Jornada
PROA
hospitalari
a Catalunya

14 març de 2024 de 9 a 17 h

Recinte Modernista de Sant Pau
Hospital de la Santa Creu i Sant Pau
C/ Sant Antoni Maria Claret, 167
Barcelona

Discussió de l'evidència científica per a síndromes - què sabem i què podem fer?

PROA en bacterièmia

Oriol Gasch Blasi

Servei de malalties infeccioses

Hospital Parc Taulí

I3PT Institut d'Investigació i Innovació Parc Taulí
UAB Universitat Autònoma de Barcelona
Parc Taulí Consorci Corporació Sanitària

Què sabem i què podem fer?

Open Forum Infectious Diseases

PERSPECTIVES

Can the Future of ID Escape the Inertial Dogma of Its Past? The Exemplars of Shorter Is Better and Oral Is the New IV

Kusha Davar,[1] Devin Clark,[1] Robert M. Centor,[2] Fernando Dominguez,[1] Bassam Ghanem,[3] Rachael Lee,[4] Todd C. Lee,[5] Emily G. McDonald,[6] Matthew C. Phillips,[7,8] Parham Sendi,[9] and Brad Spellberg[1]

[1]Los Angeles County + University of Southern California (LAC+USC) Medical Center, Los Angeles, California, USA, [2]Department of Medicine, Birmingham Veterans Affairs (VA) Medical Center, Birmingham, Alabama, Birmingham, Alabama, USA, [3]King Abdulaziz Medical City, Jeddah, Saudi Arabia, [4]Department of Medicine, Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, Alabama, USA, [5]Division of Infectious Diseases, Department of Medicine, McGill University, Montreal, Canada, [6]Division of General Internal Medicine, Department of Medicine, McGill University, Montreal, Quebec, Canada, [7]Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA, [8]Harvard Medical School, Boston, Massachusetts, USA, and [9]Institute for Infectious Diseases, University of Bern, Bern, Switzerland

…it is time for the field of infectious diseases to adopt evidenced-based over eminence-based medicine.

- Fallacy of static versus cidal antibiotics
- Double coverage in the treatment of *Pseudomonas* and/or sepsis
- Continuation of antibiotics for neutropenic fever until resolution of neutropenia
- Use of aminoglycoside or rifampin for staphylococcal endocarditis
- Inability to shorten antimicrobial therapy in patients with immune dysfunction
- Advantage of antistaphylococcal penicillin over cefazolin for *S aureus* bacteremia
- Anaerobic coverage for aspiration pneumonia

Què sabem?

- Tractament empíric
- Ajust segons antibiograma
- Pas a via oral
- Durada

Què sabem?

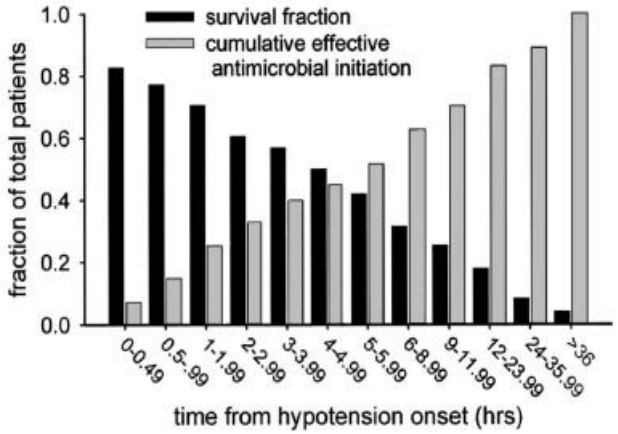
Tractament empíric

Ajust segons antibiograma

Pas a via oral

Durada

septic shock



Kumar A et al. Crit Care Med 2006 Vol. 34, No. 6

Clinical Infectious Diseases

VIEWPOINTS

IDSA Infectious Diseases Society of America · hivma hiv medicine association

Infectious Diseases Society of America (IDSA) POSITION STATEMENT: Why IDSA Did Not Endorse the Surviving Sepsis Campaign Guidelines

IDSA Sepsis Task Force*

2018

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Check for updates

Time to antibiotics

Recommendations

12. For adults with possible septic shock or a high likelihood for sepsis, we **recommend** administering antimicrobials immediately, ideally within 1 h of recognition

Strong recommendation, low quality of evidence (Septic shock)

Strong recommendation, very low quality of evidence (Sepsis without shock)

13. For adults with possible sepsis without shock, we **recommend** rapid assessment of the likelihood of infectious versus non-infectious causes of acute illness

Best Practice Statement

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association

Infectious Diseases Society of America Position Paper: Recommended Revisions to the National Severe Sepsis and Septic Shock Early Management Bundle (SEP-1) Sepsis Quality Measure

Chanu Rhee,[1,2] Kathleen Chiotos,[3,4] Sara E. Cosgrove,[4,5] Emily L. Heil,[5,6] Sameer S. Kadri,[8,9] Andre C. Kalil,[7,9] David N. Gilbert,[4] Henry Masur,[4] Edward J. Septimus,[13] Daniel A. Sweeney,[10] Jeffrey R. Strich,[4] Dean L. Winslow,[11] Michael Klompas,[1,2], for the Infectious Diseases Society of America Sepsis Task Force[#]

2021

Què sabem?

- **Tractament empíric**
- Ajust segons antibiograma
- Pas a via oral
- Durada

Clinical Microbiology and Infection 27 (2021) 175–181

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

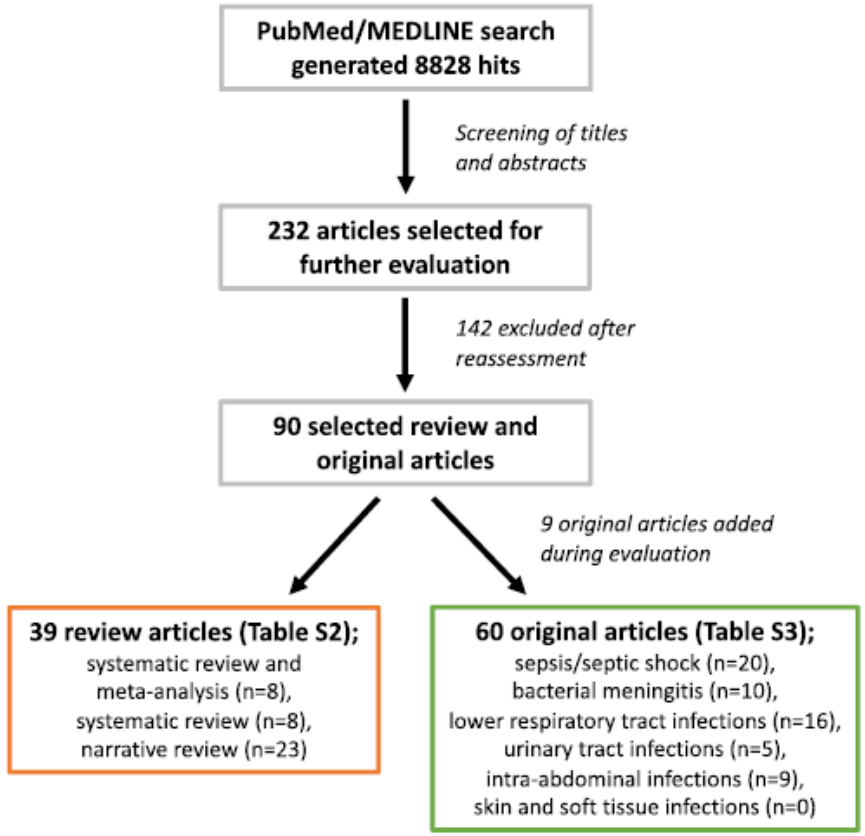
Narrative Review

Impact of time to antibiotic therapy on clinical outcome in patients with bacterial infections in the emergency department: implications for antimicrobial stewardship

P. Nauclér [1], A. Huttner [2], C.H. van Werkhoven [3], M. Singer [4], P. Tattevin [5], S. Einav [6], T. Tängdén [7,*]

Objectives: To explore the existing evidence on the impact of time to antibiotics on clinical outcomes in patients presenting to the emergency department with bacterial infections of different severity of illness and source of infection.

