

Antibiotics on Trial:

Long-term suppression in hardware infections and recurrent cystitis

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Objectives

- **Summarize** evidence for long-term suppressive antibiotics vs discontinuation in hardware infections and recurrent cystitis
- **Apply** antimicrobial stewardship principles to clinical decision-making
- **Identify** patient and infection factors guiding therapy selection

Financial disclosures

- None

Other disclosures

- The views expressed in this presentation are assigned for the purpose of academic debate and do not necessarily reflect the individual opinions or clinical practice of the presenter

Long-term suppressive antimicrobial therapy in retained hardware infections

Pro

Dr. Chuka Enwezor

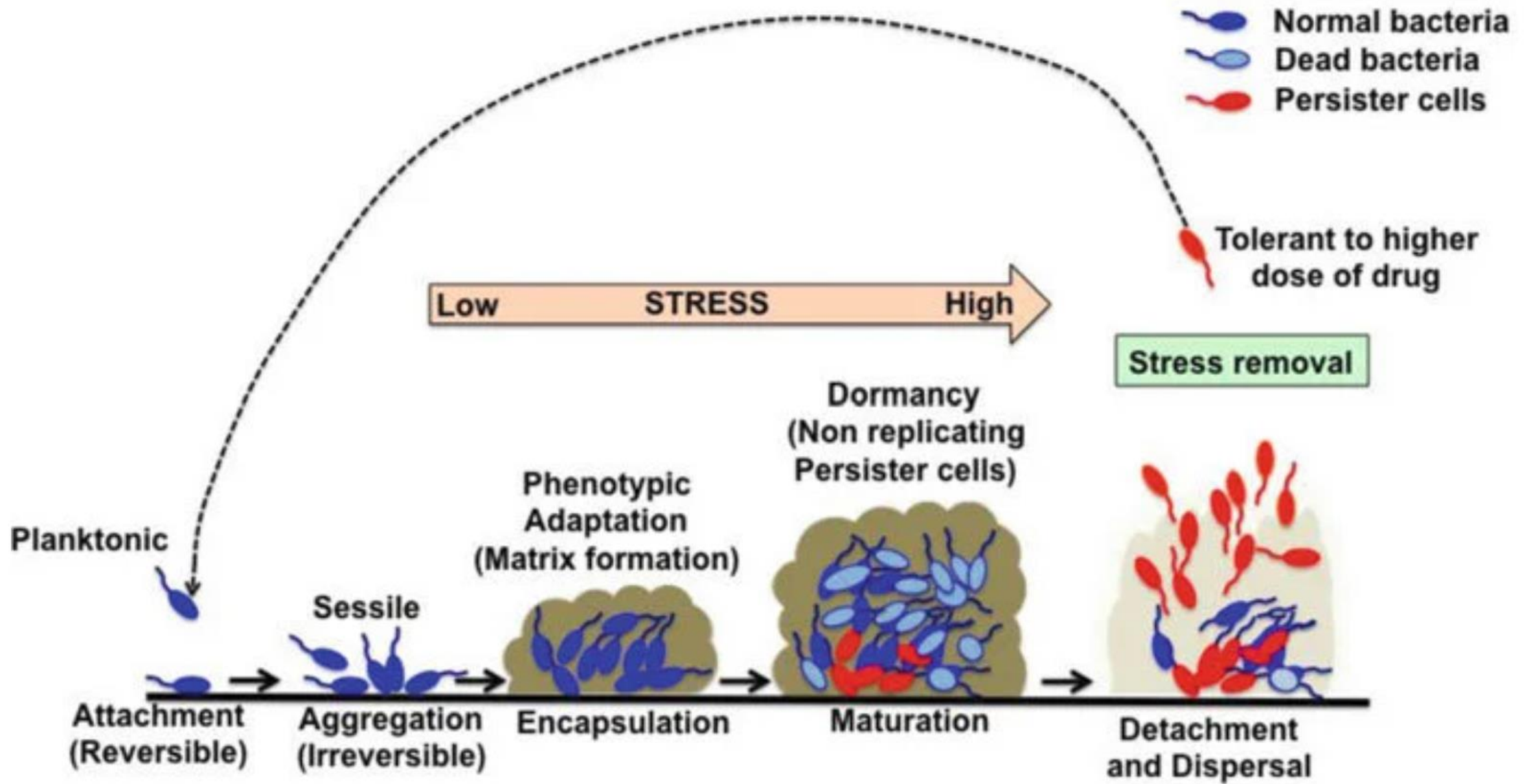
Con

Dr. Sarah Battle

Opening statements

Support long-term antibiotics for hardware

- A select group of patients may benefit from Suppression Antibiotic Therapy (SAT) when there is retained hardware
- Definition – extended antibiotic therapy beyond the initial treatment phase, typically more than 6 months



