Antibiotics Reimagined: Shorter, Smarter, and More Oral Than Ever

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Faculty Disclosure

Nothing to disclose

Educational Need / Practice Gap

Gap = Prolonged IV antibiotic courses remain common despite evidence supporting shorter, oral regimens

Educational Need = Clinicians require updated knowledge and tools to confidently apply shorter durations and oral step-down in practice

Objectives

By the end of this session, participants will be able to:

1. **Choose shorter antibiotic durations** for common infections when appropriate
2. **Decide when oral step-down therapy is appropriate** in conditions like osteomyelitis, bacteremia, and endocarditis
3. **Apply simple bedside criteria** to safely switch from IV to oral therapy
4. Recognize how AI tools may support clinical decision-making

Poll Question #1

A 65 yr old male is admitted with CAP. He is afebrile and stable on day 3 of therapy and ready for discharge. How long would you treat?

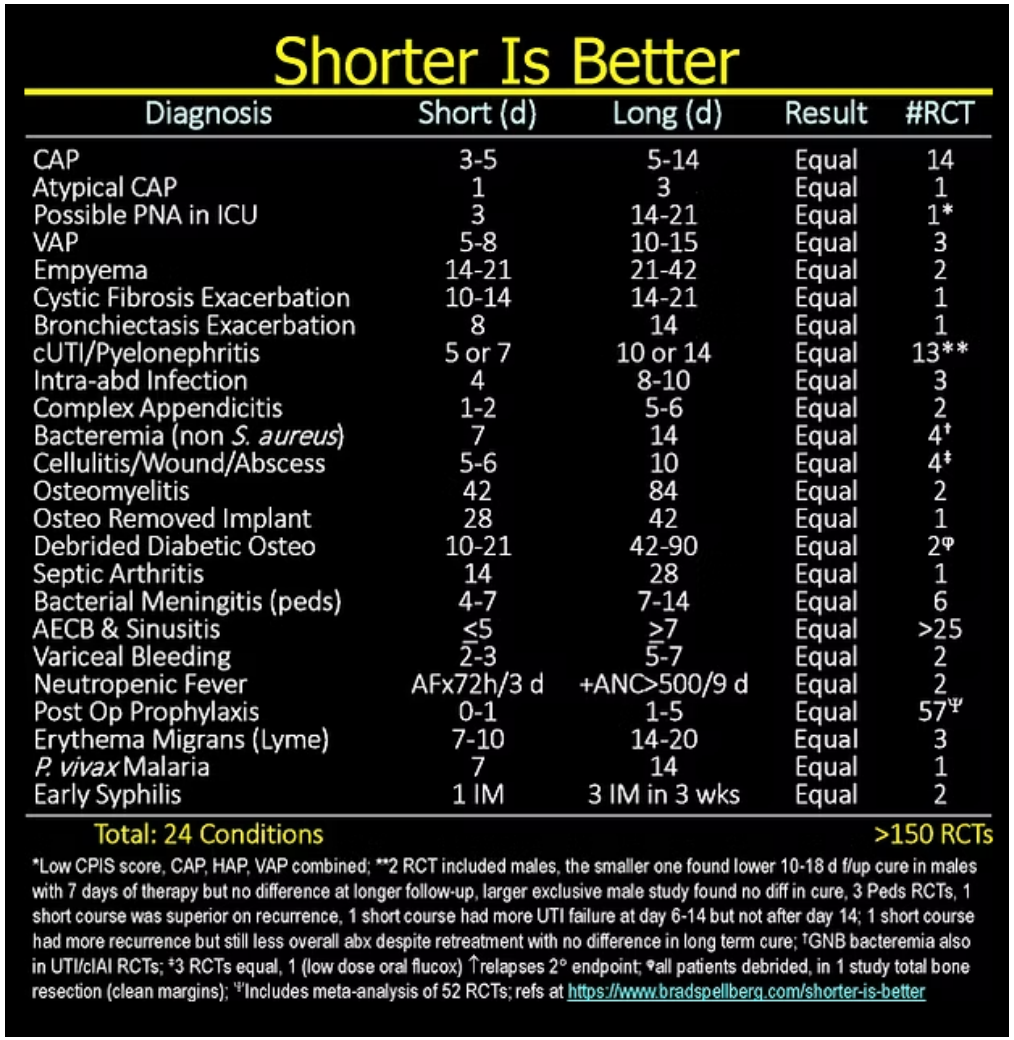
A. 3-5 days
B. 7 days
C. 10 days
D. > 10 days

Poll Question #2

A 60 yr old female is admitted with fever and found to have E. coli bacteremia and pyelonephritis without abscess. She defervesces within 48 hours of starting abx and feels much improved by HD#3. What duration of abx therapy would you choose?

A. 5-7 days
B. 10 days
C. 14 days
D. > 14 days

Less is More – The Modern Duration



Shorter Is Better

Diagnosis	Short (d)	Long (d)	Result	#RCT
CAP	3-5	5-14	Equal	14
Atypical CAP	1	3	Equal	1
Possible PNA in ICU	3	14-21	Equal	1*
VAP	5-8	10-15	Equal	3
Empyema	14-21	21-42	Equal	2
Cystic Fibrosis Exacerbation	10-14	14-21	Equal	1
Bronchiectasis Exacerbation	8	14	Equal	1
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	13**
Intra-abd Infection	4	8-10	Equal	3
Complex Appendicitis	1-2	5-6	Equal	2
Bacteremia (non *S. aureus*)	7	14	Equal	4†
Cellulitis/Wound/Abscess	5-6	10	Equal	4‡
Osteomyelitis	42	84	Equal	2
Osteo Removed Implant	28	42	Equal	1
Debrided Diabetic Osteo	10-21	42-90	Equal	2ᵠ
Septic Arthritis	14	28	Equal	1
Bacterial Meningitis (peds)	4-7	7-14	Equal	6
AECB & Sinusitis	≤5	≥7	Equal	>25
Variceal Bleeding	2-3	5-7	Equal	2
Neutropenic Fever	AFx72h/3 d	+ANC>500/9 d	Equal	2
Post Op Prophylaxis	0-1	1-5	Equal	57Ψ
Erythema Migrans (Lyme)	7-10	14-20	Equal	3
P. vivax Malaria	7	14	Equal	1
Early Syphilis	1 IM	3 IM in 3 wks	Equal	2

Total: 24 Conditions >150 RCTs

*Low CPIS score, CAP, HAP, VAP combined; **2 RCT included males, the smaller one found lower 10-18 d f/up cure in males with 7 days of therapy but no difference at longer follow-up, larger exclusive male study found no diff in cure, 3 Peds RCTs, 1 short course was superior on recurrence, 1 short course had more UTI failure at day 6-14 but not after day 14; 1 short course had more recurrence but still less overall abx despite retreatment with no difference in long term cure; †GNB bacteremia also in UTI/cIAI RCTs; ‡3 RCTs equal, 1 (low dose oral flucox) ↑relapses 2° endpoint; ᵠall patients debrided, in 1 study total bone resection (clean margins); ΨIncludes meta-analysis of 52 RCTs; refs at https://www.bradspellberg.com/shorter-is-better

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Narrative review

Short-course antibiotics for common infections: what do we know and where do we go from here?

