Syndromic Antimicrobial Stewardship: Focused Stewardship Initiatives Directed Towards Shorter Courses & Reducing Prophylactic Antimicrobial Use



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KDHE-KHC Syndromic Antibiotic Stewardship Series

Session #1 - April 5 - Focused Initiatives for the Prevention and Treatment of UTI

Session #2 - May 3 - Focused Initiatives for Wounds, Skin, and Soft Tissue

Session #3 – June 7 – Focused Initiatives for Upper & Lower Respiratory Infections

Session #4 - July 12 - Focused Initiatives Directed Toward Sepsis

Session #5 – August 2 – Focused Initiatives Directed Toward Shorter Courses and Reducing Prophylactic Antimicrobial Use

To protect and improve the health and environment of all Kansans

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Continuing Educational Credit Instructions

Steps to Obtain CNE or CPE:

- 1. Fill out the CNE or CPE Sign-In Form
- 2. Participate in the polls. Each participant must be logged in separately.
- 3. Email *fully* completed form to: jdaughhetee@khconline.org

Presenters

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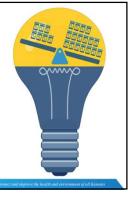
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Objectives

- Examine the evidence suggesting shorter antibiotic durations are as effective for common infectious disease conditions (e.g., pneumonia, skin infections, UTI)
- Formulate ways to incorporate shorter duration options into facility guidelines
- Discuss prophylactic antimicrobial use and overuse
- Design and implement evidence based prophylactic antibiotic guidelines



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Disease	Pre-Antibiotic Death Rate	Death with Antibiotics	Change in Death
Community Associated Pneumonia	35%	10%	-25%
Hospital Associated Pneumonia	60%	30%	-30%
Endocarditis	100%	25%	-75%
Gram negative bacteremia	80%	10%	-70%
Meningitis	>80%	<20%	-60%
Skin infection	11%	<0.5%	-10%

Polling Question 1

Shorter courses of antibiotics are associated with which of the following?

- A. Decreased risk of antibiotic resistance
- B. Increased side effects
- C. Decreased compliance
- D. Decreased cure rates

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Shorter the course the better As quickly as 4 days of antibiotic therapy, 3-fold increased resistant S. pneumoniae in throat swabs Changes in macrolide-resistant S. pneumoniae while on macrolides compared to placebo (no antibiotic) By day 4 antibiotic, resistance over 3 fold Carithromycin Placebo-1 Placebo-1 Placebo-2 Dourse Mahotra-Kumar 5, et al Lacot 2007;380(9505) 482-90.

Polling Question 2

More than 120 randomized trials have found that shorter courses of antibiotics are noninferior to longer courses for 17 conditions?

A. True

B. False

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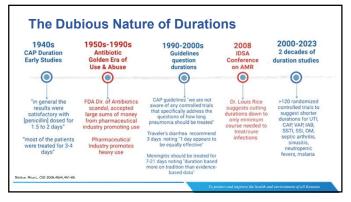
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Polling Question 2

More than 120 randomized trials have found that shorter courses of antibiotics are noninferior to longer courses for 17 conditions?

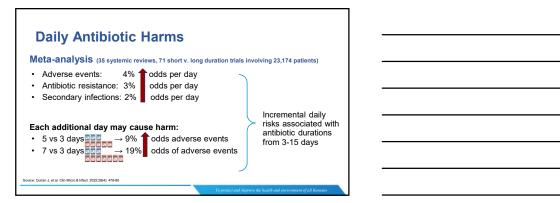
A. True

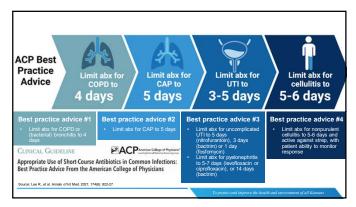
B. False

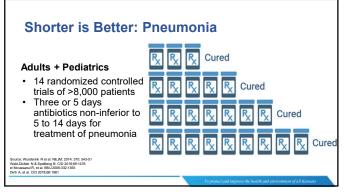




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Adults 1 randomized trial of atypical pneumonia (confirmed *C. pneumoniae, C. psittaci, C. burnetii*, or *L. pneumophila* infections)