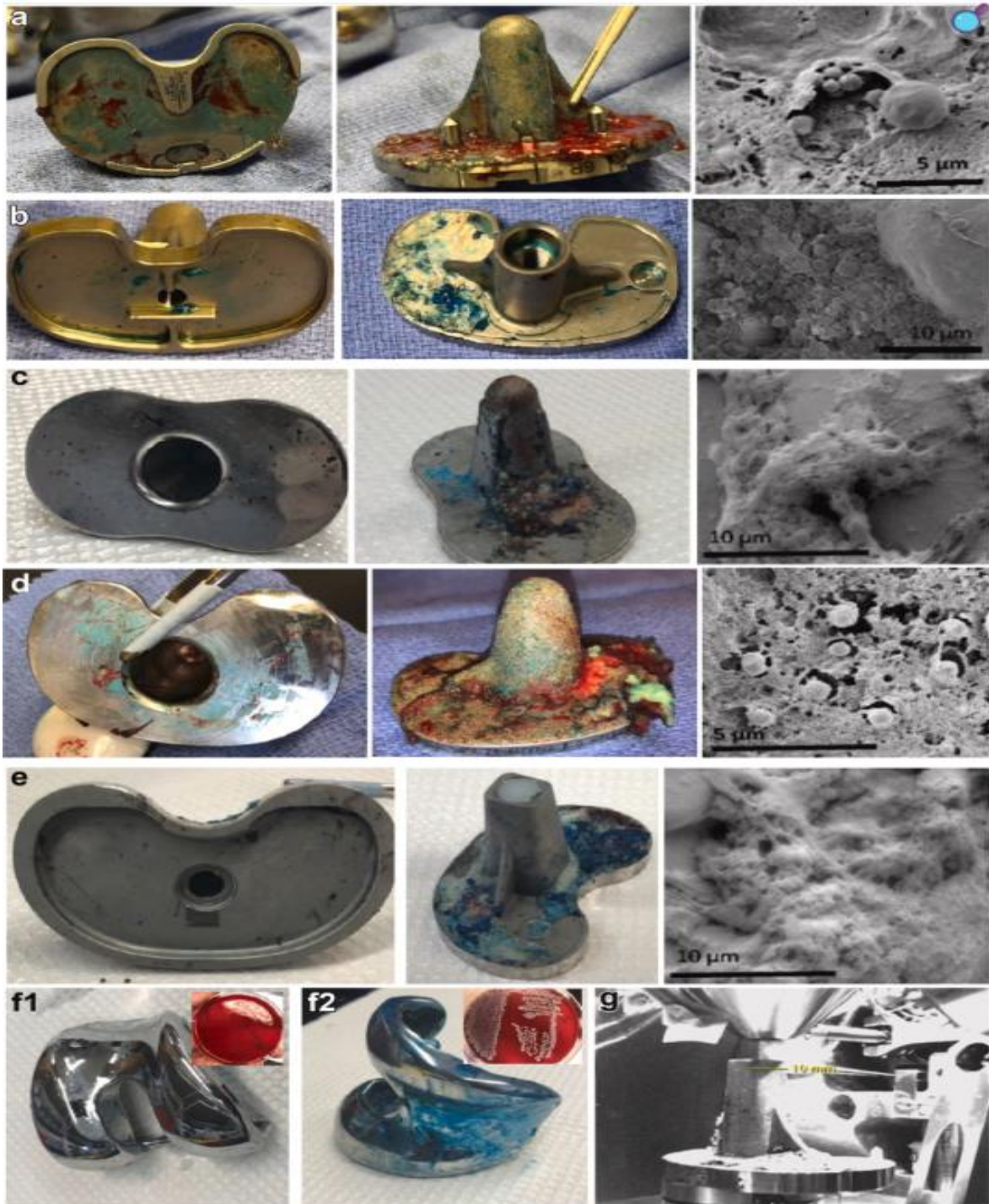


Figure 1. Location of biofilms on explanted tibial components.

- (a) *Staphylococcus aureus* PJI with biofilms located on both the bone - prosthetic interface and the interface in contact with the joint. *S. aureus* biofilm with bacterial cells seen under biofilm matrix at 24,000 magnification, 2 kV, working distance 5.0 mm; B1,
- (b) *Candida glabrata* PJI with biofilm located predominately on the bone-prosthetic interface. *C. glabrata* biofilm at 5000 magnification 2 kV, working distance 14.5 mm;
- (c) culture-negative PJI with biofilms located predominately on the bone-prosthetic interface. Culture-negative biofilm at 10,000 magnification, 2 kV, working distance 6.7 mm;
- (d) *S. aureus* PJI with biofilms located on both interfaces. *S. aureus* biofilm at 20,000 magnification, 2 kV, working distance 5.0 mm;
- (e) culture-negative PJI with biofilms located predominately on the bone-prosthetic interface. Culture-negative biofilm at 10,000 magnification, 2 kV, working distance 4.7 mm;
- (f) negative control with sterilized femoral component placed in methylene blue where no staining occurred, and no bacteria were cultured from prosthetic;
- (g) positive control with femoral component placed in broth of *S. aureus* for 24 hours and then stained with methylene blue in which large areas of biofilm can be observed. In addition, *S. aureus* could be recovered by culturing these areas stained with methylene blue;
- (h) image showing a tibial component on the SEM stage with limited capability to move the prosthetic under the electron beam.

