Stafilokokna sepsa in antibiotično zdravljenje – kaj je novega?

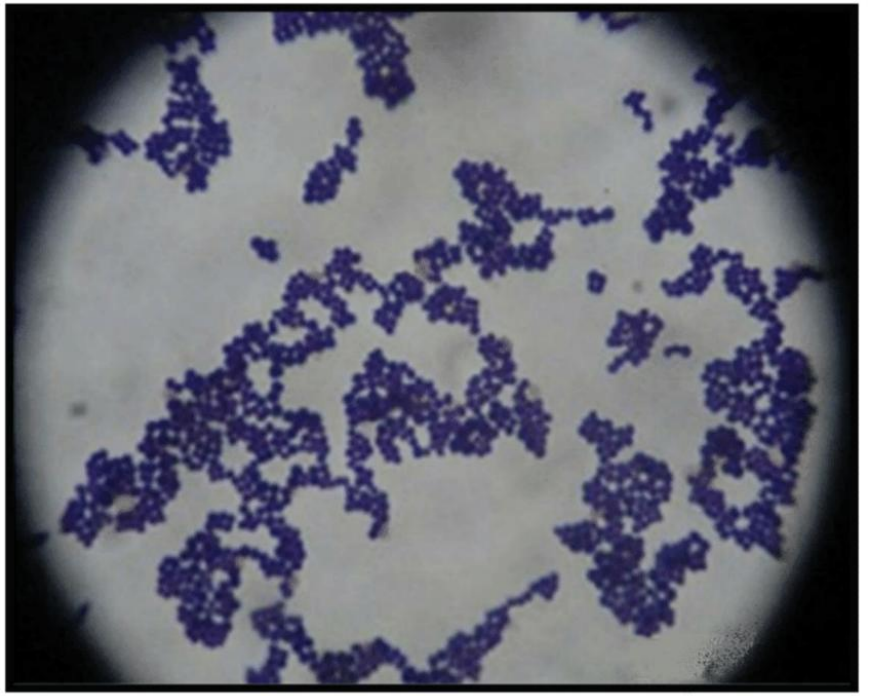
Doc. dr. Mateja Logar, dr. med.
KIBVS; UKC Ljubljana
SPOBO; UKC Ljubljana
MF UL

Razkritje

- Predavanja: Lek, Lenis, MSD, Pfizer, Pharmamed, Medis, SOBI
- Delnice: Krka

Uvod

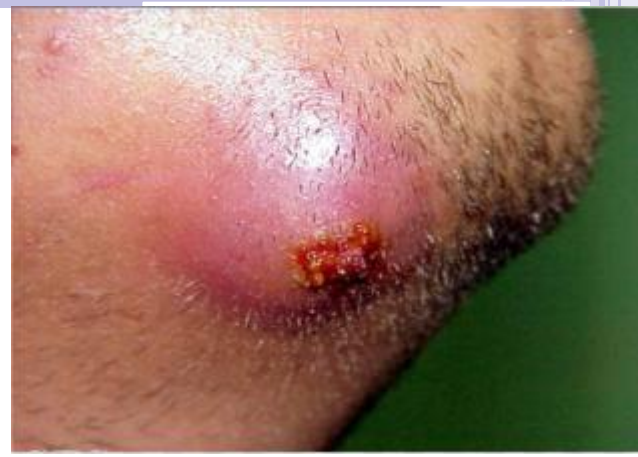
- *Staphylococcus aureus*
  - Po Gramu pozitivna bakterija
  - V skupinah
  - Ime iz grščine:
    - ”staphyle”- skupek
    - ”kokkos” - jagode
  - Prvi opisal britanski kirurg Alexander Ogston 1889
    - Gnoj iz abscesa po kirurškem posegu



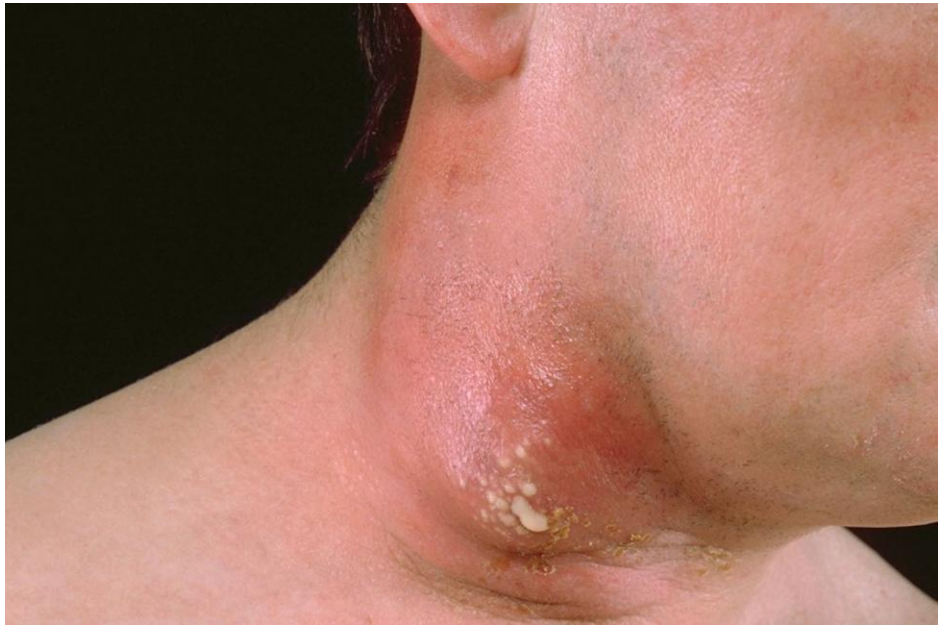
Tawhid, Tasfia. (2022). COMPREHENSIVE STUDY OF ANTIBACTERIAL ACTIVITIES OF MEDICINAL PLANTS AND ESSENTIAL OILS AGAINST Staphylococcus aureus. 10.13140/RG.2.2.24466.99529.

https://www.yourhealthremedy.com/health-tips/staphylococcus-aureus-facts-symptoms/