P. Naucler, Clin Microbiol Infect 2021;27:175



Sèpsia (0 RCT i 20 observacionals)

- Increment en la mortalitat en els pacients amb xoc sèptic

LIMITACIONS:

- Diferents definicions de '*time 0*' (arribada a urg, triatge, dx de xoc, inici de mesures de tractament)
- No hi ha un *cut-off* per identificar el benefici en mortalitat
- Qualitat d'evidència baixa

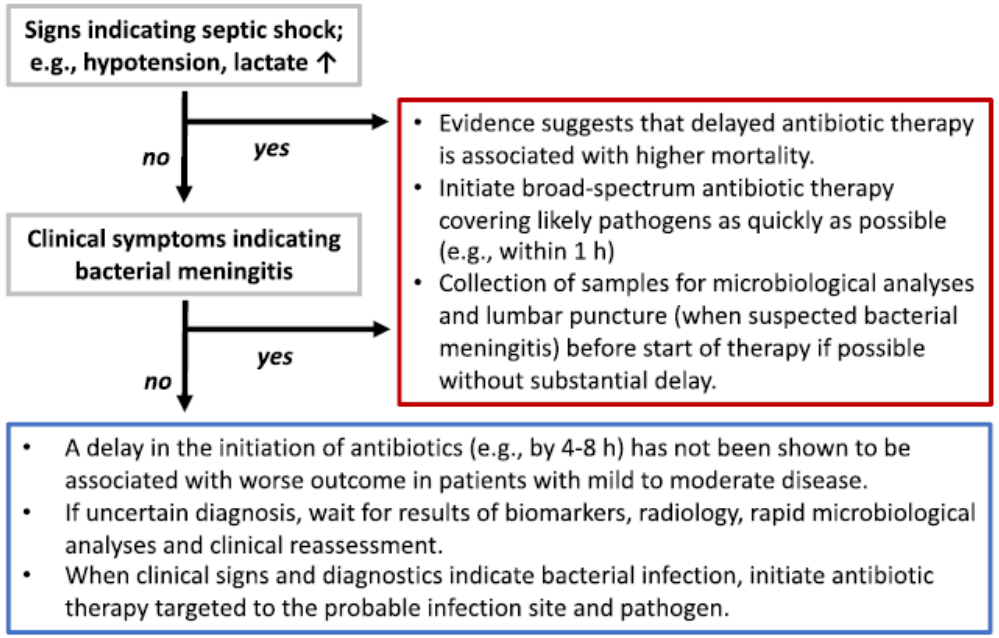


Fig. 2. Suggested approach to early or delayed antibiotic therapy for patients presenting to the emergency department with suspected bacterial infections

Què sabem?

- Tractament empíric
- Ajust segons antibiograma
- Pas a via oral
- Durada

Inappropriate empirical antibiotic therapy for bloodstream infections based on discordant in-vitro susceptibilities: a retrospective cohort analysis of prevalence, predictors, and mortality risk in US hospitals

Sameer S Kadri, Yi Ling Lai, Sarah Warner, Jeffrey R Strich, Ahmed Babiker, Emily E Ricotta, Cumhur Y Demirkale, John P Dekker, Tara N Palmore, Chanu Rhee, Michael Klompas, David C Hooper, John H Powers 3rd, Arjun Srinivasan, Robert L Danner, Jennifer Adjemian, forming the National Insititutes of Health Antimicrobial Resistance Outcomes Research Initiative (NIH-ARORI)

Critical Care Medicine Department (S S Kadri MD, S Warner MPH, J R Strich MD, C Y Demirkale PhD, R L Danner MD) **and Hospital Epidemiology Service** (T N Palmore MD), **National Institutes of Health Clinical Center, Bethesda, MD, USA; Department of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA** (S S Kadri); **Epidemiology Unit, Division of Intramural Research** (Y L Lai MPH, E R Ricotta PhD, J Adjemian PhD) **and Laboratory of Clinical Immunology and Microbiology** (J P Dekker MD), **National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA; United States Public Health Service, Commissioned Corps, Rockville, MD, USA** (J R Strich, J Adjemian); **Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, GA, USA** (A Babiker MBBS); **Brigham and Women's Hospitals, Boston, MA, USA** (C Rhee MD, Prof M Klompas MD); **Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA** (C Rhee,

Methods:

- Retrospective cohort analysis of electronic health record
- Patients with suspected—and subsequently confirmed—bloodstream infections who were treated empirically with systemic antibiotics

- Prevalence of discordant empirical antibiotic (not susceptible in vitro)
- Predictors of receiving discordant empirical antibiotic therapy

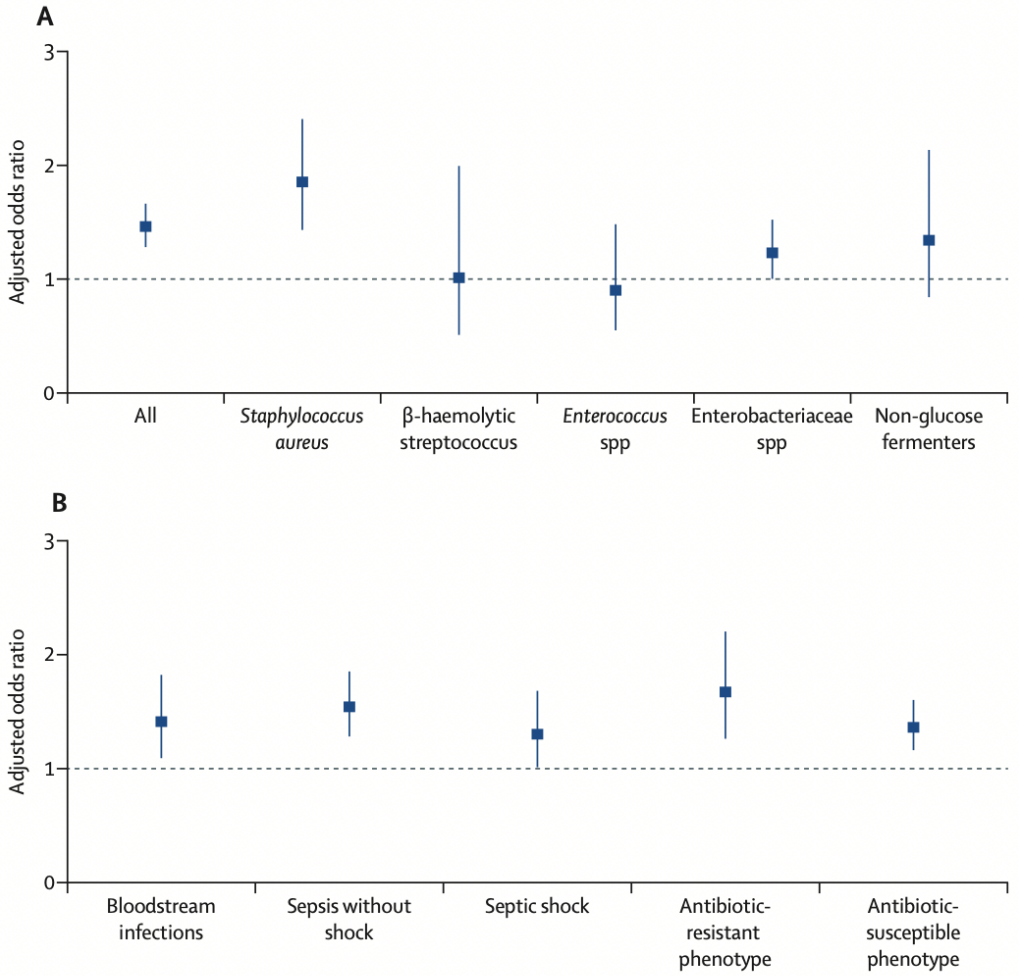
Lancet Infect Dis 2021; 21: 241–51

Tractament empíric

Ajust segons antibiograma

Pas a via oral

Durada



21 608 patients

19% discordant → aOR 1·46 [95% CI, 1·28–1·66] (death)

Unaffected by the presence or absence of sepsis or septic shock.

Lancet Infect Dis 2021; 21: 241–51

Què sabem?