Clinical Infectious Diseases

REVIEW ARTICLE



The Use of Long-term Antibiotics for Suppression of Bacterial Infections

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RESEARCH ARTICLE



Comparative *In Vitro* Study of Biofilm Formation and Antimicrobial Susceptibility in Gram-Negative Bacilli Isolated from Prosthetic Joint Infections

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TABLE 5 Comparison of planktonic and biofilm-growing bacteria antimicrobial activity^a

Antibiotic	Species (n)	Range	MIC (mg/liter)		MBC (mg/liter)		MBIC (mg/liter)		MBEC (mg/liter)	
			p50	p90	p50	p90	p50	p90	p50	p90
AMK	E.cl (9)	0.125 to 128	4	8	16	32	4	16	>128	>128
	K.p (7)		4	16	8	16	8	32	>128	>128
	P.m (9)		4	8	16	32	4	8	>128	>128
	P.a (8)		4	4	4	16	4	32	>32	>32
CRO	E.cl (9)	0.03125 to 32	<0.03125	>32	0.125	>32	2	>32	>32	>32
	K.p (7)		>32	>32	>32	>32	>32	>32	>32	>32
	P.m (9)		<0.03125	<0.03125	<0.03125	<0.03125	<0.03125	<0.03125	>32	>32
	P.a (8)		NT	NT	NT	NT	NT	NT	NT	NT
CAZ	E.cl (9)	0.03125 to 32	0.0625	16	0.25	16	2	16	>32	>32
	K.p (7)		16	32	32	>32	8	>32	>32	>32
	P.m (9)		<0.03125	<0.03-125	0.0625	0.125	<0.03125	4	>32	>32
	P.a (8)		1	2	2	4	>32	>32	>32	>32
CIP	E.cl (9)	0.03125 to 32	<0.03125	>32	<0.03125	>32	0.5	>32	>32	>32
	K.p (7)		4	32	8	>32	8	>32	>32	>32
	P.m (9)		<0.03125	4	0.125	32	<0.03125	4	>32	>32
	P.a (8)		0.125	16	0.5	32	0.25	32	>32	>32
GE	E.cl (9)	0.125 to 128	4	4	16	32	4	16	>32	>32
	K.p (7)		>128	>128	>128	>128	>128	>128	>128	>128
	P.m (9)		2	8	16	64	2	4	>128	>128
	P.a (8)		2	>128	4	>128	4	>128	>128	>128
CO	E.cl (9)	0.125 to 128	<0.125	<0.125	<0.125	0.5	0.5	4	>128	>128
	K.p (7)		0.5	16	8	64	8	32	>32	>32
	P.m (9)		NT	NT	NT	NT	NT	NT	NT	NT
	P.a (8)		0.25	0.5	0.5	1	4	8	128	128
MP	E.cl (9)	0.03125 to 32	<0.03125	<0.03-125	<0.03125	0.25	<0.03125	0.5	>32	>32
	K.p (7)		0.0625	1	0.5	2	0.5	2	>32	>32
	P.m (9)		<0.03125	0.0625	0.125	0.5	<0.03125	0.0625	>32	>32
	P.a (8)		0.5	2	2	4	4	16	>32	>32

^aThe table compares planktonic (MIC and minimal bactericidal concentration [MBC]) and biofilm-growing bacteria (minimal biofilm inhibitory concentration [MBIC] and minimal biofilm eradication concentration [MBEC]) antimicrobial activity. E.cl, *Escherichia coli*; K.p, *Klebsiella pneumoniae*; P.m, *Proteus mirabilis*; P.a, *Pseudomonas aeruginosa*; AMK, amikacin; CRO, ceftriaxone; CAZ, ceftazidime; CIP, ciprofloxacin; GE, gentamicin; CO, colistin; MP, meropenem; NT, not tested.



4 groups identified as needing suppressive antibiotics

- Prosthetic joint infections
- Vascular graft infection (VGI) and other vascular infections including infective endocarditis and mycotic aneurysm
- CIEDI Cardiovascular implantable electronic device infections
- Osteomyelitis and other orthopedic hardware infections

Graphical Abstract

Monitoring Therapy			
Three-monthly monitoring (physical and biomarker) in the first year of suppressive therapy, then 6-12 monthly review			
Prosthetic Joint Infection	Vascular Grant Infection	Cardiac Implantable Electronic Device	Prosthesis Infection Associated with Osteomyelitis (not joint)
Consider ceasing suppressive antibiotic therapy after one year if inflammatory biomarkers have normalised.	Consider PET CT and biomarker normalisation to guide cessation of suppressive antibiotic therapy.	Tailor therapy to the individual with close monitoring of biomarkers and surveillance for relapse.	Consider cessation of suppressive antibiotic therapy after 6-12 months in individuals who had early debridement and good clinical response.
Staphylococcal infections should be treated for longer before considering cessation due to higher rates of relapse.	Patients who retain the original infected prosthesis are more likely to relapse, and may not be suitable for cessation of therapy.		
Considerations After Ceasing Suppressive Antibiotic Therapy			
Monthly monitoring (including blood cultures for vascular graft infections) for the first 6-12 months after cessation of therapy. Frequency of monitoring can reduce after 12 months.			

