UWTASP
tele-antimicrobial stewardship program

Oct 12, 2021

Agenda

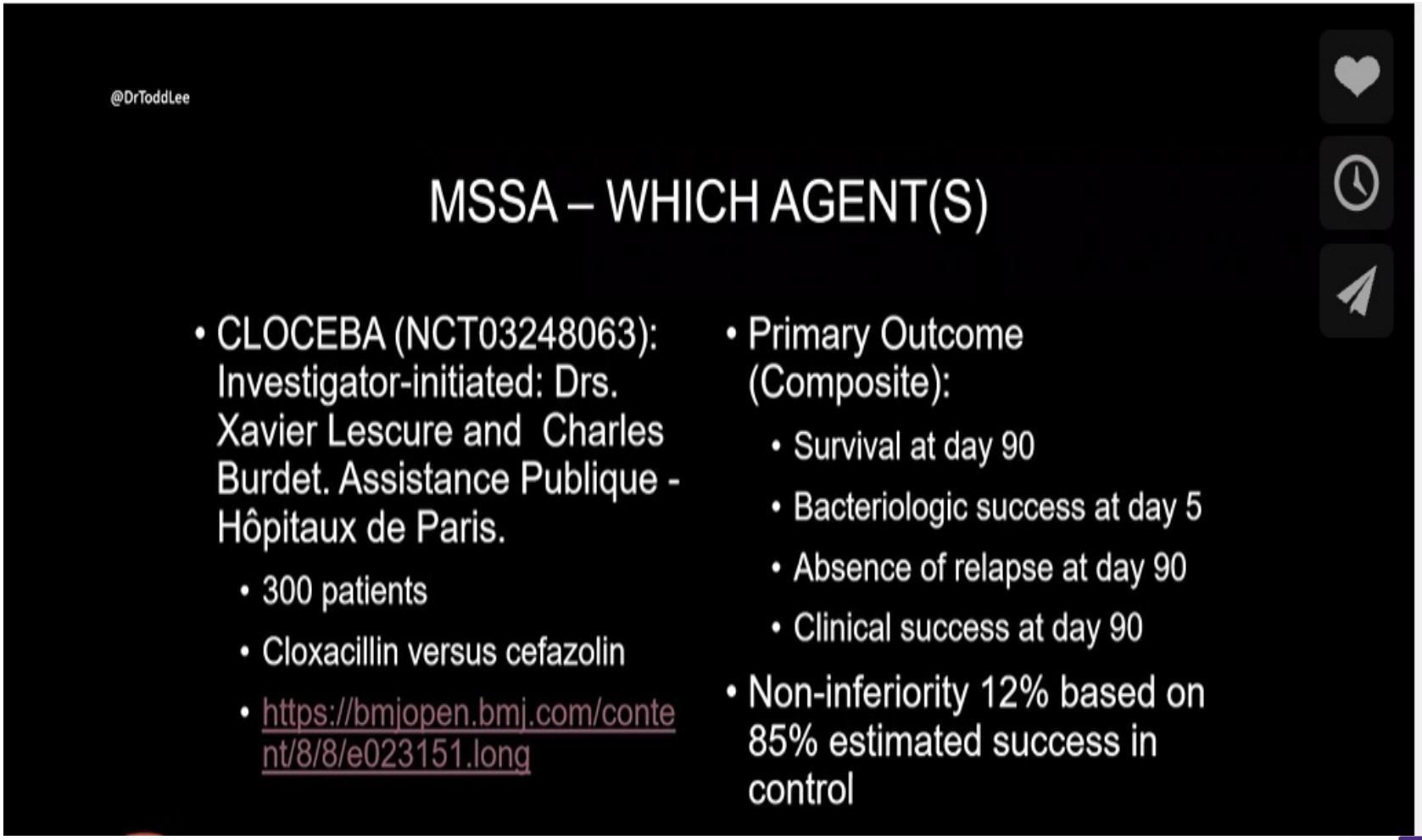
- ID Week Highlights
- Case Discussions
- Open Discussion

Staph aureus bacteremia (SAB)

- Many important SAB clinical trials are being conducted
  - Choice
  - Combination
  - IV to oral step down
  - Duration

Choice: Dalbavancin

Choice: Cloxacillin vs. Cefazolin



Combination: CAMERA-2

JAMA Network™

QUESTION In adults with methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia, does the addition of 7 days of an antistaphylococcal β-lactam to standard antibiotic therapy (vancomycin or daptomycin) lead to improved clinical outcomes at 90 days?

CONCLUSION This randomized trial found that the addition of an antistaphylococcal β-lactam to standard antibiotic therapy did not significantly reduce the prima cteremia.

98% received vancomycin

POPULATION

231 Men
121 Women

Adults hospitalized with MRSA bacteremia

Mean age: 62 years

LOCATIONS

27
Hospitals in Australia, Singapore, New Zealand, and Israel

INTERVENTION

345 Patients analyzed

170
Combination therapy
IV vancomycin or daptomycin for 14-42 days plus IV β-lactam for 7 days

175
Standard therapy
IV vancomycin or daptomycin for 14-42 days

PRIMARY OUTCOME

Composite at 90 days of all-cause mortality, persistent bacteremia at day 5, microbiological relapse, and microbiological failure

FINDINGS

All-cause mortality, persistent bacteremia at day 5, microbiological relapse, and microbiological failure

Combination therapy
59 of 170 patients

Standard therapy
68 of 175 patients

The primary outcome was not significant:

