Infezioni protesiche in ortopedia

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Il sottoscritto

ai sensi dell’art. 76, comma 4 dell’Accordo Stato-Regioni del 2 febbraio 2017 e del paragrafo 4.5. del Manuale nazionale di accreditamento per l'erogazione di eventi ECM

dichiara che

negli ultimi due anni ha avuto i seguenti rapporti con soggetti portatori di interessi commerciali in ambito sanitario

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Infection Associated with Prosthetic Joints

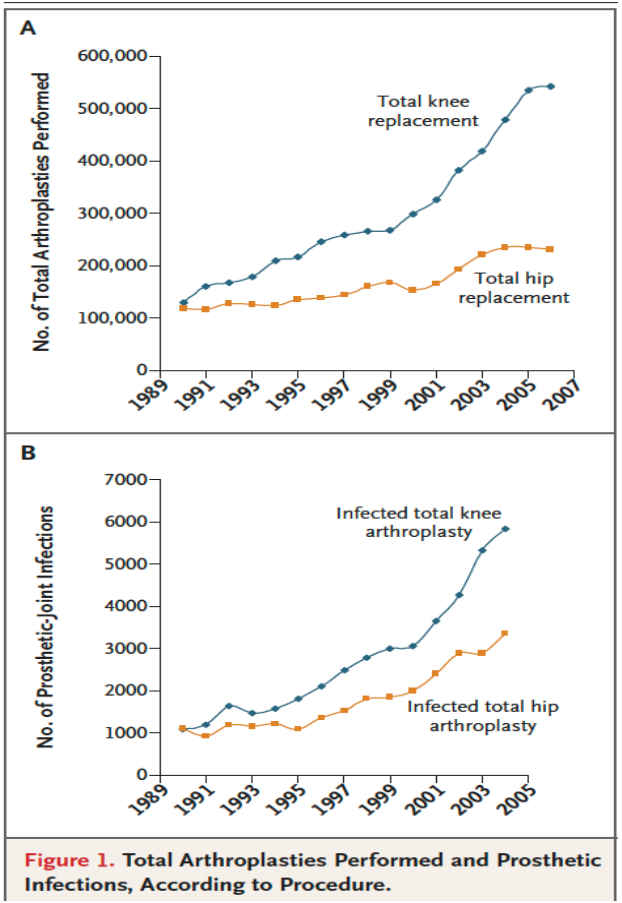


Figure 1. Total Arthroplasties Performed and Prosthetic Infections, According to Procedure.

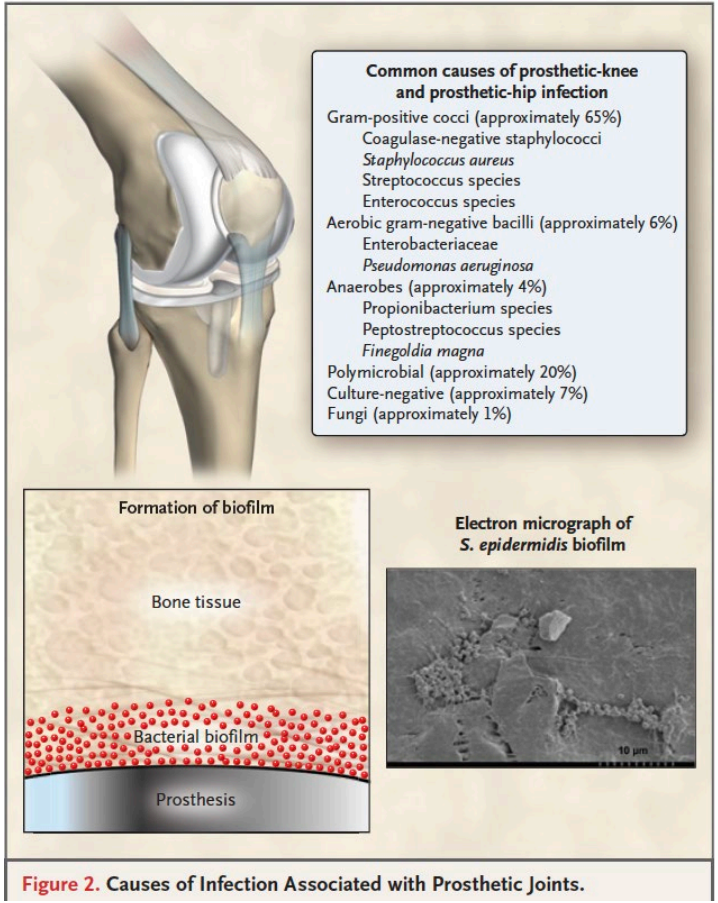


Figure 2. Causes of Infection Associated with Prosthetic Joints.

Del Pozo and Patel, NEJM 2009

Infection Associated with Prosthetic Joints

Table 1. Criteria for the Diagnosis of a Prosthetic-Joint Infection.*

The presence of at least one of the following findings:

Acute inflammation detected on histopathological examination of periprosthetic tissue

Sinus tract communicating with the prosthesis

Gross purulence in the joint space

Isolation of the same microorganism from two or more cultures of joint aspirates or intraoperative periprosthetic-tissue specimens, isolation of the organism in substantial amounts (e.g., ≥20 CFU per 10 ml from the implant in a total volume of 400 ml of sonicate fluid), or both

Del Pozo and Patel, NEJM 2009

Infection Associated with Prosthetic Joints

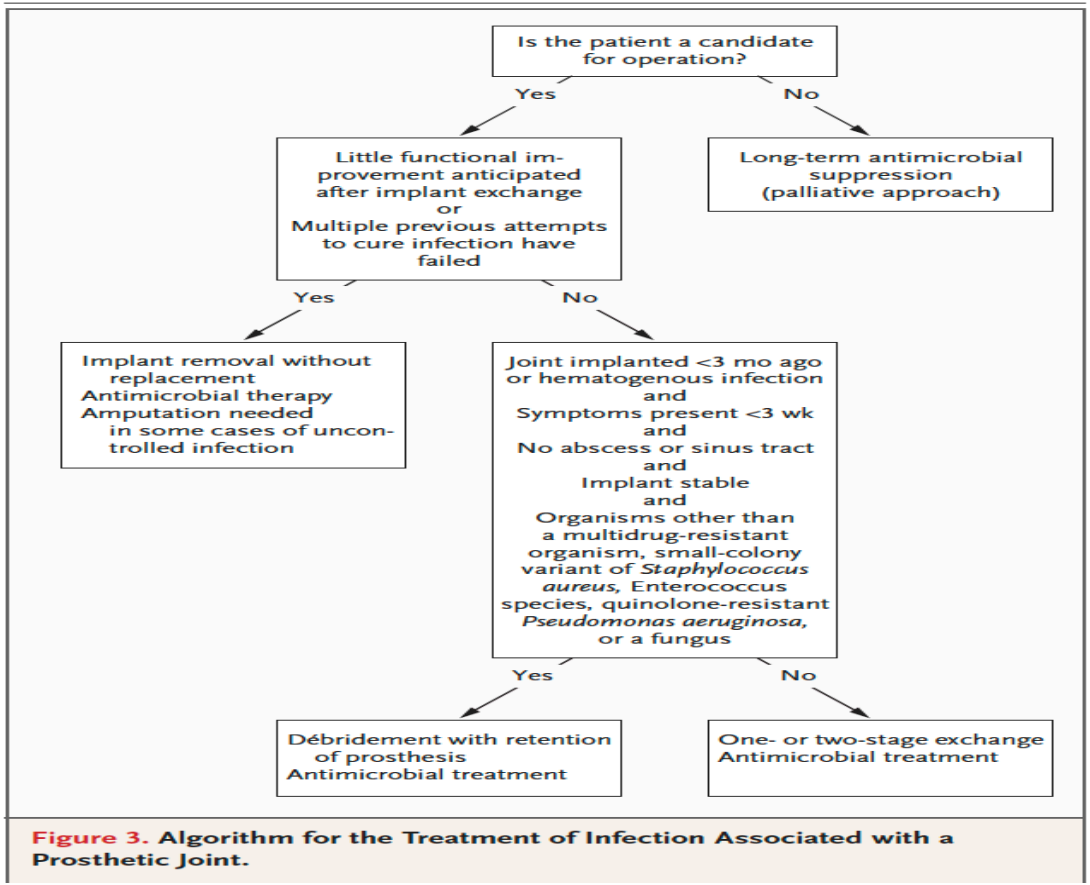


Figure 3. Algorithm for the Treatment of Infection Associated with a Prosthetic Joint.

Del Pozo and Patel, NEJM 2009

BATTERI GRAM-POSITIVI

Anaerococcus prevotii/vaginalis
Clostridium perfringens
Cutibacterium avidum/granulosum
Enterococcus faecalis
Enterococcus faecium
Finegoldia magna
Parvimonas micra
Peptoniphilus
Peptostreptococcus anaerobius
Staphylococcus aureus
Staphylococcus lugdunensis
Streptococcus spp.
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

BATTERI GRAM-NEGATIVI

Bacteroides fragilis
Citrobacter
Enterobacter cloacae complex
Escherichia coli
Haemophilus influenzae
Kingella kingae
Klebsiella aerogenes
Klebsiella pneumoniae group
Morganella morganii
Neisseria gonorrhoeae
Proteus spp.
Pseudomonas aeruginosa
Salmonella spp.
Serratia marcescens