Arguments against long-term suppressive antibiotics in hardware infections:

Stewardship = “Shorter is better”

So how short can we go?

Diagnosis	Short (d)	Long (d)	Result
Community-acquired pneumonia [6–14]	3 or 5	7, 8, or 10	Equal
Hospital-acquired/ventilator-associated pneumonia [15, 16]	7–8	14–15	Equal
Complicated urinary tract infections/pyelonephritis [17–22]	5 or 7	10 or 14	Equal
Complicated/postoperative intraabdominal infections [23, 24]	4 or 8	10 or 15	Equal
Gram-negative bacteremia [25]	7	14	Equal
Acute exacerbation of chronic bronchitis/chronic obstructive pulmonary disease (meta-analysis of 21 trials [26])	≤5	≥7	Equal
Acute bacterial skin and skin structure infections (cellulitis/major abscess) [27–29]	5–6	10	Equal
Chronic osteomyelitis [30]	42	84	Equal
Empiric neutropenic fever [31]	Afebrile and stable × 72 h	Afebrile and stable × 72 h and with absolute neutrophil count > 500 cells/μL	Equal

Diseases for which short-course antibiotic therapy has been found to be equally effective to longer traditional courses of therapy



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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*

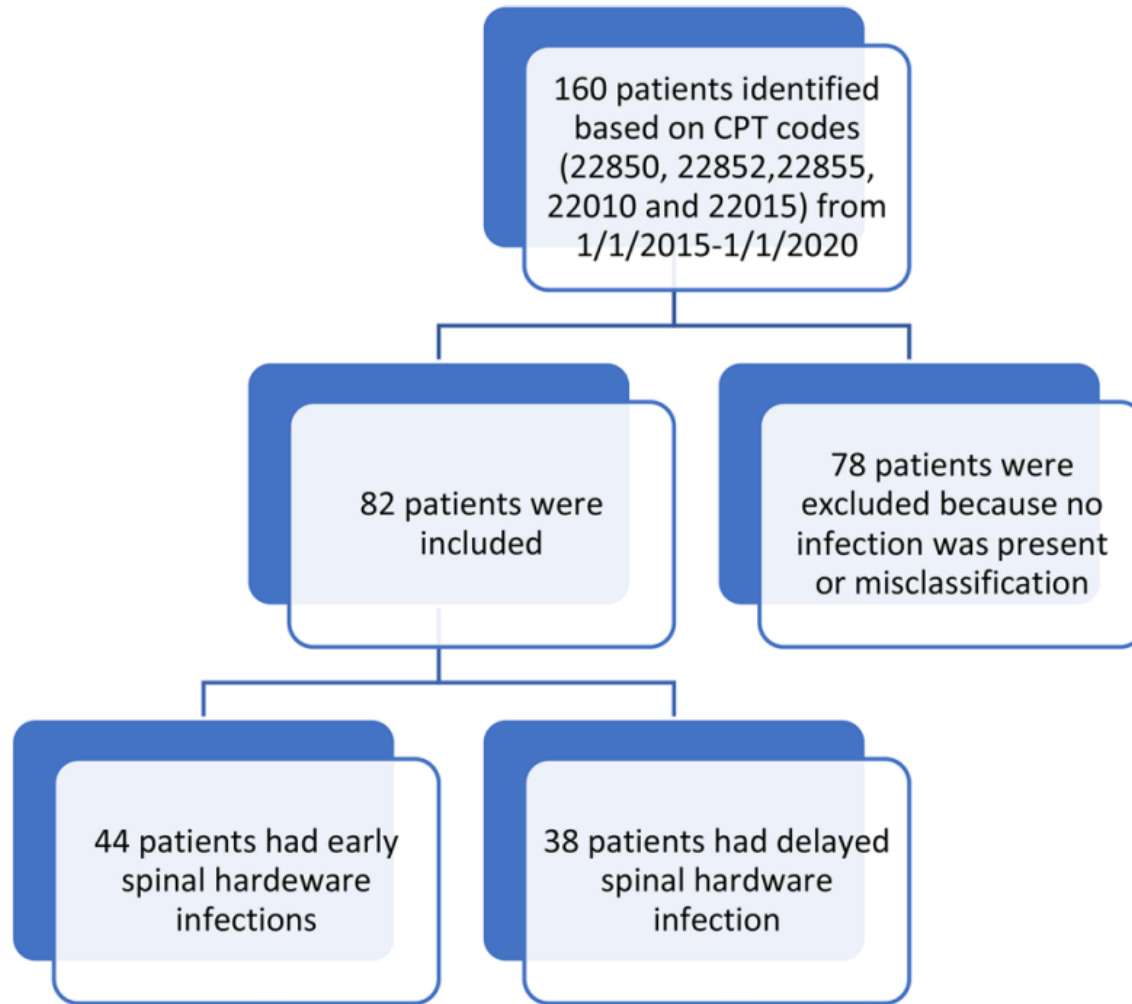
* 6 vs. 12 week inferior for all-comers in largest trial, driven primarily but not entirely by DAIR cohort, but other RCT from Shorter Is Better table demonstrated 4-6 weeks may be non inferior, and small RCT of PJI within 1 month of implant showed non-inferiority of 8 vs. 12-26 wks;