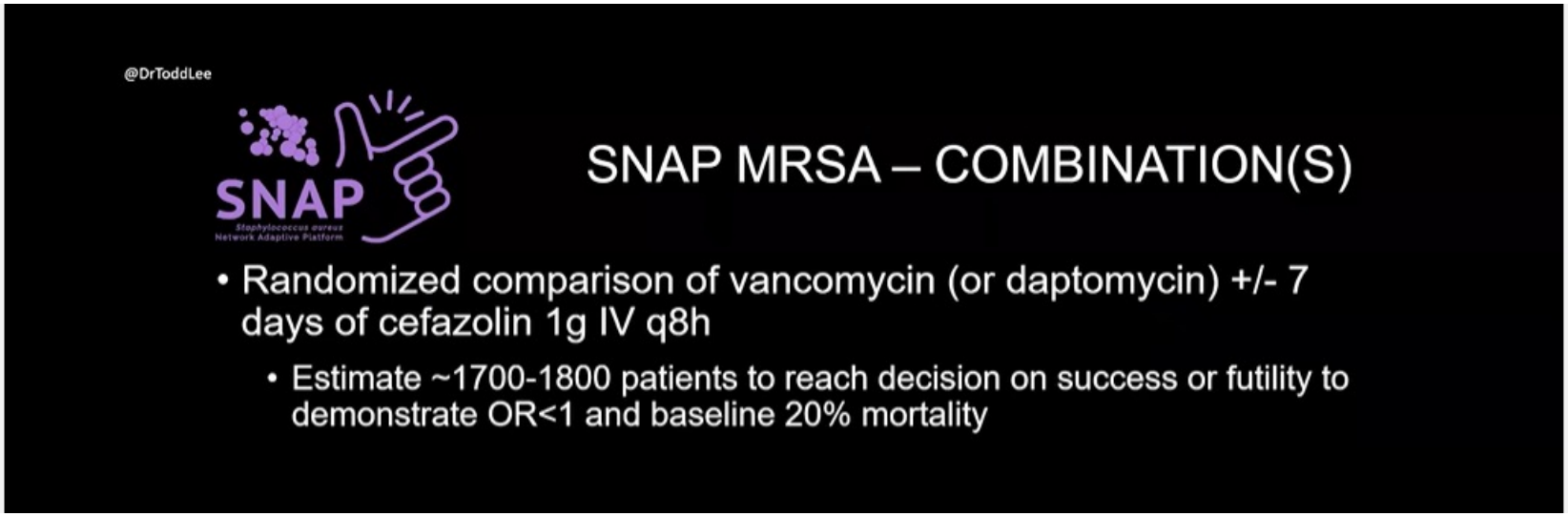
Between-group difference: **−4.2%**
(95% CI, −14.3% to 6.0%)

Tong SYC, Lye DC, Yahav D, et al. Effect of vancomycin or daptomycin with vs without an antistaphylococcal ß-lactam on mortality, bacteremia, relapse, or treatment failure in patients with MRSA bacteremia: a randomized clinical trial [published February 11, 2020]. *JAMA*. doi:10.1001/jama.2020.0103

CAMERA-2

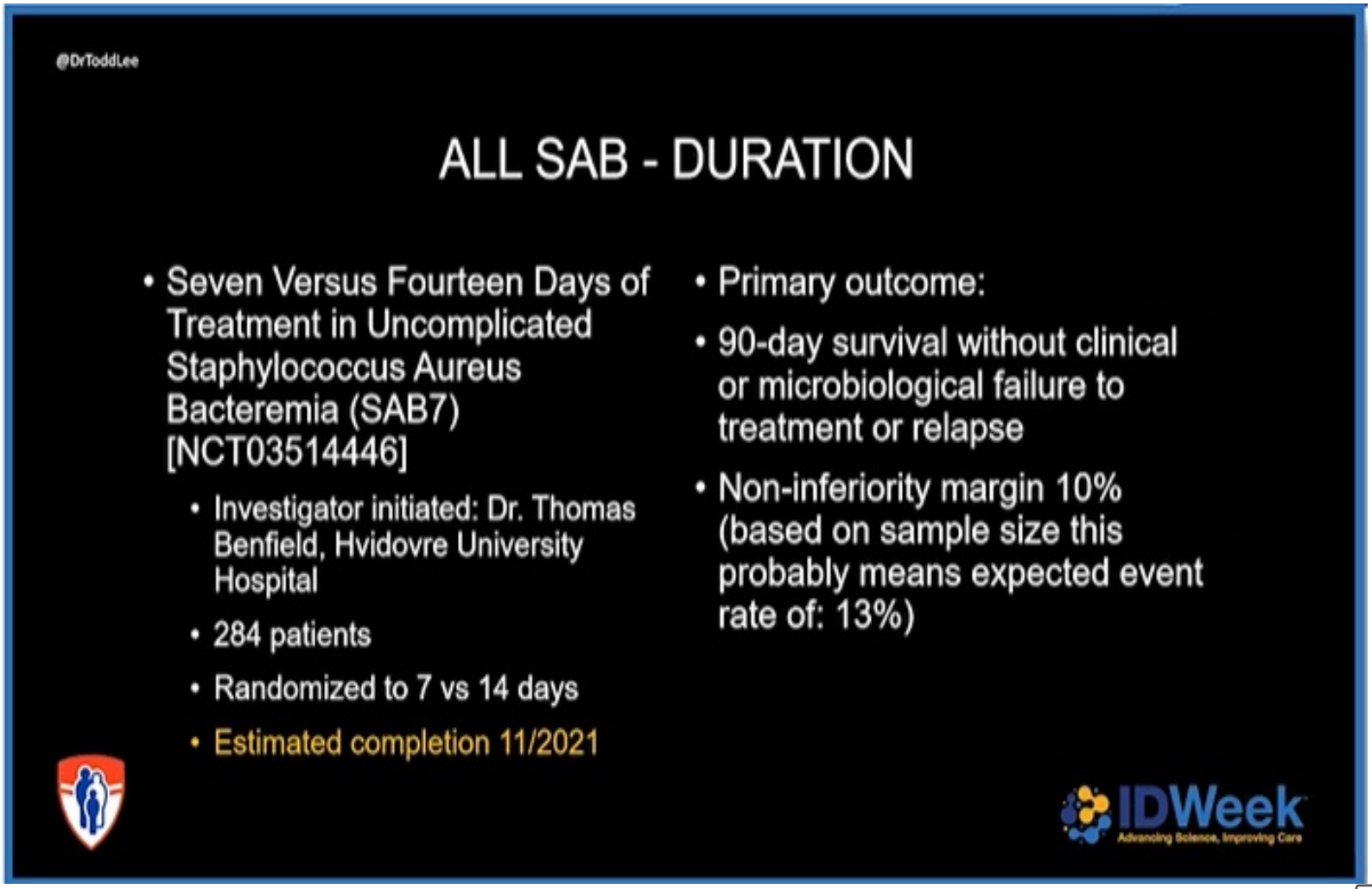
- AKI occurred in 23% combination arm vs 6% monotherapy arm ($p<0.001$)
- AKI occurred in 27% of patients who received flucloxacillin or cloxacillin compared to 3.7% who received cefazolin
- Early trial termination for safety concerns and the possibility that the study was underpowered to detect clinically important differences
- Combination of **vancomycin plus anti-staphylococcal PCN** did not improve clinical outcome (though shortens duration of bacteremia) with an increased risk of AKI