Tractament empíric

Ajust segons antibiograma

Pas a via oral

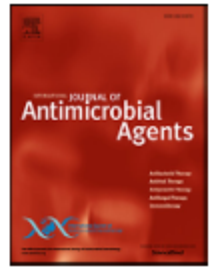
Durada

International Journal of Antimicrobial Agents 59 (2022) 106512

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag



Beta-lactam monotherapy or combination therapy for bloodstream infections or pneumonia due to *Pseudomonas aeruginosa*: a meta-analysis

Lorenzo Onorato[a], Margherita Macera[a], Federica Calò[a], Paolo Cirillo[b], Giovanni Di Caprio[b], Nicola Coppola[a,*]

[a] *Department of Mental Health and Public Medicine, Section of Infectious Diseases, University of Campania, Naples, Italy*
[b] *Infectious Diseases Unit, AORN Sant' Anna e San Sebastiano, Caserta, Italy*

→ 6 RCT, 6 prospectius de cohorts, 22 retrospectius

Int J Antimicrob Agents. 2022 Mar;59(3):106512

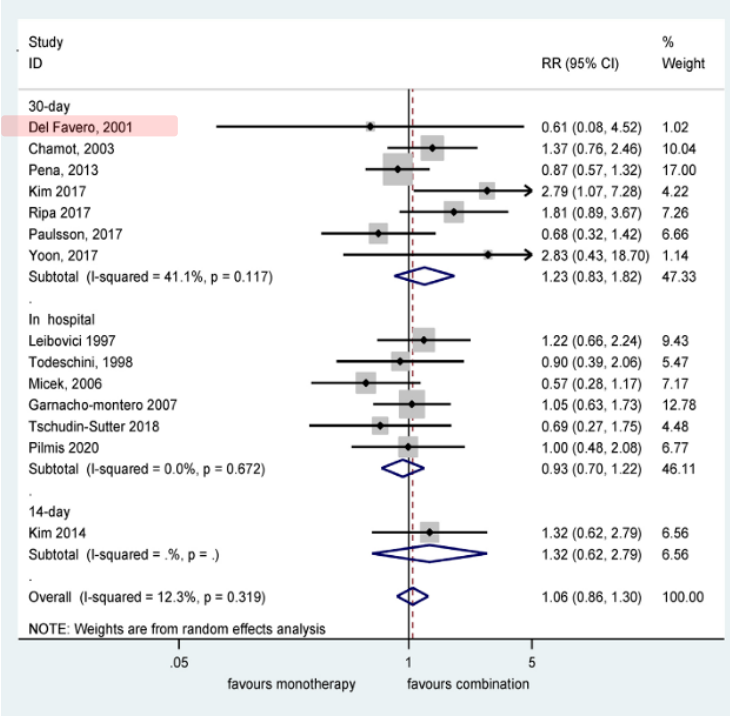


Figure 2. Forest plot of RRs of mortality in patients treated with empirical combination or monotherapy

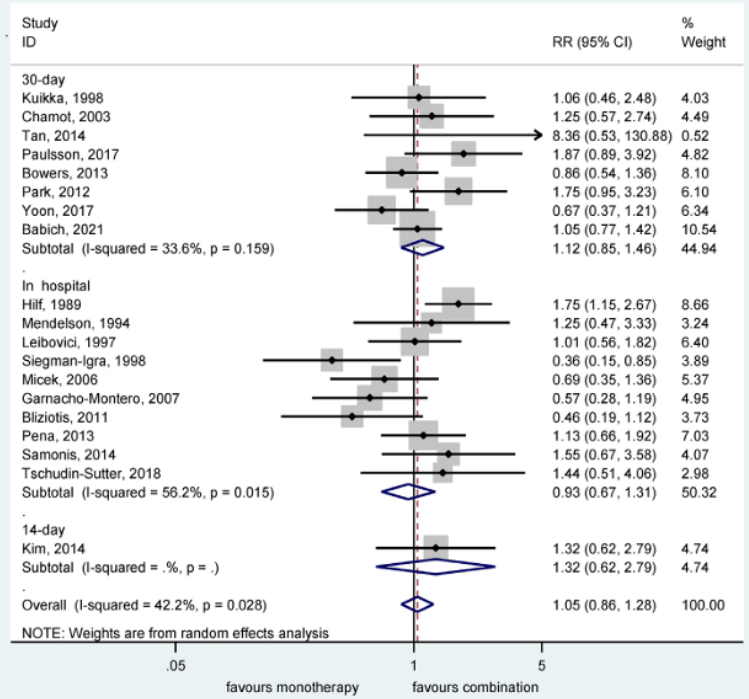
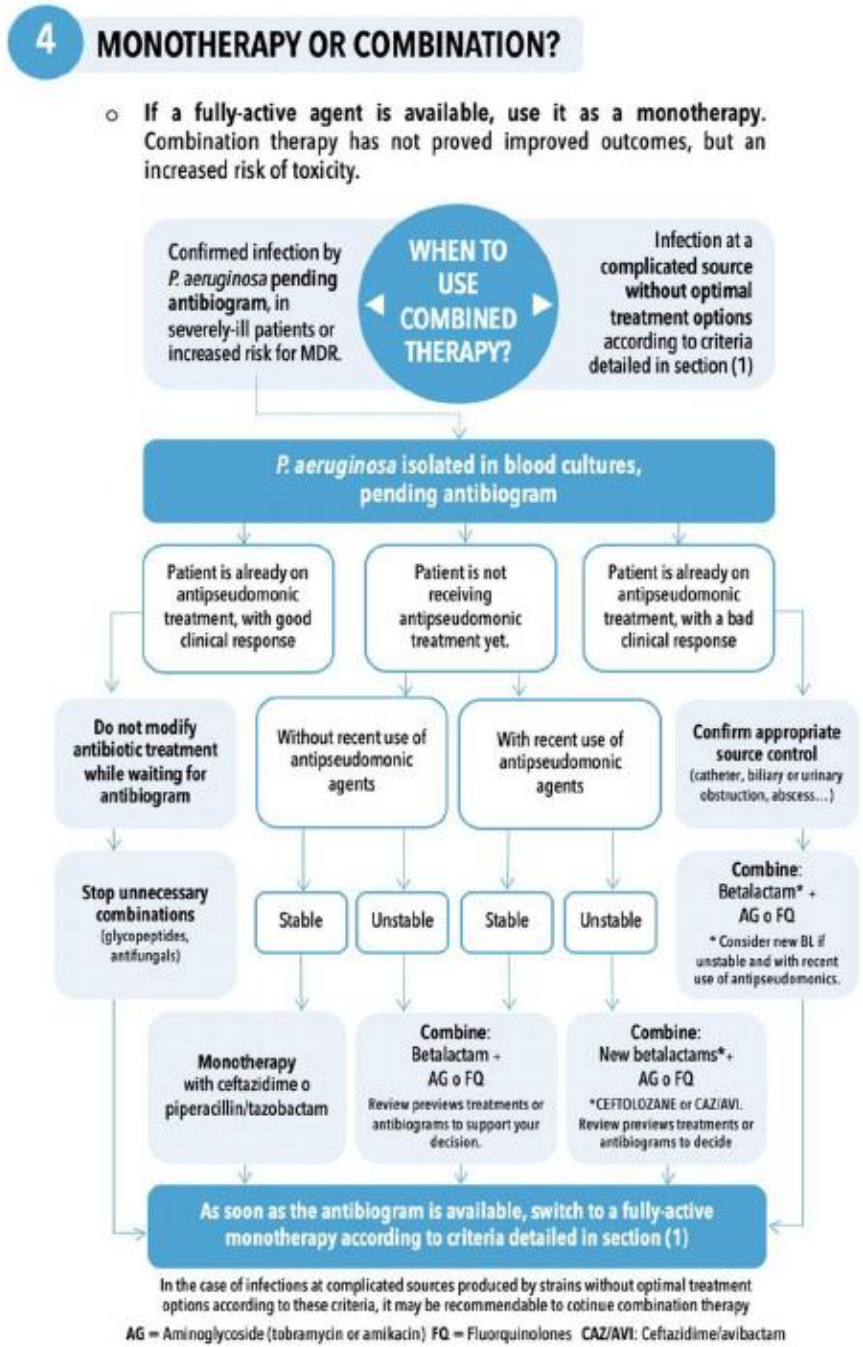


Figure 3. Forest plot of RRs of mortality in patients treated with definitive combination or monotherapy



SHORTEN-2 trial. PLoSONE 17(12): e0277333

Què sabem?