- n=96 (48 each group)
 1.5 gram azithromycin x1 dose vs 500 mg x3 days
- 98% cure in each group (followed to 4 weeks)

iource: Schonwald S., et al. Infection; 1999; 22(3):198-20

Ventilator Associated Pneumonia

- Three randomized trials of 8 days vs 15 days antibiotics
- Confirmed non-fermenting gram negatives (e.g., Acinetobacter, Pseudomonas, Stenotrophomonas)
- 9-17% recurrences, no statistical difference b/w shorter or longer, similar median days mechanical ventilation, ICU LOS, no change in mortality (followed to 90 days), lower rates of multi-resistance development

Source: Chastre J., et al. JAMA 2003; 290(19):2588-98 Capellier G., et al. PLoS One 2012; 7(8):e41290 Bougle A., et al. Intensive Care Med 2022; 48(7): 841-49.

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Additional Support - Pneumonia Shorter Courses				
Year	Regimen of shorter course	Regimen of comparator	Outcome	N
Siegel et al 1999	Cefuroxime 7 days	Cefuroxime 10 days	No difference	52
Leophonte et al 2002	Ceftriaxone x 5 days	Ceftriaxone x 10 days	No difference (& bacteriological) cure	244
Dunbar et al 2003	Levofloxacin x 5 days	Levofloxacin x 10 days	No difference	528
Dunbar et al 2004	Levofloxacin x 5 days	Levofloxacin x 10 days	No difference	149
Leophonte et al 2004	Gemifloxacin x 7 days	Amox/clav x 10 days	No difference (or bacteriological or radiographic) cure	320
Tellier et al 2004	Telithromycin x 5 or 7 days	Clarithromycin x 10 days	No difference (or bacteriological) cure	559
El Moussaoui 2006	Amoxicillin x 3 days	Amoxicillin x 8 days	No difference (or radiographic) cure	119
File et al 2007	Gemifloxacin x 5 days	Gemifloxacin x 7 days	No difference (or bacteriological) cure	510
Uranga et al 2016	Standard of treatment x 5 days	Standard of treatment x 10 days	No difference	312
		To protect and im	prove the health and environment of all Kan	sans

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	Мо	rtalit	y (28	day)			Recu	ırrent	Pneu	moni	ia
Study or subgroup	Short course Profe	rigad source	Odds Ratio Milk Random, MNs. O	Starget	Odds facto Militaration 50% CI	Study or subgroup	Shert course P	relanged stories	Colds Ratio Mini Renders, NSA CI	Mary In	Odds Racin Mrs. Random 20% C
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Sell-(2812	8.92	9.25	-	14%	1.691 9.66, 8.181	Medina 2027	1297	592		141.5	2.72 (0.78. 9.52
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Chartre 2000s	401	5-93		91.6	1.28(0.02.319)	Madica 2007	10	16		115	\$1,001,028,403,80
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inhtestal (95% CE	117	120	-	27.0%	1.65 [0.73, 3.73]	Wedne 2001	552	29		11%	1361136,1786
atel events. 16 (Short or	urse), 13 (Prolenged co	note)				Capellar 2552	7114	9009	-	64%	1,17 (9.37, 9.6)
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Unspecified imperiors field Herren 2009	524	100		115	19111271-4111	Tatal events: 54 (Short or materiagenesty Tayl or 5: Test for overall effect 2		2 17 + 2 241 7 +4%			
NATIONAL 2007	547	1058		1815	1377451.181		*930 F = 84D				
Added then con	43			26.4 %	1.22 [0.53, 2.78]	A impacified organism Faich Hassen 2009	234	204	-	37%	1271034.939
etal events: 14 l'Short or teranspensity, Taul = 0.5 act for overall effect; 2 =	unal, 16 Protosped to		T	24.5	111(431,134)	Subtotal (55% CD) fotal events 2 filters on retemperate and expen- ted for event effect 2		16		3.7%	1.17 [0.14, 9.59
Fotal (95% CI) http://www.55/libert.co fotoropenetty Faul = 0.1 het for owned effect 2 = feet for outgroup differen	0.76 (7 + 0.45)	4 8 701 F + 8 0%	•	100.0%	1.18 [0.77, 1.80]	Total (95% CI) Total events II (Dect or nationappearing Test of II Test for events effect 2 - test for events effect 2 -	12 (00 - 135 of -	10-130-15	•	100.0 %	1.41 (0.94, 2.12
	Femore	short course	Pasters prolonged	180 reurse			fasc	urs short course	favours prolong	ed course	

Longer Courses Warranted

- Initial therapy not active against isolated pathogen
 Extrapulmonary infection (eg.. meningitis or endocarditis)
 Pneumonia caused by *P.aeruginosa, S.aureus*, or unusual pathogens (*Burkholderia spp*, fungus)
 Necrotizing pneumonia

- EmpyemaLung abscess

Pletz M.,et al. Chest 2020; 158(5):1912-18.