Uvod



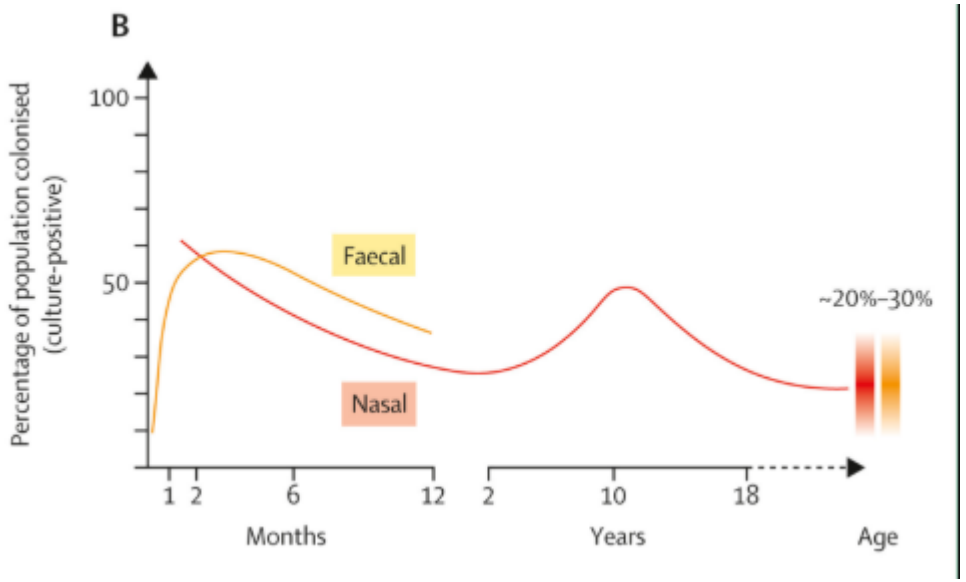
- *Staphylococcus aureus*
  - Najpogostejši povzročitelj okužb kože in podkožja
    - Lokalizirane okužbe: folikulitis, furunkel, karbunkel, absces
    - Difuzne okužbe: celulitis
  - Okužbe kosti in sklepov
  - Pljučnice
  - Infekcijski endokarditisi
  - Sepsa in septični šok
    - Smrtnost pred odkritjem AB: 82 %

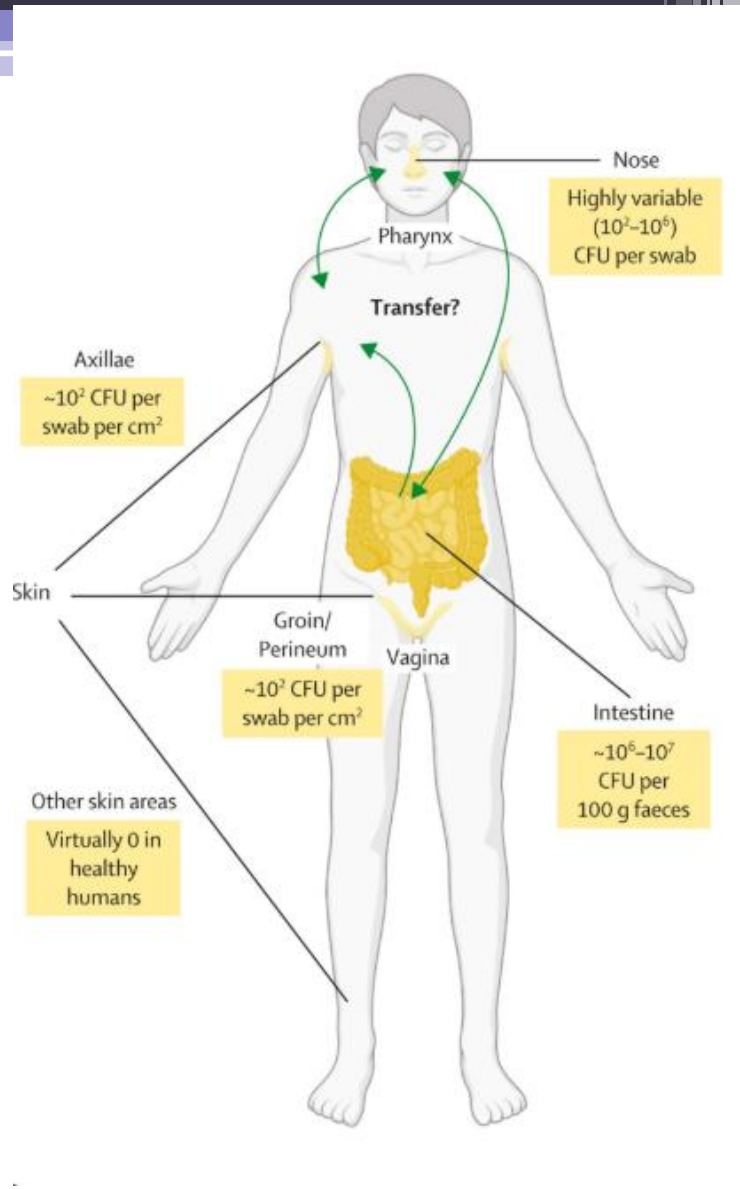


https://www.yourhealthremedy.com/health-tips/staphylococcus-aureus-facts-symptoms/

Kolonizacija

- Določen delež ljudi trajno koloniziranih
- Pri nekaterih občasna kolonizacija





Piewngam P, Otto M. Staphylococcus aureus colonisation and strategies for decolonisation. Lancet Microbe. 2024;5(6):e606-e618.