Rachael A. Lee [1, 2, *], Joshua T. Stripling [1, 2], Brad Spellberg [3], Robert M. Centor [2, 4]

- Review of > 120 RCTs illustrating short courses to be non-inferior to long courses of antibiotics for common bacterial infections
- Evaluated 7 common infections: pneumonia, UTI, intra-abdominal infection, bacteremia, skin and soft tissue infection, bone and joint infections, pharyngitis and sinusitis
- **Shorter courses evaluated are non-inferior as long as…**
  - Diagnosis is confirmed
  - Appropriate antimicrobials are used
  - Patients show clinical signs of improvement

Microbiol Infect 2023;29:150

BMJ Open Optimal duration of antibiotic treatment for community-acquired pneumonia in adults: a systematic review and duration-effect meta-analysis

- Systematic review and duration-effect meta-analysis
  - Tested non-inferiority with primary outcome being clinical improvement at day 15
  - 9 trials were included (2399 patients)
  - Absolute Clinical Improvement Rates
    - 3 days of treatment – 75%
    - 5 days of treatment – 72%
    - 7 days of treatment – 69%
  - **Conclusions**
    - **Shorter treatment durations of 3-5 days probably offers the optimal balance between efficacy and treatment burden for treating CAP in adults if they reach clinical stability**

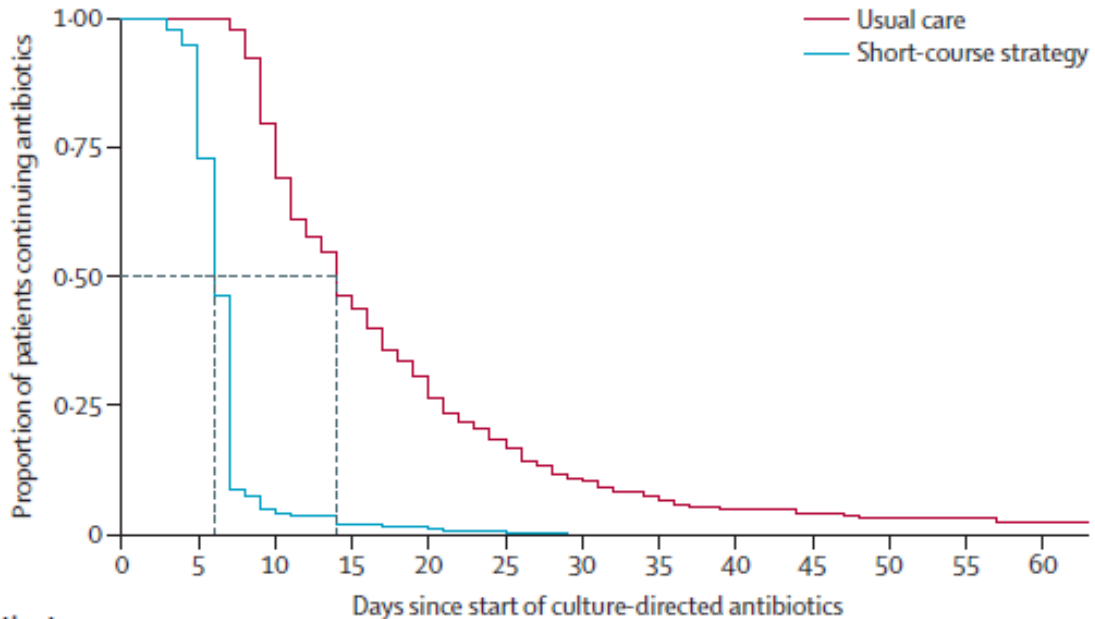
Furukawa Y, *et al. BMJ Open* 2023;**13**:e061023.

Individualised, short-course antibiotic treatment versus usual long-course treatment for ventilator-associated pneumonia (REGARD-VAP): a multicentre, individually randomised, open-label, non-inferiority trial

- Randomized, open-label, non-inferiority-superiority trial of adults who met CDC NHSN definition for VAP
- Participants randomized to receive <= 7 days vs >= 8 days (usual care)
- Primary outcome was a 60 day composite endpoint of death or pneumonia recurrence
- 435 patients
  - 231 in the <= 7 days group and 229 in the >=8 days group (usual care)

Lancet Respir Med 2024;
12: 399-408

Individualised, short-course antibiotic treatment versus usual long-course treatment for ventilator-associated pneumonia (REGARD-VAP): a multicentre, individually randomised, open-label, non-inferiority trial



Number of patients continuing antibiotics				
Usual care	229	70	11	6
Short-course therapy	231	4	0	0

Median Abx Duration

- Short course – 6 days
- Usual course – 14 days

Lancet Respir Med 2024; 12: 399-408

Individualised, short-course antibiotic treatment versus usual long-course treatment for ventilator-associated pneumonia (REGARD-VAP): a multicentre, individually randomised, open-label, non-inferiority trial

	Mortality (%)	Recurrence of pneumonia (%)	Primary outcome (%)	Unadjusted absolute risk difference (one-sided 95% CI)	Adjusted absolute risk difference (one-sided 95% CI)
Intention-to-treat (n=460)	..	..	..	−3%(−∞ to 5%)	−2%(−∞ to 5%)
Short-course group (n=231)	81 (35%)	33 (14%)	95 (41%)	..	..
Usual care group (n=229)	88 (38%)	30 (13%)	100 (44%)	..	..
Per-protocol (n=435)	..	..	..	−3%(−∞ to 5%)	−2%(−∞ to 4%)
Short-course group (n=211)	76 (36%)	29 (14%)	87 (41%)	..	..
Usual care group (n=224)	87 (39%)	30 (13%)	99 (44%)	..	..