MRSA Combination



IV to PO: Levo + Rifampin

Duration


@DrToddLee
ALL SAB - DURATION
• Seven Versus Fourteen Days of Treatment in Uncomplicated Staphylococcus Aureus Bacteremia (SAB7) [NCT03514446]
• Investigator initiated: Dr. Thomas Benfield, Hvidovre University Hospital
• 284 patients
• Randomized to 7 vs 14 days
• Estimated completion 11/2021
• Primary outcome:
• 90-day survival without clinical or microbiological failure to treatment or relapse
• Non-inferiority margin 10% (based on sample size this probably means expected event rate of: 13%)
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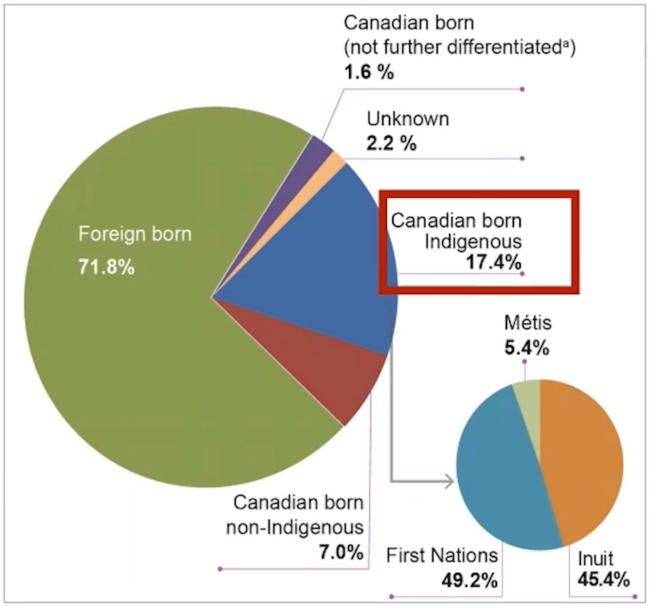
Impact of Infectious Diseases on First Nations and Indigenous Populations

Native Americans and infections

- High burden of infectious diseases amongst Native American populations due to:
- High rates of:
  - Comorbidities
  - Lack of water/electricity
  - Crowded homes
  - Food insecurity
  - Addiction/substance use
- Underfunded healthcare system
- Historical trauma

Tuberculosis

Tuberculosis in Canada



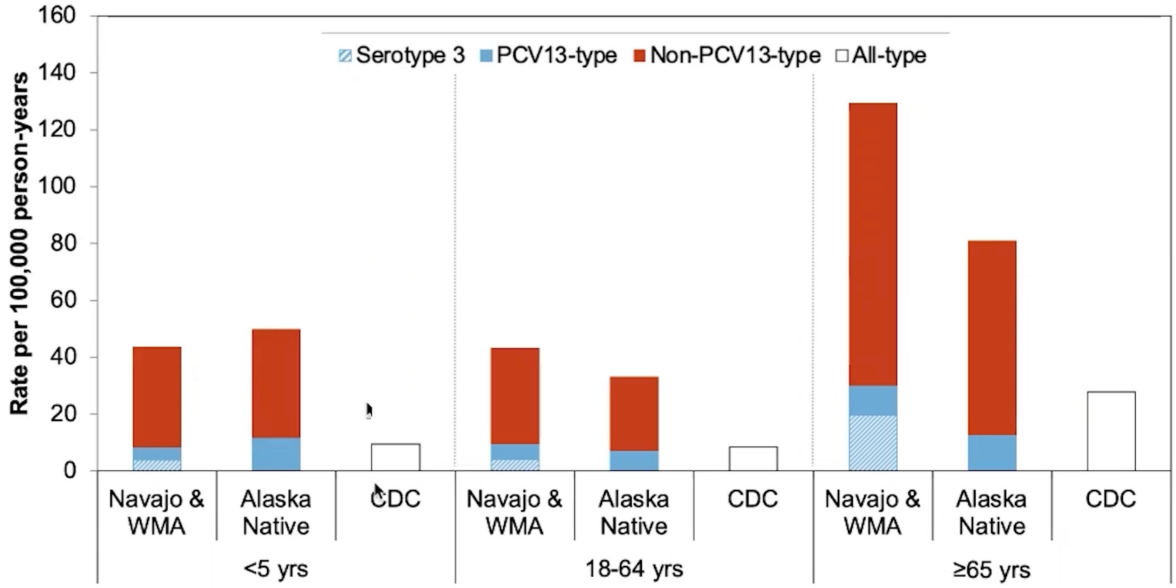
Incidence rate per 100,000	
Canadian-born, non-Indigenous	0.5
First Nations Off-Reserve	9.6
First Nations On-Reserve	21.7
Inuit	205.8

LaFreniere M, Hussain H, He N, McGuire M. Tuberculosis in Canada: 2017. Can Commun Dis Rep 2019;45(2/3):68–74.

