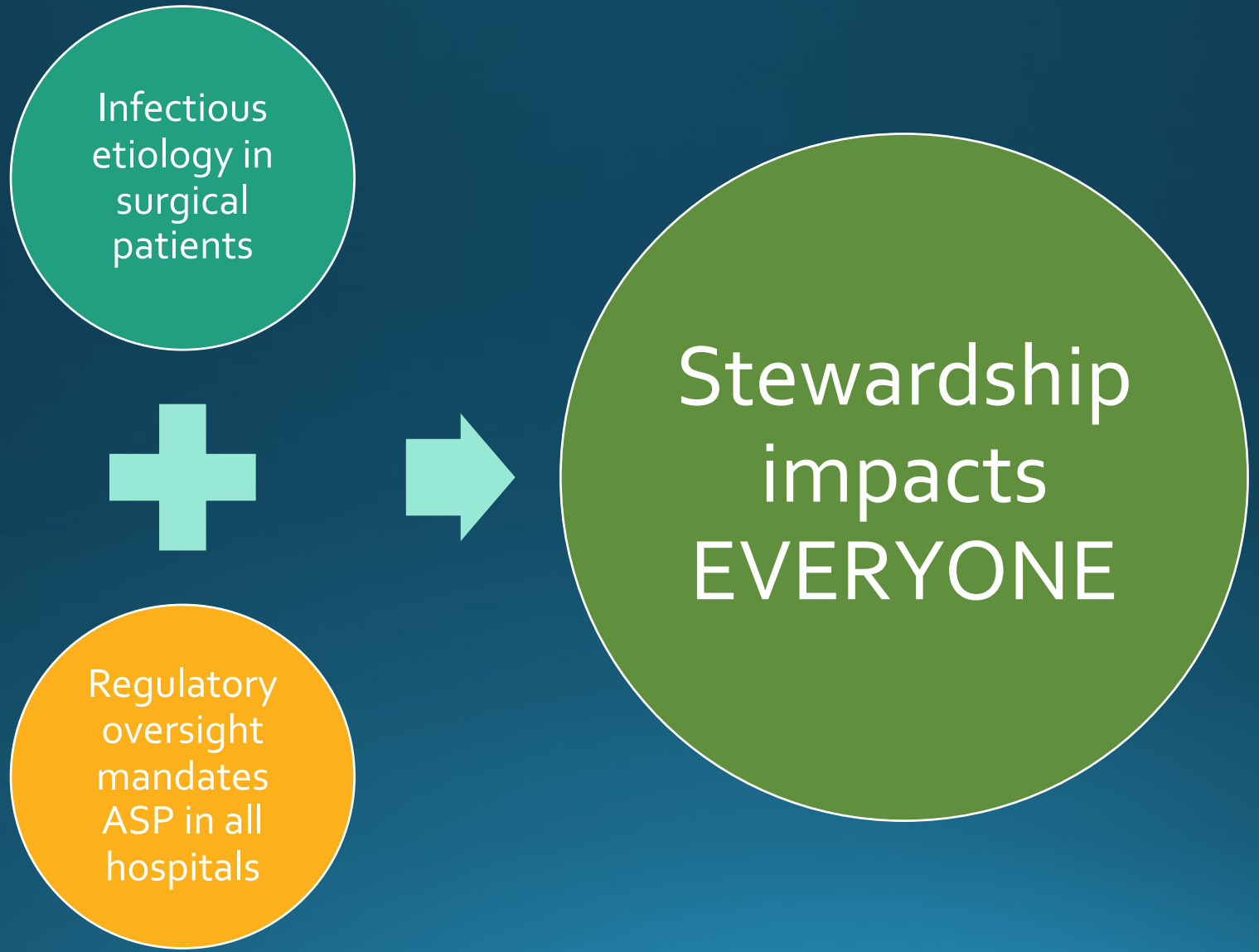
- Define what antimicrobial stewardship (ASP) is and how programs interact with surgery departments
- Recognize the Joint Commission ASP standards that relate to surgery practices
- Discuss intra-abdominal infection treatment and treatment durations with corresponding evidence
- Explain skin and soft tissue infection treatment as outlined by the Infectious Disease Society of America (IDSA) guidelines
- Identify updated guidance for *Clostridiodes difficile* (CDI) management
- Relate penicillin allergy status to surgical site infection risk

# What is Antimicrobial Stewardship?




The world focusing on COVID-19
Antibiotic Resistance

# What does ASP have to do with surgery?



# The Joint Commission ASP Standard

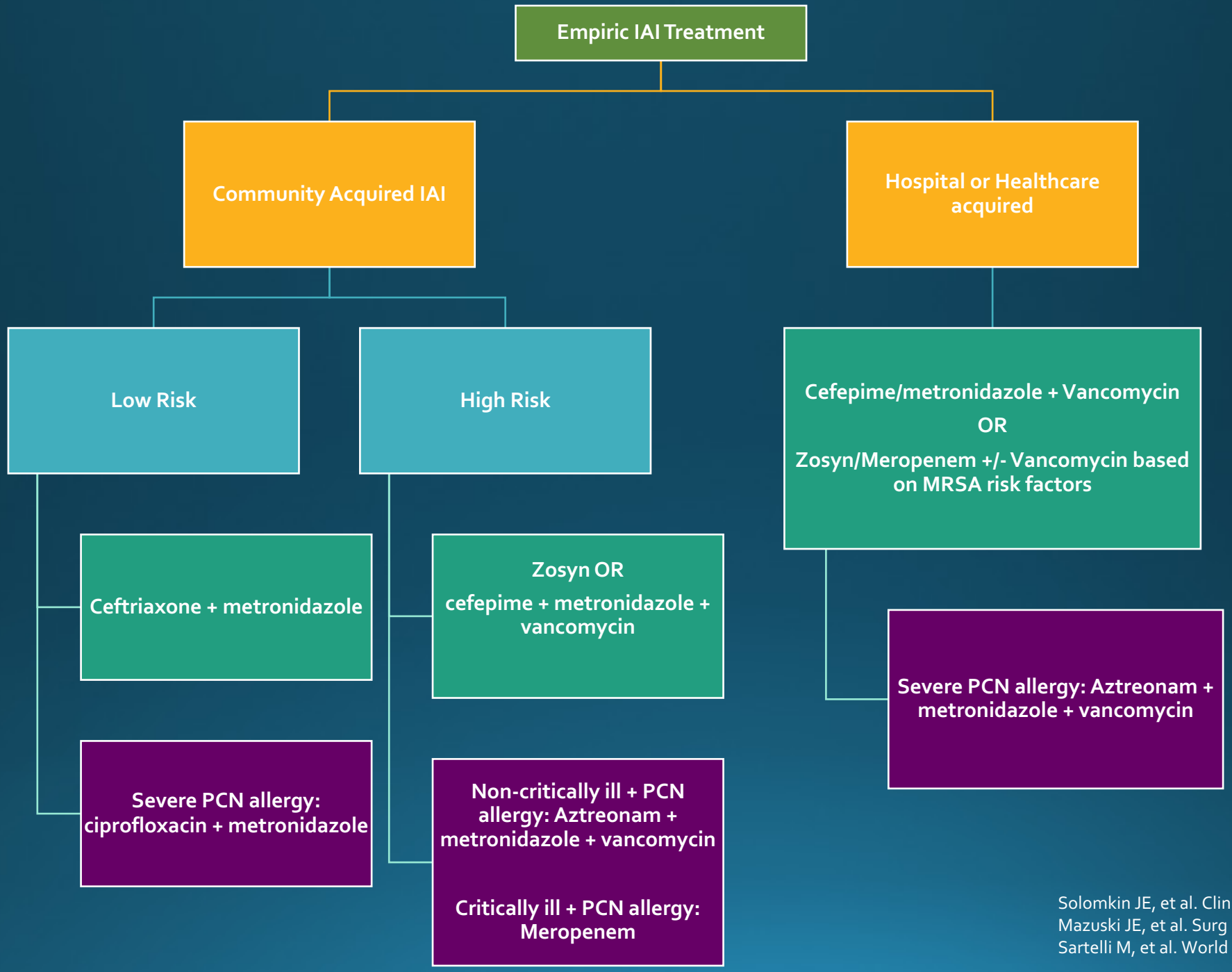
- Inpatient stewardship standard-Update effective January 1, 2023