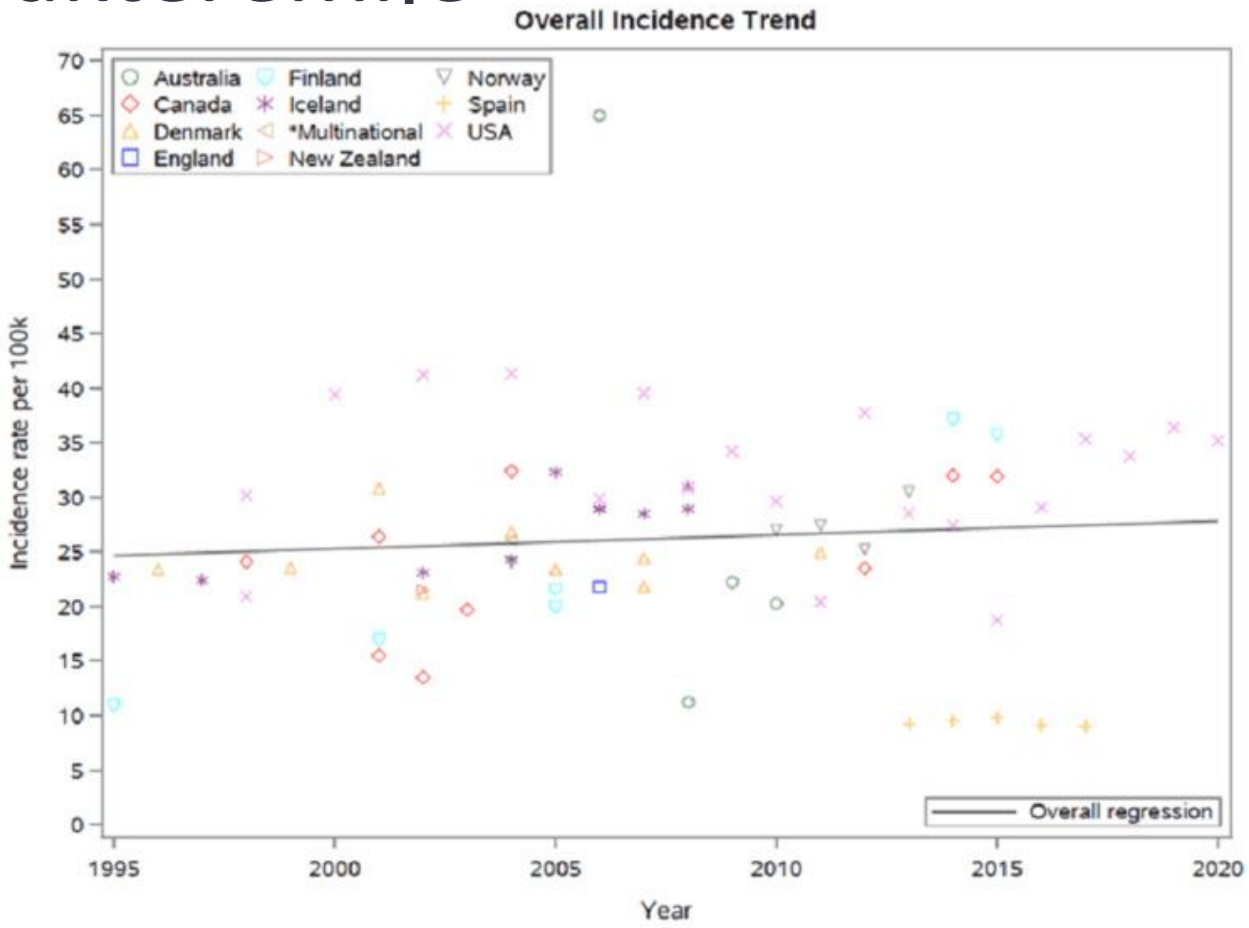
Kolonizacija

- Najpogosteje nosna sluznica
  - Trajna kolonizacija pri 12 – 30 %
  - Občasna kolonizacija cca 30 %
  - 5 % *S. aureus* znotrajcelično
  - Povezano z večjo pojavnostjo okužb kirurške rane
- Kolonizacija tudi v črevesu
  - Možen izvor bakteremije

Piewngam P, Otto M. Staphylococcus aureus colonisation and strategies for decolonisation. Lancet Microbe. 2024;5(6):e606-e618.

Epidemiologija *S. aureus* bakteremiie

- Pregled literature
  - 2001 – 2020
  - 26 populacijskih raziskav
    - 9,3 – 65/100.000/leto



Hindy JR, et al. Incidence Trends and Epidemiology of Staphylococcus aureus Bacteremia: A Systematic Review of Population-Based Studies. Cureus. 2022;14(5):e25460..

Epidemiologija *S. aureus* bakteremije

- Mediana starost 65 – 72 let
  - Odvisno od države
  - V dveh desetletjih trend poraščanja
  - Večji delež starejših od 75 let
- Charlsonov indeks pridruženih bolezni
  - Trend porasta
    - Sladkorna bolezen 13 – 38 %
    - KLB na HD 7,5 – 18,6 %
    - 10 % TEP
    - 6 % vsadne elektronske srčne naprave

Hindy JR, et al. Incidence Trends and Epidemiology of Staphylococcus aureus Bacteremia: A Systematic Review of Population-Based Studies. Cureus. 2022;14(5):e25460..

Epidemiologija *S. aureus* bakteremije

- Islandija in Kanada
  - Bakteriemije povezanih z zdravstvom 39 % – 46 %
- Norveška, ZDA in Danska
  - Bakteriemije povezanih z zdravstvom 42 – 59 %
- Nova Zelandija in Avstralija
  - Doma pridobljene okužbe 58 – 64 %

Hindy JR, et al. Incidence Trends and Epidemiology of Staphylococcus aureus Bacteremia: A Systematic Review of Population-Based Studies. Cureus. 2022;14(5):e25460..

Epidemiologija *S. aureus* bakteremije

- Izvor okužbe
  - Intravenski katetri
  - Okužbe kože in podkožja
  - Okužbe kosti in sklepov
  - Infekcijski endocarditis
  - Dihala
  - Neznano
    - V nekaterih raziskavah najpogostejše

Hindy JR, et al. Incidence Trends and Epidemiology of Staphylococcus aureus Bacteremia: A Systematic Review of Population-Based Studies. Cureus. 2022;14(5):e25460..