Data are n (%) unless otherwise stated.

Table 2: **Primary outcome: the composite endpoint of death or pneumonia recurrence within 60 days of enrolment**

Results

- Shorter courses were non inferior to longer durations and associated with less abx related side effects

Lancet Respir Med 2024; 12: 399-408

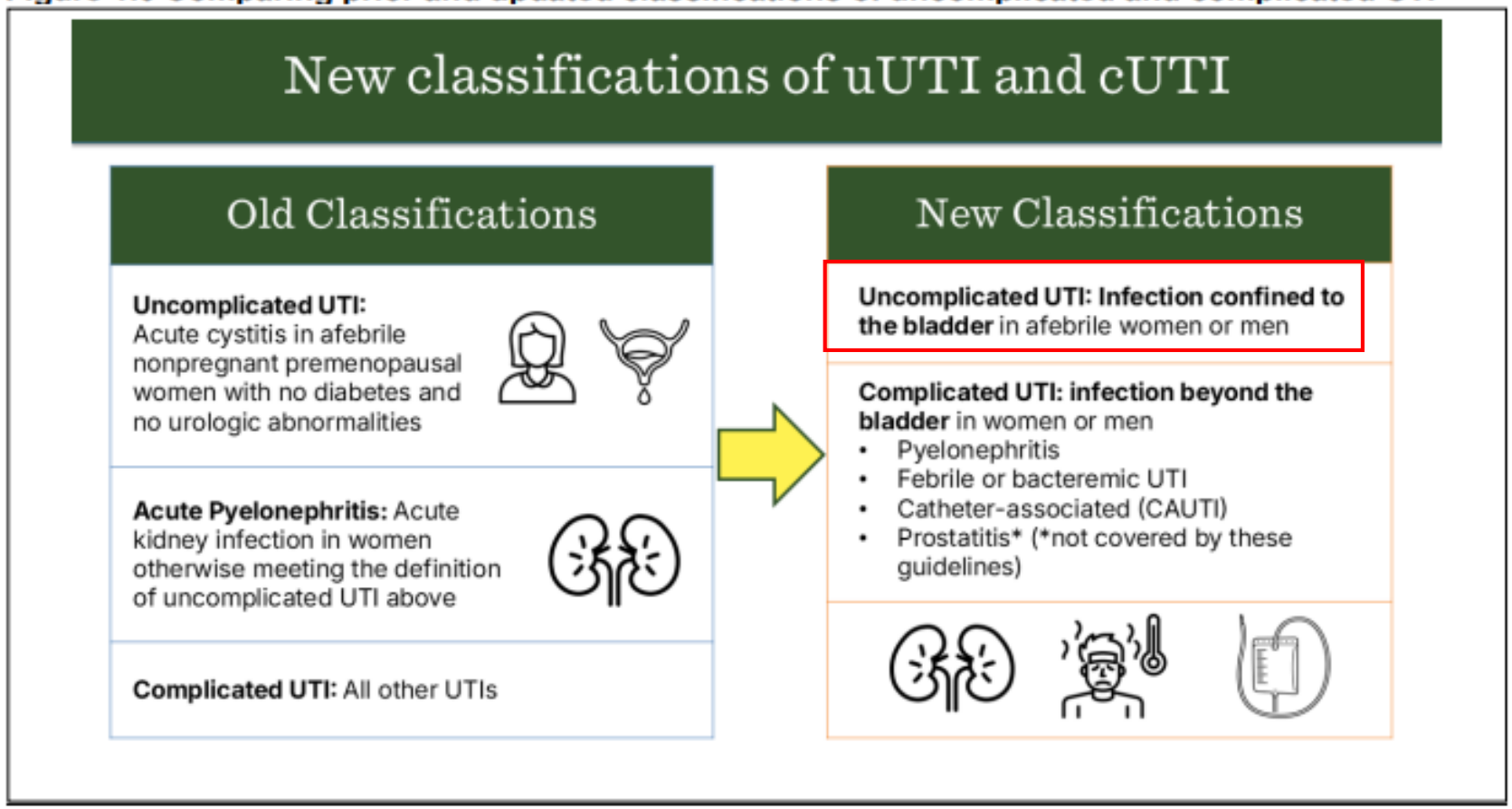
Antibiotic Treatment for 7 versus 14 Days in Patients with Bloodstream Infections

- Multicenter, noninferiority trial, randomly assigned hospitalized patients with bloodstream infections to receive abx for 7 or 14 days
  - Exclusions: severe immunosuppression, foci requiring prolonged treatment, single cultures with possible contaminants, and cultures yielding staphylococcus aureus
- Primary outcome was death from any cause by 90 days
- 3608 patients underwent randomization
  - 1814 assigned to 7 days of abx treatment, and 1794 to 14 days
- Gram negatives made up 71% of BSIs, gram positives 17.3%
- Sources of bacteremia
  - Urinary tract 42.2%; Intra-abdominal 18.8%; Lung 13%; Vascular catheter 6.3%; Skin/soft tissue 5.2%
- Results
  - 14.5% of patients had died in the 7 day group vs 16.1% in the 14 day group (non-inferior) at 90 days

N Engl J Med 2025;392:1065-78.

Clinical Practice Guideline by Infectious Diseases Society of America (IDSA): 2025 Guideline on Management and Treatment of Complicated Urinary Tract Infections: Executive Summary

Figure 1.0 Comparing prior and updated classifications of uncomplicated and complicated UTI



Men are now uncomplicated!

Published July 17, 2025

Clinical Practice Guideline by Infectious Diseases Society of America (IDSA): 2025 Guideline on Management and Treatment of Complicated Urinary Tract Infections: Executive Summary

In patients presenting with complicated UTI (cUTI) with a clinical response to therapy, should total duration of antibiotics be prolonged to >7 days rather than shorter (<=7 days)?

Recommendations:

I. In patients presenting with complicated UTI (including acute pyelonephritis) and who are improving clinically on effective therapy, we suggest treating with a shorter course of antimicrobials, using either 5-7 days of a fluoroquinolone (conditional recommendation, moderate certainty of evidence) or 7 days of a non-fluoroquinolone antibiotic (*conditional recommendation, very low certainty of evidence*), rather than a longer course (10-14 days).