| | | |
|---|---|---|
| Physician and pharmacist leads with multidisciplinary team | Monitor antibiotic use and take action on improvement opportunities | Documentation of evidence-based use of antibiotics in all depts and services of the hospital |
| Use of pre-authorization for specific antibiotics and/or prospective review and feedback to optimize antibiotic prescribing | Implementation of at least 2 evidence-based guidelines (*C.diff*, SSTI, surgical prophylaxis, etc.) | Evaluate adherence to at least 1 of the guidelines implemented |

# Intra-Abdominal Infections (IAI)

# Intra-Abdominal Infections

- Intra-abdominal infections are managed by source control and antimicrobial therapy
- Growing evidence for shorter durations or no antibiotic therapy
- Increasing gram negative resistance
- Guidelines for therapeutic recommendations
  - Infectious Disease Society of America/Surgical Infection Society 2010
  - Surgical Infection Society (SIS) 2017
  - World Society of Emergency Surgery (WSES) 2017




Solomkin JE, et al. Clin Infect Dis 2010
Mazuski JE, et al. Surg Infect (Larchmt) 2017
Sartelli M, et al. World J Emerg Surg 2017

# Community-Acquired IAI Treatment

- Classify patients by risk for treatment failure or death (high/low risk)

TABLE 6. FACTORS POTENTIALLY IDENTIFYING PATIENTS WITH INTRA-ABDOMINAL INFECTION AT HIGHER RISK

| |
|---|
| *Phenotypic/physiologic risk factors* |
| Advanced age (≥70 y) |
| Malignancy |
| Significant cardiovascular compromise |
| Significant liver disease or cirrhosis |
| Significant renal disease |
| Hypoalbuminemia |
| *Extent of infection/adequacy of initial source control* |
| Diffuse, generalized peritonitis |
| Elevated MPI score |
| Delayed initial source control |
| Inability to achieve adequate source control |
| Microbiologic characteristics |
| Suspected infection with resistant pathogens |

MPI=Mannheim Peritonitis Index.

- Consider ESBL risk when initiating treatment
  - Known colonization or infection with ESBL
  - Recent GI/GU outpt procedure in last 30 days
  - TWO or more courses of 3rd gen cephalosporin or FQ in the last 90 days
  - CA- low risk: ertapenem
  - CA-high risk: meropenem
- Consider empiric antifungal coverage if critically ill with upper GI perforation

Augustine MR, et al. ICHE 2017
Mazuski JE, et al. Surg Infect (Larchmt) 2017

# Hospital or Healthcare Acquired IAI

- Risk factors for Hospital or Healthcare Acquired IAI
  - Infection developing more than 48 hours after source control
  - Hospitalized for greater than 48 hours during current admission or within previous 90 days
  - Residence in skilled nursing home or LTC facility within past 30 days
  - Use of IV antibiotics, wound care, or RRT in the past 30 days
  - Post-operative infection
  - Known colonization with resistant pathogen
- Consider anti-fungal coverage if upper GI perf, recurrent bowel perfs, or surgically treated pancreatitis, and known colonization with Candida
- Tailor empiric treatment based on patient's clinical condition, individual risk factors for resistant pathogens (ESBL, VRE, MRSA, etc.), and local resistance

Solomkin JE, et al. Clin Infect Dis 2010
Mazuski JE, et al. Surg Infect (Larchmt) 2017

# Resistant Pathogen Risk Factors

| | IDSA Guidelines | SIS Guidelines |
|---|---|---|
| **Enterococcus risk factors** | • Post-operative infection<br>• Immunocompromised<br>• Valvular heart disease<br>• Prosthetic intravascular material | • Post-operative infection<br>• Recent broad-spectrum antibiotics<br>• Signs of severe sepsis or septic shock |
| **VRE risk factors** | • Known colonization<br>• Liver transplant patient with IAI in hepatobiliary tree | • Known colonization |
| **MRSA risk factors** | • MRSA colonization<br>  • **~97% NPV for MRSA infection**<br>• Prior treatment failure<br>• Significant antibiotic exposure | • MRSA colonization<br>• Advanced age<br>• Co-morbid medical conditions<br>• Previous hospitalization or surgery<br>• Significant recent antibiotic exposure |

Solomkin JE, et al. Clin Infect Dis 2010; Mazuski JE, et al. Surg Infect (Larchmt) 2017; Hennessy SA, et al. Surg Infect (Larchmt) 2015

# Uncomplicated Diverticulitis

- Increasing evidence that antibiotics may NOT be needed for some uncomplicated diverticulitis
- SIS guidelines recommend no antibiotics in low-risk patients
- American Gastroenterology Association (AGA) suggests selective use in severe disease, immunosuppression, pregnancy and significant comorbidity
- Cochrane Review 2022

Mazuski JE, et al. Surg Infect (Larchmt) 2017
Peery AF, et al. Gastroenterology 2021

# Uncomplicated Diverticulitis

## Study Title

- Antibiotics for uncomplicated diverticulitis
  - Cochrane review

## Patient Population/Studies Included

- Randomized controlled trials including all types of patients with a radiologically confirmed diagnosis of uncomplicated acute diverticulitis
- Localized inflammation with or without small abscess formation confined to the large bowel wall

## Intervention

- Comparator and interventions included antibiotics compared to no antibiotics

Dichman ML, et al. Cochrane Database Syst Rev 2022

# Uncomplicated Diverticulitis

## Primary Outcome

- Complications and emergency surgery

## Results

- 3 studies compared no antibiotics to antibiotics
- Little or no difference found for the primary outcome between antibiotics and no antibiotics (RR 0.89; 95% CI 0.30 to 2.62; 3 studies, 1329 participants; low-certainty evidence)
- **All studies excluded immunocompromised, pregnant, septic patients**