LIEVITI

Candida spp.
Candida albicans

GENI DI RESISTENZA ANTIMICROBICA

Carbapenemasi

IMP
KPC
NDM
OXA-48-like
VIM

ESBL

CTX-M

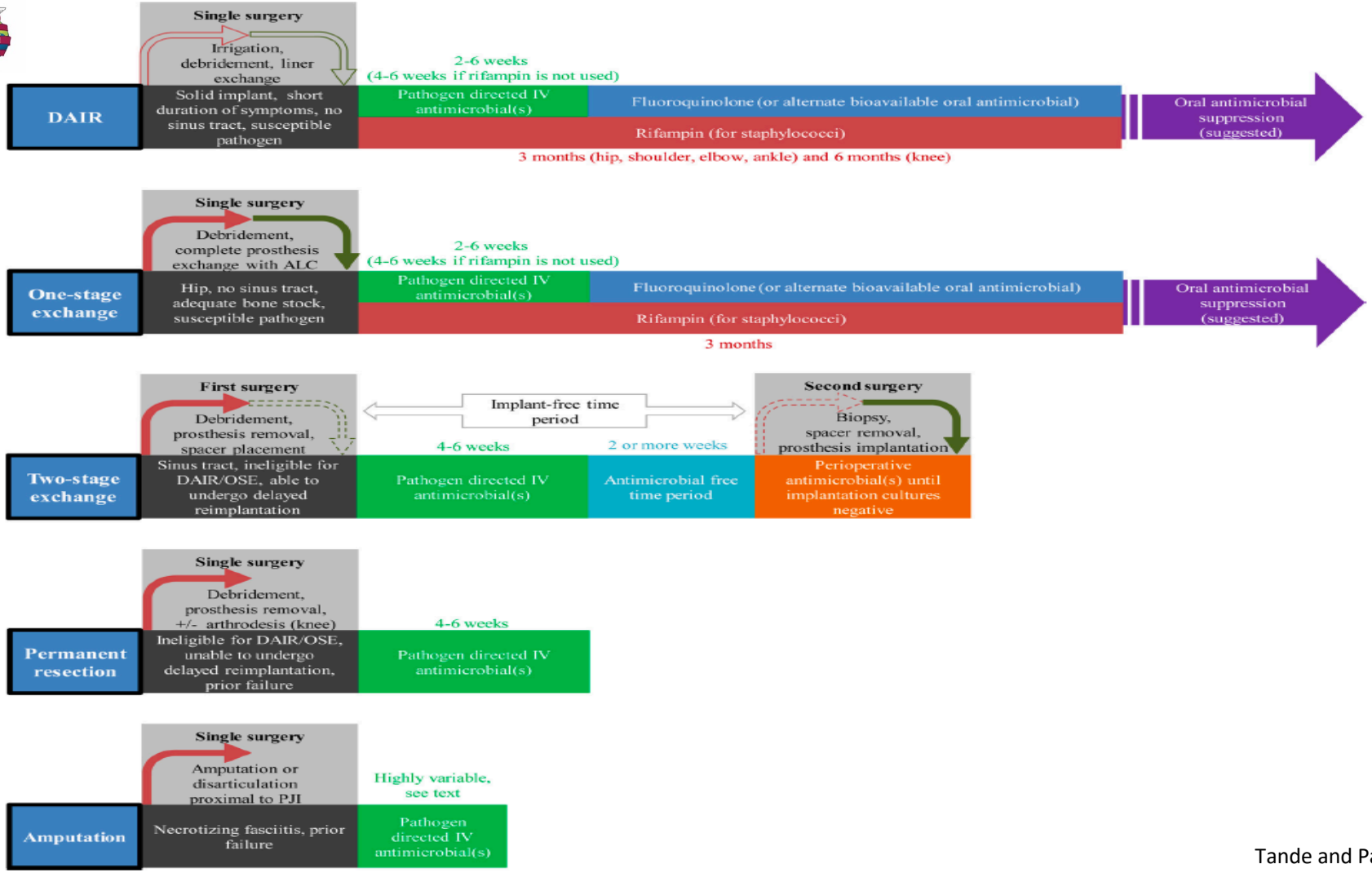
Resistenze alla meticillina

mecA/C e MREJ

Resistenze alla vancomicina

vanA/B

Labetoulle et al, JCM 2022



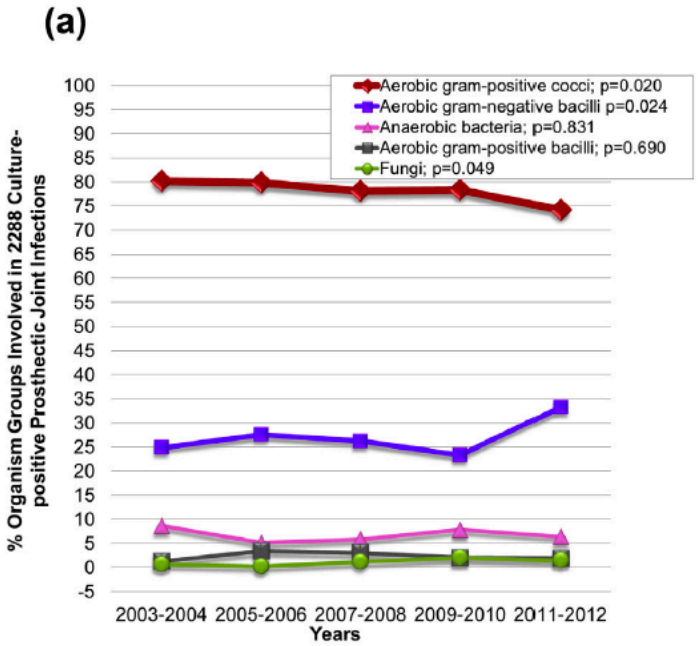
Tande and Patel, CRM 2014

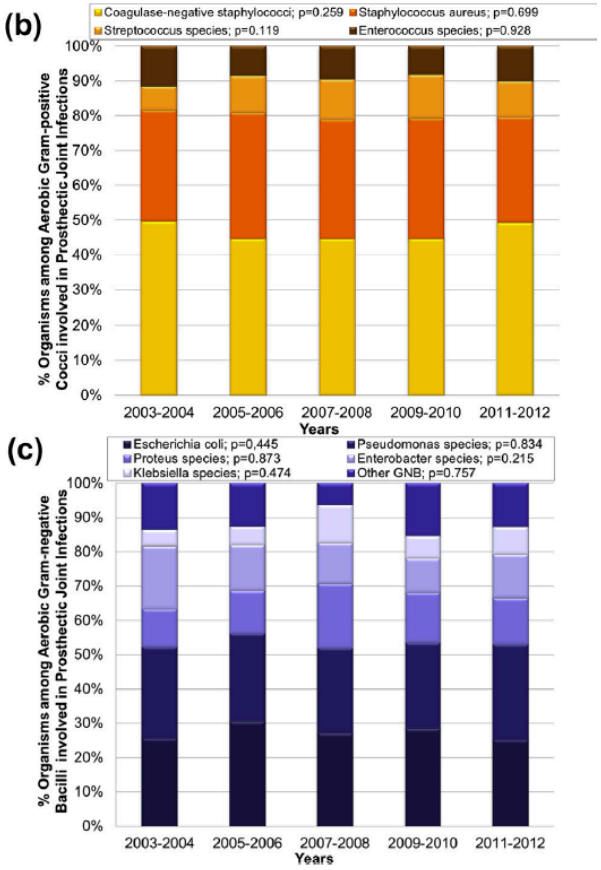
Debridement and retention of prosthesis (DAIR)

- Diagnosis of PJI within approximately 30 days of prosthesis implantation, or within approximately three weeks of symptom onset, in patients with a well-fixed prosthesis with no sinus tract. In such cases, eradication of infection occurs in up to 70 percent of patients.

- Patients who are poor surgical candidates for resection arthroplasty; in such cases, the likelihood of relapsed infection is greater than for patients who undergo resection arthroplasty.

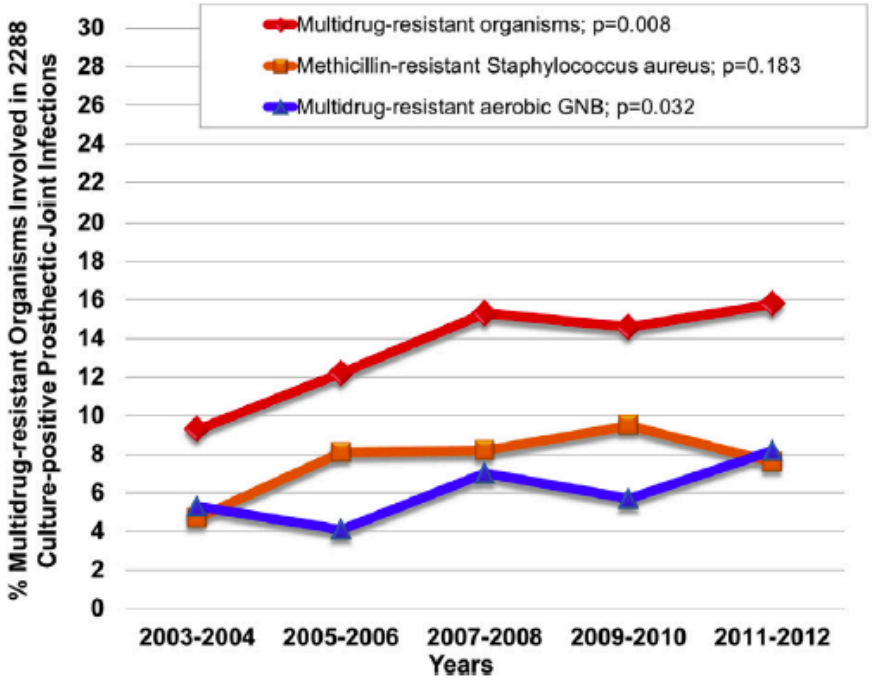
Time trends in the aetiology of prosthetic joint infections





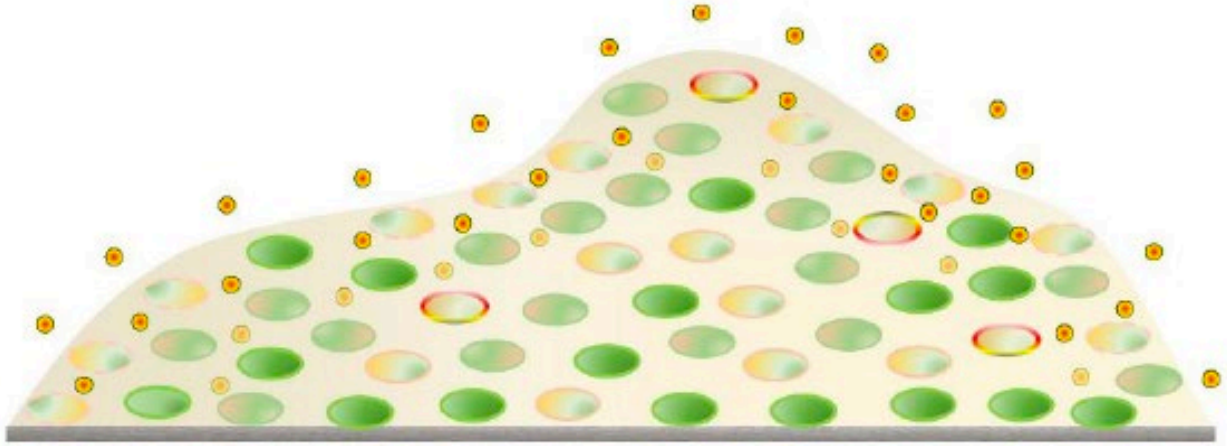
Benito et al, CMI 2016

Time trends in the aetiology of prosthetic joint infections



Benito et al, CMI 2016

Biofilm



Cells killed by biocide
Susceptible cells
Phenotype A
Phenotype B
Cells can now survive direct exposure outside of the biofilm
Antimicrobial
Degraded antimicrobial

Hulme, Pharmaceutics 2022

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

TABLE 2 Comparison between EB and NFGBN biofilm formation[a]

Family group	No. of strains			Total
	Biofilm formation (Q1 to Q3) (*n*-fold OD_c)	Nonbiofilm producer (%)	Biofilm producer (%)	
EB	3.28 (1.72 to 5.68)	1 (2.1%)	37 (97.9%)	38
NFGNB	10.06 (5.60 to 22.78)	0	8 (100%)	8

[a]EB, Enterobacteriaceae; NFGBN, nonfermenting Gram-negative bacilli; OD_c, cutoff value three standard deviations (SD) above the mean optical density; Q, quartile.