Clinical Infectious Diseases

IDSA GUIDELINES

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections (IWGDF/IDSA 2023)

Table 5. Duration of antibiotic therapy according to the clinical situation.

	Route	Duration
Infection severity (skin and soft tissues)		
Class 2: Mild	Oral	1–2 weeks
Class 3/4: Moderate/severe	Oral/initially iv	2–4 weeks[a]
Bone/joint		
Resected	Oral/initially iv	2–5 days
Debrided (soft tissue infection)	Oral/initially iv	1–2 weeks
Positive culture or histology of bone margins after bone resection	Oral/initially iv	3 weeks
No surgery or dead bone	Oral/initially iv	6 weeks

Abbreviation: iv, intravenous.

[a]10 days following surgical debridement.

Clinical Infectious Diseases
IDSA GUIDELINES

IWGDF/IDSA Guidelines on the Diagnosis and Treatment of Diabetes-related Foot Infections (IWGDF/IDSA 2023)

Recommendation 16. Consider a duration of up to 3 weeks of antibiotic therapy after minor amputation for diabetes-related osteomyelitis of the foot and positive bone margin culture and 6 weeks for diabetes-related foot osteomyelitis without bone resection or amputation. (Conditional; Low).

SOLARIO Trial – ESCMID 2025

- Multicenter, randomized, controlled trial in adults with bone and joint infections undergoing curative surgery with licensed local antibiotic implanted products
  - SOLARIO – Short or Long Antibiotic Regimes in Orthopedics
  - Long treatment duration (>= 4 weeks) vs short treatment <= 7 days after surgery
- 500 patients enrolled; 251 in short duration (median DOT 6) and 249 in long duration (median DOT 42)
- Non-inferiority across all populations for primary outcomes, saw a difference in adverse events with long course having increased reported events
- **Pending publication of the complete study – more to come**

Advancing the management of prosthetic joint infections: a review of randomized controlled trials and emerging evidence. ***Antimicrobial Agents and Chemotherapy*** Online First. Aug 14, 2025

Shorter is Better — Practical Durations

- □ CAP: 3–5 days
- □ VAP: 7 days
- □ Complicated UTI: 5–7 days
- □ Bacteremia (non-SA): 7 days
- □ Diabetic foot osteo (after debridement): ~21 days

- Key Principles
  - ☑ Confirm diagnosis
  - ☑ Use an appropriate agent
  - ☑ Clinical improvement occurs

PO Is the Way to Go!

Oral antibiotics for complex infections

Benefits of Oral Abx

- Thrombophlebitis and catheter-related bloodstream infections are consequences that result from the presence of an IV line (McCarthy & Avent, 2020)
- It is estimated that ~9% of patients discharged on outpatient parenteral antimicrobial therapy (OPAT) will have a vascular complication (Kaul et al., 2022)
- Oral abx may serve as a safe discharge alternative for the treatment of patients with certain invasive infections
- May offer costs savings for patients and health-care institutions (Davar et al., 2023; McMeekin et al., 2020)
- Switching to oral is associated with decreased hospital length of stay (Iversen et al., 2019; McMeekin et al., 2020; Mouwen et al., 2020)

Oral Is the New IV. Challenging Decades of Blood and Bone Infection Dogma: A Systematic Review

Noah Wald-Dickler, MD,[a,b,c] Paul D. Holtom, MD,[a,b] Matthew C. Phillips, MD,[a] Robert M. Centor, MD,[d,e] Rachael. A. Lee, MD,[d,e] Rachel Baden, MD,[a] Brad Spellberg, MD[a]

- Systematic review of published, prospective, controlled trials that compared IV-only to oral stepdown regimens in the treatment of 3 invasive bacterial infections: osteomyelitis, bacteremia, and infective endocarditis

Am J Med. 2022 March ; 135(3): 369–379

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- Bone and Joint Infections

Study or Subgroup	Oral Events	Oral Total	IV Events	IV Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Greenberg 1987	7	14	11	16	1.2%	-0.19 [-0.53, 0.16]	1987
Mader 1990	11	14	10	12	1.7%	-0.05 [-0.35, 0.25]	1990
Gentry 1990	24	31	22	28	3.3%	-0.01 [-0.22, 0.20]	1990
Gentry 1991	14	19	12	14	2.1%	-0.12 [-0.39, 0.15]	1991
Gomis 1999	11	16	8	16	1.3%	0.19 [-0.15, 0.52]	1999
Schrenzel 2004	18	22	11	17	1.9%	0.17 [-0.11, 0.45]	2004
Euba 2009	17	21	21	27	2.8%	0.03 [-0.20, 0.26]	2009
Li 2019	457	527	450	527	85.6%	0.01 [-0.03, 0.06]	2019
Total (95% CI)		664		657	100.0%	0.01 [-0.03, 0.05]	
Total events	559		545				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.74$, df = 7 (P = 0.69); $I^2 = 0\%$

Test for overall effect: Z = 0.61 (P = 0.54)

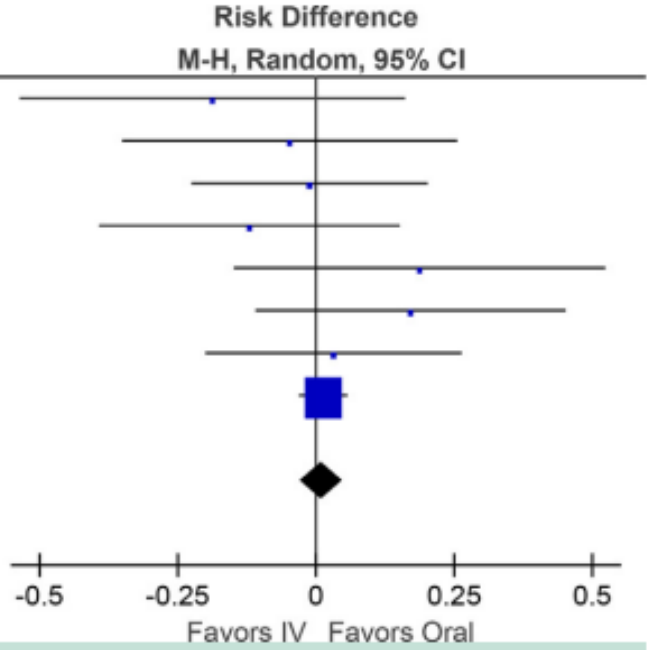

Figure 2 Meta-analysis forest plot of osteomyelitis treatment success. Overall treatment success was not significantly different.