Dichman ML, et al. Cochrane Database Syst Rev 2022

# Duration of Antimicrobial Therapy for the Treatment of IAI

# Surgical Infection Society Guidelines

- Limit to no more than 24 hours in post-operative patients with:
  - Acute or gangrenous appendicitis/cholecystitis in the absence of perforation
  - Ischemic, non-perforated bowel
  - Traumatic bowel perforations operated on within 12 hours
  - Gastroduodenal perforations operated on within 24 hours
- Limit to 4 days in patients with adequate source control
- Consider limiting to 5-7 days in patients with established IAI in whom definitive source control is not performed
  - Use clinical parameters such as fever, leukocytosis, and adequacy of GI function to determine if therapy can be discontinued sooner
  - Reassess patients who do not respond to therapy within 5-7 days for potential source control intervention
- Insufficient data to evaluate duration of therapy in immunosuppressed patients

Mazuski JE, et al. Surg Infect (Larchmt) 2017

# Evidence for Duration of Therapy

# Complicated Intra-Abdominal Infection and Source Control

## Study Title

- Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection (STOP-IT Trial)

## Patient Population

- 16 years of age or older
- 518 patients with **complicated IAI and adequate source control**
  - Complicated defined as fever, leukocytosis, or GI dysfunction due to peritonitis
  - Mean APACHE II score for index infection was 10 (range 0-29), most common origin of infection was colon/rectum, percutaneous procedure was source control in one third of patients
- Included small number of immunosuppressed patients
- Excluded patients with simple appendicitis/cholecystitis without perf, pts without bacterial or fungal cultures, SBP, pregnancy, peritoneal dialysis related infection, perf gastric ulcer treated within 24 hours, traumatic injury to the bowel treated within 12 hours of injury, etc.

## Intervention

- Control group: patients received antibiotics until 2 days after the resolution of fever, leukocytosis, and ileus, with a maximum of 10 days of therapy
- Experimental group: patients received a fixed course of antibiotics for 4±1 calendar days.
- Antibiotics considered appropriate if consistent with SIS-IDSA guidelines

Sawyer RG, et al. N Engl J Med 2015

# Complicated Intra-Abdominal Infection and Source Control

## Primary Outcome

- A composite of surgical-site infection, recurrent intraabdominal infection, or death within 30 days after the index source-control procedure, according to treatment group.
- Secondary outcomes included the duration of therapy and rates of subsequent infections

## Results

- Primary outcome occurred in **56 of 257 patients in the experimental group (21.8%),** as compared with **58 of 260 patients in the control group (22.3%)** (absolute difference, −0.5 percentage point; 95% confidence interval [CI], −7.0 to 8.0; P=0.92).
- Median duration of antibiotic therapy was **4 days** (IQR, 4.0 to 5.0) in experimental group and **8 days** (IQR 5.0 to 10.0) in the control group (absolute difference, −4.0 days; 95% CI, −4.7 to −3.3; P<0.001
- Subsequent infection rate was no different between the groups (p=0.62)
- Nonadherence to protocol was 18% in experimental group but outcomes were not statistically significant in per protocol analysis also

## Conclusion

- In patients with IAI who had adequate source control, the outcomes after fixed-duration antibiotic therapy (~ 4 days) were similar to those after a longer course of antibiotics (~ 8 days) that extended until after the resolution of physiological abnormalities.

Sawyer RG, et al. N Engl J Med 2015

# Complicated Appendicitis with Source Control

## Title

- 2 days versus 5 days of postoperative antibiotics for complex appendicitis: a pragmatic, open-label, multicentre, non-inferiority randomized trial (APPIC trial)

## Patient Population

- 1005 patients included 8 years or older with complex appendicitis
- Complex appendicitis defined as necrosis, perforation, or abscess
- Excluded immunocompromised, severe sepsis, and pregnancy

## Intervention

- **2 days of antibiotics vs 5 days after appendectomy**
- IV cefuroxime 1.5g IV q8h/ceftriaxone 2g IV q24h and metronidazole 500mg IV q8h or culture-directed treatment
- 95% of patients had laparoscopic appendectomy

De Wijkerslooth EML, et al. Lancet 2023

# Complicated Appendicitis with Source Control

## Primary Outcome

- Composite of infectious complications (intraabdominal abscess and SSI) and mortality within 90 days
  - 7.5% non inferiority margin established
- Secondary outcomes were rate of intraabd abscess, SSI, adverse effects to antibiotics, readmission to hospital, length of hospital stay, etc.

## Results

- Overall rate of complications 10% in 2 day group and 8% in 5 day group, risk difference of 2% CI -1.6-5.6
- Intraabd abscess (9% vs 7%) and SSI (2% vs 1%) rates were similar
- Hospital LOS was 2 days shorter in 2 day group
- Readmission to hospital were higher in 2 days group (12%) vs 5 day group (6%) OR 2.135, CI 1.342-3.396)
  - 53% were attributed to infectious complications
- Adverse effects of antibiotics was not statistically different (9% vs 22%, p=0.344)
- Nonadherence to protocol was 14% in 2 day treatment group

## Conclusion

- 2 days of IV antibiotics is noninferior to 5 days in patients who had laparoscopic appendectomy