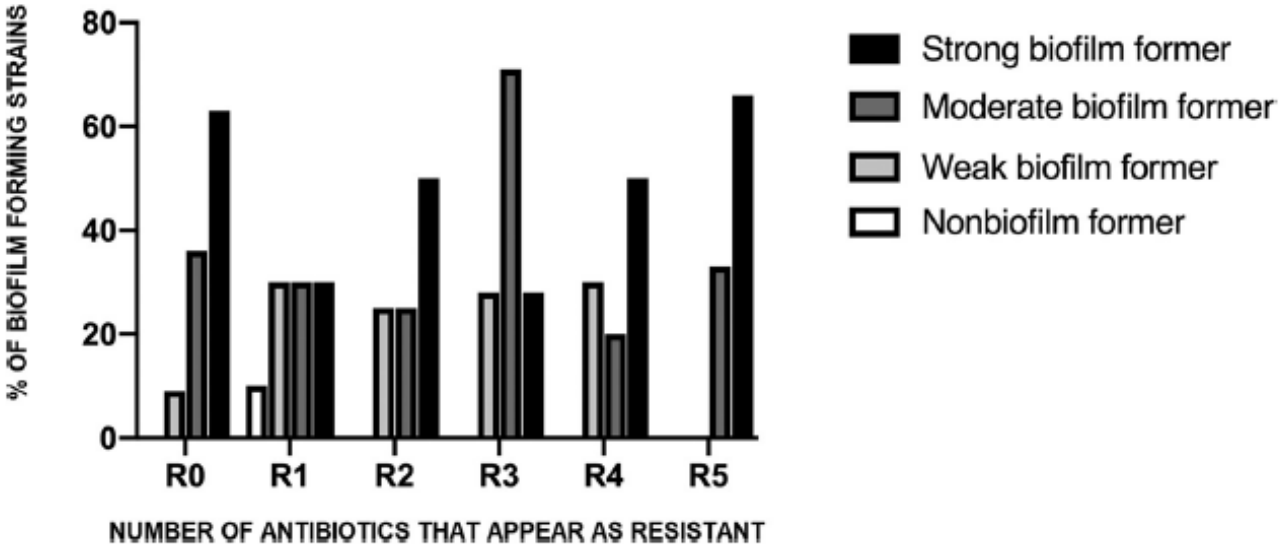
TABLE 3 GNB biofilm formation[a]

Strain (*n*)	Biofilm formation (Q1 to Q3) (*n*-fold OD_c)	Percentage biofilm producer (%)			
		Strong	Moderate	Weak	No producer
A. baumanii (1)	2.5 (1.9 to 4)	0	1 (100%)	0	0
C. freundii (1)	3.4 (1.9 to 3.9)	0	1 (100%)	0	0
C. koseri (1)	1.3 (0.7 to 1.6)	0	0	1 (100%)	0
E. cloacae (2)	7.2 (5.6 to 8.4)	2 (100%)	0	0	0
E. hormaechei (2)	1.7 (0.7 to 3.6)	0	1 (50%)	1 (50%)	0
E. coli (8)	2.1 (1.2 to 3.3)	1 (12.5%)	4 (50%)	3 (37.5%)	0
K. pneumoniae (7)	4.9 (2.3 to 7.4)	4 (71.4%)	2 (14.3%)	1 (14.3)	0
M. morganii (3)	5.9 (2.1 to 13.45)	2 (66.7%)	0	1 (33.3%)	0
P. mirabilis (8)	3.3 (2.2 to 5)	2 (25%)	5 (62.5%)	1 (12.5%)	0
P. vulgaris (1)	1.3 (1.1 to 2.4)	0	0	1 (100%)	0
P. stuartii (1)	2.9 (2.3 to 4.6)	0	1 (100%)	0	0
P. aeruginosa (7)	10.2 (6.4 to 19.6)	7 (100%)	0	0	0
R. ornithinolytica (1)	0.9 (0.7 to 1.3)	0	0	0	1 (100%)
S. marcescens (3)	2.6 (1.7 to 5)	1 (33.3%)	1 (33.3%)	1 (33.3%)	0
Total	3.6 (1.8 to 6.8)	19 (41.3%)	16 (34.8%)	10 (21.8%)	1 (2.1%)

[a]GNB, Gram-negative bacilli; OD_c, cutoff value three standard deviations (SD) above the mean optical density; Q, quartile.

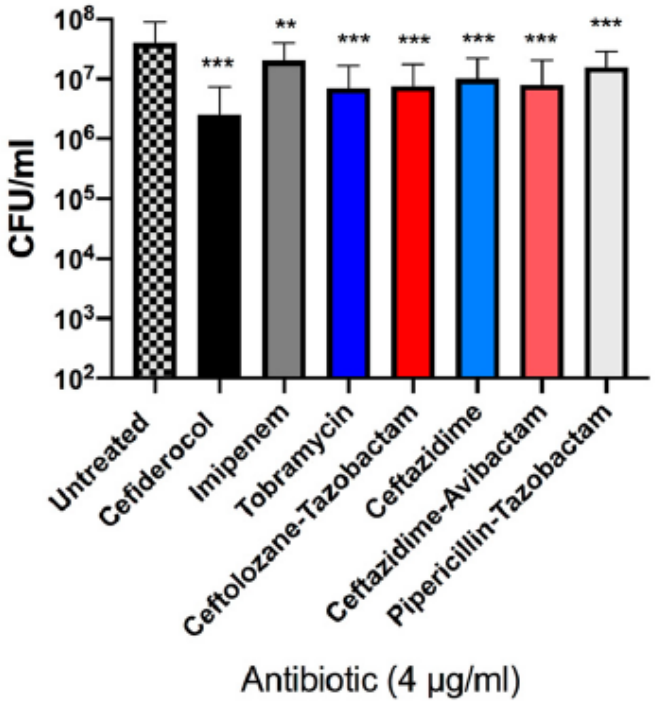
Macias-Valcajo et al, Microbiology Spectrum 2022

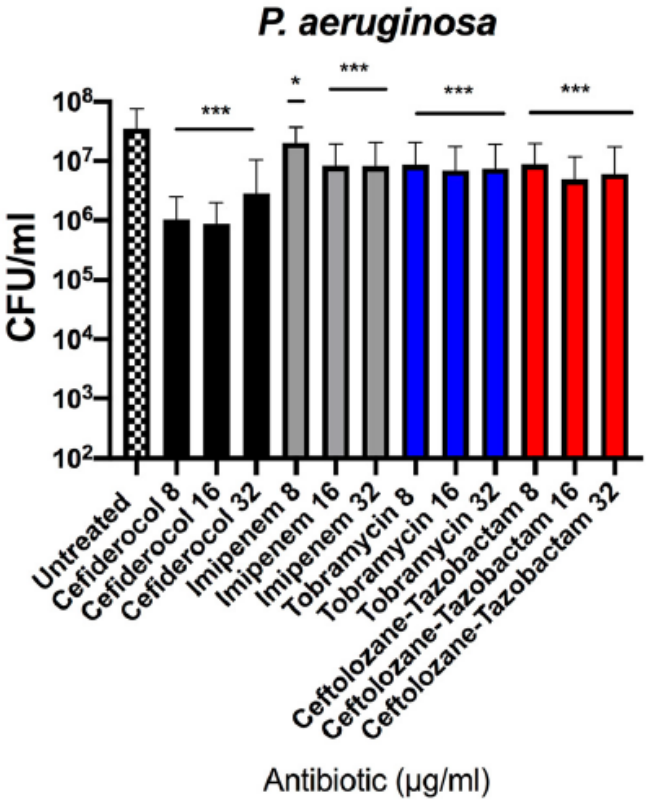
Comparative *In Vitro* Study of Biofilm Formation and Antimicrobial Susceptibility in Gram-Negative Bacilli Isolated from Prosthetic Joint Infections



Macias-Valcajo et al, Microbiology Spectrum 2022

Biofilm and Gram-negative





Pybus et al, AAC 2021

Principi di terapia antibiotica delle infezione di dispositivo ortopedico

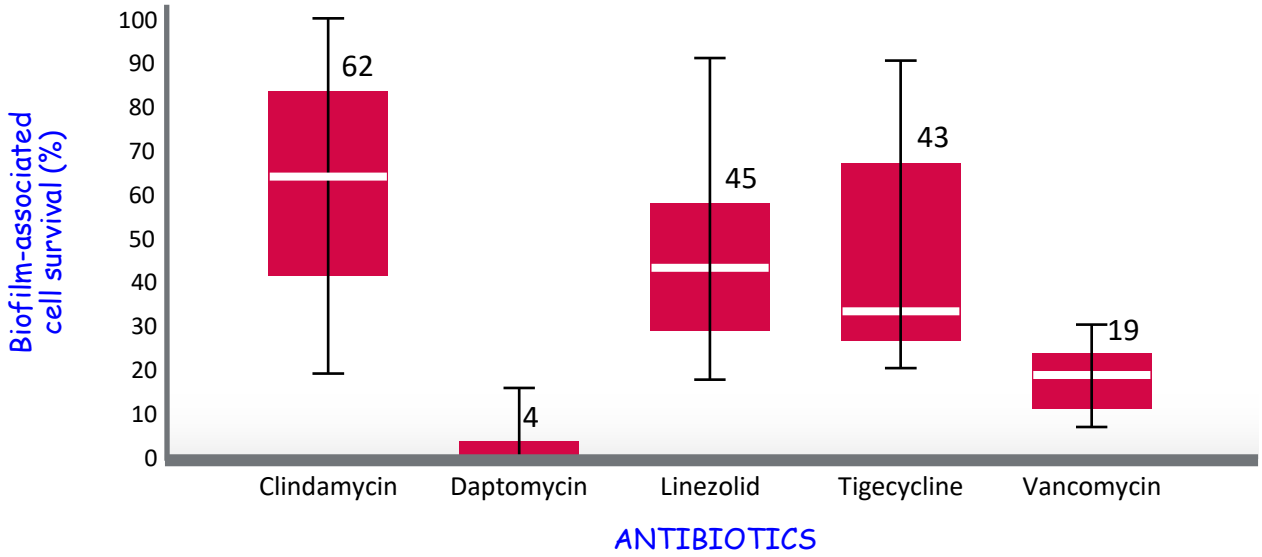
- Antibiotico battericida
- Attivo sul biofilm
- Buon profilo cinetico-dinamico
- Scarse interazioni con altri farmaci
- Potenziale per terapia di associazione
- Scarsi effetti collaterali
- Dati clinici convincenti

Armamentarium for treatment of PJIs

TABLE 5 Suggested antimicrobials for treatment of PJI[a]

Microorganism(s)	Preferred treatment	Alternate treatment	Combination therapy[b]
Methicillin-susceptible staphylococci	Cefazolin or nafcillin	Vancomycin, daptomycin, or linezolid	Rifampin for DAIR and one-stage exchange
Methicillin-resistant staphylococci	Vancomycin	Daptomycin or linezolid	Rifampin for DAIR and one-stage exchange
Penicillin-susceptible enterococci	Penicillin or ampicillin	Vancomycin, daptomycin, or linezolid	Consider aminoglycoside
Penicillin-resistant enterococci	Vancomycin	Daptomycin or linezolid	Consider aminoglycoside
Pseudomonas aeruginosa	Cefepime or meropenem	Ciprofloxacin or ceftazidime	Consider aminoglycoside or fluoroquinolone
Enterobacter species	Cefepime or ertapenem	Ciprofloxacin	No
Enterobacteriaceae	Beta-lactam or ciprofloxacin		No
Beta-hemolytic streptococci	Penicillin or ceftriaxone		No
Propionibacterium acnes	Penicillin or ceftriaxone		No