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- Bacteremia

Study or Subgroup	Oral Events	Oral Total	IV Events	IV Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Amodio Groton 1996	20	24	20	26	8.4%	0.06 [-0.16, 0.28]	1996
San Pedro 2002	27	29	15	22	8.7%	0.25 [0.03, 0.46]	2002
Deville 2003	20	25	7	11	4.6%	0.16 [-0.16, 0.49]	2003
Jantausch 2003	54	75	18	28	9.3%	0.08 [-0.13, 0.28]	2003
Kaplan 2003	47	57	17	23	9.3%	0.09 [-0.12, 0.29]	2003
Schrenzel 2004	34	39	25	28	13.0%	-0.02 [-0.18, 0.13]	2004
Wilcox 2004	23	26	17	30	8.7%	0.32 [0.10, 0.53]	2004
Wilcox 2009	70	93	59	73	16.0%	-0.06 [-0.18, 0.07]	2009
Monmaturopaj 2012	6	6	10	11	6.3%	0.09 [-0.18, 0.36]	2012
Park 2014	27	29	28	30	15.7%	-0.00 [-0.13, 0.13]	2014
Total (95% CI)		**403**		**282**	**100.0%**	**0.07 [-0.01, 0.15]**	
Total events	328		216				

Heterogeneity: Tau² = 0.01; Chi² = 14.28, df = 9 (P = 0.11); I² = 37%
Test for overall effect: Z = 1.83 (P = 0.07)

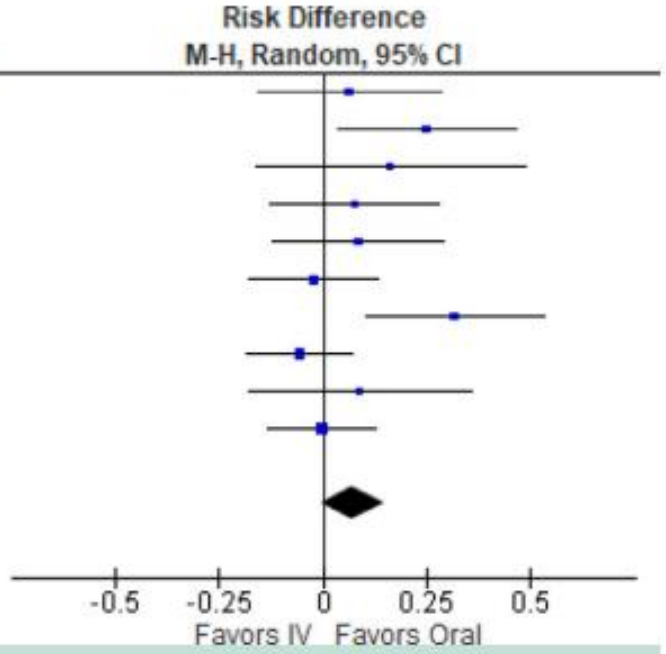

Figure 3 Meta-analysis forest plot of bacteremia treatment success. Overall treatment success was not significantly different, although the confidence interval favored oral therapy.

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- Endocarditis

Study or Subgroup	Oral Events	Oral Total	IV Events	IV Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Stamboulian 1991	15	15	15	15	19.8%	0.00 [-0.12, 0.12]	1991
Heldman 1996	18	19	22	25	11.0%	0.07 [-0.09, 0.23]	1996
Iversen/Bungard 2019	146	199	125	201	34.5%	0.11 [0.02, 0.20]	2019
Tissot-Dupont 2019	138	171	119	170	34.6%	0.11 [0.02, 0.20]	2019
Total (95% CI)		**404**		**411**	**100.0%**	**0.08 [0.03, 0.14]**	
Total events	317		281				

Heterogeneity: Tau² = 0.00; Chi² = 3.05, df = 3 (P = 0.38); I² = 2%
Test for overall effect: Z = 3.01 (P = 0.003)

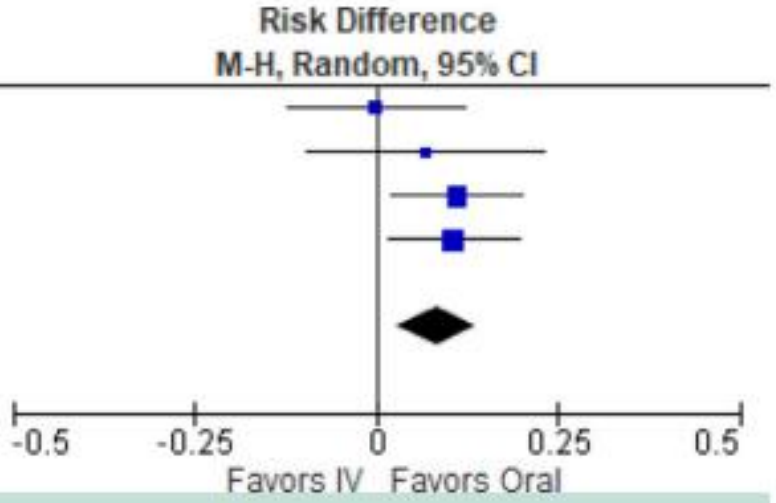

Figure 4 Meta-analysis forest plot of endocarditis treatment success. Oral therapy was significantly more effective.