Slide credit: Laura Hammitt, MD

Pneumococcus

All Serotype IPD: Native Americans, Alaska Natives and General US, 2011-2017

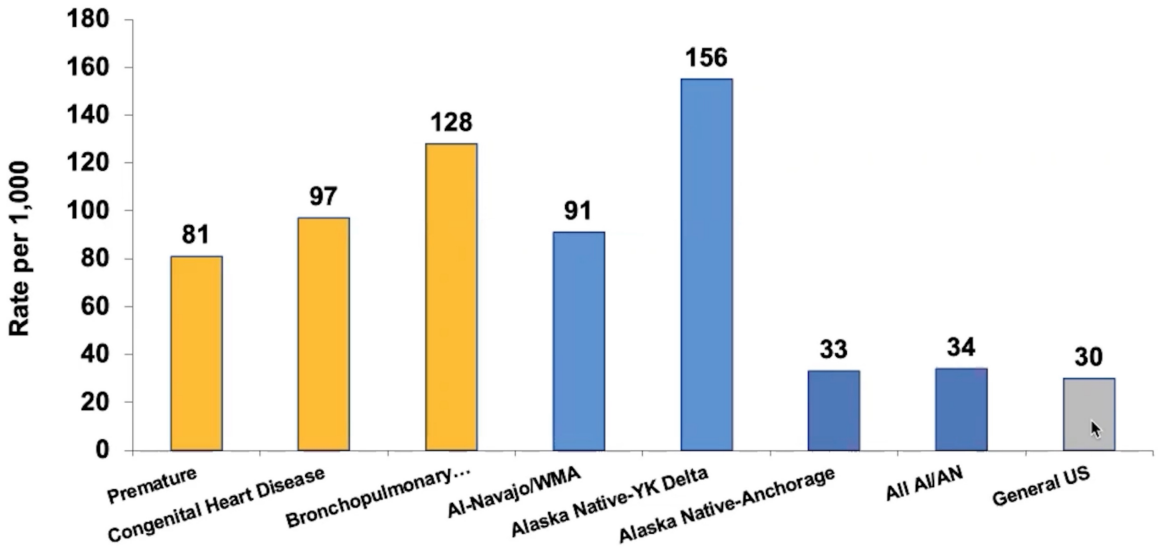


Hammitt et al, Navajo Human Research Review Board Conference, 2019; Alaska Native data courtesy of CDC/AIP; CDC data from ABCs surveillance reports

Slide credit: Laura Hammitt, MD

RSV

RSV Hospitalization Rates in Various Groups Age <1 year, 1990s-2000



Boyce TG et al. J Pediatr 2000;137:865-70
Karron RA et al. JID 1999;180:41-9
Impact Pediatrics 1998;102(3):531-7

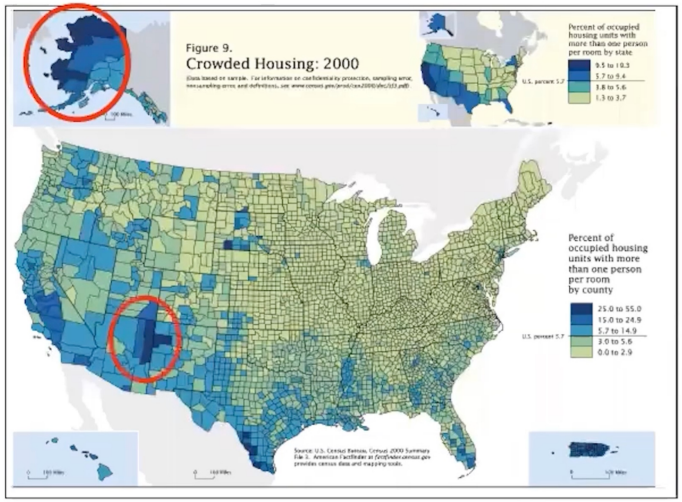
Feltes J Peds 2003;143:532-40
Bockova Pediatrics 2002:110(2):e20
Holman Pediatrics 2004, 114 (4) e437-e444

Slide credit: Laura Hammitt, MD

RSV risk factors

Risk factors for RSV hospitalization in AI/AN infants

- Medically high-risk
- Absence of breastfeeding
- Household crowding
- <2 rooms with sinks
- No piped water
- Woodstove in the house
- Low parent education
- Low household income

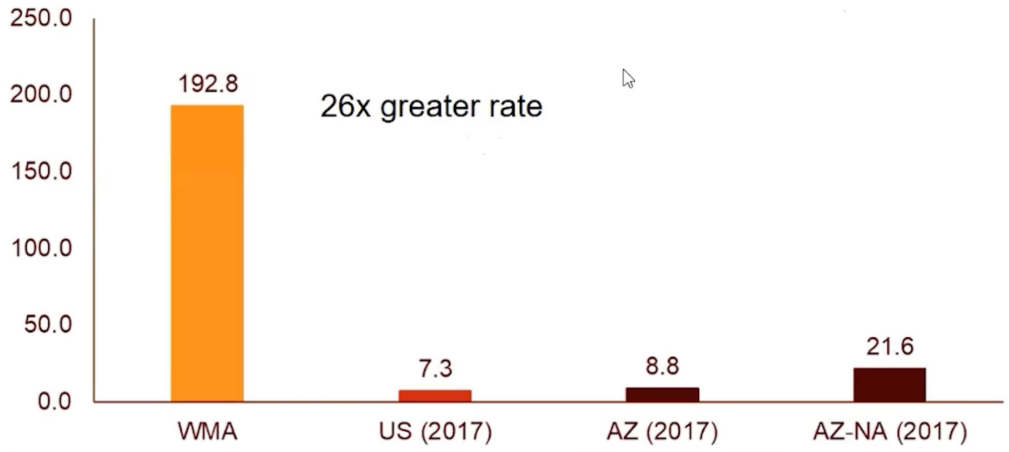


Bruden et al, 18 years of RSV Surveillance. Ped Infect Dis J, 2015.
Bulkow LR et al. Risk Factors for Hospitalization With LRTIs in Children in Rural Alaska. Pediatrics 2012
Bulkow LR et al. Risk factors for severe RSV infection among Alaska native children. Pediatrics 2002
Morris K, et al. Woodburning stoves and lower respiratory infection in American Indian Children AJDC 1990
Robin LF et al. Woodburning stoves and lower respiratory infection in Navajo children PIDJ 1996

Slide credit: Laura Hammitt, MD

Invasive Group A Strep

COMPARISON OF IGAS ON THE WMA TRIBAL LANDS TO THE US GENERAL POPULATION



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Slide credit: James B. McAuley, MD MPH FIDSA

GAS AS A HEALTH DISPARITIES DISEASE

PERSPECTIVE

Disparate Effects of Invasive Group A *Streptococcus* on Native Americans

Ryan M. Close, James B. McAuley

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 26, No. 9, September 2020

- Significant disparities in iGAS rates between indigenous and non-indigenous populations of Australia, New Zealand, and Canada, but much less is understood regarding iGAS among AI/AN in the United States.
- 46% of iGAS in Alaska is among AI/AN (20% of population)
- Post-strep sequelae (RF, PSGN) without recent data
- Role of SES needs to be defined, role of historical trauma not yet understood (ACEs and chronic disease)

Slide credit: James B. McAuley, MD MPH FIDSA

Conclusions

- Native Americans have some of the worst health outcomes and highest rates of infection in the country
- There are many socioeconomic factors that contribute to this and conditions are often worst on reservations
- Think about these patients' unique risk factors when caring for them
- It may be worth considering how some of these factors affect our non-Native American patients