De Wijkerslooth EML, et al. Lancet 2023

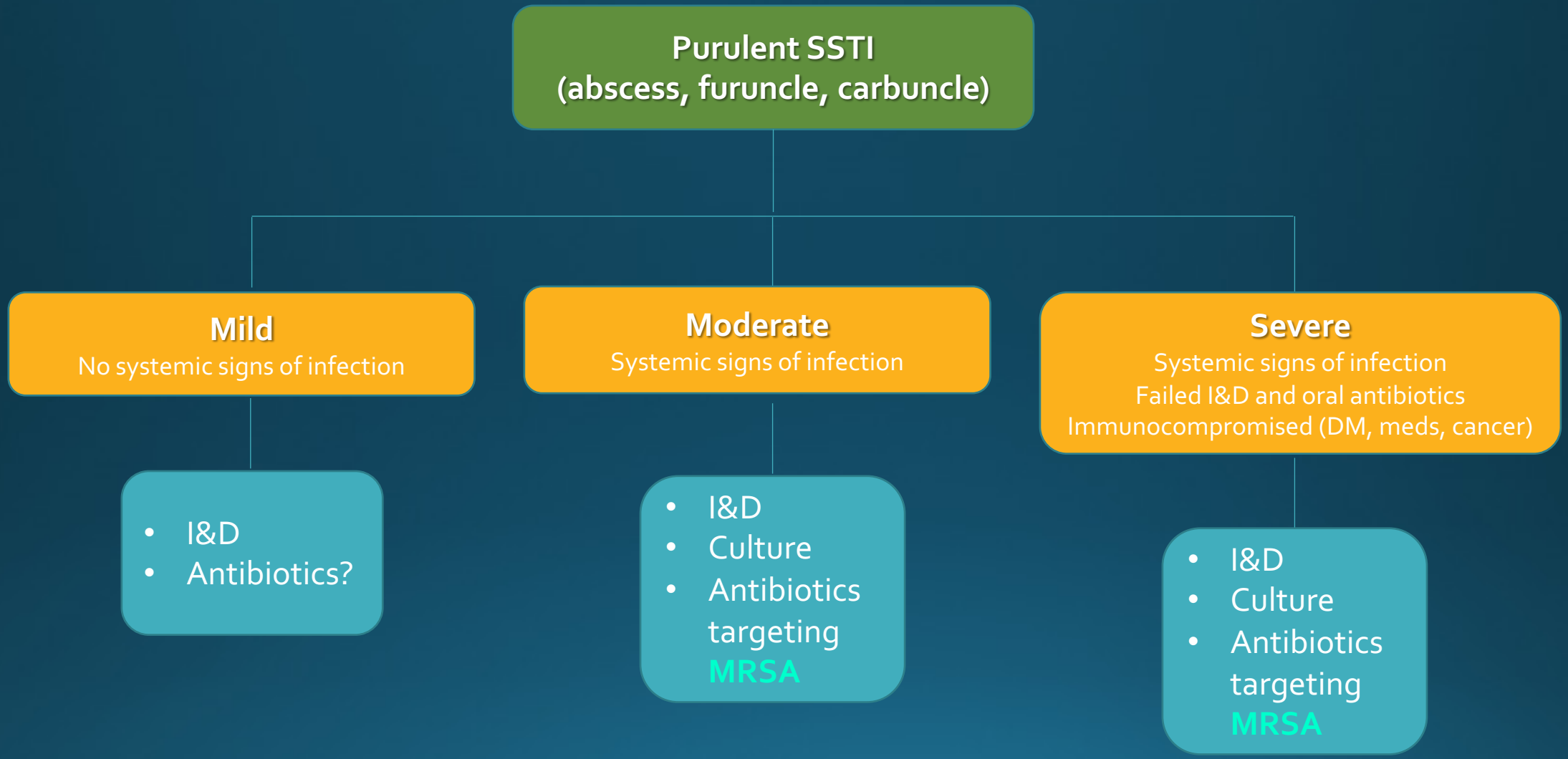
# Stewardship for IAI

- Use narrow spectrum antibiotics for low risk CA-IAI patients
- Consider deferring antibiotic treatment for low risk uncomplicated diverticulitis patients
- Shorter treatment durations for uncomplicated and complicated IAI did not lead to worse clinical outcomes **if source control was achieved**
  - Discontinue antibiotics within 24 hours of appendectomy/cholecystectomy for uncomplicated infections
  - Consider 4 days of antibiotics if adequate source control is achieved in complicated infections

# Skin and Soft Tissue Infections (SSTI)

# Skin and Soft Tissue Infections

- Common infectious condition caused by staph and strep
  - Purulent SSTI: abscess, purulent cellulitis
  - Nonpurulent SSTI: cellulitis, necrotizing fasciitis
- Disease state targeted for ASP intervention by TJC
- Controversial evidence on when to prescribe antibiotics in addition to incision and drainage in the management of abscesses




Stevens DL, et al. Clin Infect Dis 2014

# Treat or Don't Treat?

- Guideline recommendations for antibiotic treatment s/p I&D for abscess
  - **MRSA IDSA guideline**: treat if multiple sites of infection, systemic illness, associated comorbidities with MRSA or immunosuppression (DM, HIV, cancer), extremes of age, difficult area to drain, septic phlebitis, lack of response to I&D alone (2011)
  - **IDSA guideline**: no antibiotics for mild severity infection (2014)
  - **Global consensus**: treat if abscess is greater than 5cm, in area difficult to drain (face, hand, genitalia), or multiple localizations (2022)

Stevens DL, et al. Clin Infect Dis 2014
Sartelli M, et al. World J Emerg Surg 2022
Liu C, et al. Clin Infect Dis 2011

# Treat or Don't Treat?

## Title

- Trimethoprim-Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess

## Patient Population

- 1247 patients included that were 12 years of age or older who had cutaneous lesion that was found to have purulent material on surgical exploration
- Lesion had been present for less than 1 week and at least 2cm in diameter
- Excluded  perirectal perineal or paronychial lesions, IVDU, fever, immunocompromised, CrCl less than 50, LTC residence, etc.

## Intervention

- Multicenter, double-blind randomized controlled trial
- Bactrim 4 SS tab po BID x 7 days vs placebo s/p I&D

Talan DA, et al. N Engl J Med 2016

# Treat or Don't Treat?

## Outcomes

- Primary: Clinical cure of abscess lesion at the test-of-cure visit (7 to 14 days after end of treatment)
- Secondary: surgical drainage procedures, invasive infections, skin infections at same or different site, etc.

## Results

- Clinical cure rate was 80.5% in Bactrim group and 73.6% in placebo group (mITT) p=0.005, CI 2.1-11.7
- Lower rates of subsequent surgical drainage procedures with Bactrim (3.4%) vs placebo (8.6%) and lower rates of skin infections at a new site (3.1% vs 10.3%)
- Similar rates of invasive infections
- Adverse events were similar between Bactrim and placebo

## Conclusion

- Treatment with Bactrim after abscess drainage had higher clinical cure rates and fewer subsequent surgical drainage procedures and new skin infections

Talan DA, et al. N Engl J Med 2016

# Treat or Don't Treat?

## Title

- A Placebo-Controlled Trial of Antibiotics for Smaller Skin Abscesses

## Patient Population

- 786 adults and children who had single skin abscess that was 5cmin diameter or smaller
- Excluded  abscess located at body sites that require specialized management (perirectal, genital, hand), human/animal bite, fever, SIRS, immunosuppressed, BMI over 40, SSI, prosthetic device infection, systemic anti-staph abx in past 14 days, require hospitalization, live in LTCF, etc.

## Intervention

- Multicenter, double-blind randomized controlled trial
- Bactrim 2 SS tab po BID vs clindamycin 300mg PO TID vs placebo x 10 days s/p I&D

Daum RS, et al. N Engl J Med 2017

# Treat or Don't Treat?

## Outcomes

- Primary: Clinical cure of abscess lesion at the test-of-cure visit (7 to 10 days after end of treatment)
- Secondary: cure rate at the end of treatment, cure rate in adults and children, cure rates in MRSA pts, and adverse event rates

## Results

- Cure rate at test of cure visit was 83.1% in clindamycin group, 81.7% in Bactrim group and 68.9% in placebo group (ITT) $p<0.001$ for both compared to placebo
- Cure rate was ~83% for Bactrim and clindamycin group in MRSA patients compared to 63.8% with placebo ($p<0.001$ for both groups)
- Non staph aureus infections had the same cure rates in all treatment groups (~83%)
- Adverse events were highest in clindamycin group (21.9%) vs Bactrim group (11.1%) vs placebo (12.5%)

## Conclusion

- There is clinical benefit to antibiotic therapy in addition to incision and drainage for staph aureus infections