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- From the authors:
  - All 20 published randomized controlled trials demonstrated oral antibiotic therapy was at least as effective as IV
  - In no published studies was IV superior in efficacy
  - “The data are overwhelmingly clear regarding the relative efficacy of oral to IV only therapy for these diseases; it is time to change how we practice

Am J Med. 2022 March ; 135(3): 369–379

Oral Antibiotics for Bone and Joint Infections

Oral vs. IV Abx for Osteomyelitis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Greenberg	'87	30	Ciprofloxacin vs. std IV	50% (7/14) v 65% (11/16)
Gentry	'90	59	Ciprofloxacin vs. βL+aminoglyc	77% (24/31) v 79% (22/28)
Mader	'90	26	Ciproflox vs. βL/clinda+aminoglyc	79% (11/14) v 83% (10/12)
Gentry	'91	33	Ofloxacin vs. cephalosporin	74% (14/19) v 86% (12/14)
Gomis	'99	32	Ofloxacin vs. imipenem	69% (11/16) v 50% (8/16)
Schrenzel	'04	39	Fleroxacin+rifampin v βL/vanco	82% (18/22) v 65% (11/17)
Euba	'09	48	TMP-SMX+rifampin vs. cloxacillin	81% (17/21) v 77% (21/27)
Li	'19	1054	Std oral vs. std IV	87% (457/527) v 85% (450/527)
Manning	'22	60	PJI/DAIR: Std oral vs. std IV	71% (22/31) v 76% (22/29)
METRC*	'25	233	Std oral vs. std IV	63% (73/115) v 64% (76/118)
Total (N=10 RCT)		1,614		81% (654/810) v 80% (643/804)

*Fracture-related infections; treatment success was a secondary endpoint
Success = absence of osteo at long term follow up (most studies >1 year); std = standard of care, protocol specified; all RCTs comparing oral to IV-only are in adults, however there are also 9 other adult and 10 pediatric RCTs or quasi-experimental studies comparing mostly oral vs. mostly oral, with high cure rates; refs at https://www.bradspellberg.com/oral-antibiotics

Oral versus intravenous antibiotics for bone and joint infections: the OVIVA non-inferiority RCT

- Randomized, open-label, non inferiority trial
  - 1054 patients enrolled, 26 centers in the United Kingdom

- Acute and chronic bone and joint infection, including:
  - Native osteomyelitis of the extra axial skeleton
  - Native joint infection requiring excision arthroplasty
  - Prosthetic joint infection
  - Orthopedic fixation device infection
  - Vertebral osteomyelitis with or without associated diskitis or soft-tissue infection

HEALTH TECHNOLOGY ASSESSMENT 2019 VOL. 23 NO. 38

Oral versus intravenous antibiotics for bone and joint infections: the OVIVA non-inferiority RCT

- Specifically required good quality microbiological data (i.e., deep tissue cultures or aspirates)
- Randomized at <=7 days after definitive surgery or start of antibiotic therapy
- Followed for 1 year
- Primary outcome was treatment failure within 1 year

HEALTH TECHNOLOGY ASSESSMENT 2019 VOL. 23 NO. 38

Oral versus intravenous antibiotics for bone and joint infections: the OVIVA non-inferiority RCT

- Antibiotic therapy >6 weeks for 805 of 1049 patients (76.7%)
  - IV group median total duration of therapy = 78 days
  - PO Group median total duration of therapy = 71 days

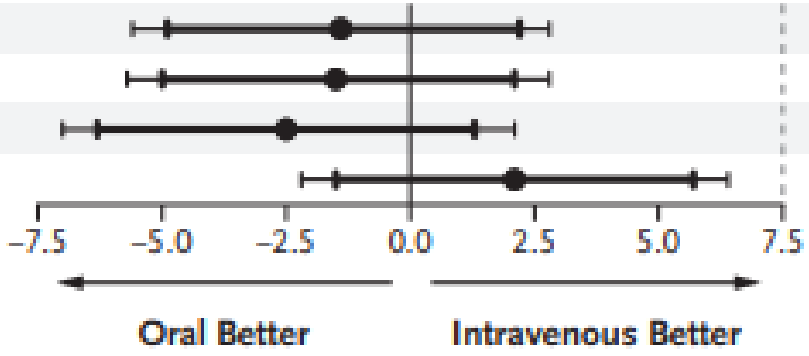
- Treatment failure:
  - IV group: 74/506 (14.6%)
  - PO Group: 67 of 509 (13.2%)

- Similar rates of adverse events
  - IV Group 27.7% vs PO Group 26.2%

HEALTH TECHNOLOGY ASSESSMENT 2019 VOL. 23 NO. 38

Oral versus intravenous antibiotics for bone and joint infections: the OVIVA non-inferiority RCT

Subgroup	Oral Group	Intravenous Group	Risk Difference (90% CI; 95% CI)
	patients with treatment failure/ total no. of participants		
Intention-to-treat population	70.0/527	77.3/527	−1.4 (−4.9 to 2.2; −5.6 to 2.9)
Modified intention-to-treat population	67/509	74/506	−1.5 (−5.0 to 2.1; −5.7 to 2.8)
Per-protocol population	61/466	69/443	−2.5 (−6.3 to 1.3; −7.0 to 2.1)
Worst-case sensitivity analysis	85/527	74/527	2.1 (−1.5 to 5.7; −2.2 to 6.4)



Subgroup analysis showed bias toward IV antibiotics with culture-negative infection or infections with retained implants

Oral versus intravenous antibiotics for bone and joint infections: the OVIVA non-inferiority RCT

- OVIVA Caveats
  - “We relied on the expertise of the consulting infectious-disease specialist to select and adjust antibiotic regimens”
  - No date on adequacy of surgical debridement
  - Patients could be randomized to PO group and subsequently go back on IV if cultures subsequently showed no oral abx options
  - Patients in PO group could receive up to 5 days of IV antibiotics for other infections

HEALTH TECHNOLOGY ASSESSMENT 2019 VOL. 23 NO. 38

Principles for oral antibiotic therapy in bone and joint infections

- Ideally would have mechanical/surgical source control (e.g., drainage of abscesses, removal of implants; resection of chronically infected bone)
- Good quality deep tissue and/or bone cultures to guide abx therapy
- There is well-tolerated, well-absorbed oral antibiotic option
- No contraindications to switch to PO antibiotic therapy (later slide)
- Probably best for initial lead in course of IV abx therapy (~ 1 week) then switch to oral abx to complete therapy