But this is for initial treatment → What about subsequent suppressive antibiotics?

When is it safe to stop antimicrobials in orthopedic hardware infections?

- Relapse rates for orthopedic hardware infections are high
- Identifying who needs to be treated for how long is critical to improve patient outcomes while avoiding unnecessary antibiotics

Spinal hardware infections



- 81/82 received IV antibiotics as initial therapy (median duration 6 weeks)
 - 1 patient received levofloxacin

Fig. 1 Patient enrollment

Spinal hardware infections

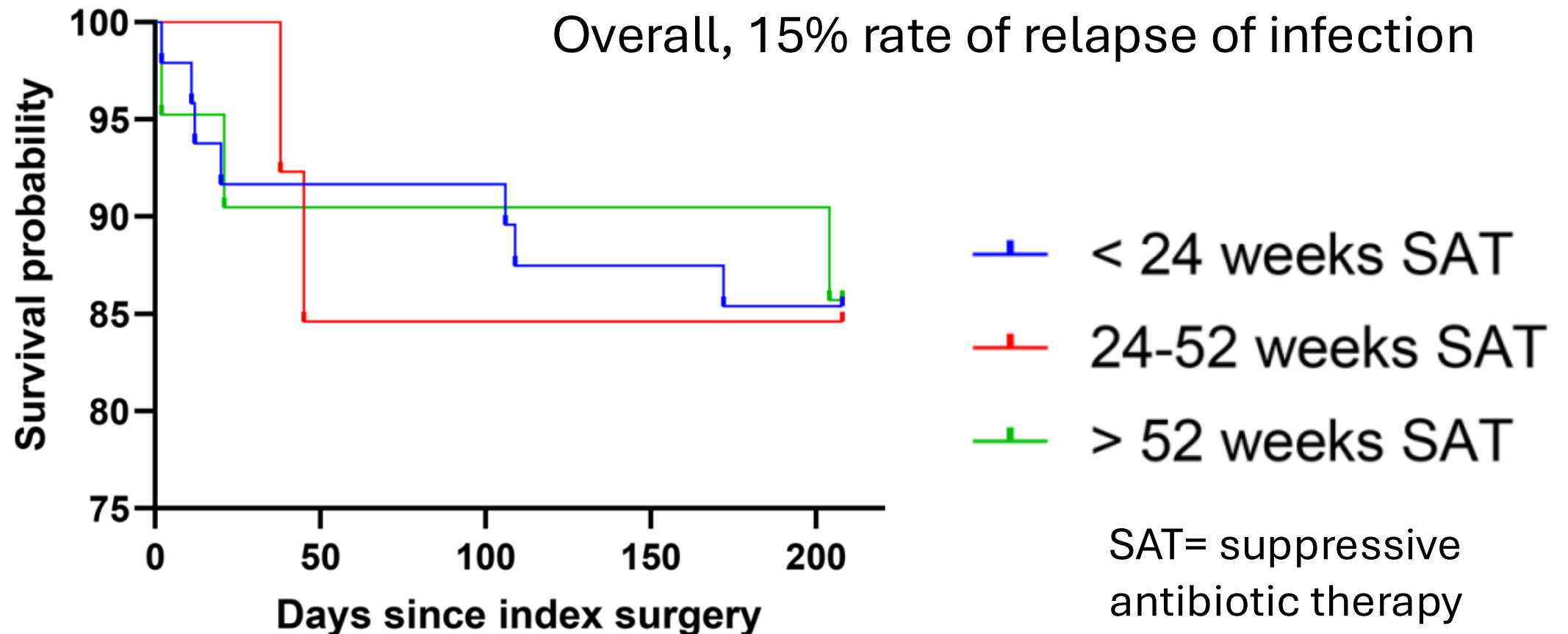


Fig. 2 Kaplan-Meier plot of survival probability (Recurrence) in all patients ($N=82$) by the different SAT durations. Log rank (Mantel-Cox) test $\chi^2(2)=0.01, p=0.10$

