

Everyday antibiotic stewardship

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1


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The following presentation represents my views at the time of the presentation. This information is meant for educational purposes, and should not replace other sources of information or your medical judgment.

I will be sharing personal experiences, reflections, or opinions during this presentation.

Learning Objectives:

1. Determine ideal treatment duration for common infections, applying emerging evidence.
2. Apply principles of antibiotic stewardship in everyday practice.



2


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Conflict Disclosures

Definition: A Conflict of Interest may occur in situations where the personal and professional interests of individuals may have actual, potential or apparent influence over their judgment and actions.

"I have the following conflicts to declare:"

	Company/Organization	Details
Advisory Board or equivalent		
Speakers bureau member		
Payment from a commercial organization. (including gifts or other consideration or "in kind" compensation)		
Grant(s) or an honorarium	FRQS, CHR, M4	Research salary support, Operating grants
Patent for a product referred to or marketed by a commercial organization.	MedSafer Corp.	Software providing medical reference for identifying deprescribing opportunities
Investments in a pharmaceutical organization, medical devices company or communications firm.		
Participating or participated in a clinical trial	Numerous	




3

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Some of the drugs, devices, or treatment modalities mentioned in this presentation are:

Antibiotics

I *might* make therapeutic recommendations for medications that have not received regulatory approval or for their use in ways which do not match the Canadian product monographs.




4

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How long should we treat?

- The example of Community Acquired Pneumonia:
 - When I started training:
 - 10-14 days
 - When I finished training:
 - 7 days
 - Modern randomized controlled trials
 - 3-5 days



5

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journal homepage: www.clinicalmicrobiologyandinfection.com

Why it matters

Systematic review
Estimating daily antibiotic harms: an umbrella review with individual study meta-analysis

Jennifer Curran^{1,2}, Jennifer Lo^{3,4}, Valerie Leung^{5,6}, Kevin Brown^{6,7}, Kevin L. Schwartz^{8,9}, Nick Dastaman^{10,11}, Gary Garber^{12,13}, Julie H.C. Wu¹⁴, Bradley J. Langford^{15,16}

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6

Why it matters

Estimating Daily Antibiotic Harms

Umbrella Review and Meta-Analysis

35 Systematic Reviews | 71 Short to Long Antibiotic Duration Trials | 92% studies evaluated respiratory tract and urinary tract infections | 23,174 patients evaluated


Adverse Events: 41% ↑ (n=2,345) | Each Additional Day Can Cause Harm: 5 vs 3 Days: 9% ↑ Adverse Events; 7 vs 3 Days: 19% ↑ Adverse Events

Antibiotic Resistance: 3% ↑ (n=189) | Adverse Events: 1.04 (1.02 to 1.07) (n=20,340 patients)

Superinfections: 2% ↑ (n=178) | Adverse Events: 1.03 (0.98 to 1.07) (n=20,330 patients)

Superinfection: 0.98 (0.92 to 1.06) (n=20,170 patients)

Fig. 6. Forest plots of odds ratios for primary outcomes.




7

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Key areas where we can embrace “less is more”

- Community acquired pneumonia
 - There are 15 randomized controlled trials which have compared shorter durations of therapy to longer, including in hospitalized patients
 - The uniform conclusion is that less therapy is non-inferior to more therapy for clinical outcomes [but has fewer side effects]
 - If the patient is afebrile and off oxygen by day 3-5, the antibiotics can stop

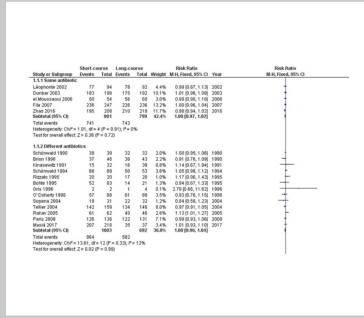


8

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Key areas where we can embrace “less is more”

- Community acquired pneumonia
- 2018 meta-analysis
 - Relative risk of clinical cure in adults – 1.00




9

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Key areas where we can embrace “less is more”

- UTI
 - Step one:
 - Is this really a urinary tract infection, or is this asymptomatic bacteriuria or a contaminated specimen?



10

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Symptom-Free Pee: LET IT BE

A national initiative to stop inappropriate antibiotic use for asymptomatic bacteriuria in long-term care residents.


STOP treating asymptomatic bacteriuria. It is not an infection.

STOP testing foul-smelling, dark, or cloudy urine.

WAIT and hydrate residents who develop changes in mental status, behavior, or function without typical urinary tract infection symptoms.

GO to urinalysis and urine culture if typical signs and symptoms of urinary tract infection are present.