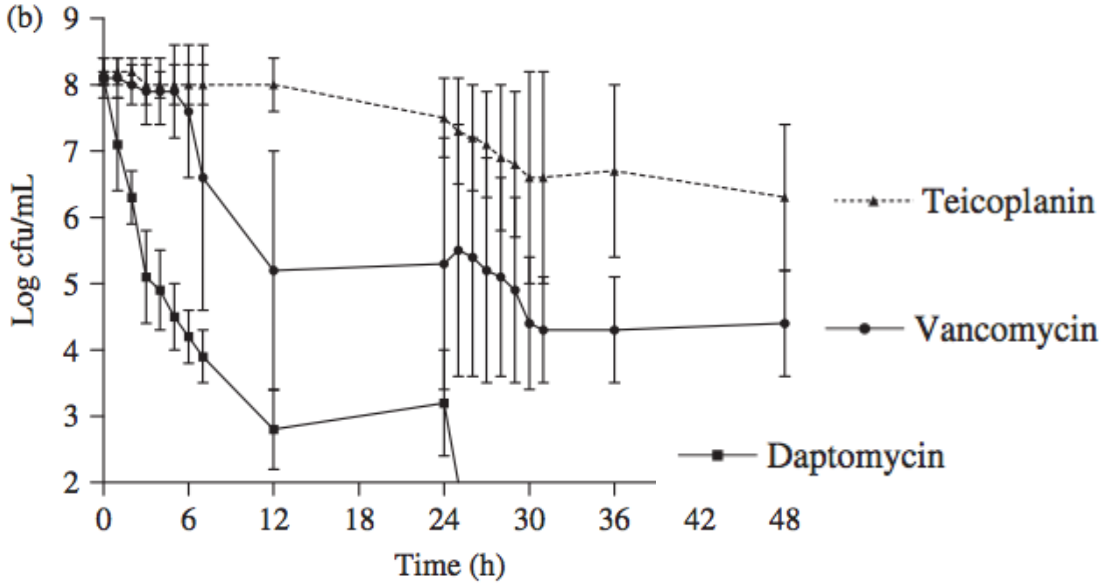
Sopravvivenza cellulare associata a biofilm in 12 isolati di MRSA



Smith, et al. Int J Antimicrob Agents 2008

Comparative antibacterial effects of daptomycin, vancomycin and teicoplanin studied in an *in vitro* pharmacokinetic model of infection

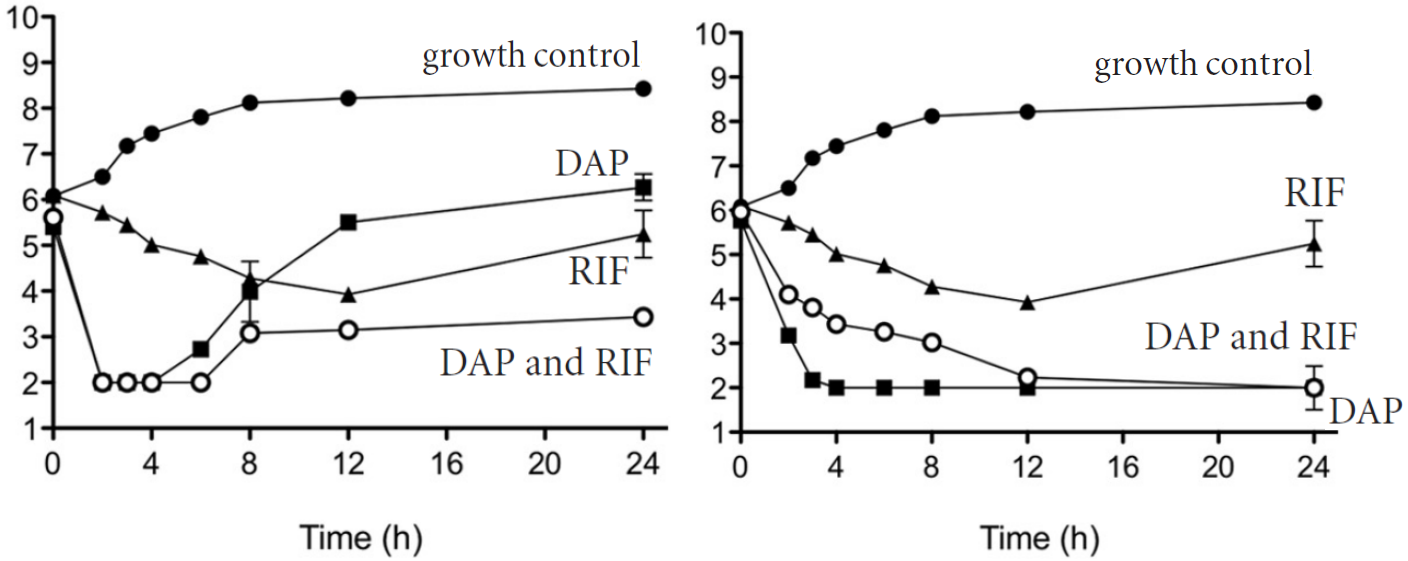
Karen E. Bowker*, Alan R. Noel and Alasdair P. MacGowan



Journal of Antimicrobial Chemotherapy (2009) 64, 1044–1051

Possibili sinergismi

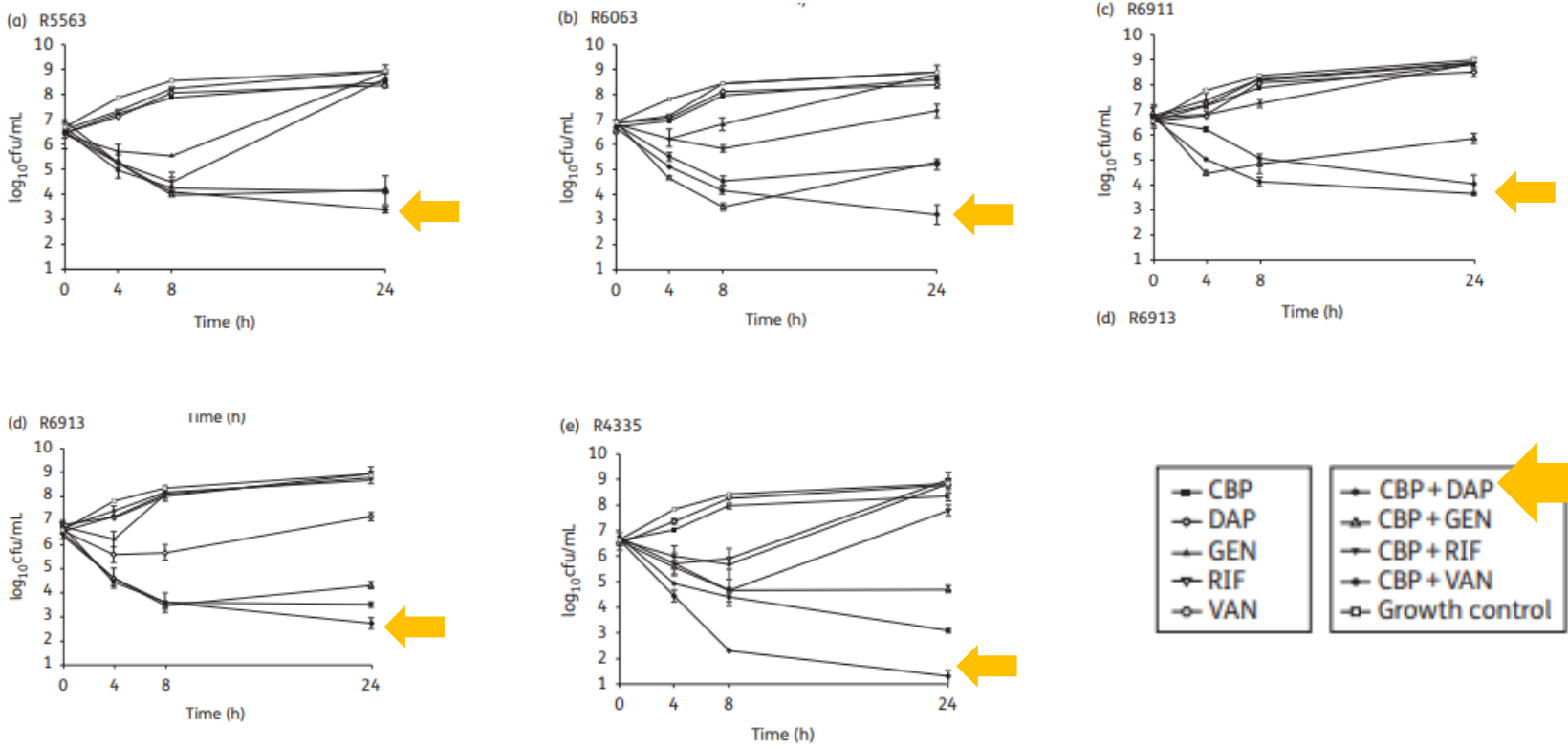
The analysis shows synergy with low concentrations of both DAP and RIF but early antagonism as DAP concentrations increased.



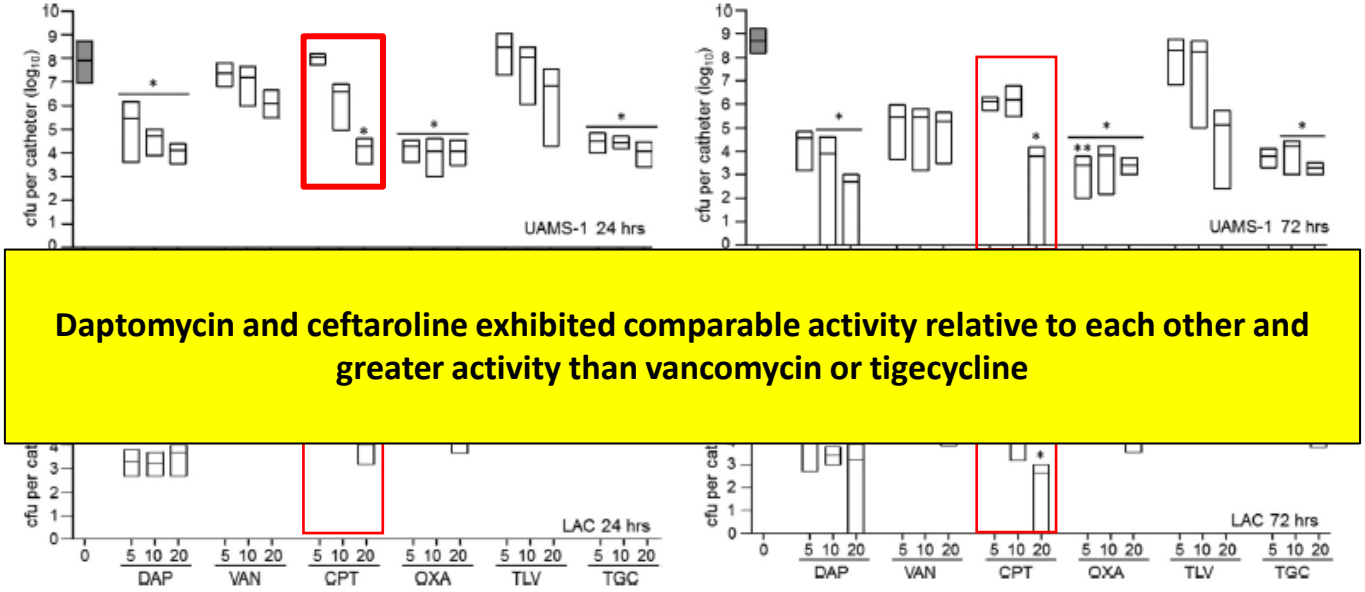
Warren E. Rose Antimicrobial Agents and Chemotherapy p. 3450–3452 July 2013 Volume 57 Number 7

ɔtent synergy of ceftobiprole plus daptomycin against multiple strains of Staphylococcus aureus with various resistance phenotypes.