Clinical Infectious Diseases

STATE-OF-THE-ART REVIEW

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

Contemporary Management of *Staphylococcus aureus* Bacteremia—Controversies in Clinical Practice

Daniel J. Minter,[1,] Ayesha Appa,[1,2,] Henry F. Chambers,[1,2] and Sarah B. Doernberg[1]

[1]Division of Infectious Diseases, Department of Medicine, University of California, San Francisco, San Francisco, California, USA; and [2]Division of HIV, Infectious Diseases, and Global Medicine at Zuckerberg San Francisco General Hospital, Department of Medicine, University of California, San Francisco, San Francisco, California, USA

JAMA | Original Investigation

Effect of Vancomycin or Daptomycin With vs Without an Antistaphylococcal β-Lactam on Mortality, Bacteremia, Relapse, or Treatment Failure in Patients With MRSA Bacteremia

A Randomized Clinical Trial

Steven Y. C. Tong, MBBS, PhD; David C. Lye, MBBS; Dafna Yahav, MD; Archana Sud, MD; J. Owen Robinson, MD; Jane Nelson, BN; Sophia Archuleta, MD; Matthew A. Roberts, PhD; Alan Cass, MBBS, PhD; David L. Paterson, MBBS, PhD; Hong Foo, MBBS; Mical Paul, MD; Stephen D. Guy, MBBS; Adrian R. Tramontana, MBBS; Genevieve B. Walls, MBChB; Stephen McBride, MBChB; Narin Bak, MBBS, MPH; Niladri Ghosh, MBBS; Benjamin A. Rogers, MBBS, PhD; Anna P. Ralph, MBBS, PhD; Jane Davies, MBBS, PhD; Patricia E. Ferguson, MBBS, PhD; Ravindra Dotel, MBBS; Genevieve L. McKew, MBBS; Timothy J. Gray, MBBS(Hons); Natasha E. Holmes, MBBS(Hons), PhD; Simon Smith, MBChB; Morgyn S. Warner, MD, PhD; Shirin Kalimuddin, MBBS, MPH; Barnaby E. Young, MBBS; Naomi Runnegar, MBBS; David N. Andresen, MBBS; Nicholas A. Anagnostou, MBBS; Sandra A. Johnson, BSc, MPH; Mark D. Chatfield, MSc; Allen C. Cheng, MBBS, PhD; Vance G. Fowler Jr, MD, MHS; Benjamin P. Howden, MBBS, PhD; Niamh Meagher, MBiostat; David J. Price, PhD; Sebastiaan J. van Hal, MBChB, PhD; Matthew V. N. O'Sullivan, MBBS, PhD; Joshua S. Davis, MBBS, PhD; for the Australasian Society for Infectious Diseases Clinical Research Network

Combination therapy	Standard therapy
VAN/DAP + 7 days of Beta-lactam	VAN/DAP

Table 3. Primary and Secondary Outcomes

Outcomes	No./Total No. (%) Combination Therapy	Standard Therapy	Risk Difference, % (95% CI)	*P* Value
Primary Outcome[a,b]				
Primary analysis population	59/170 (35)	68/175 (39)	−4.2 (−14.3 to 6.0)	.42
Per protocol	47/144 (33)	68/175 (39)	−6.2 (−16.7 to 4.3)	.25
Secondary Outcomes[c]				
All-cause mortality[d]				
Day 14	13/170 (8)	13/174 (7)	0.2 (−5.4 to 5.8)	.95
Day 42	25/170 (15)	19/174 (11)	3.8 (−3.3 to 10.8)	.29
Day 90	35/170 (21)	28/174 (16)	4.5 (−3.7 to 12.7)	.28
Persistent bacteremia[e]				
Day 2	50/167 (30)	61/173 (35)	−5.3 (−15.3 to 4.6)	.29
Day 5	19/166 (11)	35/172 (20)	−8.9 (−16.6 to −1.2)	.02
Microbiological relapse[a]	14/169 (8)	18/175 (10)	−2.0 (−8.1 to 4.1)	.52
Microbiological treatment failure[a]	16/170 (9)	17/175 (10)	−0.3 (−6.5 to 5.9)	.92
Acute kidney injury[f]	34/145 (23)	9/145 (6)	17.2 (9.3 to 25.2)	<.001
Duration of intravenous antibiotics, mean (SD), d	29.3 (19.5)	28.1 (17.4)		.72

Què sabem?

Characteristics	Combination Therapy (n = 174)	Standard Therapy (n = 178)
Final diagnosis of infective endocarditis, No. (%)[a]	26 (15)	16 (9)
Received vancomycin, No. (%)[b]	171 (98)	178 (100)
Received daptomycin, No. (%)[b]	7 (4)	6 (3)
Trough vancomycin level, mean (SD), µg/mL		
Day 1	15.1 (8.1)	14.7 (7.3)
Day 2	17.9 (9.1)	17.2 (8.0)
Day 3	20.1 (7.6)	19.2 (7.5)

Within the combination therapy group, 111 patients received flucloxacillin or cloxacillin and 27 received only cefazolin.

Early trial termination for safety concerns

Tong SYC, CAMERA2,JAMA 2020

Què sabem?

Daptomycin Plus Fosfomycin Versus Daptomycin Alone for Methicillin-resistant *Staphylococcus aureus* Bacteremia and Endocarditis: A Randomized Clinical Trial

Arm 1: daptomycin, 10mg/kg IV daily plus fosfomycin, 2g IV/6h (combination-therapy)
Arm 2: daptomycin 10mg/kg/24h IV (monotherapy)

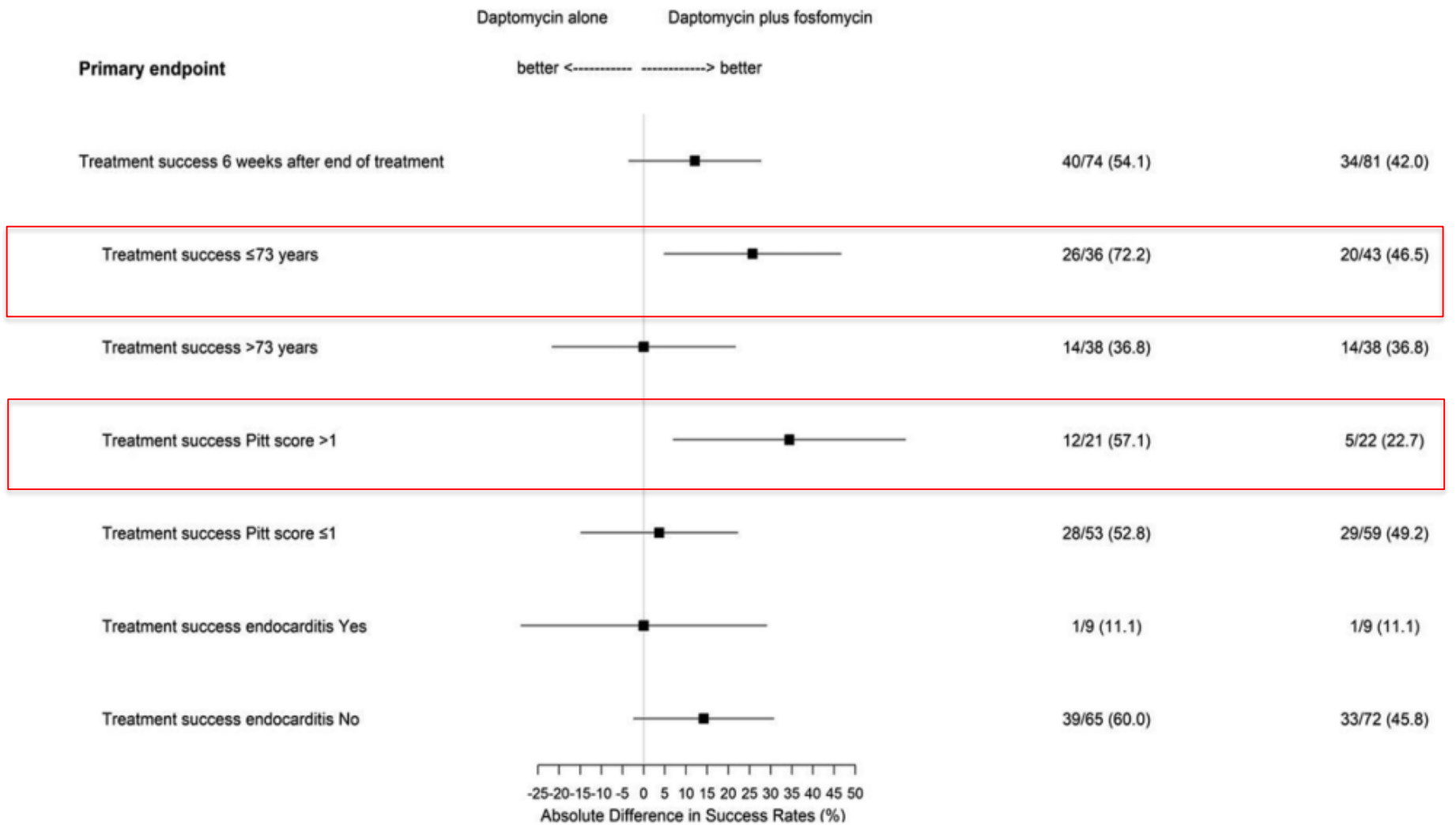
Table 3. Reasons for Treatment Failure at Test of Cure