Onset of spinal hardware infection

	Total N (%)	No Recurrence of infection N= 70 (85.4%)	Recurrence of infection N=12 (14.6%)	Odds ratio (CI) Univariate
Early	44 (53.7)	36 (43.9)	8 (9.8)	Reference
Late	38 (46.3)	34 (41.5)	4 (4.9)	0.53 (0.14-1.92)

CI= confidence interval

Organism and presence of bacteremia

	Total N (%)	No Recurrence of infection N= 70 (85.4%)	Recurrence of infection N=12 (14.6%)	Odds ratio (CI) Univariate	Odds ratio (CI) Multivariate
Non- <i>S. aureus</i>	45 (54.9)	38 (46.3)	7 (8.5)	Reference	
<i>S. aureus</i>	37 (45.1)	32 (39.0)	5 (6.1)	0.85 (0.24-2.93)	0.85 (0.24-2.96)
No bacteremia	53 (64.6)	44 (53.7)	9 (11.0)		
Bacteremia	29 (35.4)	26 (31.7)	3 (3.6)	0.56 (0.14-2.27)	

CI= confidence interval

Hardware status

	Total N (%)	No Recurrence of infection N= 70 (85.4%)	Recurrence of infection N=12 (14.6%)	Odds ratio (CI) Univariate	Odds ratio (CI) Multivariate
All hardware removed	22 (26.8)	21 (25.6)	1 (1.2)	Reference	
Partial revision	26 (31.7)	20 (24.4)	6 (7.3)	6.30 (0.70-57.07)	
All retained	34 (41.5)	29 (35.4)	5 (6.1)	3.62 (0.39-33.30)	1.03 (0.29-3.65)*

CI= confidence interval

*Ran as a binary variable. All hardware removed or partial revision versus all original hardware retained

Duration of suppressive antimicrobial therapy

	Total N (%)	No Recurrence of infection N= 70 (85.4%)	Recurrence of infection N=12 (14.6%)	Odds ratio (CI) Univariate	Odds ratio (CI) Multivariate
No suppressive antibiotics	28 (34.2)	24 (29.3)	4 (4.9)	Reference	
Yes suppressive antibiotics	54 (65.8)	46 (56.1)	8 (9.7)	1.04 (0.29-3.82)	1.04 (0.28-3.85)
Suppressive antimicrobial duration (N=54)					
>52 weeks	21 (39.6)	18 (34.0)	3 (5.7)	Reference	
24-52 weeks	13 (24.53)	11 (20.8)	2 (3.8)	1.09 (0.16-7.59)	
<24 weeks	19 (35.9)	16 (30.2)	3 (5.7)	1.13 (0.20-6.39)	

CI= confidence interval

Other variables from uni/multivariate logistic regression analysis: association with recurrence of infection

- All with confidence interval that crosses 1
 - Age <50, 50-70, >70
 - Infection location: cervical, thoracic, lumbar
 - Smoking history
 - BMI 18.5-<25, 25-<30, >30
 - Multimorbidity yes/no
 - Albumin ≥ 3.5 , <3.5

Overall, 15% rate of recurrence
spinal hardware infection.

No difference between early or
late onset infection, regardless
of suppressive antibiotic therapy
or hardware status.

Longterm suppressive antimicrobial
therapy in retained hardware infections

Pro vs. Con

Probably the truth is in the middle

When Suppressive Antibiotics Are Most Likely to Help after Debridement and Retention (DAIR)

Strongly favor SAT after DAIR if ≥ 1 present:

- Limited surgical options for future failure
(*e.g., amputation, arthrodesis, poor wound coverage outcomes*)
- Recurrent prosthetic joint infection (PJI) or prior DAIR failure
- High-risk host factors: cirrhosis, ESRD, heart failure
- Age >75 or limited life expectancy (<10 years)
- Late hematogenous infection (>2 years post-implant), especially with bacteremia
- Gram-negative infection without fluoroquinolone option
- Patient preference strongly favors suppression after shared decision-making

When Suppressive Antibiotics Likely Provide Little Benefit after Debridement and Retention (DAIR)

- **SAT generally NOT recommended if:**
 - Successful completion of adequate rifampin-based therapy for staphylococcal PJI
 - Completion of effective fluoroquinolone-based therapy for gram-negative PJI
 - Culture-negative infection
 - Good surgical source control and favorable response to standard therapy

How to apply this in practice

- SAT should be individualized risk–benefit decision
- Consider:
 - Risk of recurrence
 - Consequences of failure
 - Surgical salvage options
 - Patient goals and tolerance for long-term antibiotics
- Emphasize shared decision-making + antimicrobial stewardship

Recurrent/chronic cystitis

Con

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Pro

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Opening statements

Argument against long-term antibiotics for cystitis

- The diagnosis is often not definitive. Multiple studies have shown that cystitis can be misdiagnosed or overdiagnosed up to 50% of the time – Myreen Tomas et al 2015; Gupta et al 2022; Murray et al 2024
- Prolonged antibiotic exposure for suppression has not been shown to effective
- Beerepoot et al conducted a randomized, double-blind, noninferiority trial of trimethoprim-sulfamethoxazole (TMP/SMX) versus lactobacilli in preventing recurrent UTI in 252 postmenopausal women. TMP/SMX and lactobacilli therapies did not differ significantly in preventing recurrent UTIs over 1 year. However, after 1 month of TMP/SMX prophylaxis, resistance to TMP/SMX, TMP, and amoxicillin had increased from 20%–40% to 80%–95% among *Escherichia coli* from the feces and urine of asymptomatic women and among *E. coli* causing a UTI. Resistance did not increase during lactobacilli prophylaxis.
- Carl Ior et al retrospective analysis showed suppressive antibiotic therapy in women with recurrent UTIs is associated with a higher incidence and severity of future infections.