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ID Week Review

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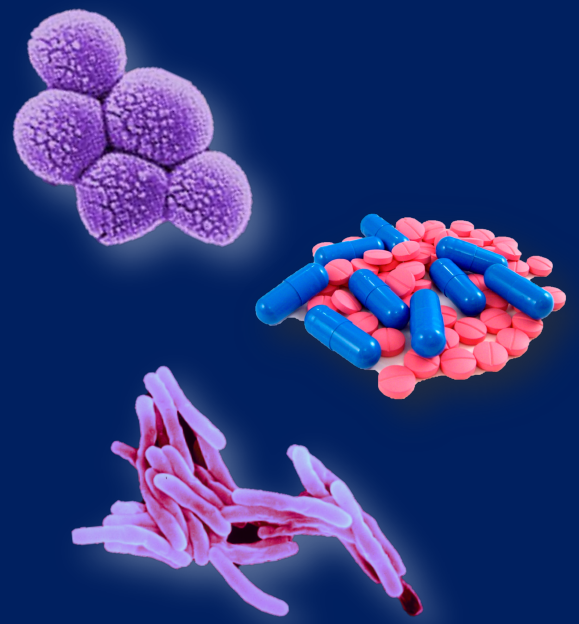
UW-TASP
12 October 2021



IDea Incubator: *Shark Tank!*

IDSA Foundation Awards: *Breakpoints Blog*

Erin McCreary PharmD

AMS Controversies: *Diagnostic Stewardship*

How Does Diagnostic Stewardship Affect Antibiotic Use?

Session: Controversies in Antimicrobial Stewardship

Erin K. McCreary, PharmD, BCPS, BCIDP
Clinical Assistant Professor, University of Pittsburgh School of Medicine
Director of Stewardship Innovation, UPMC and Infectious Disease Connect
@erinmccreary

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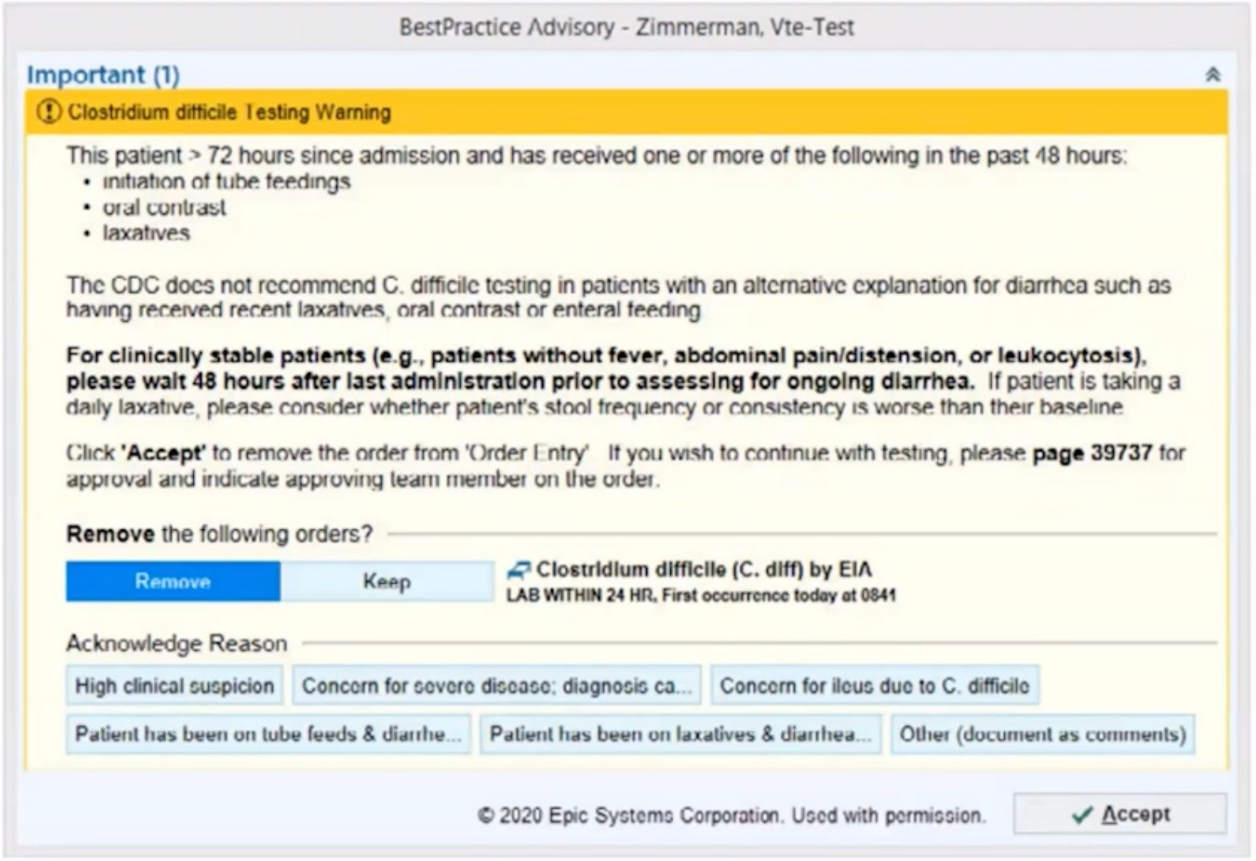
Incorporating preauthorization into antimicrobial stewardship pharmacist workflow reduces *Clostridioides difficile* and gastrointestinal panel testing

Nikki N. Tran PharmD[1], John P. Mills MD[2], Ch
Alison C. Tribble MD, MSCE[4], Lindsay A. Petty M
Gianni Scappaticci PharmD[1], Twisha Patel Phar
Kristin C. Klein PharmD[1], Laraine Washer MD[2], V
and Gregory A. Eschenauer PharmD[1]

32% absolute reduction in hospital onset CDI cases!



A “nudge” is good stewardship

Specimen:

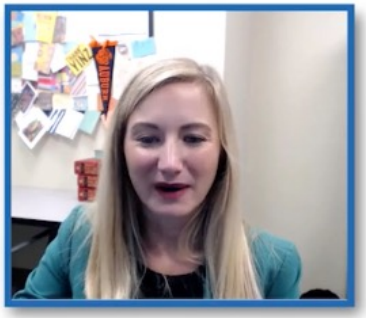
Sputum Culture

Gram Stain

When the Default Choice is No Antibiotic: Modified Reporting

In lieu of culture and susceptibility:

“The majority of positive urine cultures from inpatients without an indwelling urinary catheter represent asymptomatic bacteriuria. If you strongly suspect that your patient has developed a urinary tract infection, please call the microbiology laboratory.”