Reason for Treatment Failure	Daptomycin Plus Fosfomycin, No. (%) of Patients (n = 74)	Daptomycin Alone, No. (%) of Patients (n = 81)	Proportion Difference (95% CI)	*P* Value[a]
Treatment failure[b]	34 (45.9)	47 (58.0)	−12.1 (−27.7 to 3.6)	.133
Mortality at TOC	18 (24.3)	22 (27.1)	−2.8 (−16.6 to 10.9)	.687
Clinical failure[c]	0 (0.0)	3 (3.7)	−3.7 (−7.8 to .4)	.247[d]
Microbiological failure	0 (0.0)	9 (11.1)	−11.1 (−18.0 to −4.3)	.003[d]
Any AE leading to treatment discontinuation	13 (17.6)	4 (4.9)	12.6 (2.8–22.5)	.012
Additional antimicrobial therapy administered before TOC[e]	9 (12.1)	19 (23.4)	−11.3 (−23.2 to .6)	.068
Lack of blood cultures at TOC	8 (10.8)	4 (4.9)	5.9 (−2.6 to 14.4)	.172
Loss to follow-up	1 (1.3)	3 (3.7)	−2.4 (−7.2 to 2.5)	.622[d]

Microbiological failure: persistent bacteremia, recurrent bacteremia, emergence of resistance to study drugs during treatment.

Pujol M. Clin Infect Dis. 2020

Primary endpoint	Daptomycin plus fosfomycin no./total no. (%)	Daptomycin alone no./total no. (%)
Treatment success 6 weeks after end of treatment	40/74 (54.1)	34/81 (42.0)
Treatment success ≤73 years	26/36 (72.2)	20/43 (46.5)
Treatment success >73 years	14/38 (36.8)	14/38 (36.8)
Treatment success Pitt score >1	12/21 (57.1)	5/22 (22.7)
Treatment success Pitt score ≤1	28/53 (52.8)	29/59 (49.2)
Treatment success endocarditis Yes	1/9 (11.1)	1/9 (11.1)
Treatment success endocarditis No	39/65 (60.0)	33/72 (45.8)



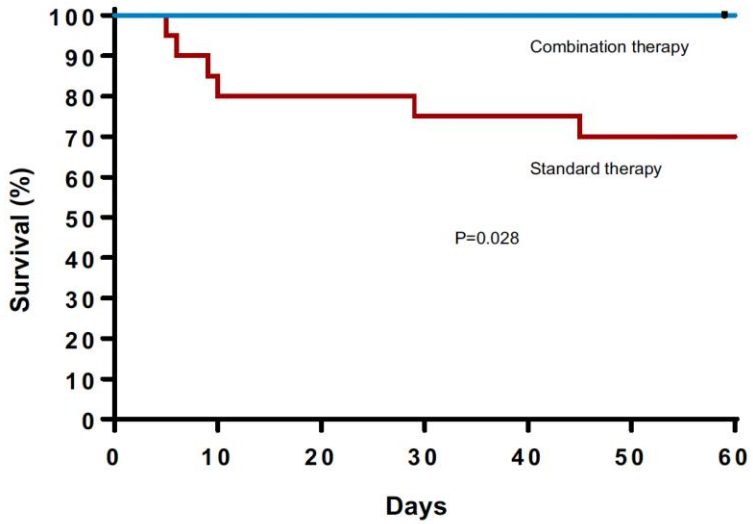
Què sabem?

Clinical Data on Daptomycin plus Ceftaroline versus Standard of Care Monotherapy in the Treatment of Methicillin-Resistant *Staphylococcus aureus* Bacteremia

Matthew Geriak,[a] Fadi Haddad,[b] Khulood Rizvi,[c] Warren Rose,[d] Ravina Kullar,[e] Kerry LaPlante,[f] Marie Yu,[b] Logan Vasina,[a] Krista Ouellette,[a] Marcus Zervos,[c] Victor Nizet,[f] George Sakoulas[a,g]

DAP + CPT (n=17)

VAN or DAP (n=23)



In-hospital mortality:

0% (0/17) for combination
26% (6/23) for monotherapy

Early trial termination for safety concerns

Geriak M, Antimicrob Agents Chemother. 2019

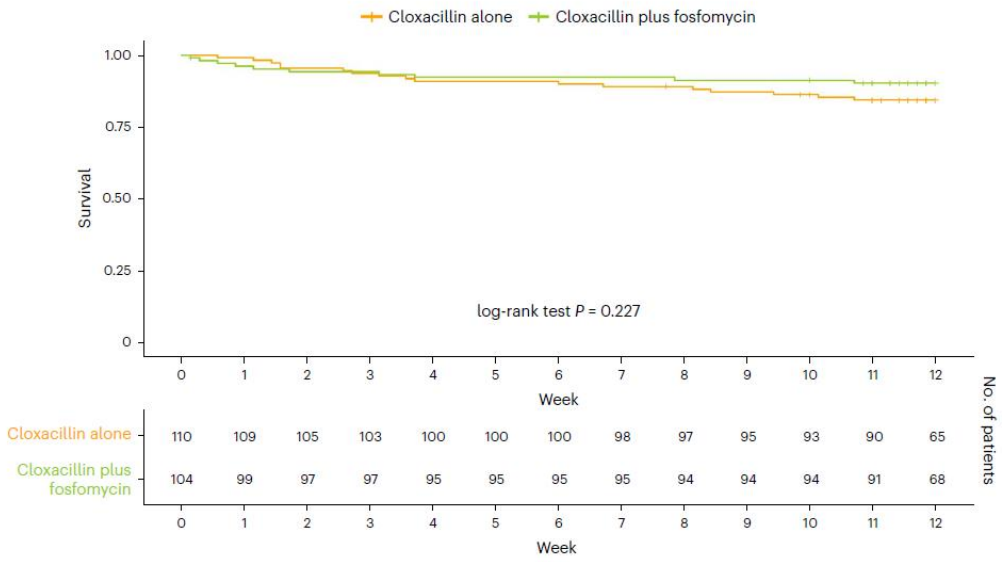
Què sabem?

nature medicine

Article

https://doi.org/10.1038/s41591-023-02569-0

Cloxacillin plus fosfomycin versus cloxacillin alone for methicillin-susceptible *Staphylococcus aureus* bacteremia: a randomized trial



Grillo S, Nature Medicine volume 29, pages2518–2525 (2023)

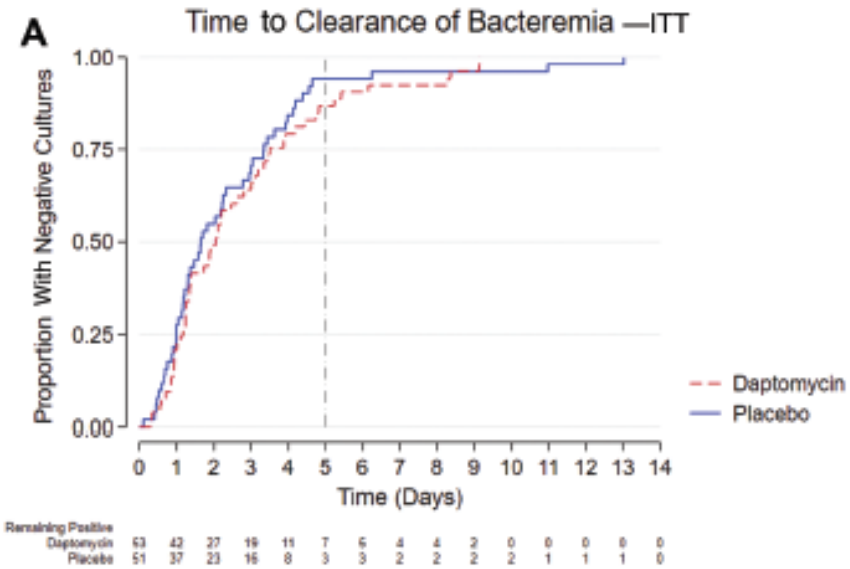
Clinical Infectious Diseases

MAJOR ARTICLE

Adjunctive Daptomycin in the Treatment of Methicillin-susceptible *Staphylococcus aureus* Bacteremia: A Randomized, Controlled Trial