Tomas ME et al. *Clin Infect Dis*. 2015;61:441–447.
Gupta A et al. *BMJ Qual Saf*. 2022;31:383–386.
Murray K et al. *Neurourol Urodyn*. 2024;44:382–389.

Beerepoot et al. *Arch Intern Med*, 2012;172:704–712
Llor C et al. *BMJ Open* 2025

Evidence to support long-term antibiotics for
cystitis in *certain populations*

Neurogenic bladder and self-catheterization

APPENDIX

URINARY TRACT INFECTION BASIC DATA SET (VERSION 1.0)

Date of data collection: YYYYMMDD

Length of time of sign(s)/symptom(s) (tick one only):

- ☐ Less than 1 day ☐ 1 to 3 days ☐ 4 days–1 week ☐ >1week–2 weeks
☐ >2weeks–1 month ☐ >1 month–3 months ☐ >3 months

Signs/symptoms (tick all that apply):

- ☐ Fever
☐ Incontinence, onset or increase in episodes, including leaking around catheter
☐ Spasticity, increased
☐ Malaise, lethargy or sense of unease
☐ Cloudy urine (with or without mucus or sediment) with increased odor
☐ Pyuria
☐ Discomfort or pain over the kidney or bladder or during micturition
☐ Autonomic dysreflexia
☐ Other _____

Neurogenic bladder and self-catheterization

Table 1 Thresholds for elevated body temperature (fever) and normal ranges for temperature variation in non-spinal cord-injured adults⁸

<i>Elevated body temperature</i>	<i>Observed normal ranges^a</i>
Oral at or above 38.2 °C (101 °F)	33.2–38.2 °C (92–101 °F)
Axillary at or above 37 °C (99 °F)	35.5–37.0 °C (96–99 °F)
Rectal at or above 37.8 °C (100 °F)	34.4–37.8 °C (94–100 °F)
Tympanic at or above 37.8 °C (100 °F)	35.4–37.8 °C (96–100 °F)

^aIndividuals with SCI who are prone to poikilothermia may need the above normal ranges to be adjusted for their normal temperature range within a given environmental temperature. The above temperature ranges are for non-SCI adults. Sund-Levander *et al.*⁸ also provide adult temperature values stratified by gender within their article.

Neurogenic bladder and self-catheterization

Urine dipstick test for nitrite (tick one only):

☐ Negative ☐ Positive ☐ Unknown

Urine dipstick test for leukocyte esterase (tick one only):

☐ Negative ☐ Positive ☐ Unknown

Urine culture (tick one only):

☐ Negative ☐ Positive ☐ Unknown

If positive, give species and amount of colony-forming units (CFU) ml⁻¹ (10¹–10⁵ CFU ml⁻¹), and the resistance pattern:

- 1) _____ species, _____ CFU ml⁻¹
Resistance pattern (tick one only): ☐ Normal ☐ Multidrug resistant (agents from 3 or more different drug classes)
- 2) _____ species, _____ CFU ml⁻¹
Resistance pattern (tick one only): ☐ Normal ☐ Multidrug resistant (agents from 3 or more different drug classes)
- 3) _____ species, _____ CFU ml⁻¹
Resistance pattern (tick one only): ☐ Normal ☐ Multidrug resistant (agents from 3 or more different drug classes)
- 4) _____ species, _____ CFU ml⁻¹
Resistance pattern (tick one only): ☐ Normal ☐ Multidrug resistant (agents from 3 or more different drug classes)
- 5) _____ species, _____ CFU ml⁻¹
Resistance pattern (tick one only): ☐ Normal ☐ Multidrug resistant (agents from 3 or more different drug classes)