Barber KE, Werth BJ et al J Antimicrob Chemother. 2014



Relative activity of different antibiotics against MRSA biofilm at 24 h



Daptomycin and ceftaroline exhibited comparable activity relative to each other and greater activity than vancomycin or tigecycline

Meeker DG, Antimicrob Agents Chemother. 2016;60:5688-94

Reduced glycopeptide and lipopeptide susceptibility in *Staphylococcus aureus* and the "seesaw effect": Taking advantage of the back door left open?

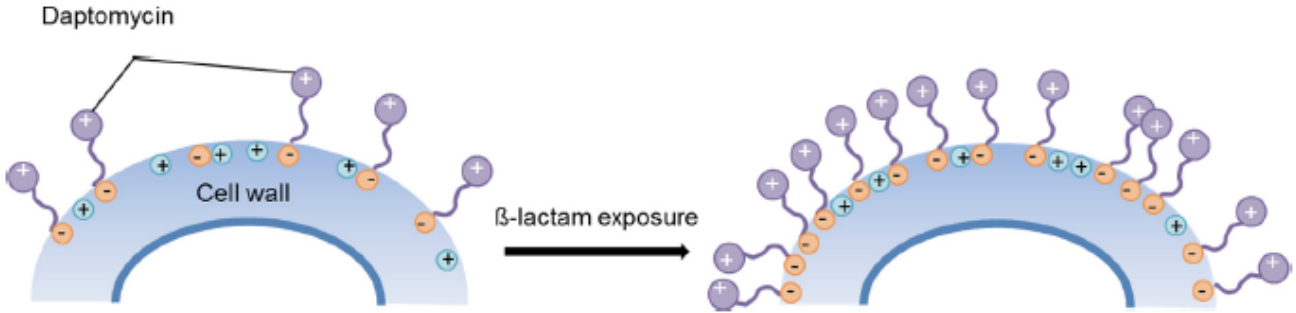
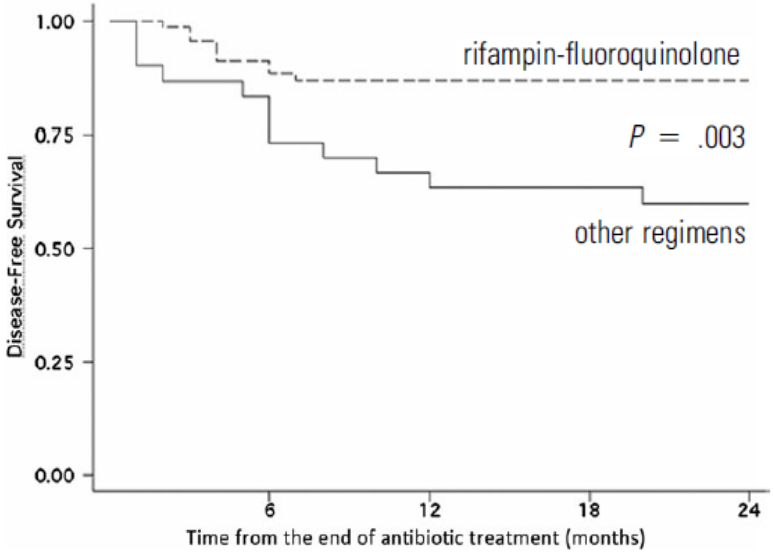


Figure 2. Proposed mechanisms for daptomycin and beta-lactam synergy. Daptomycin acts like a cationic peptide antibiotic and is attracted to the negative charge of the bacterial cell membrane. Once in contact with the cytoplasmic membrane (CM) daptomycin disrupts the CM causing a rapid release of electrolytes from the cytoplasm leading to depolarization and death of the cell. Exposure to beta-lactams increases the negative charge of the cell surface leading to an increase in daptomycin binding and improved bactericidal activity.

Ortwine et al. Drug Resistance Updates 2013

Possibili sinergismi

The results suggest that rifampin combination therapy is associated with a better outcome for patients treated for total hip and knee prosthetic infections due to MSSA or MRSA when compared with other antibiotic regimens.



	patients with remission				
	Rifampin treatment (n = 68)		No Rifampin treatment (n = 30)		
	Fluoroquinolone combinations (n = 39)	Other rifampin combinations (n = 29)	Linezolid monotherapy (n = 11)	Other treatment (n = 19)	P
Debridment / Repacement / Arthrodesis	37/39 (94.8%)	21/29 (72.4%)	9/11 (81.8%)	10/19 (52.6%)	.002

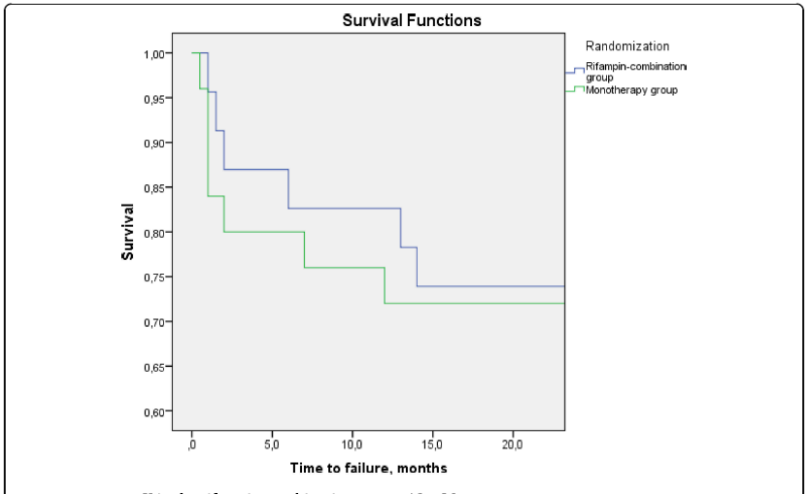
Clinical Infectious Diseases 2011;53(4):334–340

Rifampin combination therapy in staphylococcal prosthetic joint infections: a randomized controlled trial

Table 2 Bacterial findings in initial DAIR procedure

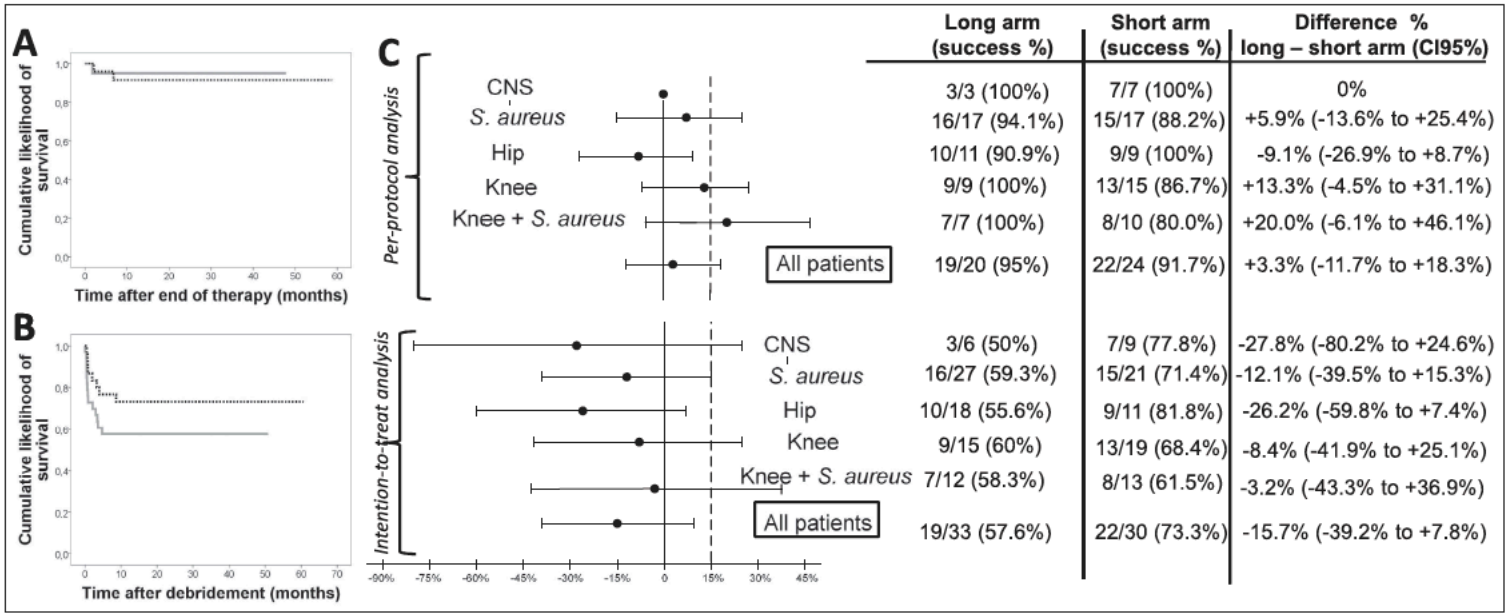
Microbes	Rifampin-combination group	Monotherapy group	Total
MSSA	15	19	34
MRSE	5	5	10
MSSA + MSSE	2	0	2
Staph lugdunensis	1	0	1
Staph capitis	0	1	1

MSSA **methicillin-susceptible** ***S. aureus, MRSE*** **methicillin-resistant** ***S. epidermidis***



Karlsen et al, JOSR 2020

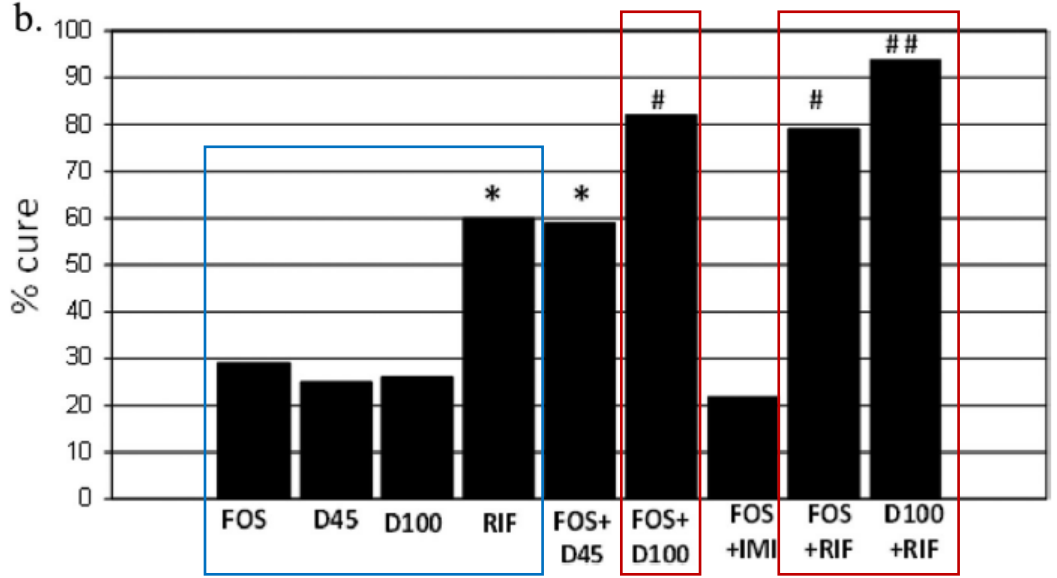
Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ☆