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Shorter is Better: UTI and Pyelonephritis R R R R R Cured Adults Nine randomized R R R R R R Cured controlled trials of >1800 patients Complicated UTI: 5-7 R R R R R R R R R R Cured days antibiotics non-inferior to 10-14 days Pyelonephritis: 5-7 days Cured Pyelonephritis: 5-7 days non-inferior to 10-14 days

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Additional Support - Pyelonephritis Shorter Courses				
Year	Regimen of shorter course	Regimen of comparator	Outcome	N
Gleckman et al 1985	Gent/Tobra → bactrim x 9- 11	Gent/Tobra→bactrim x 20-22	No difference in cure	54
Stamm et al 1987	Ampicillin x 2 weeks	Ampicillin x 6 weeks	No difference in cure	27
Stamm et al 1987	Bactrim x 2 weeks	Bactrim x 6 weeks	No difference in cure	33
Jernelius et al 1988	Pivampicilin x 7 days	Pivampicillin x 21 days	Shorter course more bacteriologic cure (28% vs 69%)	77
De Gier et al 1995	Fleroxacin x 7 days	Fleroxacin x 14 days	No difference in cure	54
Talan et al 2000	Ciprofloxacin x 7 days	Bactrim x 14 days	Improved clinical cure (96% vs 83%)	255
Klausner et al 2007	Levofloxacin x 5 days	Ciprofloxacin x 14 days	No difference in cure, micro eradication	192
Peterson et al 2008	Levofloxacin x 5 days	Ciprofloxacin x 10 days	No difference in cure	1109

Shorter is Better: Skin Infections
Adults + Pediatrics
 Four randomized controlled trials of >1400 patients Five to 6 days antibiotics non-inferior to 10 days for cellulitis
R R R R R Cured R R R R R R R R R R R Cured
Social Registers M., et al. Ann 1988 to Bad 2004, 154(15), 1660-74 Norm C. et al. Lorest for 100 2004, 146(16), 1660-74 Norm C. et al. Lorest for 100 2014, 146(1600-706 Commodors et al. Child Modellaters 2015/2006, 000-12
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Diabetic Foot Infections

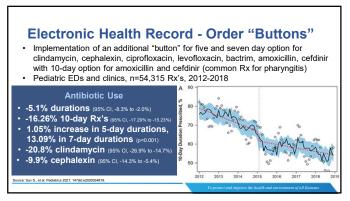
Adults

- Moderate-severe diabetic foot ulcer infections w/o osteomyelitis
- Post-debridement antibiotics for 10 or 20 days (all oral)
- No difference in cure (77% in 10-days vs 71% in 20-days, (p=0.57) $\,$
- Non-statistically greater longer-term osteomyelitis (23%, 3/35) in 10 days vs 16% (5/31) in 20 days (p=0.53)
- · Larger confirmatory trial is underway

Source: Pham T., et al. Annals of Surg 2022;276(2):233-36

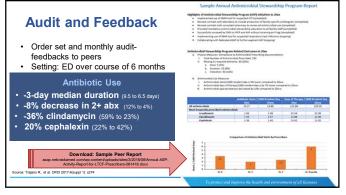
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Stewardship Initiatives to Improve Durations • EHR • Audit and feedback • Guidelines and incorporation into clinical decision support Clinical decision support Antibiotic Timeouts & Audit Feedback



Secondary Outcomes No difference in clinic or ED revisits No increase in hospital admissions No difference in abx re-orders - Optimize your EHR, many features are available without add-ons or 3rd party vendors (but may require institutional IT programming) - Optimize your EHR, many features are available without add-ons or 3rd party vendors (but may require institutional IT programming)

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Audit and Feedback

 Systematic review: interventions directed to physicians by providing advice or feedback were more effective in improving prescribing practices than those not providing feedback (29 studies)



 Interventions that applied "rules" (prior-auth) to make physicians prescribe properly resulted in delays in treatment and a breakdown in trust (n=7 studies)

Source: Davey P., et al. Cochrane Database Syst Rev 2017;2017(2): CD003543

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Polling Question 3

Does your facility have facility guidelines in place which incorporate shorter antibiotic durations?