Oral Antibiotic Therapy for Bacteremia

Oral vs. IV Abx for Bacteremia

Author	Yr	N	Regimen (Oral vs. IV)	Success
Amodio-Groton	'96	50	Ciprofloxacin oral vs. IV—GNB	83% (20/24) v 77% (20/26)
Deville	'03	36	Linezolid vs. vanco—GPC (peds)	80% (20/25) v 64% (7/11)
Jantausch	'03	103	Linezolid vs. vanco—GPC (peds)	72% (54/75) v 64% (18/28)
Kaplan	'03	80	Linezolid vs. vanco—GPC (peds)	82% (47/57) v 74% (17/23)
Schrenzel	'04	67	FQ + rif vs. βL/vanco—*Staph* (<24 h IV lead in)	87% (34/39) v 89% (25/28)
Wilcox	'04	56	Linezolid vs. teicoplanin—GPC	89% (23/26) v 57% (17/30)
Wilcox	'09	166	Linezolid vs. vancomycin—GPC	75% (70/93) v 81% (59/73)
Monmaturopaj*	'12	17	Cefditoren vs. ceftriaxone—GNB	100% (6/6) v 91% (10/11)
Park	'14	59	Ciprofloxacin vs. std IV—GNB	93% (27/29) v 93% (28/30)
Omrani	'23	165	FQ/TMPSMX/BL vs. std IV—GNB	78% (65/83) v 74% (61/82)
Kaasch	'24	213	Various Abx IV/Oral—*S. aureus*	87% (94/108) v 88% (92/105)
Total (N=11 RCTs)		1,012		81% (460/565) v 79% (354/447)

*N = 82 pts with pyelonephritis of whom 17 were bacteremic with *E. coli*, patients were randomized to continue ceftriaxone or switch to oral ceftditoren at day 3. Refs at https://www.bradspellberg.com/oral-antibiotics

Efficacy and safety of an early oral switch in low-risk *Staphylococcus aureus* bloodstream infection (SABATO): an international, open-label, parallel-group, randomised, controlled, non-inferiority trial

- Randomized, controlled, non-inferiority trial done in 31 tertiary care hospitals in Europe
- Adult patients with **low risk *S. aureus* bloodstream infection** randomly assigned **after 5-7 days of IV antimicrobial therapy** to oral antimicrobial therapy or to continue IV standard therapy
- The composite primary endpoint was the occurrence of any complication related to S. aureus bloodstream infection within 90 days such as relapsing infection, deep-seated infection and mortality attributable to infection

Lancet Infect Dis 2024;
24: 523–34

Efficacy and safety of an early oral switch in low-risk *Staphylococcus aureus* bloodstream infection (SABATO): an international, open-label, parallel-group, randomised, controlled, non-inferiority trial

- Results
  - 213 randomly assigned
    - 108 to switch to oral therapy and 105 to continue IV therapy
  - 13% in the oral switch group met the primary end point vs 12 % in the IV group
- Interpretation
  - Oral switch to antimicrobial therapy was non-inferior to intravenous standard therapy in participants with low risk *S. aureus* bloodstream infection

Lancet Infect Dis 2024;
24: 523–34

Oral Antibiotic Therapy for Endocarditis

Oral vs. IV Abx for Endocarditis

Author	Yr	N	Regimen (Oral vs. IV)	Success
Stamboulian	'91	30	Amox 1 gm qid vs. CTX—*Strep*	100% (15/15) v 100% (15/15)
Heldman	'96	93	Cipro + Rif vs. std IV—*Staph*	95% (18/19) v 88% (22/25)
Iversen/ Bungaard‡	'19	400	Std oral vs. std IV—GPC	74% (146/199) v 62% (125/201)
*Tissot-Dupont**	*'19*	*341*	*TMP-SMX+clinda vs. std IV--Staph*	*81% (138/171) v 70% (119/170)*
Totals (N=3 RCTs)	523			77% (179/233) v 70% (162/241)
(+ 1 quasi expt)*	*(864)*			*78% (317/404) v 68% (281/411)*

*Quasi-experimental, pre-post study. Italicized totals include the quasi-experimental data.
‡Iversen reported early follow up, Bungaard 3 year follow up from the same study.
Refs at https://www.bradspellberg.com/oral-antibiotics

ORIGINAL ARTICLE

Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D., Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D., Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc., Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., et al.

- Randomized controlled trial of 400 patients with left sided endocarditis
  - 201 pts received oral therapy vs 199 pts that received IV therapy
- All patients received at least 10 days of IV therapy before transitioning to oral therapy
- Studied organisms included MSSA, coagulase negative staphylococci, streptococci and enterococcus faecalis
- Primary outcome was a compositive of all cause mortality, unplanned cardiac surgery, embolic events or relapse of bacteremia with the primary pathogen for up to 6 months
- Primary outcome occurred in 12.1% in the IV group and 9.0% in the PO group

N Engl J Med 2019;380:415-24.

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Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N=199)	Oral Treatment (N=201)	Difference	Hazard Ratio (95% CI)
	number (percent)		*percentage points (95% CI)*	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (–1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (–3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (–2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (–3.1 to 3.1)	0.97 (0.28 to 3.33)