Epidemiologija *S. aureus* bakteremije

- MRSA
  - Odvisno od države
  - Velike razlike
    - Kanada 9 %
      ZDA 32 %
    - Norveška, Islandija, Danska in Nova Zelandija: 0,4 – 1,7 %

Hindy JR, et al. Incidence Trends and Epidemiology of Staphylococcus aureus Bacteremia: A Systematic Review of Population-Based Studies. Cureus. 2022;14(5):e25460.
https://www.ecdc.europa.eu/sites/default/files/documents/Country_profiles_2023_2024_1.pdf

Epidemiologija *S. aureus* bakteremije

- Slovenija:
  - 644 – 768 invazivnih izolatov/leto
  - 8 – 14 iz EIT
  - 7,5 – 10,1 % MRSA

https://www.ecdc.europa.eu/sites/default/files/documents/Country_profiles_2023_2024_1.pdf

Epidemiologija *S. aureus* bakteremije

- Umrljivost
  - 2 – 7,6/100.000 prebivalcev/leto
- 30-dnevan smrtnost
  - Večja pri starejših, imunsko oslabelih
  - Glede na vir okužbe
    - Pljučnica
    - Infekcijski endocarditis
    - Nenznano
  - Manjša smrtnost, če je bil vključen infektolog

Hindy JR, et al. Incidence Trends and Epidemiology of Staphylococcus aureus Bacteremia: A Systematic Review of Population-Based Studies. Cureus. 2022;14(5):e25460..

Epidemiologija *S. aureus* bakteremije

- Retrospektivna raziskava
  - 1991 – 2021
  - Manjša smrtnost v zadnjem desetletju
  - Večja pri MRSA kot pri MSSA
  - Smrtnost
    - 10 % v 1. tednu
    - 20 % v 1 mesecu
    - 30 % v 1 letu

Bai Ad, et al. Staphylococcus aureus bacteraemia mortality: a systematic review and meta-analysis. Clin Microbiol Infect. 2022;28(8):1076-84.

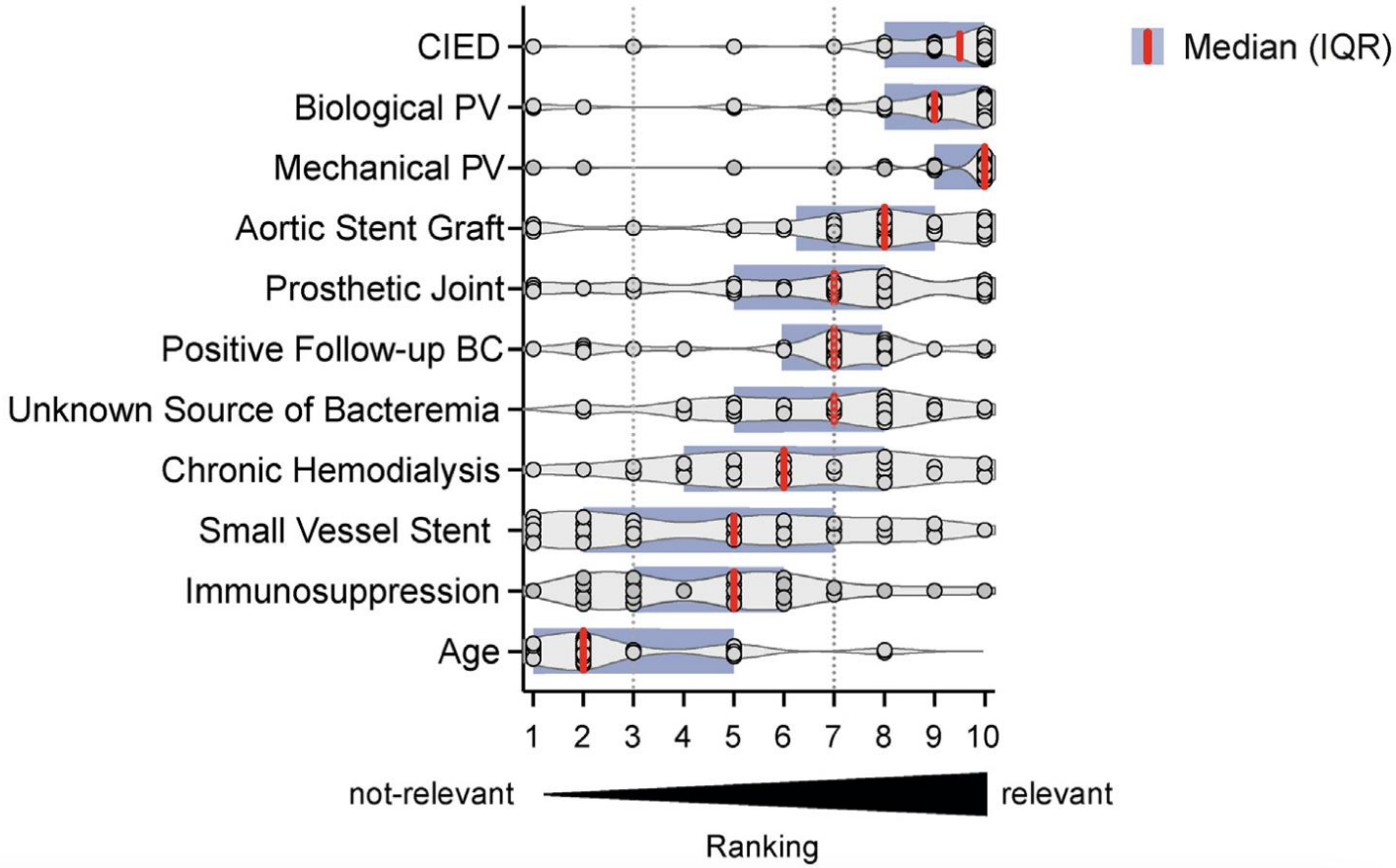
Delitev *S. aureus* bakteriemij

- Nezapletena : zapletena
- Več definicij
- Osnovni kriteriji za nezapleteno
  - Izključen infekcijski endokarditis ali TEP
  - Klinično izboljšanje manj kot 72 ur od uvedbe učinkovite terapije
  - Negativne hemokulture po 48 – 96 urah
  - Brez oddaljenih zasevkov
- Nekateri še
  - Brez imunskih pomanjkljivosti
  - Brez OŽK
  - Ni OID

Hagel S, et al. Complicated and uncomplicated S. aureus bacteraemia: an international Delphi survey among infectious diseases experts on definitions and treatment. Clin Microbiol Infect. 2022;28(7):1026.e7-1026.e11.