Matthew P. Cheng,[1,a] Alexander Lawandi,[2,a] Guillaume Butler-Laporte,[2,a] Samuel De l'Étoile-Morel,[2] Katryn Paquette,[3] and Todd C. Lee[2,4,5]

[1]Division of Infectious Diseases, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA, [2]Division of Infectious Diseases, Department of Medicine, McGill University, Montreal, Quebec, Canada, [3]Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal, Quebec, Canada, [4]Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada, and [5]Clinical Practice Assessment Unit, Department of Medicine, McGill University, Montreal, Quebec, Canada



Clinical Infectious Diseases® 2021;72(9):e196–203

Què sabem?

Tractament empíric

Ajust segons antibiograma

Pas a via oral

Durada

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)
San Pedro	'02	51	Linezolid vs. ceph—*S. pneumo*	93% (27/29) v 68% (15/22)
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*	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=12 RCTs)		1063		82% (487/594) v 79% (369/469)

*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

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

Què sabem?

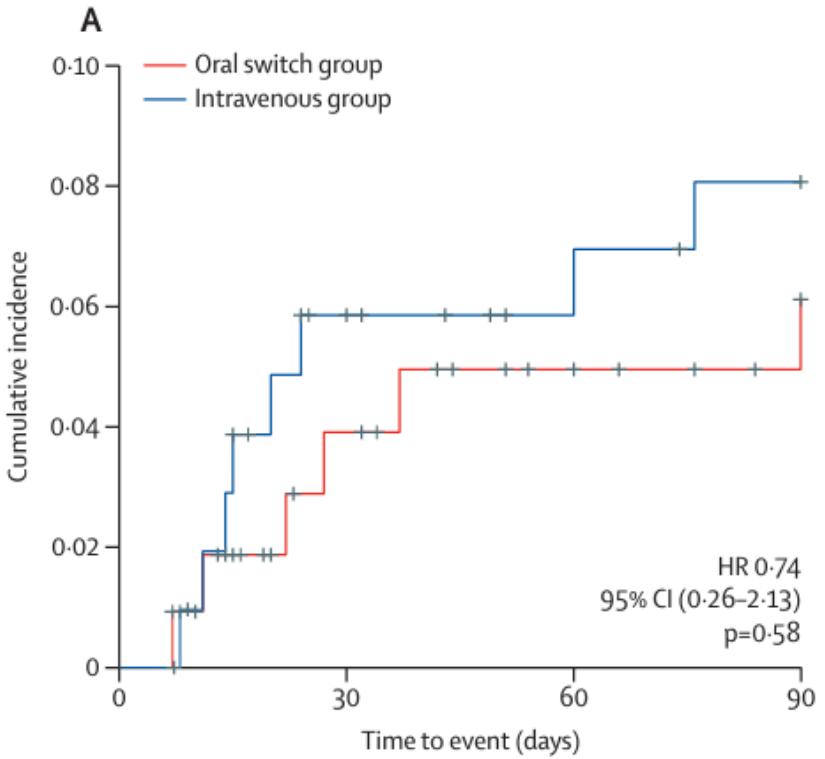
Kaasch AJ, Lopez-Cortez LE, Rodriguez-Bano J, et al. Efficacy and safety of an early oral switch in low-risk *Staphylococcus aureus* bloodstream infection (SABATO): an international, open-label, parallel-group, randomised, controlled, non-inferiority trial. Lancet Infect Dis 2024.

→ After 5–7 days of intravenous antimicrobial therapy. Oral vs intravenous standard therapy.

Exclusion criteria:

- Complicated *S aureus* BSI (52,4%)
- Deep-seated focus (47,5%)
- Septic shock (4d) (14,8%)
- Prolonged bacteraemia (>72 h) (20%)
- Tª>38°C (4,5%)
- Intravascular catheters not removed <4 days after the first HC. (5,9%)
- Recent history of *S aureus* BSI previous 3 months, (3%)
- injection drug use, (3,7%)
- severe immunodeficiency or immunosuppression, (15,5%)
- Prosthetic heart valve or deep-seated vascular graft. (26,4%)

** not meet eligibility criteria

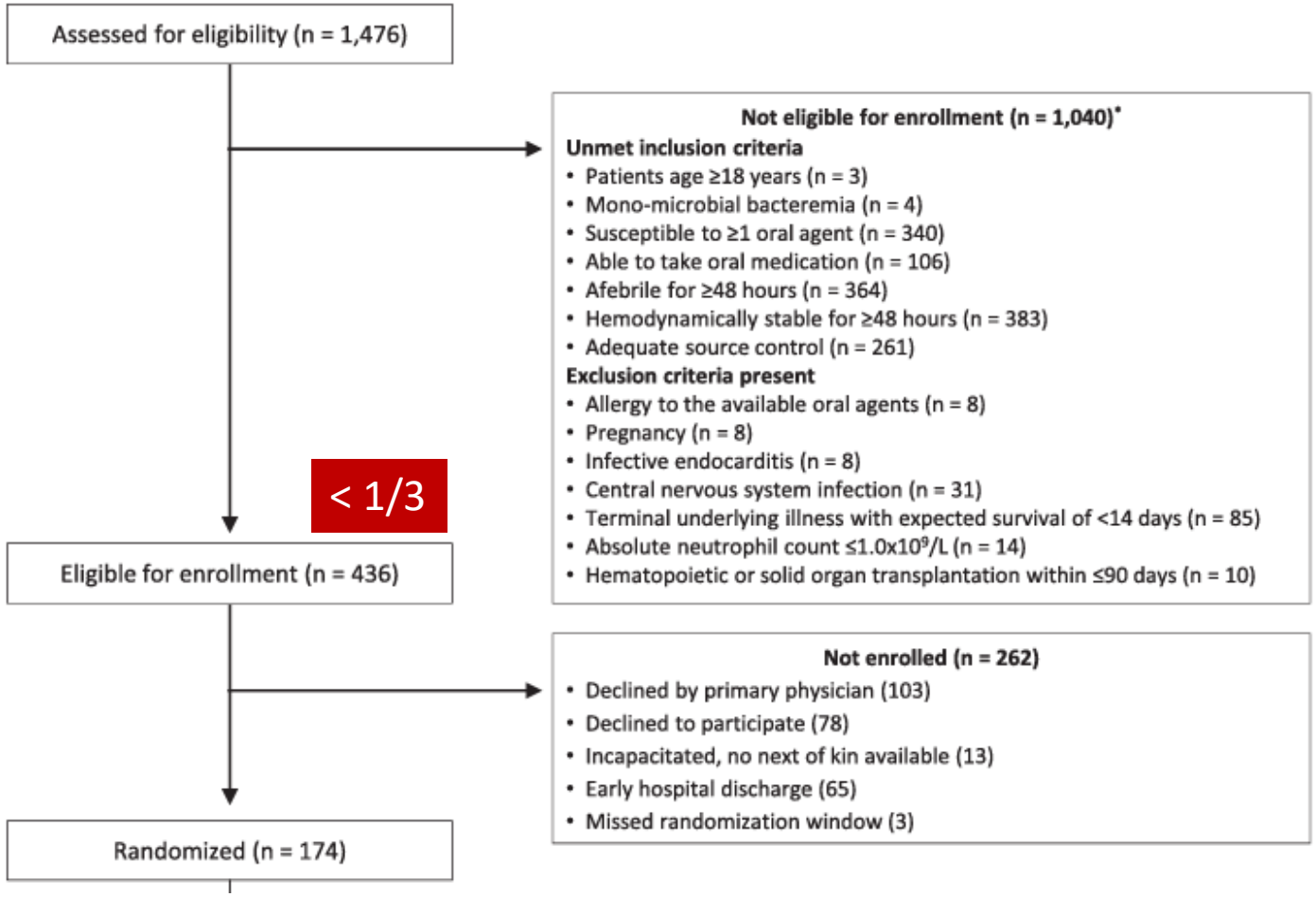


Oral switch antimicrobial therapy was non-inferior to intravenous standard therapy in participants with **low-risk** *S aureus* bloodstream infection. However, it is necessary to **carefully assess** patients for signs and symptoms of complicated *S aureus* bloodstream infection at the time of presentation and thereafter before considering early oral switch therapy.