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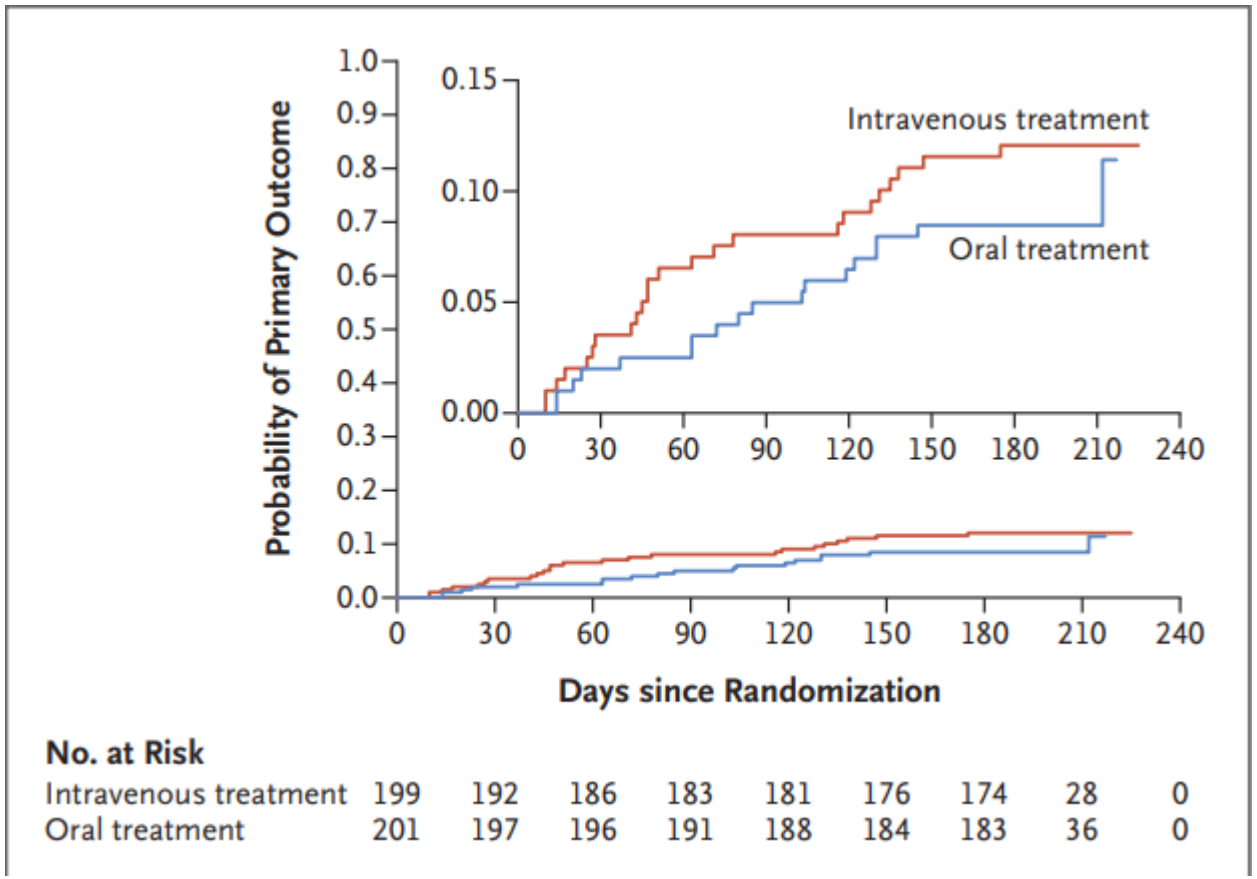

Figure 2. Kaplan–Meier Plot of the Probability of the Primary Composite Outcome.

The primary composite outcome was all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from randomization until 6 months after antibiotic treatment was completed. The oral treatment group shifted from intravenously administered antibiotics to orally administered antibiotics at a median of 17 days after the start of treatment. The inset shows the same data on an enlarged y axis.

N Engl J Med 2019;380:415-24.

When can I switch to oral?

- ☑ GI tract works – patient can absorb reliably
- ☑ Stable – afebrile & hemodynamically stable ≥48h
- ☑ Appropriate IV lead-in (~1 week)
- ☑ Susceptible bug – high bioavailability oral option
- ☑ Source controlled – abscess drained, hardware addressed
- ☑ Blood cultures cleared
- ☑ Follow-up feasible – patient reliable for monitoring

If these boxes are checked → oral step-down should be a consideration

PO Is the Way to Go!

Oral vs. IV Antibiotics RCT Master Table			
Diagnosis	Number of RCTs	Number of Patients	Result
Osteomyelitis	10	1,614	Equal
Bacteremia	11	1,012	Equal
Endocarditis	3*	523	Equal
Intra-Abdominal Infection	7	1,763	Equal
Urinary Tract Infection	5	369	Equal
Pneumonia	12	2,158	Equal
Skin Infections	2	253	Equal
Pseudomonas in Cystic Fibrosis	1	155	Equal
Neuroborreliosis	3	366	Equal
Bubonic Plague (yeah, seriously!)	1	222	Equal
Total: 10 Conditions	55	8,435	All Equal

*Not including quasi-experimental study of *S. aureus* endocarditis; Refs at https://www.bradspellberg.com/oral-antibiotics

https://www.bradspellberg.com/oral-antibiotics

Smarter(?): Stewardship in the Age of AI

Poll Question #3

Are you using AI Tools like ChatGPT or OpenEvidence in your day-to-day clinical work?

A. Yes – regularly (e.g. multiple times per week)
B. Yes – occasionally (e.g. a few times/month)
C. No – not yet, but I’m curious
D. No – and I don’t see the value
E. What’s ChatGPT?

Poll Question #4

If you've used AI tools like ChatGPT or OpenEvidence, how helpful have you found them?

A. Very helpful – saved me time, improved clarity
B. Somewhat helpful – depends on the task
C. Meh – interesting but not that useful yet
D. Not helpful – too inaccurate or generic
E. Haven't used it

Can we rely on artificial intelligence to guide antimicrobial therapy? A systematic literature review

Sulwan AlGain MD[1,2], Alexandre R. Marra MD[3,4], Takaaki Kobayashi MD[4,5], Pedro S. Marra BS[6], Patricia Deffune Celeghini MD[3], Mariana Kim Hsieh MD[4], Mohammed Abdu Shatari MD[7], Samiyah Althagafi MD[8], Maria Alayed MD[1], Jamila I Ranavaya MD[5], Nicole A. Boodhoo BS[9], Nicholas O. Meade DO[5], Daniel Fu BS[10], Mindy Marie Sampson DO[2], Guillermo Rodriguez-Nava MD[2], Alex N. Zimmet MD[2], David Ha PharmD[2], Mohammed Alsuhaibani MD[1], Boglarka S. Huddleston MA, MLIS[11] and Jorge L. Salinas MD[2]

- 17 studies used machine learning as part of the clinical decision support systems. They improved prediction of antimicrobial resistance and optimized antimicrobial use
- 6 studies focused on large language models to guide antimicrobial therapy; they had higher prescribing error rates, patient safety risks, and needed precise prompts to ensure accurate responses

Antimicrobial Stewardship & Healthcare Epidemiology (2025), **5**, e90, 1–9

Can we rely on artificial intelligence to guide antimicrobial therapy? A systematic literature review

- Conclusions
  - AI, particularly machine learning integrated into CDSS holds promise in enhancing clinical decision-making and improving antimicrobial management
  - “Large language models currently lack the reliability required for complex clinical applications”

Antimicrobial Stewardship & Healthcare Epidemiology (2025), **5**, e90, 1–9

Take Homes

- Shorter durations are just as effective
  - More refinement needed for the “optimal duration” but this will likely still be individualized
- Oral abx for complex infections are safe and effective
  - Can avoid line complications and readmissions, and reduces OPAT burden
- AI is coming whether we like it or not
  - The future should be supportive decision aids, not autopilot prescribing

THANK YOU!