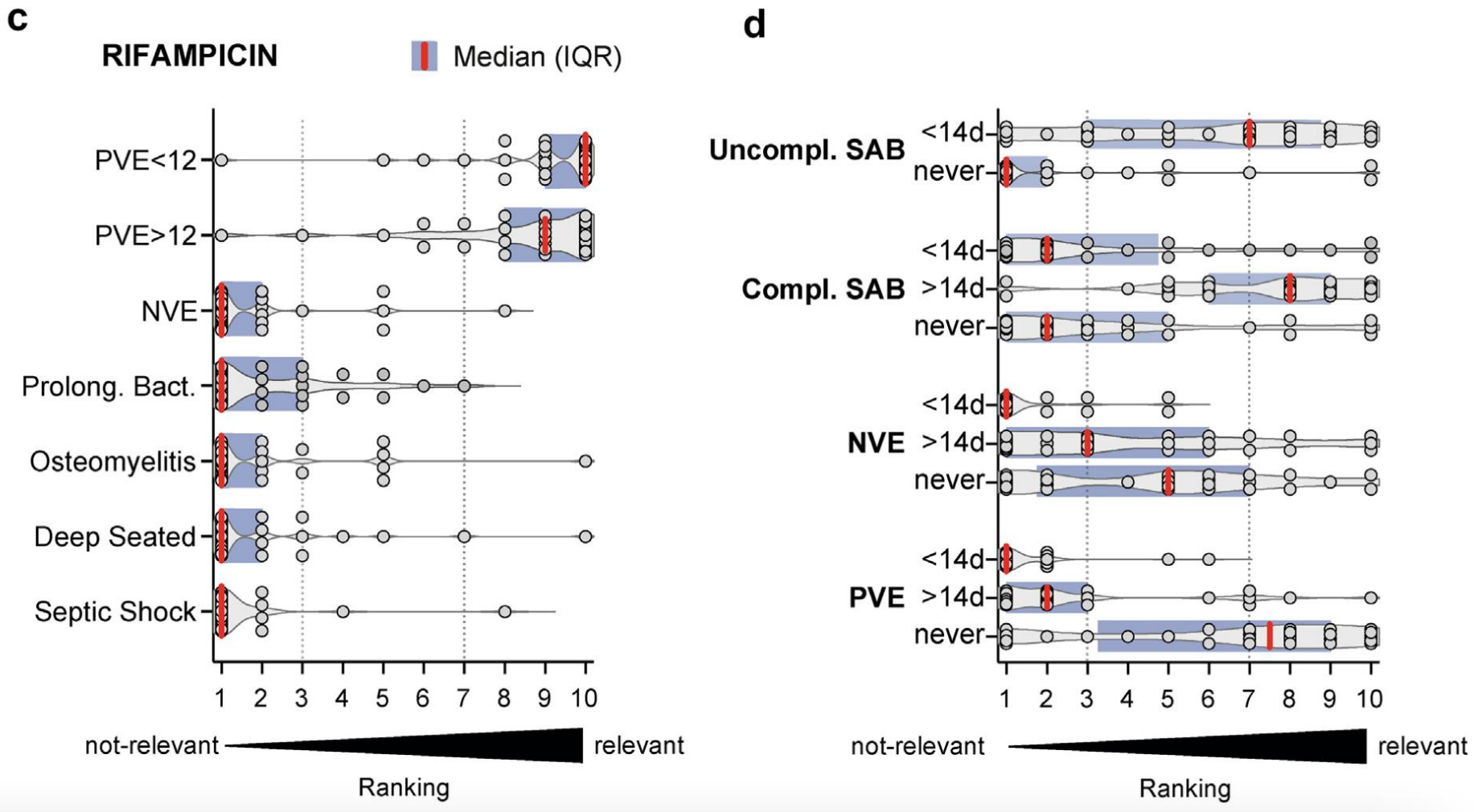
Delitev *S. aureus* bakteriemij

- 90 zdravnikov, 14 držav
  - Nezapletena : zapletena



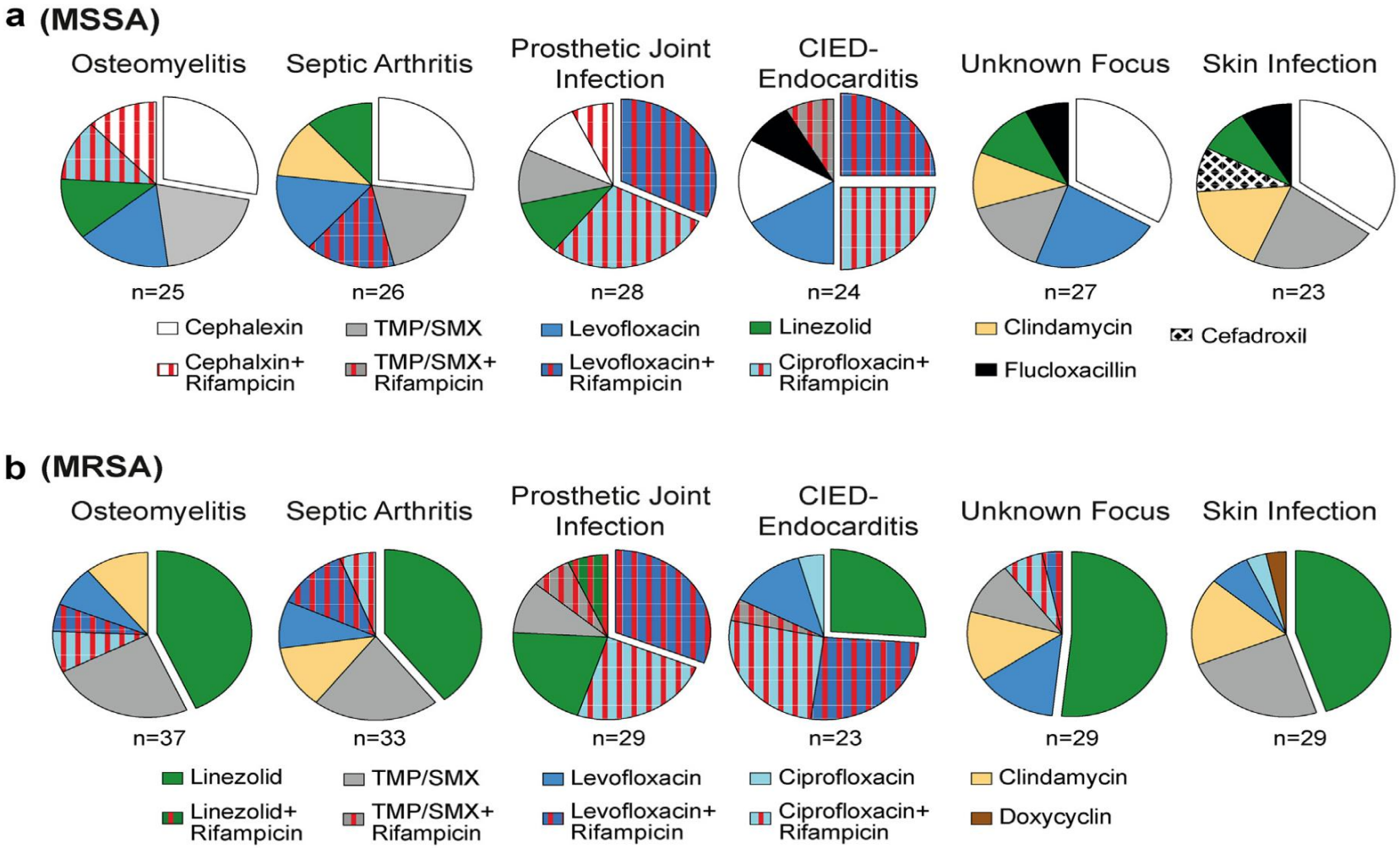
Hagel S, et al. Complicated and uncomplicated S. aureus bacteraemia: an international Delphi survey among infectious diseases experts on definitions and treatment. Clin Microbiol Infect. 2022;28(7):1026.e7-1026.e11.

S. aureus bakteriemije – uporaba rifampicina



Hagel S, et al. Complicated and uncomplicated S. aureus bacteraemia: an international Delphi survey among infectious diseases experts on definitions and treatment. Clin Microbiol Infect. 2022;28(7):1026.e7-1026.e11.

Delitev *S. aureus* bakteriemij – sestopno zdravljenje per os



Hagel S, et al. Complicated and uncomplicated S. aureus bacteraemia: an international Delphi survey among infectious diseases experts on definitions and treatment. Clin Microbiol Infect. 2022;28(7):1026.e7-1026.e11.