For more directions and guidance: www.amaa.ca




11

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Key areas where we can embrace “less is more”

- UTI
 - “Symptom free pee” exceptions
 - Pregnancy (someone should do the RCT)
 - Pre-invasive urological procedure where blood and urine will mix
 - 1st 1-2 months post renal transplant



12

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Key areas where we can embrace “less is more”

- UTI
 - Step two: So, you have a UTI?
 - Uncomplicated: Single dose fosfomycin, 5 days nitrofurantoin
 - Complicated?
 - 5-7 days is long enough
 - Even in men (without prostatitis)!
 - <https://jamanetwork.com/journals/jama/fullarticle/2782300>
 - Even in pyelo!
 - Even in most who have concomitant bacteremia!
 - <https://pubmed.ncbi.nlm.nih.gov/30535100/>
 - <https://jamanetwork.com/journals/jama/fullarticle/2766635>




13

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Key areas where we can embrace “less is more”

- Cellulitis
 - 6-7 days seems to be as good as 10-14 in most patients




14

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<https://www.bradspellberg.com/shorter-is-better>


- Brad Spellberg
 - Chief Medical Officer at the Los Angeles County-University of Southern California (LAC+USC) Medical Center
 - ID physician who spends more time on the medical inpatient units as IMP than he does as ID consultant
 - Huge advocate for higher value healthcare and rational health policy



15

Spellberg knows!

- Spellberg, JAMA: IM 2016
<https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2536180>
- Spellberg and Rice, Annals 2019
<https://www.acpjournals.org/doi/10.7326/M19-1509>
- Wald Dickler and Spellberg, CID 2019
<https://academic.oup.com/cid/article/69/9/1476/5275222>



16

Shorter Is Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	14
Atypical CAP	1	3	Equal	1
VAP	8	15	Equal	2
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	9*
Intra-abdominal Infection	4	10	Equal	2
GNB Bacteremia	7	14	Equal	3**
Cellulitis/Wound/Abscess	5-6	10	Equal	4†
Osteomyelitis	42	84	Equal	2
Osteo with Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2†
Septic Arthritis	14	28	Equal	1
AECB & Sinusitis	≤5	≥7	Equal	>25
Neutropenic Fever	AFx72 h	+ANC<500	Equal	1
Post Op Prophylaxis	0-1	1-5	Equal	54†
Z. Malaria	7	14	Equal	1
Total: 15 Conditions				122 RCTs

*2 RCT included meta, the smaller one based lower 10-18 d (14) cure in males with 7 days of therapy but no difference at longer follow-up, larger exclusive meta study based on 8 RCT cure. **DMB bacteremia also in 1/15 RCT. †3 RCTs report 11 (one double-blind) (10/10) 2 (single-blind) 1 (1/1) study and none reported adverse events. ‡Includes meta-analysis of 42 RCTs with # 1001 (www.basileia.com/shorter-is-better)

17

Shorter Is Better Exceptions

Diagnosis	Short (d)	Long (d)	Result	#RCT
Prosthetic Joint Infection	6 wk	12 wk	Inferior	1*
Early Pros. Joint Infect.	8 wk	12-26 wk	Equal	1*
Otitis Media < 2 yr old	5	10	Inferior	1
Otitis Media > 2 yr old	<10	10	Equal	49**
Strep Throat: Nml PCN	3-5	7-10	Inferior	5†
Strep Throat: Other Abx	3-5	7-10	Equal	>20†
Strep Throat: QID PCN	5	10	Equal	1
Total: 3 Diseases				>25 RCTs

*6 vs. 12 week inferior for all comers in largest trial, driven primarily but not entirely by DART cohort, but other PCN from Shorter Is Better (also demonstrated 4-6 weeks may be non-inferior, and small RCT of FU within 1 month of impact showed non-inferiority of 6 vs. 12 wk. †Meta-analysis of 63 trials. ‡No increased short-term failure, but by 1 month of follow-up, no difference; meta-analysis of >25 trials. www.basileia.com/shorter-is-better

18



19




20

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What is Stewardship?

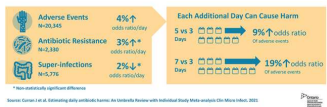
- Optimizing:
 - Selection of spectrum
 - Dose
 - Route
 - Duration
- To MAXIMIZE clinical cure or prevention of infection



21

While reducing:

- Adverse drug events (including *C. difficile*)
- Antimicrobial resistance in the community and hospital
- Costs



22

How can you lead stewardship?

- Avoid unnecessary antibiotics
 - COPD and other non-CAP RTI are often viral
 - "Dirty urine" <-> infection
 - "Symptom free pee; let it be!"
- Making choices
 - Narrow spectrum beta-lactams for more cellulitis
 - Beta-lactams preferred for CAP
- Duration of therapy

23

Questions

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24