Daum RS, et al. N Engl J Med 2017

# Antibiotics-Purulent SSTI

| Severity | Empiric Antibiotic | Precautions/ADRs |
|---|---|---|
| Moderate | Bactrim | AKI, hyperkalemia, warfarin interaction, poor strep coverage |
| | Doxycycline | Poor strep coverage |
| | Clindamycin | High resistance rates, high *C.diff* risk, dosing frequency |
| Confirmed MSSA | Cephalexin | Frequent dosing |
| Severe | Vancomycin | AKI |
| | Linezolid | Serotonin syndrome interactions, thrombocytopenia |
| | Daptomycin | CPK, interact with statins |
| | Telavancin/Oritavancin /Dalbavancin | Expensive, may require ID consultation |
| | Ceftaroline | Broad gram neg coverage |
| Confirmed MSSA | Cefazolin | |
| | Nafcillin | AKI, LFT elevation |
| **Duration: 5-10 days** | | |

Stevens DL, et al. Clin Infect Dis 2014

*Cover MRSA for cellulitis associated with penetrating wound, evidence of MRSA elsewhere, nasal colonization, IVDU, or SIRS

## Nonpurulent SSTI (cellulitis/necrotizing infection)

### Mild
No systemic signs of infection

Antibiotics targeting strep/MSSA*

Duration: 5 days if improving

### Moderate
Systemic signs of infection

Antibiotics targeting strep/MSSA*

Duration: 5 days if improving

### Severe
Systemic signs of infection
Failed I&D and oral antibiotics
Immunocompromised
Clinical signs of deeper infection

- Surgical debridement
- Culture
- Broad Antibiotics

Duration: 7 days if improving, if necrotizing depends on source control

Stevens DL, et al. Clin Infect Dis 2014

# Antibiotics-Nonpurulent SSTI

| Severity | Empiric Antibiotic | Precautions/ADRs |
|---|---|---|
| Mild/Moderate | Cephalexin | |
| | Augmentin | |
| | Cefazolin IV | |
| PCN allergy | Clindamycin PO/IV | High resistance rates, high *C.diff* risk, dosing frequency |
| | Vancomycin IV | |
| Duration: 5 days if improving | | |
| Severe | Vancomycin + Zosyn | |
| | Vancomycin + cefepime | |
| Necrotizing | Vancomycin + Zosyn + clindamycin | Clindamycin is added for group A strep toxin production |
| | Linezolid + Zosyn | MRSA and toxin production treatment with linezolid |
| **Duration: 7-14 if neutropenic**<br>**Necrotizing infection duration depends on control of necrosis** | | |

Stevens DL, et al. Clin Infect Dis 2014

# Gram Negative Coverage

- Gram negative pathogens are rare in SSTI
- Consider gram negative coverage IN ADDITION to staph/strep coverage:
  - Wound of the perineum, GI tract, or female genital tract
  - Immunocompromised patients
  - Burn wounds
  - Culture-directed
  - History of gram-negative skin infection
  - Penetrating wound (pseudomonas)
  - Water exposure (pseudomonas)

Stevens DL, et al. Clin Infect Dis 2014
Bystritsky R, et al. Ann Intern Med 2018

# Stewardship for SSTI

- Avoid MRSA coverage for nonpurulent wounds
- Only culture drainage or infected tissue, superficial swabs are unreliable
- No antibiotics may be reasonable for some uncomplicated abscesses s/p I&D
- Treatment duration for most SSTI can be 5-7 days if there is clinical improvement
- Understand antibiotic spectrum limitations
  - Bactrim and doxycycline have poor strep coverage
  - Clindamycin has high resistance rates and C diff risk
- Only use gram negative coverage when indicated

# *Clostridiodes difficile*

# *C. difficile* Infections

- *Clostridiodes difficile* is a gram-positive anaerobic bacteria that produces toxins and spores that lead to infection
- Toxin A and B cause inflammation and lead to symptoms of infection
- Antibiotics are backbone of CDI treatment but also kill healthy gut microbiome and are unable to kill spores → recurrence

# Diagnosis and Classification

## Diagnosis

- Only test if 3 or more **UNFORMED** stools in 24 hours
- No other explanation for diarrhea (laxatives, tube feeds)
- PCR alone can detect carriers
- 2-step testing is preferred to distinguish colonization from active infection

## Classification

- **Mild/moderate**: WBC less than 15,000 cells/mm3 AND Scr less than 1.5 mg/dL
- **Severe**: WBC ≥ 15,000 cells/mm3 OR Scr >1.5
- **Fulminant/Severe-complicated**: Severe criteria plus hypotension, shock, ileus, or megacolon

Kelly CR, et al. Am J Gastroenterol 2021
McDonald LC, et al. Clin Infect Dis 2018
Johnson S, et al. Clin Infect Dis 2021

# CDI Risk Factors

## Risk factors for CDI

- Age 65 or older
- Antibiotics (modifiable)
- Duration of hospitalization
- GI surgery
- GI tract manipulation
- Immunosuppression
- Chemotherapy

## Risk Factors for Recurrent CDI

- Age 65 or older
- Immunosuppression
- Severe CDI on initial episode
- History of prior CDI

Kelly CR, et al. Am J Gastroenterol 2021
McDonald LC, et al. Clin Infect Dis 2018
Johnson S, et al. Clin Infect Dis 2021