A. Yes

B. No

Note: there is no right or wrong answer ©

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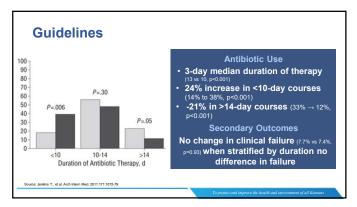
Guidelines

- Guideline development for cellulitis and suspected abscesses
 - Seven-day duration recommended
 also provided algorithm for imaging indications (that is if abscess
 - indications (that is if abscess suspected but not cellulitis)
- Included in order set
- Educational campaign
 - E-mail
 - Intranet
 Work are
 - Work areas

enkins T., et al. Arch Intern Med. 2011;171:1072-79.

Antibiotic Use
-30% gram-negative coverage (66%
→ 36%, p<0.001)
-10% anti-pseudomonal
antibiotics (28% → 18%, p=0.02)
cont to be to be store (DI and

- -32% in beta-lactam/BLase inhibitor combos (60% → 28%, p<0.001)



Example Guidelines					
Condition	Preferred	Alte	rnative		
Uncomplicated UTI	Nitrofurantoin x 5 days	Bactrim x 3 days	Cephalexin x 3-7 days Cefpodoxime Cefuroxime Cefdinir		
		Alt to above:	Levofloxacin x 3 days		
Complicated UTI	Nitrofurantoin x 7 days	Bactrim x 7 days	Cephalexin x 7 days Cefpodoxime Cefuroxime Cefdinir		
		Alt to above:	Levofloxacin x 7 days		
Pyelonephritis	Cipro or Levoflox x 7 days	Bactrim x 7-14 days	Augmentin x 10-14 days		

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Example Guidelines					
MDRO	Preferred	Alterna	tive		
VRE	Amoxicillin 500 - 1000 mg TID-BID urine drug exceeds MIC necessary for therapeutic effect	Daptomycin	Linezolid		
ESBL	Fosfomycin 3g q72h x1-3 doses not for use for pyelonephritis	Ertapenem			

Example Guidelines			
Condition	Pathogens	Treatment	Duration
Impetigo		Topical mupirocin 2% three times daily	
If numerous	Staphylococcus spp Streptococcus pyogenes	Cephalexin 500 mg TID to QID or Cefadroxil 500 mg BID	
		Penicillin Allergic Alternative: Amoxicillin/clavulanate 875 mg BID	5 days
Erysipelas	Streptococcus pyogenes Beta-hemolytic strep	Amoxicillin 500-875 mg BID to TID Penicillin Allergic Alternative: Amoxicillin/clavulanate 875 mg BID Clindamycin 300 mg QID	

	Ex	ample Guidelines	
Condition	Pathogens	Treatment	Duration
Non-purulent cellulitis	Streptococcus pyogenes / beta- hemolytic strep Staphylococcus spp	Cephalexin 500 mg TID to QID or Cefadroxil 500 mg BID	
Non-purulent cellulitis with MRSA risk factors*	Staphylococcus spp MSSA MRSA	Cephalexin or cefadroxil PLUS Bactrim 1-2 DS tab BID or Doxycycline 100 mg BID Penicillin Allergic Alternative: Clindamycin 300 mg QID	5 days (may extend based on response)
		onization, close contact with MRSA, high community patracks, prison), contact sports (wrestling, footb	

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	Exam	ple Guidelines	
Condition	Pathogens	Treatment	Duration
Purulent cellulitis	MSSA MRSA	Perform Incision and Drainage (I&D) Adjunctive antibiotics are recommended in certain scenarios if drained*	
collection	Reta hemolytic etren	* abscesses >2 cm, extensive disease (multiple abscesses or multiple sites of infection), clinical signs or symptoms of infection, inadequate response following I&D, immunosuppression	5 days (may extend based on response)
Purulent cellulitis WITHOUT drainable fluid collection	MSSA MRSA Beta-hemolytic strep (less common)	Bactrim 1-2 DS tabs BID or Doxycycline 100 mg BID	

| Common | Condition | Common | Common

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Polling Question 4

True or false? The most effective way to improve antibiotic durations are via educational initiatives

- A. True
- B. False

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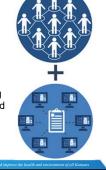
Polling Question 4

True or false? The most effective way to improve antibiotic durations are via educational initiatives

- A. True
- B. False

Clinical Decision Support

- Systematic review: antibiotic stewardship initiatives in the outpatient setting to reduce prescriptions (43 studies)
- The most effective interventions in changing abx prescribing behaviors were multi-faceted combining active clinician education with clinical decision support



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Ranji S., et al. Med Care 2008;46(8):847-62.