	Prophylaxis group (n=181)*	No prophylaxis group (n=180)*	Incidence rate ratio (95% CI)	p value
Symptomatic, antibiotic-treated urinary tract infections†				
All eligible participants	1.3 (1.1–1.6)	2.6 (2.3–2.9)	0.52 (0.44–0.61)	<0.0001
<4 infections at baseline	0.8 (0.6–1.1)	1.7 (1.4–2.2)	0.46 (0.34–0.64)	0.45‡
≥4 infections at baseline	1.7 (1.3–2.0)	3.1 (2.7–3.6)	0.54 (0.45–0.64)	..
Microbiologically confirmed urinary tract infections§				
All eligible participants	0.74 (0.58–0.94)	1.5 (1.3–1.8)	0.49 (0.39–0.60)	<0.0001
<4 infections at baseline	0.32 (0.18–0.57)	1.2 (0.9–1.5)	0.28 (0.18,0.45)	0.01‡
≥4 infections at baseline	0.99 (0.77–1.3)	1.7 (1.4–2.1)	0.57 (0.45–0.72)	..
Febrile urinary tract infections§				
All eligible participants	0.11 (0.06–0.21)	0.16 (0.10–0.25)	0.71 (0.40–1.26)	0.24
<4 infections at baseline	0.07 (0.03–0.17)	0.12 (0.06–0.23)	0.62 (0.20–1.90)	0.79‡
≥4 infections at baseline	0.14 (0.06–0.30)	0.19 (0.11–0.32)	0.74 (0.38–1.45)	..
Asymptomatic bacteriuria§				
All eligible participants	1.4 (1.2–1.6)	1.6 (1.4–1.9)	0.88 (0.74–1.04)	0.14
<4 infections at baseline	1.5 (1.2–2.0)	2.0 (1.6–2.5)	0.77 (0.60–1.00)	0.18‡
≥4 infections at baseline	1.3 (1.1–1.6)	1.4 (1.1–1.6)	0.98 (0.77–1.23)	..

*Data are incidence rate (95% CI). †Primary outcome. ‡For interaction between subgroups (<4 and ≥4 infections at baseline) and treatment group. §Secondary outcome.

Table 2: Incidence rates and incidence rate ratios of the primary and secondary outcomes, compared between the prophylaxis and control (no prophylaxis) groups

Recurrent UTIs in renal transplant

- Healthcare providers may need to consider interventions beyond standard antibiotic treatment in frequent or severe recurrent UTIs.
- Urological procedures, such as addressing anatomical abnormalities or ureteral strictures, may be necessary to reduce the risk of recurrent infections.
- *Additionally, suppressive antibiotic therapy, which involves the long-term use of low-dose antibiotics, may be considered to prevent or minimize UTI recurrence.*
- These interventions should be tailored to the patient's circumstances and risk factors.

Recurrent/chronic cystitis

Con

Dr. Chuka Enwezor

Pro

Dr. Sarah Battle

Assessment Question 1

- Which of the following are valid reasons clinicians may consider placing a patient on long-term suppressive antibiotic therapy?

Select all that apply

1. Biofilm-associated infection
2. Shared decision-making with patient after discussion of risks and benefits
3. Limited or no future surgical/interventional options for source control
4. High-risk host factors (cirrhosis, end-stage renal disease, heart failure)

Assessment Question 1

- Which of the following are valid reasons clinicians may consider placing a patient on long-term suppressive antibiotic therapy?

Select all that apply

- 1. Biofilm-associated infection**
- 2. Shared decision-making with patient after discussion of risks and benefits**
- 3. Limited or no future surgical/interventional options for source control**
- 4. High-risk host factors (cirrhosis, end-stage renal disease, heart failure)**

When Suppressive Antibiotics Are Most Likely to Help after Debridement and Retention (DAIR)

Strongly favor SAT after DAIR if ≥ 1 present:

- Limited surgical options for future failure
(*e.g., amputation, arthrodesis, poor wound coverage outcomes*)
- Recurrent prosthetic joint infection (PJI) or prior DAIR failure
- High-risk host factors: cirrhosis, ESRD, heart failure
- Age >75 or limited life expectancy (<10 years)
- Late hematogenous infection (>2 years post-implant), especially with bacteremia
- Gram-negative infection without fluoroquinolone option
- Patient preference strongly favors suppression after shared decision-making

Assessment Question 2

- Which of the following is not an indication for long-term suppressive antibiotics according to Horne et al. *Clin Infect Dis.* 2024?
 1. Prosthetic Joint Infections
 2. Vascular graft infection
 3. Cardiovascular implantable electronic device infection
 4. Osteomyelitis and other orthopedic hardware infections
 5. Recurrent cystitis

Assessment Question 2

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 1. Prosthetic Joint Infections
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 - 5. Recurrent cystitis**



4 groups identified as needing suppressive antibiotics

- Prosthetic joint infections
- Vascular graft infection (VGI) and other vascular infections including infective endocarditis and mycotic aneurysm
- CIEDI Cardiovascular implantable electronic device infections
- Osteomyelitis and other orthopedic hardware infections

Assessment Question 3

- Which of the following patients has strong evidence for the use of long-term suppressive antibiotics for cystitis?
 1. Renal transplant recipient
 2. Neurogenic bladder
 3. Presence of multidrug-resistant pathogen on urine culture
 4. None of the above

Assessment Question 3

- Which of the following patients has strong evidence for the use of long-term suppressive antibiotics for cystitis?
 1. Renal transplant recipient
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 3. Presence of multidrug-resistant pathogen on urine culture
 - 4. None of the above**

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