Slide courtesy of Brad Langford, PharmD, BCIDP, MPH(c)
@BRxAD
Daley P, et al. ICHE. 2018.
Leis JA, et al. CID. 2014.

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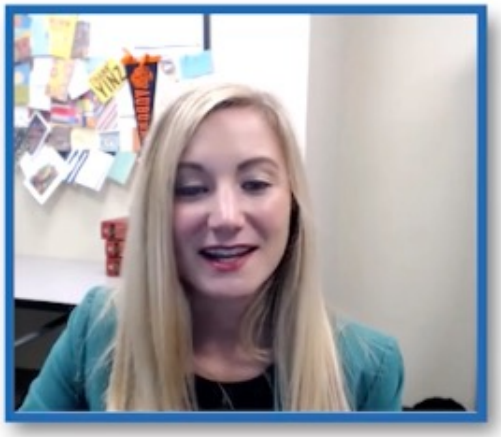
Steps Where Diagnostic Stewardship May Improve Testing

Preanalytic (Ordering/ Collecting)	• Test only if clinical presentation consistent with infection • Improve sampling techniques • Implement clinical decision support for ordering criteria
Analytic (Processing)	• Use adjunctive testing or multi-step algorithms to distinguish colonization from infection • Follow strict contamination guidance in laboratory
Postanalytic (Reporting)	• Report results in a clinician-friendly manner that guides practice • Add interpretive comments to result reports • Suppress irrelevant or confounding results

Morgan D, et al. JAMA. 2017.



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AMS Controversies: *Should We De-escalate?*

Stewardship Controversies

ANTIBIOTIC DE-ESCALATION:
Killing Bugs or Killing Time?

Meghan N. Jeffres, PharmD, BCIDP
University of Colorado Anschutz Medical Campus
@PharmerMeg

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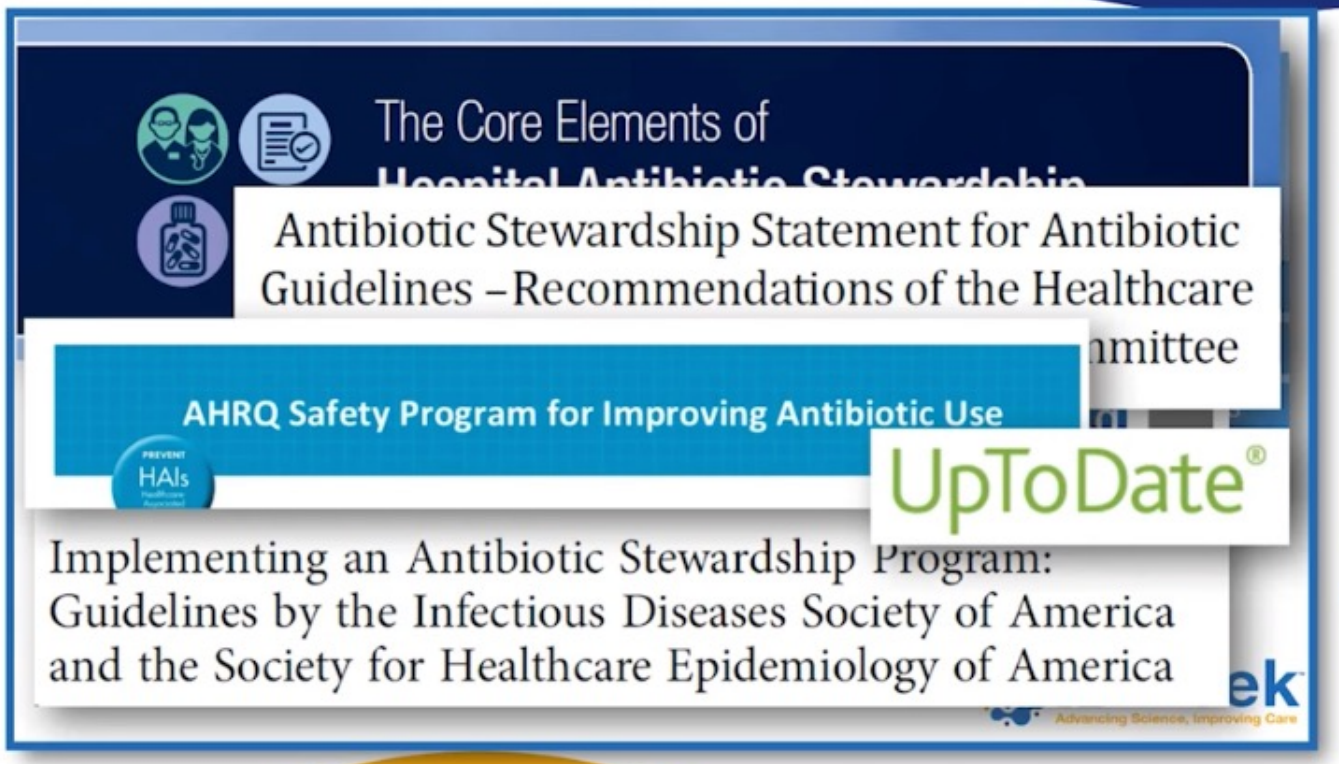
The Core Elements of
Antibiotic Stewardship Statement for Antibiotic
Guidelines –Recommendations of the Healthcare
AHRQ Safety Program for Improving Antibiotic Use
PREVENT
HAIs
UpToDate®
Implementing an Antibiotic Stewardship Program:
Guidelines by the Infectious Diseases Society of America
and the Society for Healthcare Epidemiology of America

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4 Moments of AMS: *Overview*

Boil our approach into 4 moments...

1. Does my pt have an infection that needs abx?
2. If so... have I ordered cultures before abx? And what empiric abx should I choose?
3. It's a new day... Can I stop abx, or de-escalate spectrum, or convert IV to PO?
4. If abx still needed... how long should I treat?

Tamma *JAMA* 2019

ARE THERE ADVANTAGES OF SPECTRUM DE-ESCALATION?

SHOULD WE BE INVESTING OUR TIME ON THESE INTERVENTIONS?