S. aureus bakteriemija – smernice za zdravljenje

Clinical Infectious Diseases

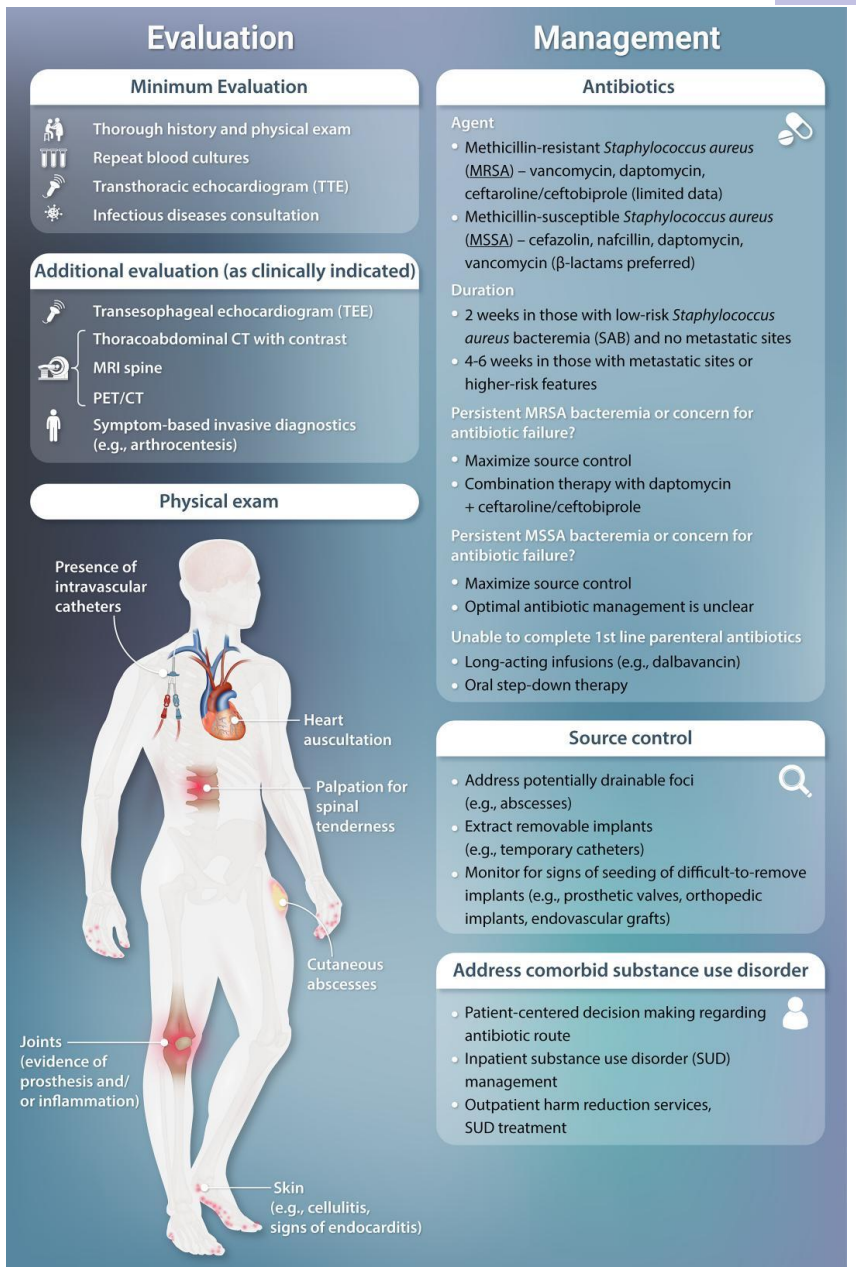
STATE-OF-THE-ART REVIEW

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

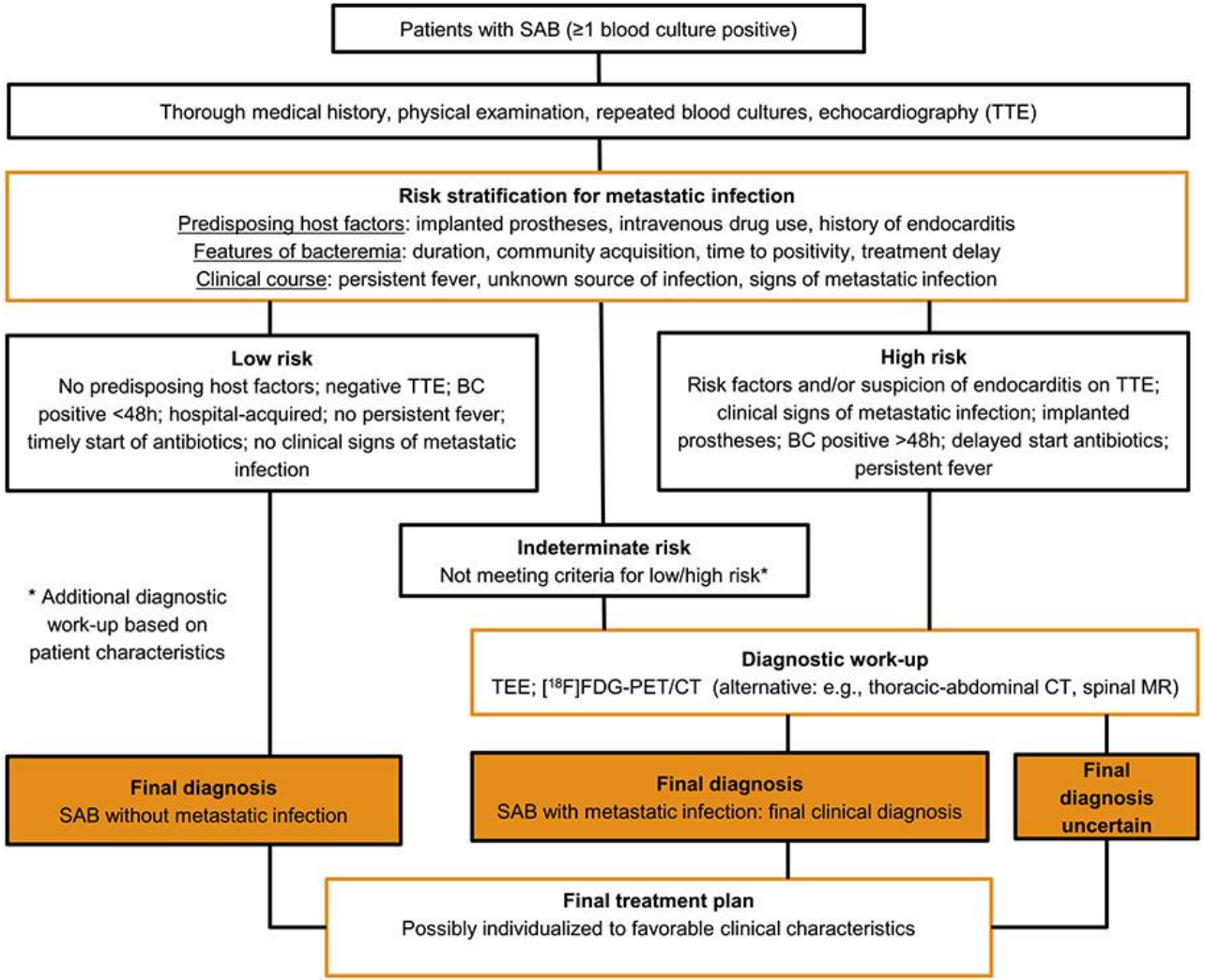
Minter DJ, Appa A, Chambers HF, Doernberg SB. Contemporary Management of Staphylococcus aureus Bacteremia-Controversies in Clinical Practice. Clin Infect Dis. 2023 77(11):e57-e68.