	Long arm (success %)	Short arm (success %)	Difference % long – short arm (CI95%)
CNS	3/3 (100%)	7/7 (100%)	0%
S. aureus	16/17 (94.1%)	15/17 (88.2%)	+5.9% (-13.6% to +25.4%)
Hip	10/11 (90.9%)	9/9 (100%)	-9.1% (-26.9% to +8.7%)
Knee	9/9 (100%)	13/15 (86.7%)	+13.3% (-4.5% to +31.1%)
Knee + *S. aureus*	7/7 (100%)	8/10 (80.0%)	+20.0% (-6.1% to +46.1%)
All patients	19/20 (95%)	22/24 (91.7%)	+3.3% (-11.7% to +18.3%)
CNS	3/6 (50%)	7/9 (77.8%)	-27.8% (-80.2% to +24.6%)
S. aureus	16/27 (59.3%)	15/21 (71.4%)	-12.1% (-39.5% to +15.3%)
Hip	10/18 (55.6%)	9/11 (81.8%)	-26.2% (-59.8% to +7.4%)
Knee	9/15 (60%)	13/19 (68.4%)	-8.4% (-41.9% to +25.1%)
Knee + *S. aureus*	7/12 (58.3%)	8/13 (61.5%)	-3.2% (-43.3% to +36.9%)
All patients	19/33 (57.6%)	22/30 (73.3%)	-15.7% (-39.2% to +7.8%)

Lora-Tamayo, IJAA 2016

Fosfomycin-Daptomycin and Other Fosfomycin Combinations as Alternative Therapies in Experimental Foreign-Body Infection by Methicillin-Resistant *Staphylococcus aureus*



Daptomycin-rifampin was confirmed as the most effective therapy against MRSA foreign-body infections. Fosfomycin combinations with high doses of daptomycin and rifampin were efficacious alternative therapies in this setting. Fosfomycin-imipenem was relatively ineffective and did not protect against resistance.

Garrigós et al. Antimicrobial Agents and Chemotherapy January 2013 Volume 57 Number 1 p. 606–610

Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

Subgroup	6-Wk Therapy	12-Wk Therapy	Risk Difference (95% CI)
	no. of patients with event/total no. (%)		*percentage points*
All patients	32/190 (16.8)	15/188 (8.0)	8.9 (2.2 to 15.6)
Surgical procedure			
Débridement	23/75 (30.7)	11/76 (14.5)	16.2 (2.9 to 29.5)
Two-stage revision	6/40 (15.0)	2/41 (4.9)	10.1 (–3.1 to 23.3)
One-stage revision	3/75 (4.0)	2/71 (2.8)	1.2 (–4.8 to 7.1)
Affected joint			
Hip	19/122 (15.6)	9/117 (7.7)	7.9 (–0.2 to 16.0)
Knee	13/68 (19.1)	6/71 (8.5)	10.7 (–0.9 to 22.2)
Episode of prosthetic joint infection			
First	27/162 (16.7)	13/160 (8.1)	8.5 (1.4 to 15.7)
At least the second	5/28 (17.9)	2/28 (7.1)	10.7 (–7.0 to 28.4)

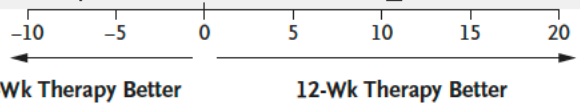


Figure 2. Exploratory Subgroup Analyses of Persistent Infection within 2 Years after the Completion of Antibiotic Therapy (Primary Outcome).

Bernard et al, NEJM 2021

Short- versus standard-course intravenous antibiotics for peri-prosthetic joint infections managed with debridement and implant retention: a randomised pilot trial using a desirability of outcome ranking (DOOR) endpoint

Table 2
Primary, secondary and exploratory outcomes according to treatment allocation

	Total (n=60)	Short-course (n=31)	Standard-course (n=29)
Prosthesis removal within 120 days	8 (13.3%)	4 (12.9%)	4 (14%)
Duration of IV (d) (median [IQR])****	26 (15-42)	15 (14-17.5)	42 (42-44)
Death at 1 year	3 (5%)	2 (6.4%)	1 (3.4%)
Prosthesis removal 120-365	5	1 (3.2%)	4 (13.8%)
Ongoing antibiotics at 365	5	2 (6.4%)	3 (10.3%)
DOOR (median [IQR])	2 (1-4)	2 (1-4)	2 (1-3.5)
DOOR Score1234567	162266613	81222502	81044111
Clinical cure (DOOR values 1-3)	44 (73%)	22 (71%)	22 (76%)
Oxford Score at 12 months	43 (33-46)	34 (30-46)	41.5 (32-45)
At least 1 major AE	9	4	5
CRP Change at 2 weeks (% of baseline)	81.5 (71.4-91.1)	85.5 (74.2-91.4)	79.3 (71.1-90.3)
CRP Change at 4 weeks (% of baseline)	89.6 (80.0-94.4)	90 (82.7-96.4)	85.0 (66.7-94.0)
CRP Change at 12 weeks (% of baseline)	97.1 (92.3-98.9)	97.9 (90.2-98.9)	95.6 (93.8-98.7)

IV, intravenous; d, days; IQR, interquartile range; DOOR, desirability of outcome ranking; AE, adverse event; CRP, C-reactive protein.

**** $P<0.0001$ compared between short-course and standard-course groups.

Manning et al, IJAA 2022

Four versus six weeks of antibiotic therapy for osteoarticular infections after implant removal: a randomized trial

ITT analysis	Six weeks	Four weeks	p-	PP analysis	Six weeks	Four weeks	p-
n = 123	n = 61	n = 62	value *	n = 117	n = 60	n = 57	value *
Duration of intravenous therapy (median)	**5 days**	**3.5 days**	**.09**	**Duration of intravenous therapy (median)**	**4 days**	**3.5 days**	**.23**
Complete clinical remission	58 (94%)	58 (95%)	.71	Complete clinical remission	54 (95%)	57 (95%)	.95
Complete microbiological remission	60 (97%)	60 (98%)	.57	Complete microbiological remission	55 (97%)	59 (98%)	.53
Significant antibiotic-related adverse events	22 (35%)	17 (28%)	.36	Significant antibiotic-related adverse events	19 (33%)	17 (28%)	.56
Visible osteosynthesis material	**7 (11%)**	**11 (18%)**	**.29**	**Visible osteosynthesis material**	**5 (9%)**	**11 (18%)**	**.13**
Removed arthroplasties	24 (39%)	15 (25%)	.09	Removed Arthroplasties	23 (40%)	15 (25%)	.08
- **with temporary spacers**	18 (30%)	13 (21%)	.28	- with temporary spacers	18 (30%)	13 (23%)	.38
- **re-implantation after infection**	17 (29%)	13 (21%)	.37	- re-implantation after infection	17 (28%)	13 (23%)	.49
- **median interval between stages**	8 weeks	6 weeks	.01	- median interval between stages	8 weeks	6 weeks	.01

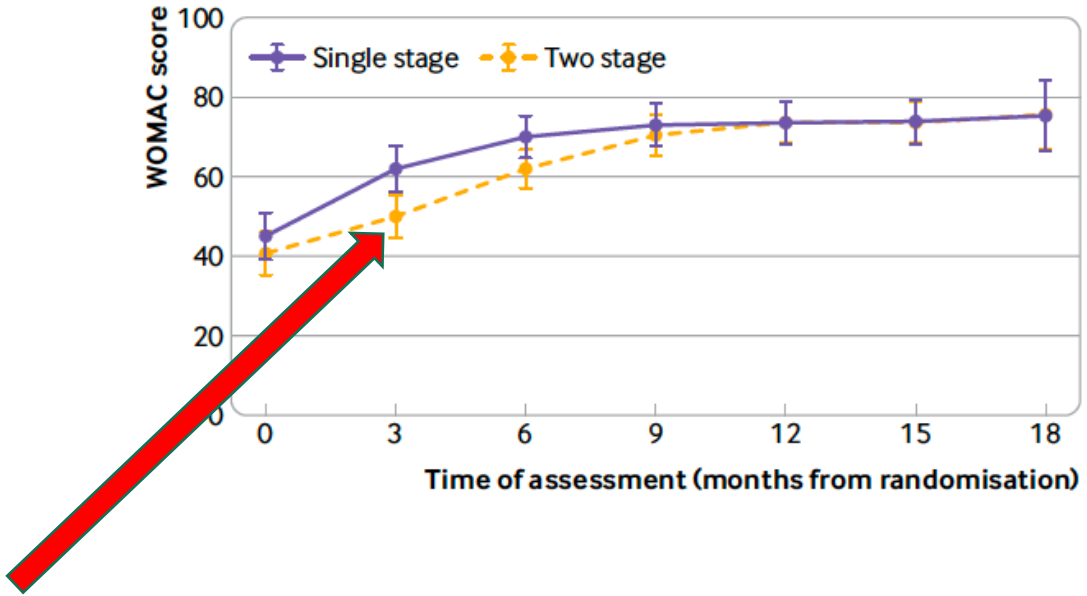
Benkabouche et al, JAC 2019

Four versus six weeks of antibiotic therapy for osteoarticular infections after implant removal: a randomized trial

	Six weeks		Four weeks	
Pathogen group	Parenteral antibiotics	Oral antibiotics	Parenteral antibiotics	Oral antibiotics
MSSA, n=42	Flucloxacillin (n=4) Cefazolin (n=3) Co-amoxiclav (n=4) Cefuroxim (n=3) Daptomycin (n=1)	Co-trimoxazole (n=3) Clindamycin (n=8) Quinolones (n=8) Beta-lactams (n=4) Rifampicin (n=3)	Flucloxacillin (n=3) Cefazolin (n=3) Co-amoxiclav (n=3) Cefuroxim (n=1) Daptomycin (n=0)	Co-trimoxazole (n=3) Clindamycin (n=10) Quinolones (n=5) Beta-lactams (n=6) Rifampicin (n=3)
Streptococci, n=14	Cefuroxim (n=3) Ampicillin (n=2) Vancomycin (n=2)	Levofloxacin (n=2) Clindamycin (n=2) Ampicillin (n=1)	Cefuroxim (n=1) Ampicillin (n=2) Vancomycin (n=1)	Levofloxacin (n=2) Clindamycin (n=2) Ampicillin (n=3)
Gram-negatives, n=28	Cephalosporins (n=5) Carbapenems/tazobactam (n=3)	Quinolones (n=8) Co-trimoxazole (n=3)	Cephalosporins (n=3) Carbapenems/tazobactam (n=2)	Quinolones (n=10) Co-trimoxazole (n=2)
Skin commensals°, n=43	Vancomycin/daptomycin (n=8) Aminopenicillins (n=7) Cephalosporins (n=9)	Ampicillin (n=4) Clindamycin (n=2) Quinolones (n=8) Tetracyclines (n=9) Rifampicin (n=5)	Vancomycin/daptomycin (n=6) Aminopenicillins (n=4) Cephalosporins (n=3)	Ampicillin (n=3) Clindamycin (n=6) Quinolones (n=6) Tetracyclines (n=8) Rifampicin (n=3)