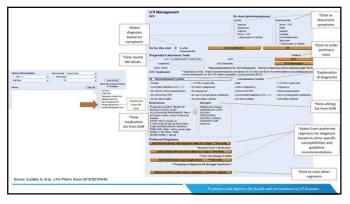
Clinical Decision Support

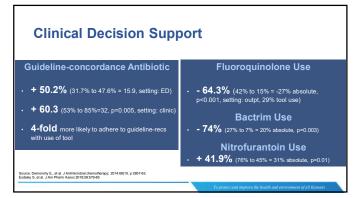
- · Systematize the decision-making process
- Akin to checklist approach
- CDSS tools provided the greatest benefit for providers in non-teaching settings, had been practicing the longest, and in facilities/regions with limited access to consultation and subspecialty services

Source: AHRQ interventions to Decrease Antibiotic Overuse; ahrq.gov/hai/patient-safety-resources/advances-in-hai/hai-article6.html

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EMR-Treatment Support Best practice alert auto-triggered upon antibiotic-Rx for UTI Clinician enters dx (UTI, chronic prostatitis, pyelonephritis) Pop-up w/ relevant info extracted EMR Abx recommended based on guideline Clinician can opt-out





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Surgical Prophylaxis (ppx) is to reduce the burden of microorganisms present at the surgical site during the operative procedure • Patients who receive ppx abx 1-2 hours before surgery have significantly reduced rates of surgical site infections Time of Admin. Ssi Odds Ratio SSW CI Early (2-24h before incision) 3.8% 4.3 18-10.4 Peri-operative (w/in 3hrs after incision) 0.6% 1 08-7.4 Post-operative (more than 3 hours after 3.3% 2.1 24-13.8 Incision)

Surgical Prophylaxis Guidelines					
Recommendation	American College of Surgeons & Surgical Infection Society	World Health Organization	Centers for Disease Control & Prevention		
IV antibiotic ppx	Given w/in 60 minutes of incision (redosing should be based on the half-life of the antibiotic and blood loss)	Given w/in 120 minutes of incision	Given so that bactericidal concentration of agent is present during incision		
Post-op ppx	Antibiotics should stop at closure incision, with few exceptions	Antibiotics should not be given after operation	Stop at closure of incision for clean/clean- contaminated incisions		
MRSA/MSSA Colonization	Cardiac & orthopedic patients colonized with MSSA/MRSA should be decolonized	Nasal carriers of MSSA/MRSA should be decolonized prior to surgery			

Surgical Prophylaxis • Meta-analysis of 21 randomized trials (n>14,000) • or 1.19 (95% CI, 0.94 − 1.50) • No benefit of post-op ppx, with increased risk of C. diff, adverse events | Study or Subgroup | Events | Total | Events | Even

50

Polling Question 5

True or false: Dental antibiotic prophylaxis is recommended before dental cleanings for people who have had a joint replacement?

- A. True
- B. False

Polling Question 5

True or false: Dental antibiotic prophylaxis is recommended before dental cleanings for people who have had a joint replacement?

A. True

B. False

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Dental Prophylaxis

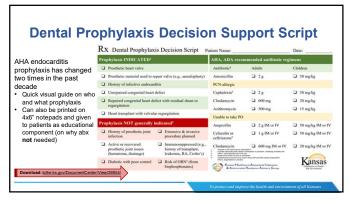
- Although frequently implicated in endocarditis, dental procedures contribution is low (temporal relationships estimated at 4%)
- Three case-control studies no change in endocarditis post-dental treatment
- UK before-after NICE guideline changes (2008 rec to stop all abx
 - No associated change in endocarditis over 10 year period

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Dental Prophylaxis

In a systematic review of case-control and randomized controlled trials no studies could be found relating periodontal disease to prosthetic joint infection





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- Participate in the polls. Each participant must be logged in separately.
- 3. Email *fully* completed form to: jdaughhetee@khconline.org

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