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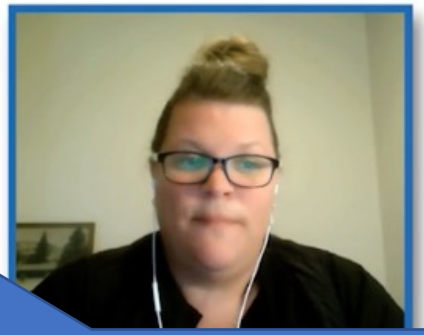
AMS Controversies: *Pro*-De-escalation

DURATION OF ANTIPSEUDOMONAL B-LACTAM AND DEVELOPMENT OF NEW RESISTANCE

	AP beta-lactam, n=7118	Cefepime, n=5274	Meropenem, n=3625	Pip-tazo, n=2463
Each additional day of exposure	1.04 (1.04-1.05)	1.08 (1.07-1.09)	1.02 (1.01-1.03)	1.08 (1.06-1.09)

	Cefepime, n=61	Meropenem, n=103	Pip-tazo, n=108
P. aeruginosa	18%	65%	12%
E. coli	23%	2%	9%
A. baumannii	20%	11%	5%
Enterobacter sp.	13%	9%	41%

Teshome BF. Pharmacotherapy. 2019;39(3):261-270.



Increased risk of resistance per day of exposure: 4%

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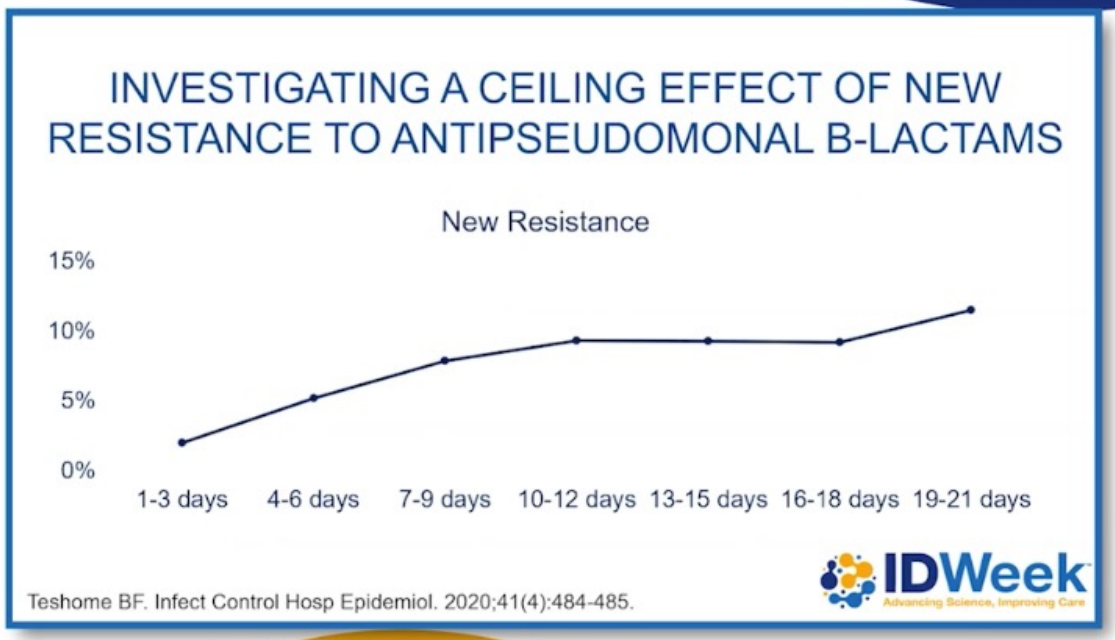

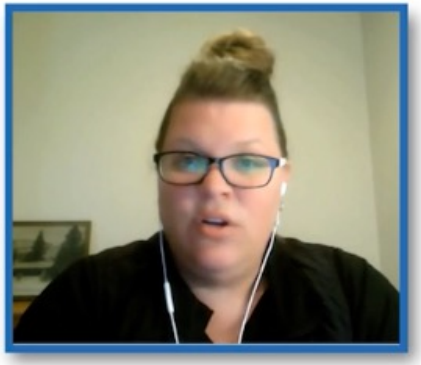

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AMS Controversies: *Pro*-De-escalation

EARLY DE-ESCALATION AND RISK OF *CLOSTRIDIOIDES DIFFICILE* INFECTION

AP BL > 48 hrs, n=394 **vs** AP BL < 48 hrs, n=414

CDI within 90 days of index GN BSI

23 (6%) **vs** 6 (1%)

- Risk factors for receiving > 48 hrs of AP
  - Age, female, Charlson score, Pitt bacteremia score, hospital LOS before GN BSI, intra-ab infection

AP BL = antipseudomonal beta-lactam
CDI = *Clostridioides difficile* infection
GN BSI = gram negative bloodstream infection

Seddon MM. CID 2019;69(3):414-420.

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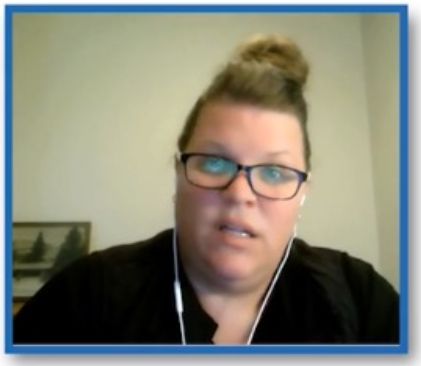

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DE-ESCALATION WITH NEGATIVE CULTURES IN PNEUMONIA

PNA, empiric antibiotics for MRSA and *P. aeruginosa*, n=11,357

De-escalated by day 4, n=913

NOT De-escalated, n=10,444

Lower:
ICU transfer
LOS
Costs (3k)
Duration (5 vs 7d)

No difference:
Mortality, CDI

- De-escalated pts were younger, less comorbid diseases

CDI = *Clostridioides difficile* infection

Deshpande A. CID 2021;72(8):1314-1322.

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AMS Controversies: *Indifferent to De-escalation*

DE-ESCALATION VS. CONTINUATION IN SEVERE SEPSIS: RCT

Severe sepsis w appropriate antibiotics, n=120

De-escalated PP, n=59

Continued PP, n=57

Higher:
Antibiotic days (14 vs. 10)
Super infections (27% vs. 11%)
Lower:
Antipseudomonal days (2 vs. 3)

Super infections
Same index pathogen:
DE = 7/16 (44%)
Cont = 4/6 (67%)

PP = per protocol, DE = de-escalation, Cont = continued

Leone M. Intensive Care Med. 2014; 40:1399-1408.