Què sabem?

Omrani AS, Abujarir SH, Ben Abid F, et al. Switch to Oral Antibiotics in Gram-negative Bacteraemia; a Randomised, Open-label, Clinical Trial. Clin Microbiol Infect. 2023.

→ After 3–5 days of intravenous antimicrobial therapy. Oral vs intravenous standard therapy.



In patients with Enterobacterales bacteraemia, oral switch, after initial IV antimicrobial therapy, **clinical stability and source control**, is non-inferior to continuing IV therapy.

Què sabem?

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 31, 2019 VOL. 380 NO. 5

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., Emil L. Fosbøll, M.D., Ph.D., Flemming Rosenvinge, M.D., Henrik C. Schønheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc., Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc., Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

International Journal of Antimicrobial Agents 54 (2019) 143–148
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International Journal of Antimicrobial Agents
journal homepage: www.elsevier.com/locate/ijantimicag

High-dose trimethoprim-sulfamethoxazole and clindamycin for *Staphylococcus aureus* endocarditis

Hervé Tissot-Dupont[a], Frédérique Gouriet[a], Leopold Oliver[c], Matthieu Jamme[d], Jean-Paul Casalta[a], Marie-Thérèse Jimeno[e], Florent Arregle[b], Cécile Lavoute[b], Sandrine Hubert[b], Mary Philip[b], Hélène Martel[b], Alberto Riberi[f], Gilbert Habib[b], Didier Raoult[a,*]

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: $Tau^2 = 0.00$; $Chi^2 = 3.05$, df = 3 (P = 0.38); $I^2 = 2\%$
Test for overall effect: Z = 3.01 (P = 0.003)

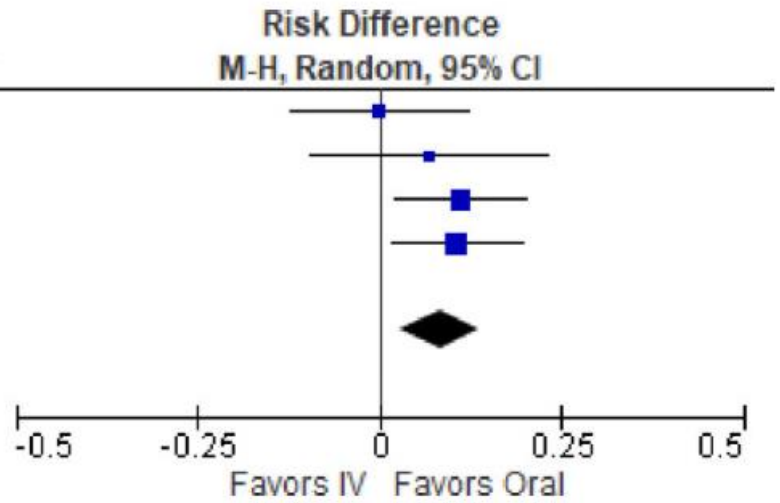


Figure 4. Meta-Analysis Forest Plot of Endocarditis Treatment Success.
Oral therapy was significantly more effective.

N Engl J Med. 2019 Jan 31;380(5):415-424
Int J Antimicrob Agents. 2019 Aug;54(2):143-148.
Am J Med. 2022 March ; 135(3): 369–379.e1.

Què sabem?

- Tractament empíric
- Ajust segons antibiograma
- Pas a via oral
- **Durada**

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 Excerbation	10-14	14-21	Equal	1
cUTI/Pyelonephritis	5 or 7	10 or 14	Equal	11**
Intra-abd Infection	4	8-10	Equal	3
Complex Appendicitis	1-2	5-6	Equal	2
GNB Bacteremia	7	14	Equal	3†
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	3	7	Equal	1
Neutropenic Fever	AFx72h/3 d	+ANC>500/9 d	Equal	2
Post Op Prophylaxis	0-1	1-5	Equal	55Ψ
Erythema Migrans (Lyme)	7-10	14-20	Equal	3
P. vivax Malaria	7	14	Equal	1

Total: 22 Conditions >130 RCTs

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

Clinical Infectious Diseases

MAJOR ARTICLE

Seven Versus 14 Days of Antibiotic Therapy for Uncomplicated Gram-negative Bacteremia: A Noninferiority Randomized Controlled Trial

Dafna Yahav,[1,2] Erica Franceschini,[3] Fidi Koppel,[4] Adi Turjeman,[2,5] Tanya Babich,[2,5] Roni Bitterman,[4] Ami Neuberger,[4,6] Nesrin Ghanem-Zoubi,[4] Antonella Santoro,[3] Noa Eliakim-Raz,[1,2] Barak Pertzov,[5] Tali Steinmetz,[5] Anat Stern,[4] Yaakov Dickstein,[4] Elias Maroun,[4] Hiba Zayyad,[4] Jihad Bishara,[1,2] Danny Alon,[7] Yonatan Edel,[2,8] Elad Goldberg,[9] Claudia Venturelli,[3] Cristina Mussini,[3] Leonard Leibovici,[2,5] Mical Paul[4,6]; for the Bacteremia Duration Study Group[a]

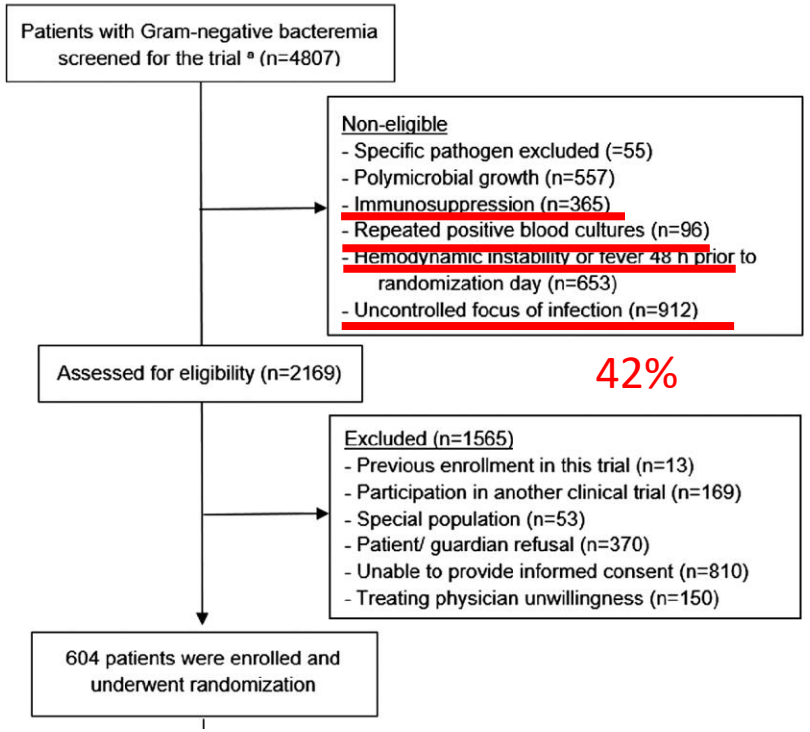
ORIGINAL ARTICLE | VOLUME 28, ISSUE 4, P550-557, APRIL 2022