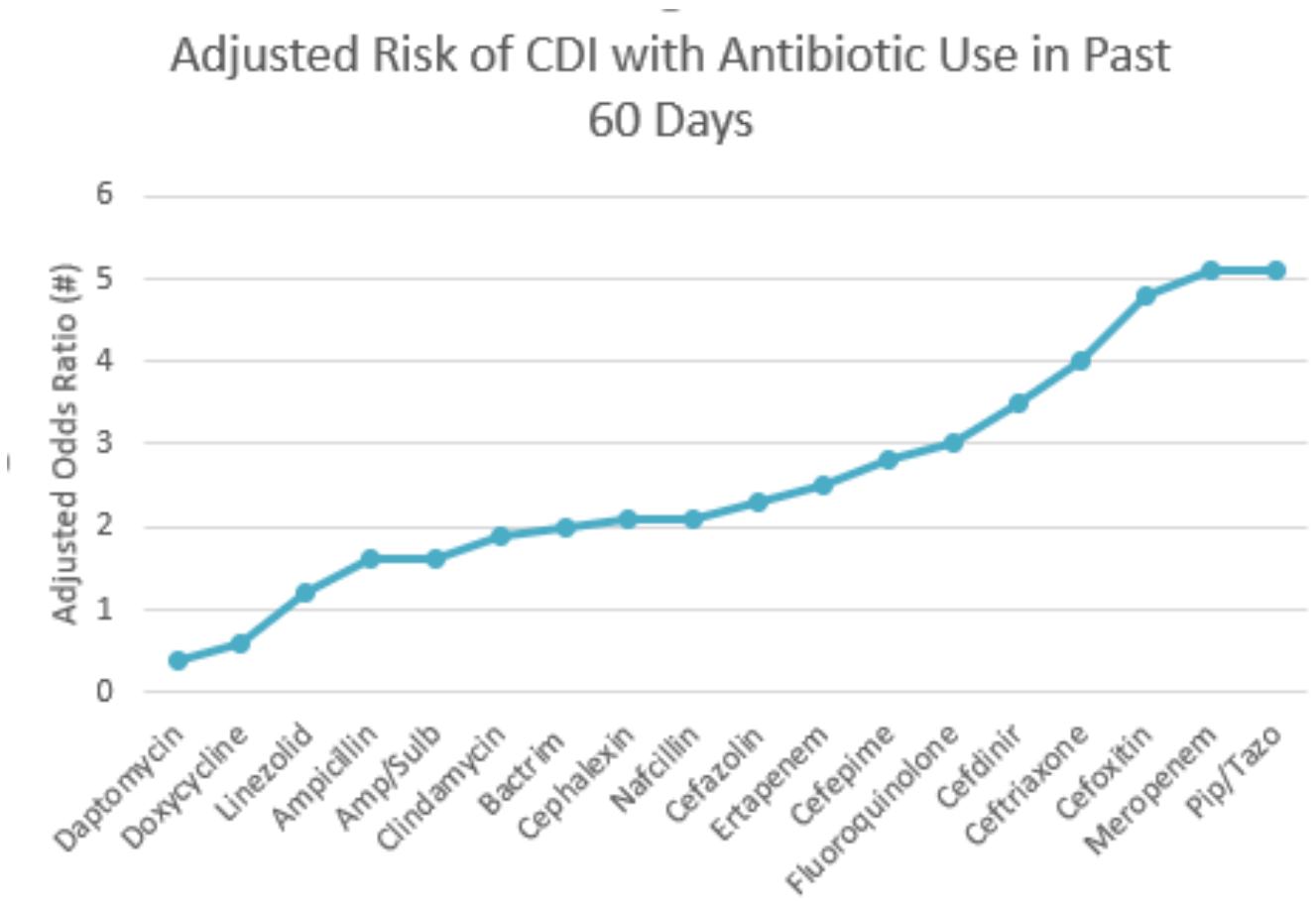
# CDI Risk and Antibiotics

- Systemic antibiotics disrupt the normal gut microbiome
- CDI infection is 7 to 10 times more likely to occur in patients while taking antibiotics and for one month after
- A single-dose of antibiotics (ex surgical prophylaxis) increases risk for CDI
- Antibiotic selection, number of antibiotics, and duration impact CDI risk
  - HR of 2.5 for patients who received 2 antibiotics vs 1 antibiotics
  - Longer duration antibiotic treatment increase the risk for CDI
  - Higher risk antibiotic use increases risk for CDI

McDonald LC, et al. Clin Infect Dis 2018
Hensgens MP, et al. J Antimicrob Chemother 2012

# CDI Risk and Antibiotics

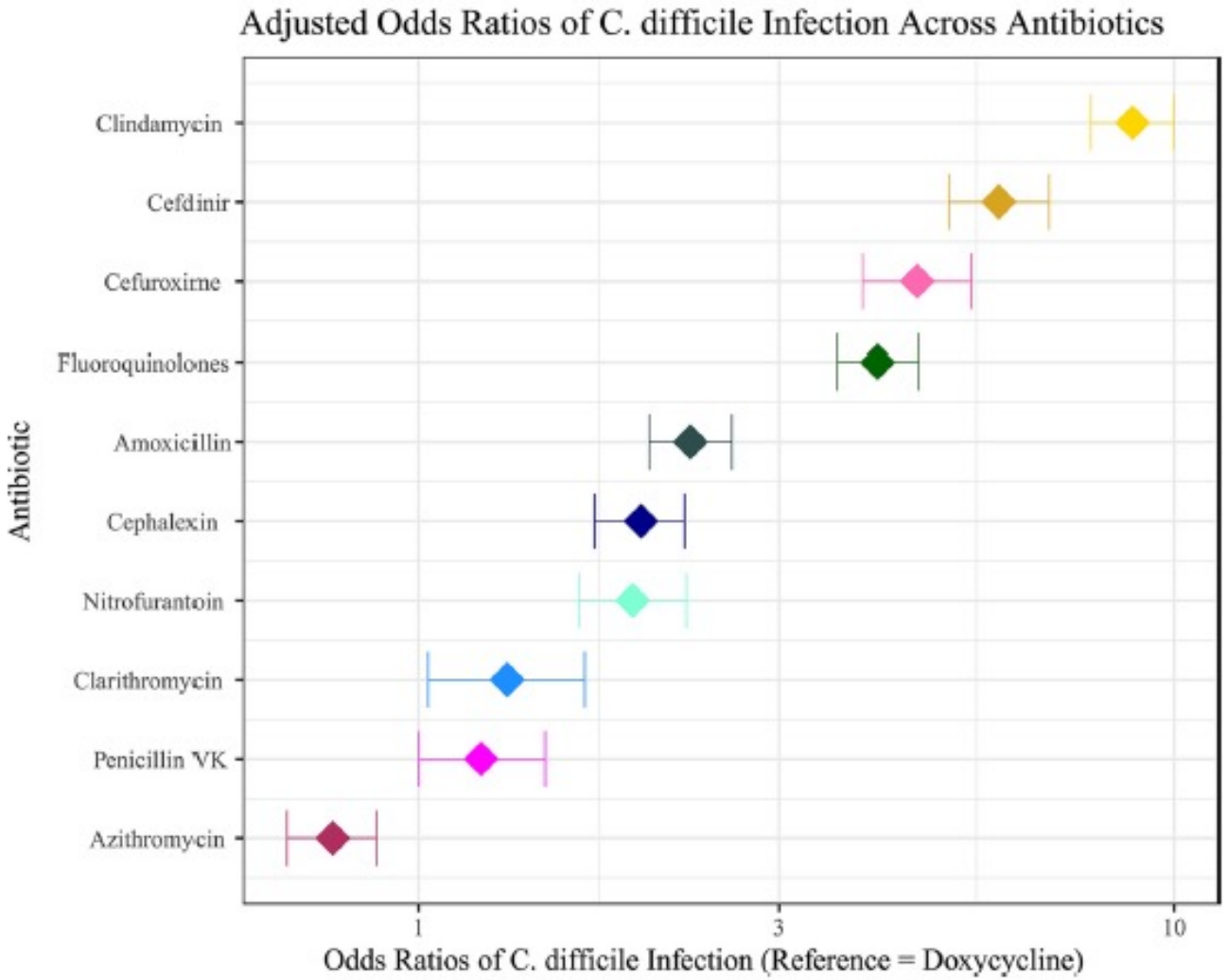
- Webb et al.
  - Retrospective cohort
  - 2,356 CDI cases evaluated
  - Evaluated hospital-associated CDI risk associated with antibiotic use during index visit and within past 60 days
  - Multivariable logistic regression to evaluate antibiotic-specific risk