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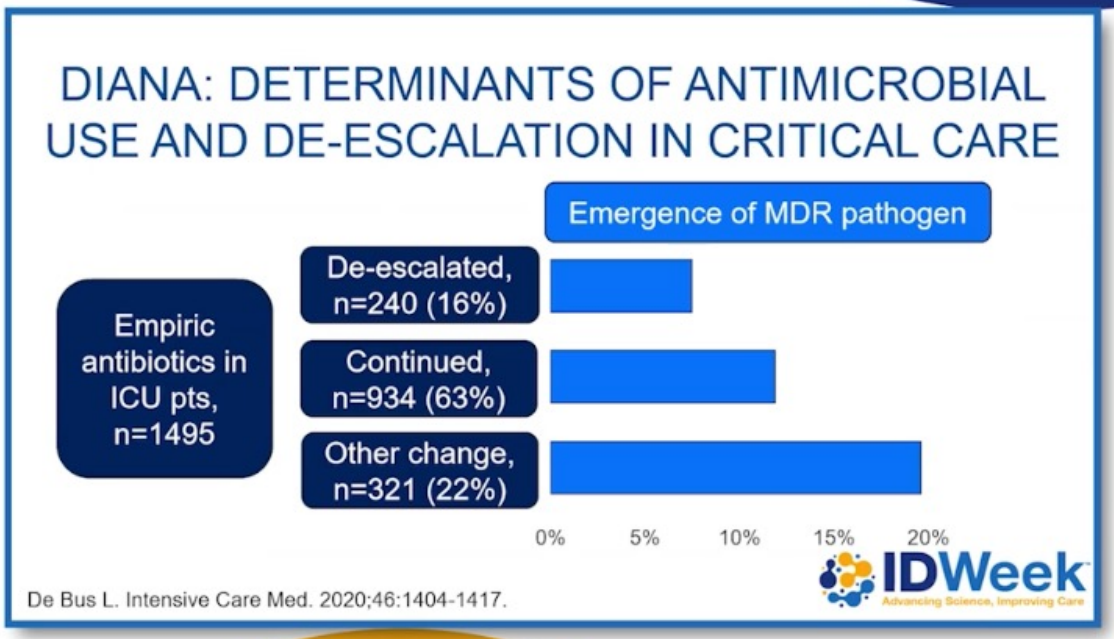
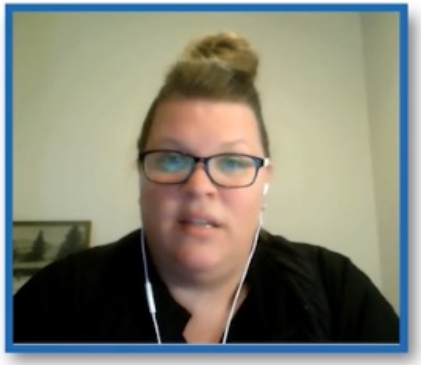
AMS Controversies: *Indifferent to De-escalation*





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AMS Controversies: *Should We De-escalate?*

INTERIM SUMMARY
CONTINUE VS. SPECTRUM DE-ESCALATION

- Probably equal mortality and clinical outcomes
  - In all retrospective studies, de-escalated pts healthier
- Mixed results
  - Duration of antibiotics
  - Antibiotic resistance and super infections
    - Strongest study design showed more resistance with de-escalation
- Is their rationale for exposure to fewer antibiotics?

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RISKS OF SPECTRUM DE-ESCALATION

Hospitalized w ≥ 2 days of antibiotics n=10,154

CDI, n=241

No CDI, n=9913

Higher: GI procedure, HIV, previous CDI, level of care, LOS, PPI/H2RA, GI meds, immuno-suppression, chemotherapy

Adjusted hazard ratios for number of antibiotics received:

1: reference
2: 2.5 (1.6-4.0)
3 or 4: 3.3 (2.2-5.2)
≥5: 9.6 (6.1-15.1)

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Stevens V. Clin Infect Dis. 2011;53(1):42-8.

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FEWER ANTIBIOTICS

Patient 1 — Cefepime x 7 days

Decrease in *E. coli* and bifidobacterial bacteria
Stable for Bacteroides and clostridia class

Patient 2 — Cefepime x 3 days | Ceftriaxone x 4 days

Decrease in Enterobacteriaceae, *E. coli*, lactobacilli, bifidobacterial, and clostridia
Increase in enterococci
Stable for Bacteroides

Bhalodi AA. J Antimicrob Chemother. 2019;74:I6-15.

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AMS Controversies: *Should We De-escalate?*

PRACTICE IMPROVEMENT

- Spectrum de-escalation has not conclusively shown to improve patient outcomes or prevent resistance
- Opportunity costs of stewardship time
  - IV to PO transitions
  - Shortening durations
  - Allergy stewardship

@PharmerMeg

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AMS Controversies: *Handshake Stewardship*

HANDSHAKE STEWARDSHIP: THE FUTURE FOR ASP?

Alison Tribble, MD, MSCE
Associate Professor of Pediatrics
Division of Pediatric Infectious Diseases
C.S. Mott Children's Hospital
University of Michigan

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AMS Controversies: *Handshake Stewardship*

ROUNDING FACILITATES IMPROVED COMMUNICATION AND UNDERSTANDING

- Increased communication between and among ASP and clinical teams
  - Reduces pager/phone tag
  - Direct communication with decision-makers
- Opportunity for teams to ask questions of ASP
- Increased opportunities for education (24% of interventions at CHCO)
- Builds rapport with clinical teams, improves image of ASP, and is likely more enjoyable for ASP teams
- Increases understanding of the practices and cultures of different units and team
- Review of all antimicrobials may identify previously missed inappropriate use, particularly among previously considered "low-yield" targets (e.g. cefazolin)
  - Identifies targets for future ASP efforts and collaborations
- Perhaps more pronounced Hawthorne effect

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AMS Controversies: *Handshake Stewardship*

DOWNSIDES OF HANDSHAKE STEWARDSHIP

Time, time, time:

Physician and Pharmacist at CHCO each dedicate 3-4 hours per day to Handshake Stewardship

Other possible pitfalls:

ASP Fatigue?

If no evaluation after 48-72 hours, may result in missed opportunities to limit duration of use

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