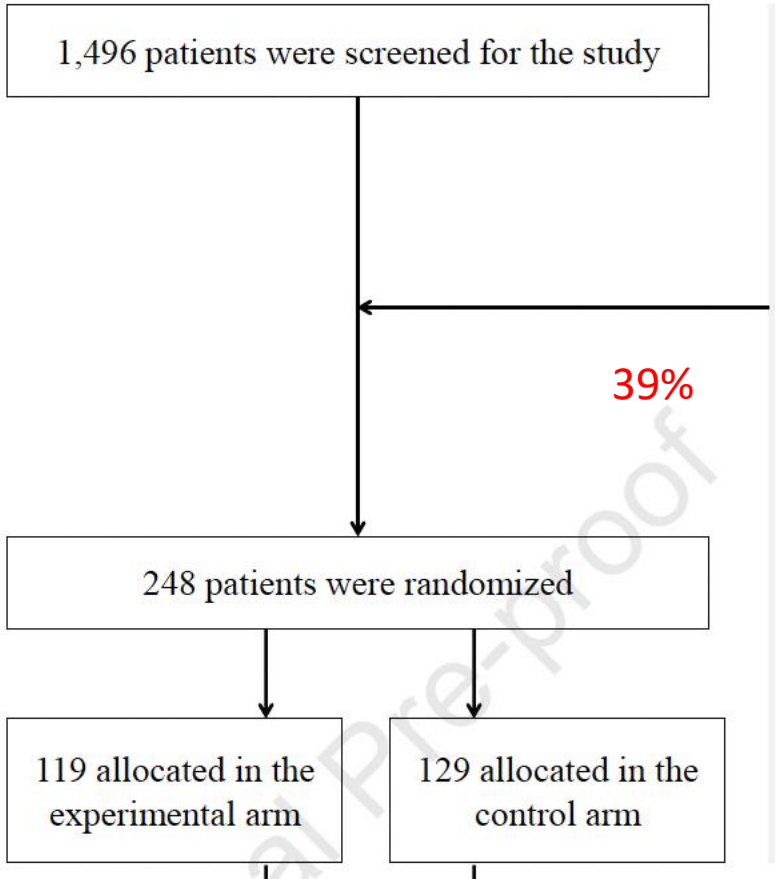
Download Full Issue

Seven-versus 14-day course of antibiotics for the treatment of bloodstream infections by Enterobacterales: a randomized, controlled trial

José Molina • Enrique Montero-Mateos • Julia Praena-Segovia • ... Jesús Rodríguez-Baño • José Miguel Cisneros • on behalf of the SHORTEN trial team † • Show all authors • Show footnotes

Published: September 08, 2021 • DOI: https://doi.org/10.1016/j.cmi.2021.09.001





Criteria of exclusion:

327 patients presented an uncontrolled source.

302 failed to be randomised within 72h from the diagnosis, or impossibility for the follow-up.

173 presented BSI due to, or associated with infections requiring prolonged antibiotic use.

111 had a expected survival inferior to 48h.

89 patients had polymicrobial BSI

76 patients presented prolonged neutropenia.

75 patients refused to participate.

95 patients were excluded due to other criteria.

Strategies for Reduction in Duration of Antibiotic Use in Hospitalized Patients

Antimicrobial therapy of established infection should be limited to **4–7 days**, unless it is difficult to achieve adequate source control. Longer durations of therapy have not been associated with improved outcome (B-III).

Excepcions:

1.Infeccions ‘peculiars’

- Antimicrobians tenen problemes d’activitat o penetració (endocarditis, infecció osteoarticular, focus supratiu no controlat, PNA, prostatitis, SNC)
- Alt risc emboligen (bacterièmia per *S. aureus* o *Candida sp.*)

2.Evolució clínica no satisfactòria

3.Factors predictors de mala evolució (Immunosupresió)

Adaptat de Hayashi Y, Clin Infect Dis, 2011

Què sabem?

Optimisation of empirical antimicrobial therapy in patients with haematological malignancies and febrile neutropenia (How Long study): an open-label, randomised, controlled phase 4 trial

Manuela Aguilar-Guisado, Ildefonso Espigado, Almudena Martín-Peña, Carlota Gudiol, Cristina Royo-Cebrecos, José Falantes, Lourdes Vázquez-López, María Isabel Montero, Clara Rosso-Fernández, María de la Luz Martino, Rocío Parody, José González-Campos, Sebastián Garzón-López, Cristina Calderón-Cabrera, Pere Barba, Nancy Rodríguez, Montserrat Rovira, Enrique Montero-Mateos, Jordi Carratalá, José Antonio Pérez-Simón, José Miguel Cisneros

www.thelancet.com/haematology Vol 4 December 2017

Què sabem?

Accelerated treatment of endocarditis—The POET II trial: Rationale and design of a randomized controlled trial

Lauge Østergaard, MD, [a,1] Mia Marie Pries-Heje, MD, [a,1] Rasmus Bo Hasselbalch, MD, [b] Magnus Rasmussen, MD, PhD, [c] Per Åkesson, MD, [c] Robert Horvath, MD, [d] Jonas Povlsen, MD, PhD, [e] Sabine Gill, MD, PhD, [f] Niels Eske Bruun, MD, DMSc, [g] Katrine Müllertz, MD, PhD, [h] Christian Ditlev Tuxen, MD, PhD, [i] Nikolaj Ihlemann, MD, PhD, [a] Jannik Helweg-Larsen, MD, DMSc, [j] Claus Moser, MD, PhD, [k] Emil Loldrup Fosbøl, MD, PhD, [a] Henning Bundgaard, MD, DMSc, [a,2] and Kasper Iversen, MD, DMSc [b,2] *Copenhagen, Aarbus, Odense, Roskilde, Hillerød, Denmark; Lund, Sweden; and Brisbane, Australia*

ClinicalTrials.gov ID NCT05144399

Sponsor Herlev Hospital

Information provided by Kasper Iversen, Herlev Hospital (Responsible Party)

Last Update Posted 2024-01-18

Què sabem?

STUDY PROTOCOL

Study protocol for a randomized clinical trial to assess 7 *versus* 14-days of treatment for *Pseudomonas aeruginosa* bloodstream infections (SHORTEN-2 trial)

José Molina[1,2,3], Clara María Rosso-Fernández[4], Enrique Montero-Mateos[5], José Ramón Paño-Pardo[3,6,7], María Solla[1,4], Ana Belén Guisado-Gil[1,2,3,8], Rocío Álvarez-Marín[1,2,3], María Eugenia Pachón-Ibáñez[1,2,3], Adelina Gimeno[1,2,3], Guillermo Martín-Gutiérrez[1,2,3], José Antonio Lepe[1,2,3], José Miguel Cisneros[1,2,3]*, on behalf of the SHORTEN-2 trial team[¶]

SHORTEN-2 trial. PLoSONE 17(12): e0277333

Què sabem?

STUDY PROTOCOL Open Access

Efficacy of seven and fourteen days of antibiotic treatment in uncomplicated *Staphylococcus aureus* bacteremia (SAB7): study protocol for a randomized controlled trial

Louise Thorlacius-Ussing[1*], Christian Østergaard Andersen[2], Niels Frimodt-Møller[3], Inge Jenny Dahl Knudsen[2], Jens Lundgren[4] and Thomas Lars Benfield[1]

Thorlacius-Ussing et al. Trials (2019) 20:250

Jornada *PROA hospitalari* a Catalunya

14 març de 2024 de 9 a 17 h

Recinte Modernista de Sant Pau
Hospital de la Santa Creu i Sant Pau
C/ Sant Antoni Maria Claret, 167
Barcelona

Discussió de l'evidència científica per a síndromes - què sabem i què podem fer?

PROA en bacterièmia

Recollida de mostres

Processament de mostres

Diagnòstic clínic

Control de focus

Tractament empíric

Ajust segons antibiograma

Pas a via oral

Durada

Al·lèrgia a Beta-lactàmics

Què podem fer? Proposta de decàleg

1. Seleccionar bé els pacients que requereixen tractament empíric precoç
2. Seleccionar bé els pacients que es poden beneficiar de tractaments combinats (endocarditis, SARM, *P aeruginosa*)
3. Estratificar els factors de risc de mala evolució.
4. Bacterièmia de baix risc → clarament pautes curtes i tractament oral
5. Controlar el focus sempre que sigui possible
6. Millorar el diagnòstic sindròmic dels pacients amb infeccions
7. Escurçar els temps per obtenir resultats microbiològics (micro 24/7)
8. Recollida de mostres adequada prèvia a l'inici dels antibiòtics
9. Millorar la història i maneig de pacients amb etiqueta d'al·lèrgia

10.- Interpretar bé els estudis per aplicar-los correctament a la nostra activitat clínica.

…it is time for the field of infectious diseases to adopt evidenced-based **with experience**-based medicine.

ogasch@tauli.cat