Webb BJ, et al. Antimicrob Agents Chemother 2020

# CDI Risk and Antibiotics

- Zhang et al.
  - Retrospective cohort
  - 11,607 patients included
  - Evaluated community-acquired CDI risk for specific antibiotics
  - Doxycycline was reference




Zhang J, et al. Antimicrob Agents Chemother 2022

# Guideline Treatment Recommendations

| | ACG 2021 | IDSA |
|---|---|---|
| **Mild or Moderate** | • Vancomycin 125mg po q6h x 10 days OR fidaxomicin 200mg po BID x 10 days<br>• Metronidazole 500mg po TID x 10 days for low-risk patients (young and minimal comorbidities) | • Preferred: Fidaxomicin x 10 days<br>• Alt: Vancomycin 125mg po q6h<br>• If vanc and fidaxomicin are unavailable: metronidazole 500mg TID x 10-14 days |
| **Severe** | • Vancomycin 125mg po q6h x 10 days OR fidaxomicin 200mg po BID x 10 days | • Preferred: Fidaxomicin x 10 days<br>• Alt: Vancomycin 125mg po q6h |
| **Fulminant/ Severe-complicated** | • Vancomycin 500mg po q6h x48-72h then reduce dose to 125mg +/- metronidazole 500mg IV q8h<br>• Add vancomycin 500mg PR q6h (enema) if ileus | • Vancomycin 500mg po q6h + metronidazole IV q8h<br>• Add vancomycin PR 500mg q6h if ileus |
| **First Recurrence** | • Vancomycin tapered/pulse dosed regardless of initial treatment OR fidaxomicin if previously treated with vancomycin or metronidazole | • Preferred: Fidaxomicin standard or extended/pulse regimen<br>• Alternative:<br>  • Vancomycin standard or tapered/pulse<br>  • Bezlotoxumab 10mg/kg IV x1 with SOC antibiotics if within 6 months from initial CDI |
| **Second Recurrence** | FMT | Same as above PLUS<br>Alt: Vancomycin po followed by rifaximin<br>*Don't recommend FMT until more than 2 recurrences |

Kelly CR, et al. Am J Gastroenterol 2021; McDonald LC, et al. Clin Infect Dis 2018; Johnson S, et al. Clin Infect Dis 2021

# Fidaxomicin vs Oral Vancomycin

- Updated literature review found fidaxomicin had higher sustained response compared to oral vancomycin (RR 1.16, CI 1.09-1.24)
- Similar initial clinical cure as oral vancomycin(RR 1.00, CI 0.96-1.04)
- Fidaxomicin is EXPENSIVE!!
  - $282 per 200mg tablet
  - $5640 per 10 day course
- Selective use of fidaxomicin first-line may be needed
  - Use for initial infection in patients that are high risk for recurrence
  - Use for recurrent infection

Johnson S, et al. Clin Infect Dis 2021
Lexicomp. Fidaxomicin

# CDI Treatment Pipeline

- Ridinilazole: antibiotic that targets CDI, in phase III clinical trials
- Live biotherapeutic products: new "FMT" products, 3 being studied
  - Oral capsule x2
  - Suspension enema
- Toxoid vaccines: 2 being studied
  - Bivalent toxoid vaccine contains detoxified version of toxin A and B
  - Completed phase III trials, neutralizes CDI toxins

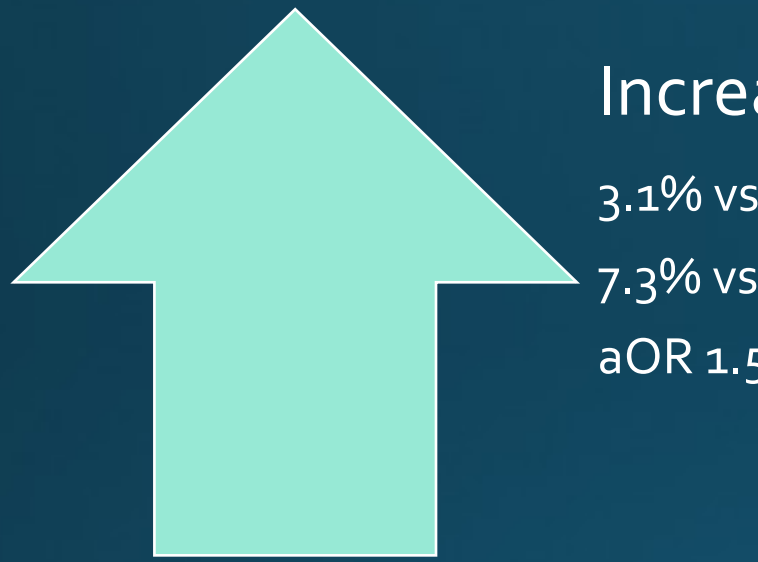
Gonzales-Luna AJ, et al. Drugs 2023

# Stewardship and CDI

- Only test when clinically appropriate
  - Only test patients if 3 or more unformed and unexplained stools in 24 hours
  - Discontinue agents that can cause diarrhea and reassess in 24 hours
- Minimize use and duration of high-risk antibiotics
- Fidaxomicin has less recurrence but is very expensive
  - Consider for patients at high risk for recurrence
  - Oral vancomycin is still a reasonable first-line treatment option

# Penicillin Allergy and Surgical Site Infections

# Impact of PCN allergy on SSI

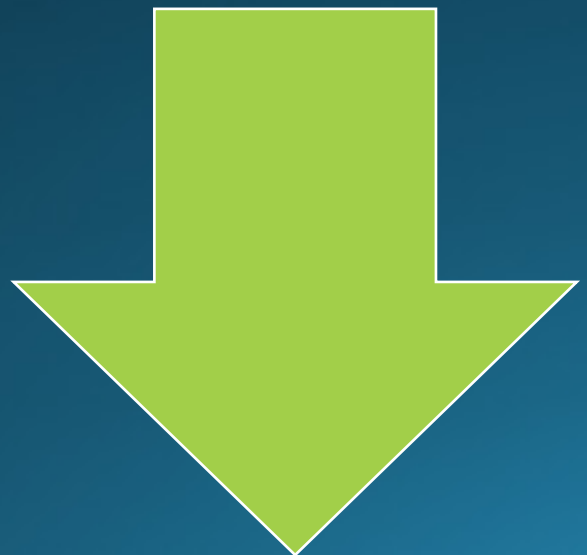


## Increased SSI risk

3.1% vs 1.5%, OR 2.015 p=0.023 (Wilhelm)

7.3% vs 4.8%, aOR 1.61 p=0.03 (Lam)

aOR 1.51, CI 1.02-2.22 (Blumenthal)