Benkabouche et al, JAC 2019

Clinical and cost effectiveness of single stage compared with two stage revision for hip prosthetic joint infection (INFORM): pragmatic, parallel group, open label, randomised controlled trial



Blom et al, BMJ 2022

Clinical and cost effectiveness of single stage compared with two stage revision for hip prosthetic joint infection (INFORM): pragmatic, parallel group, open label, randomised controlled trial

Table 4 | Rates of complications in groups randomised to single or two stage revision for prosthetic joint infection. Data are number (%) of participants, unless otherwise specified

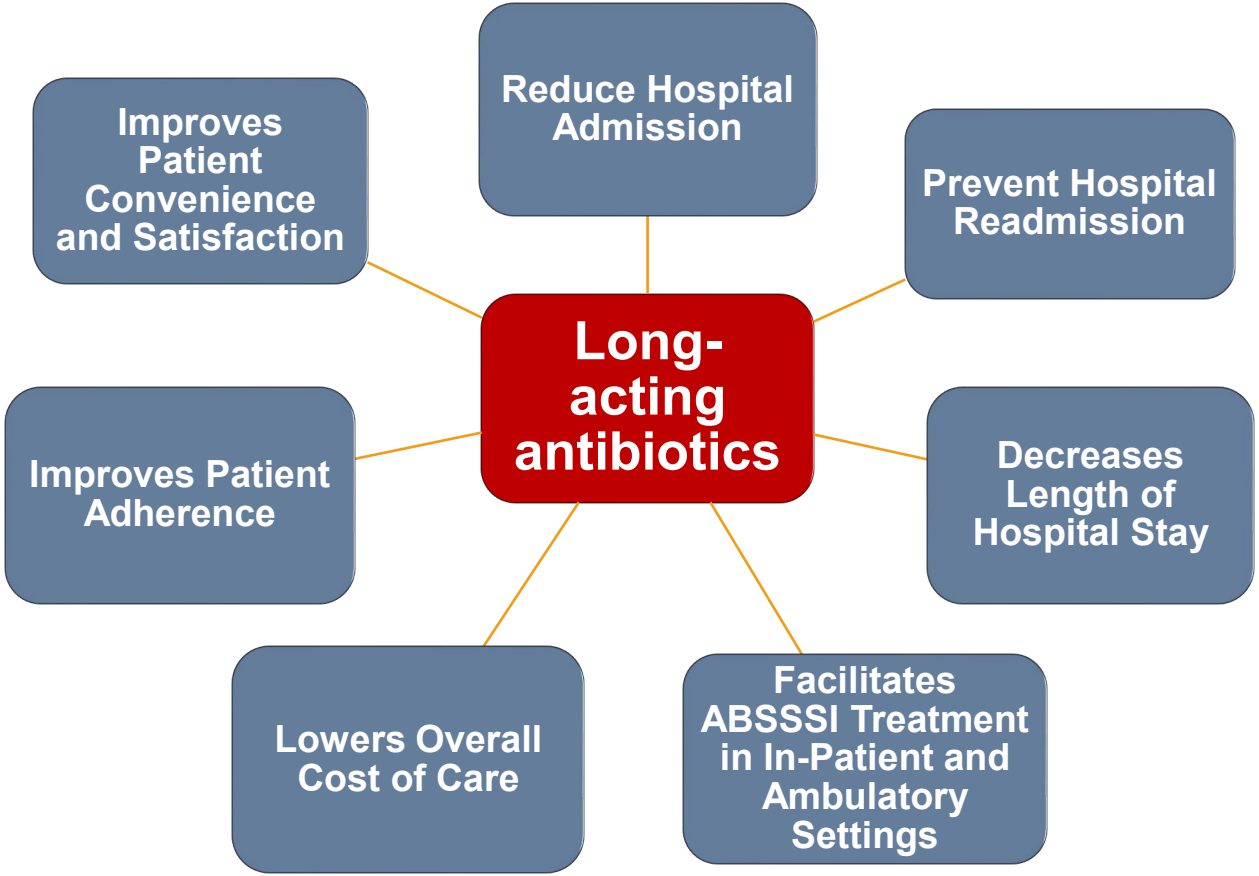
Complication	Single stage revision surgery (n=65)	Two stage revision surgery (n=75)	P value
Death	2 (3)	5 (7)	0.45
Serious adverse event	11 (17)	16 (21)	0.51
Complication of surgery	27 (42)	43 (57)	0.04
Intraoperative event	5 (9)	20 (27)	0.01
Readmission to hospital	22 (34)	31 (41)	0.47
Reoperation	10 (15)	20 (27)	0.08
Readmission to hospital owing to prosthetic joint infection	10 (15)	17 (23)	0.33
Reoperation owing to prosthetic joint infection	6 (9)	9 (12)	0.55
Possible prosthetic joint infection at 15-18 months	9 (14)	8 (11)	0.62
Prescribed antibiotics at 15-18 months	4 (6)	4 (5)	—

Blom et al, BMJ 2022

4 punti critici

Dispositivo:	Microrganismo:	Strategia:	Antibiotico
Ginocchio	MRSA (Gram negativi?)	DAIR	Biofilm (MDR)

Personal view


Long-acting antibiotics
Reduce Hospital Admission
Improves Patient Convenience and Satisfaction
Prevent Hospital Readmission
Improves Patient Adherence
Decreases Length of Hospital Stay
Lowers Overall Cost of Care
Facilitates ABSSSI Treatment in In-Patient and Ambulatory Settings

Long-acting for MRSA

- Dalbavancin
- Oritavancin

Dalbavancin off-label use

Table 6 Cumulative Efficacy Reported with the Use of Dalbavancin for off-Label Therapeutic Indications

Off-Label Therapeutic Indications	Clinical Success	Relapse	Resistance Development
Endocarditis	120/148 (81.1%)	7/114(6.1%)	3/114(2.6%)
Bloodstream infections	117/144(81.3%)	7/140(5.0%)	1/140(0.7%)
Bone and joint infections	408/483(84.5%)	31/387(8.0%)	0/387(0.0%)
Others	23/25(92.0%)	2/25(8.0%)	0/25(0.0%)
Deep sternal wound infections	15/16(93.8%)	1/16(6.2%)	0/16(0.0%)
Intrabdominal infection	3/3(100.0%)	0/3(0.0%)	0/3(0.0%)
Mediastinitis	1/2(50.0%)	1/2(50.0%)	0/2(0.0%)
Pneumonia	2/2(100.0%)	0/2(0.0%)	0/2(0.0%)
Sinusitis	1/1(100.0%)	0/1(0.0%)	0/1(0.0%)
Pyelonephritis	1/1(100.0%)	0/1(0.0%)	0/1(0.0%)

Gatti et al, Drug Design, Development and Therapy 2021

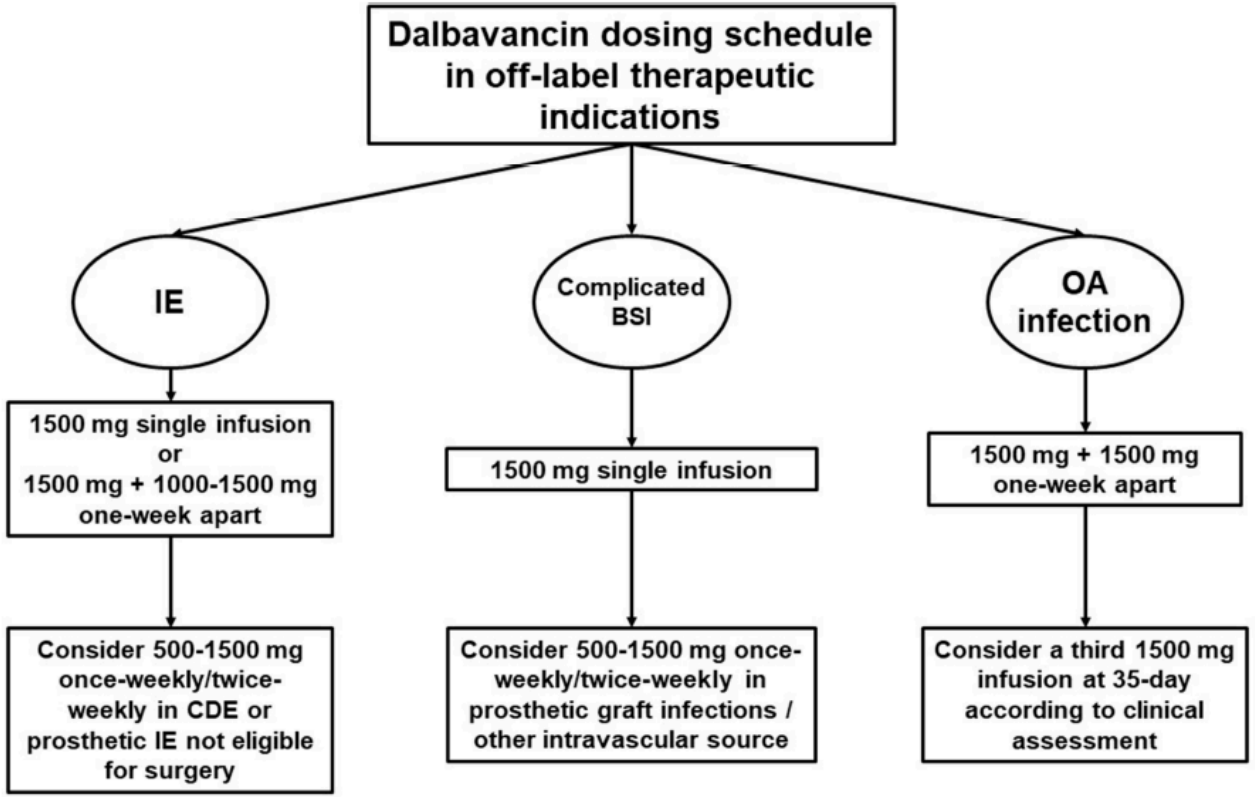
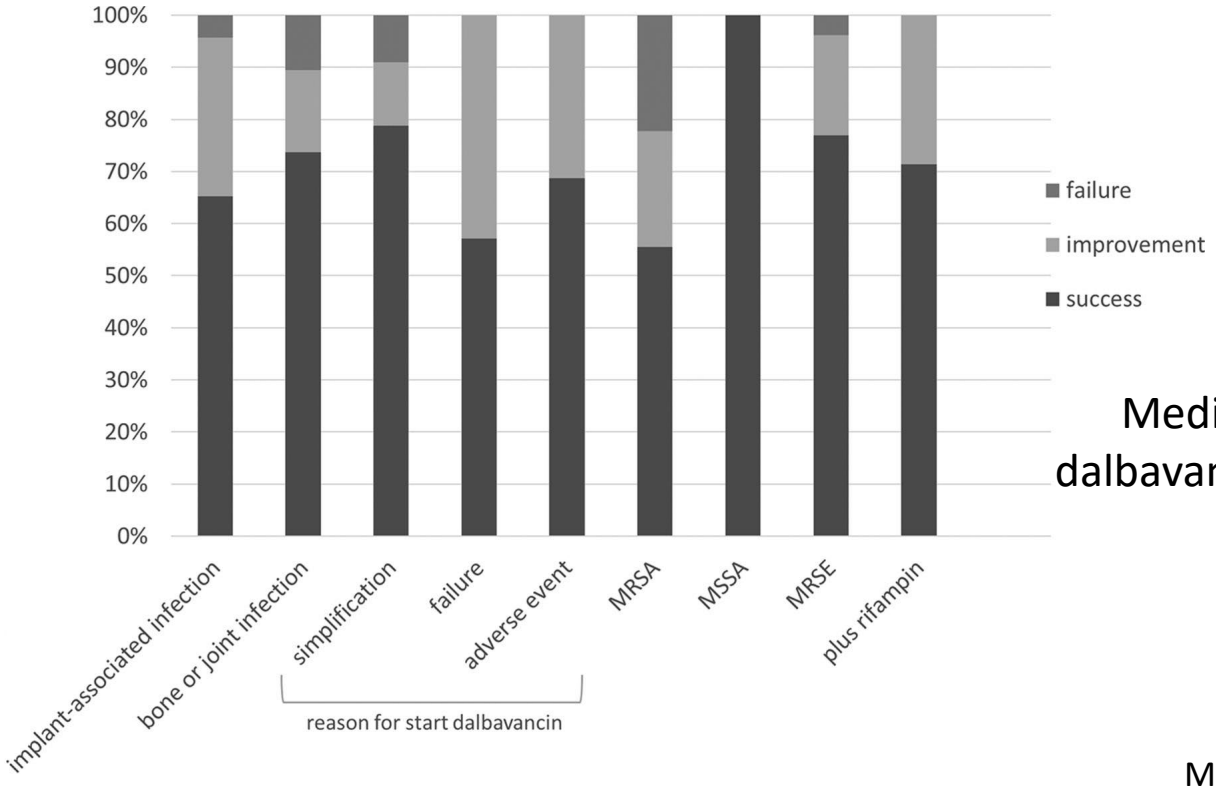