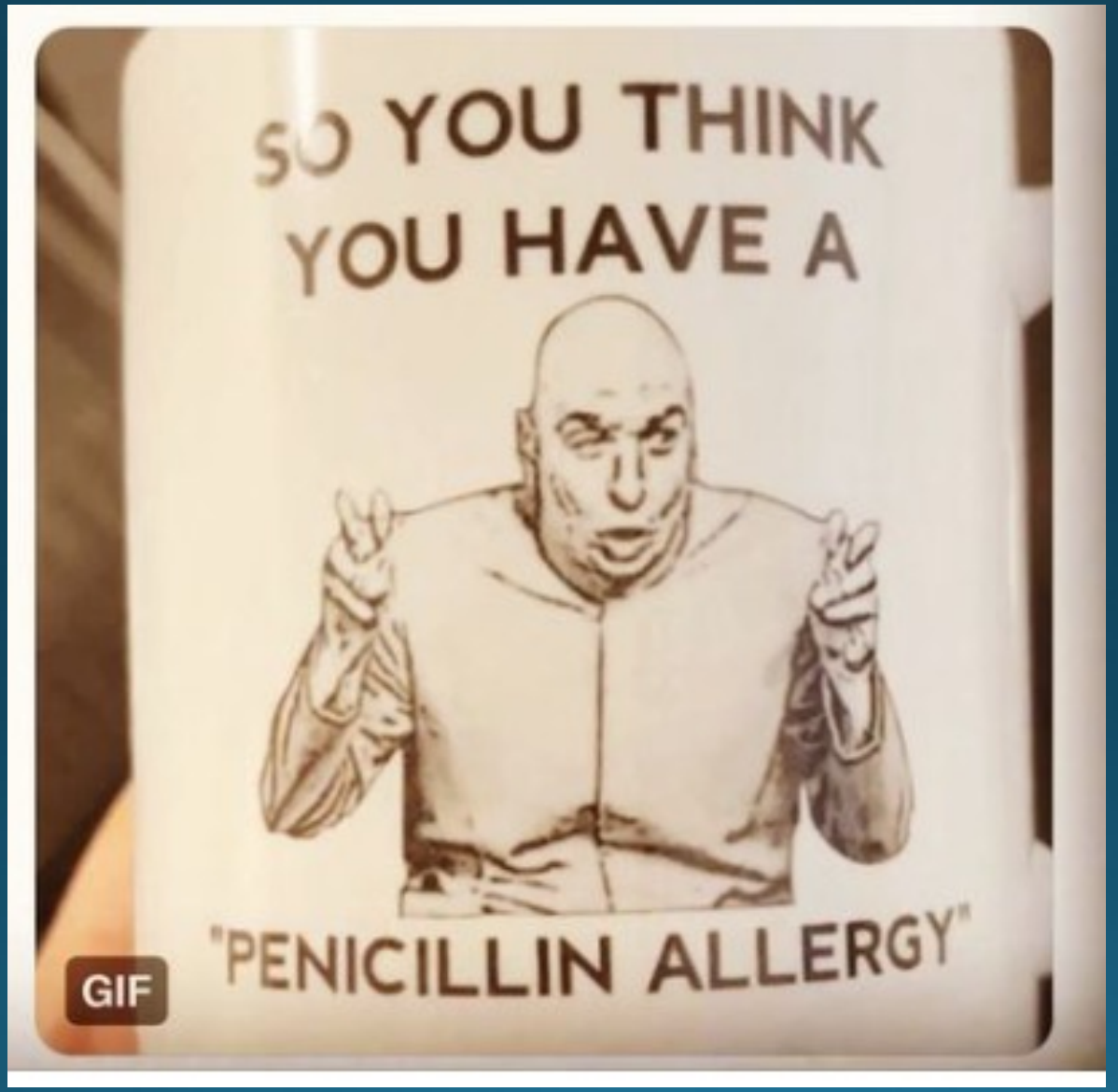
Less likely to receive first-line pre-op antibiotics

Wilhelm NB, et al. Ann Surg 2022
Blumenthal KG, et al. Clin Infect Dis 2018
Lam PW, et al. Infect Control Hosp Epidemiol 2020

# Penicillin Allergy

- PCN allergy is over reported
  - 5-10% of reported allergies were confirmed with skin testing
  - Correlates to 1% of US population that has a true allergy
- Less than 3% cross reactivity between PCN and cephalosporins
- Classification of reaction
  - IgE mediated allergic reaction (anaphylaxis and non-anaphylaxis)
  - Delayed hypersensitivity reaction
  - Non-allergy reactions

Wilhelm NB, et al. Ann Surg 2022
Blumenthal KG, et al. Clin Infect Dis 2018


SO YOU THINK
YOU HAVE A
"PENICILLIN ALLERGY"
GIF

# De-labeling Penicillin Allergies

- Non-allergic reactions should be removed from the medical record
- Delayed hypersensitivity reactions should NOT be removed or re-tried
- IgE reactions can be de-labeled
  - PCN skin testing (medium risk allergy)
  - Oral amoxicillin challenge (low risk allergy)
- IgE reactions can be modified and sometimes de-labeled with a thorough PCN allergy assessment
  - 68% of patients were cleared to receive an alternative beta-lactam at the Memphis VAMC with assessment alone
  - 35% of patients could receive cefazolin based on assessment at CVAHCS

Shenoy ES, et al. JAMA 2019

# Penicillin Allergy Assessment

What medicine cause your allergic reaction? (prompt with brand/generic names)

- Consider R side chain similarities
- Unable to do any skin testing for cephalosporins

How long ago did the reaction occur?

- IgE allergies wane over time

After how many doses or days of the medicine did the reaction occur? Was it within 24 hours of the first dose or days after the first dose?

- Immediate IgE reaction vs delayed reaction

What happened when you took the medicine?

- Did you experience any SOB, wheezing, throat or mouth swelling, hives, anaphylaxis?
- If a rash occurred please describe the rash appearance and location

Shenoy ES, et al. JAMA 2019

# Penicillin Allergy Assessment

Did you seek medical attention for the reaction? Did they give you any medicine to help with your symptoms?

Since your reaction, have you received another penicillin or cephalosporin (prompt with names)? If so, did you tolerate this medicine?

- Check medical records available to see if the patient has taken amoxicillin, Augmentin, cephalexin, or cefazolin

Shenoy ES, et al. JAMA 2019

# Interpreting Assessment for Surgery

- If the patient reports a non-allergic reaction like stomach upset, family history of allergy, etc. → give cefazolin pre-op
- If the patient has tolerated amoxicillin, Augmentin, cephalexin, or cefazolin since the allergy → give cefazolin pre-op
- Initiate a process at your institution for oral amoxicillin challenge or PCN skin testing!

# Summary

- Antimicrobial stewardship is a multidisciplinary team that can collaborate with surgery depts to improve patient outcomes by optimizing antimicrobial therapy
- Uncomplicated IAI can be treated without antibiotics in certain instances or with short antibiotic durations if source control is achieved
- MRSA coverage is not clinically indicated in most nonpurulent SSTI
- Fidaxomicin has lower CDI recurrence rates but its use may be prioritized for patients at high risk of recurrence due to cost
- Penicillin allergy assessments can be used to identify patients with PCN allergies that can receive first-line pre-op antibiotics which can improve SSI rates

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# Questions?

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