Figure 1 A proposal of algorithm for dalbavancin dosing schedule in off-label therapeutic indications.
Abbreviations: BSI, bloodstream infection; CDE, cardiac device-associated endocarditis; IE, infective endocarditis; OA, osteoarticular infection.

Gatti et al, Drug Design, Development and Therapy 2021

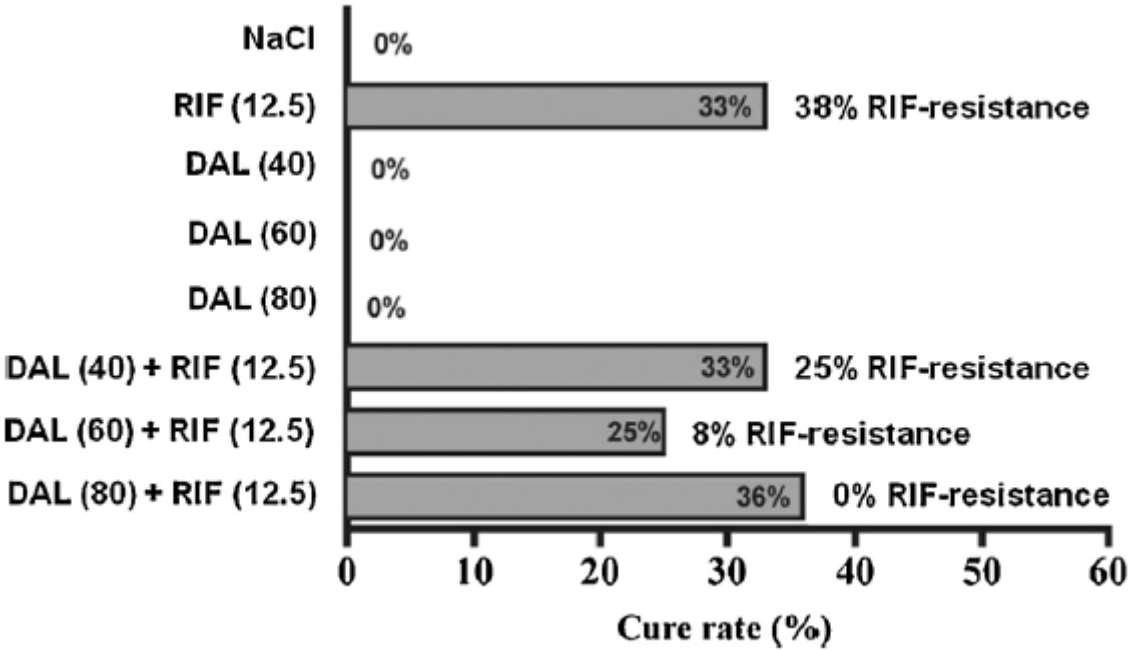
Dalbavancin for PJIs



Median (IQR) no. of dalbavancin doses: 5 (3–8)

Morata et al, AAC 2019

Activity of dalbavancin, alone and in combination with rifampicin, against meticillin-resistant *Staphylococcus aureus* in a foreign-body infection model



International Journal of Antimicrobial Agents 42 (2013) 220–225

Evaluation of Oritavancin Combinations with Rifampin, Gentamicin, or Linezolid against Prosthetic Joint Infection-Associated Methicillin-Resistant *Staphylococcus aureus* Biofilms by Time-Kill Assays

TABLE 1 MIC and MBBC values for 10 MRSA isolates

Isolate	MIC (μg/ml) of[a]:				MBBC (μg/ml) of[a]:			
	ORI	RIF	GEN	LZD	ORI	RIF	GEN	LZD
IDRL-6169	0.03	0.004	0.25	2	4	4	1	>128
IDRL-7126	0.03	0.008	0.25	4	4	16	0.5	>128
IDRL-7680	0.06	0.008	0.25	2	16	4	2	>128
IDRL-8302	0.06	0.008	0.25	2	4	16	0.5	>128
IDRL-8454	0.015	0.008	0.25	2	8	4	2	>128
IDRL-8459	0.12	0.008	0.25	2	16	8	16	>128
IDRL-8508	0.06	0.004	0.25	2	4	0.03	0.25	>128
IDRL-9121	0.015	0.008	0.12	4	8	16	2	>128
IDRL-9337	0.12	0.008	1	4	4	8	2	>128
IDRL-11468	0.015	0.008	0.25	4	4	8	4	>128

[a]ORI, oritavancin; RIF, rifampin; GEN, gentamicin; LZD, linezolid.

Yan et al, AAC 2018

Chronic suppressive therapy

Suppressive therapy is warranted only for individuals with retained hardware and/or necrotic bone not amenable to complete debridement.

The optimal duration of oral suppressive antibiotic therapy is uncertain.

Requisiti della terapia soppressiva cronica

1. Attività nei confronti del patogeno
2. Attività nel biofilm e sul patogeno in fase «sessile»
3. Efficacia di schedule di somministrazione facilmente praticabili
4. Controllo del rispetto della schedula di somministrazione
5. Minima interazione con altri farmaci
6. Minima tossicità associata
7. Concentrazioni adeguata nel focolaio di infezione
8. Adeguatezza posologica

Predictors of Success With Chronic Antibiotic Suppression for Prosthetic Joint Infections

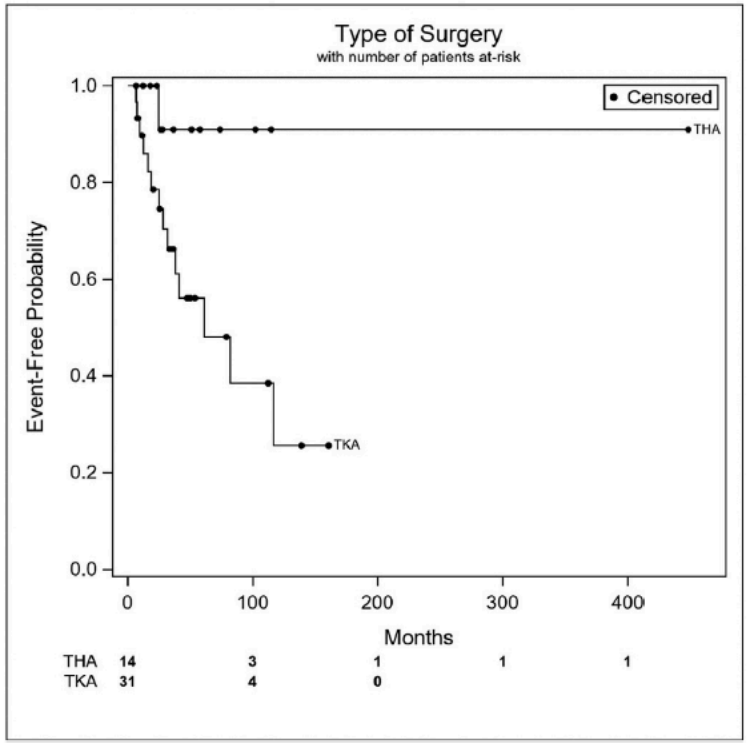


Fig. 1. Cumulative event-free estimates for surgery type. THA, total hip arthroplasty; TKA, total knee arthroplasty.

Burr et al, Journal of Arthroplasty 2022

Predictors of Success With Chronic Antibiotic Suppression for Prosthetic Joint Infections

Table 3
Risk of Reoperation.

Variable	Unadjusted		Adjusted	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
Age (per 5-y increase)	1.04 (0.83-1.30)	.72		
Gender: male vs female	0.92 (0.32-2.58)	.87		
Race: non-White vs White	0.61 (0.13-2.78)	.52		
BMI (per 5 kg/m^2 increase)	1.19 (0.93-1.53)	.16	1.15 (0.88-1.50)	.31
Prior surgeries (per 1 count increase)	1.03 (0.74-1.42)	.88		
Spacer type		.74[a]		
Articulating vs static	1.39 (0.34-5.71)	.58		
Articulating vs none	1.63 (0.31-8.74)	.48		
Static vs none	1.18 (0.20-6.78)	.82		
Surgery type: THA vs TKA	0.14 (0.01-0.72)	.01	0.18 (0.01-0.96)	.04
Infection-free duration (per year increase)	0.99 (0.88-1.12)	.90		
CCI (per 1-point increase)	1.07 (0.84-1.36)	.58		
Ambulatory status (per 1-stage increase)	1.05 (0.56-2.00)	.87		
Infection type				
Staphylococcus (yes vs no)	0.37 (0.10-1.37)	.21		
MRSA (yes vs no)	1.20 (0.28-5.17)	.99		
Gram status (positive vs negative)	0.21 (0.04-1.21)	.10	0.22 (0.05-0.88)	.03

Burr et al, Journal of Arthroplasty 2022

Conclusioni

- Le protesi ortopediche sono oggi presidi irrinunciabili
- Le infezioni protesiche rappresentano una problematica destinata a crescere
- Necessità di diagnostica precoce
- Trattamento con farmaci battericidi e attivi sul biofilm
- Epidemiologia locale delle infezioni