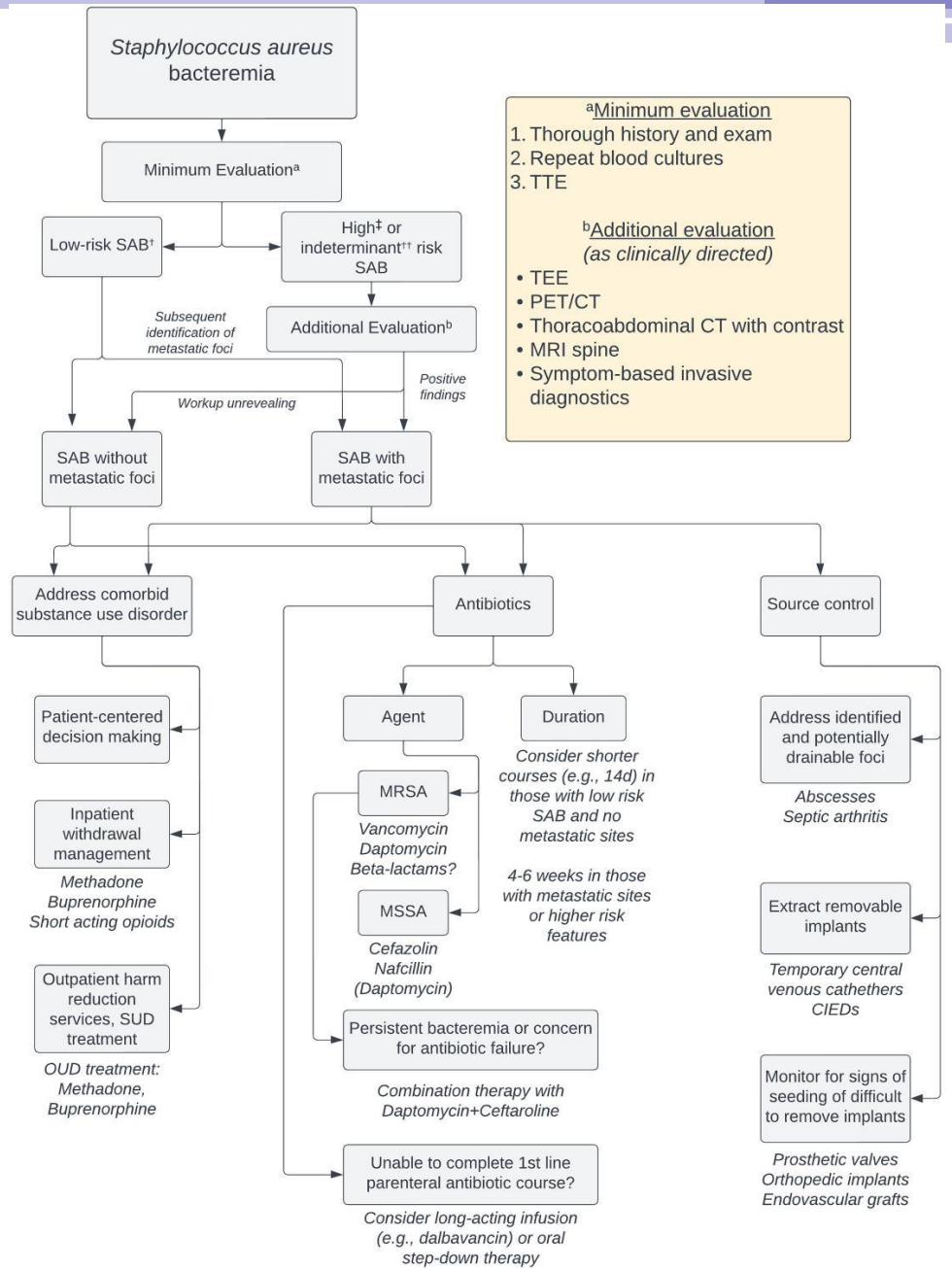
!

Minter DJ, Appa A, Chambers HF, Doernberg SB. Contemporary Management of Staphylococcus aureus Bacteremia-Controversies in Clinical Practice. Clin Infect Dis. 2023 77(11):e57-e68.

S. aureus bakteriemija – predlog nove razdelitve



S. aureus bakteriemija – smernice za zdravljenje



Minter DJ, Appa A, Chambers HF, Doernberg SB. Contemporary Management of Staphylococcus aureus Bacteremia-Controversies in Clinical Practice. Clin Infect Dis. 2023 77(11):e57-e68.

Chong *et al.* 2013 (n=111)		
	<14 day	**≥14 days**
Median Antibiotics	8.5 (7-11) days	16 (14-21) days
Treatment failure	26%	22%
Relapse	**8%**	**0%**

Disadvantage to shorter therapy
more relapses

Taupin *et al.* 2020 (n=64)		
	14 day	**>14 days**
Median Antibiotics	14 (14-14) days	28 (28-40) days
Treatment failure	0	5%
Relapse	0	5%

No advantage to longer therapy
High risk of bias (longer therapy group had a higher risk profile, eg. deep vein thrombosis)

Zgodnji prehod na per os zdravljenje

THE LANCET
Infectious Diseases

ARTICLES · Volume 24, Issue 5, P523-534, May 2024 Download Full Issue

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

Prof Achim J Kaasch, MD [a] · Luis Eduardo López-Cortés, MD [b,d] · Prof Jesús Rodríguez-Baño, MD [b,d] · Prof José Miguel Cisneros, MD [c,d] · M Dolores Navarro, MD [c,d] · Prof Gerd Fätkenheuer, MD [e] · et al. Show more

Kaasch AJ, López-Cortés LE, Rodríguez-Baño J, et al SABATO study group. Efficacy and safety of an early oral switch in low-risk Staphylococcus aureus bloodstream infection (SABATO): an international, open-

Zgodnji prehod na per os zdravljenje

- Prospektivna, randomizirana raziskava (SABATO)
- Težave z vključevanjem
- 5063 bolnikov s *S. aureus* bakteriemijo
  - 218 izpolnjevalo kriterije za nezapleteno okužbo
  - 213 ranodmiziranih
    - 108 prehod na per os po 5 – 7 dneh
    - 105 14 dni parenteralna terapija

Kaasch AJ, et al SABATO study group. 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;24(5):523-534.

Zgodnji prehod na per os zdravljenje

- Kriteriji
  - Odrasli bolniki
  - Nezapletena *S. aureus* bakteriemija
  - Dodatni izključitveni kriteriji
    - *S. aureus* bakteriemija v zadnjih 3 mesecih
    - UID
    - Huda imunska pomanjkljivost
    - Zdravljenje z imunosupresivi
    - Prisotnost umetne srčne zaklopke ali velikega žilnega vsadka

Kaasch AJ, et al SABATO study group. 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;24(5):523-534.

Zgodnji prehod na per os zdravljenje

	Intention-to-treat population		Clinically evaluable population	
	Oral switch group (n=108)	Intravenous group (n=105)	Oral switch group (n=86)	Intravenous group (n=79)
Age, years	64·4 (16·8)	62·6 (17·6)	62·4 (17·1)	62·1 (17·8)
Sex				
Male	71 (66%)	77 (73%)	59 (69%)	58 (73%)
Female	37 (34%)	28 (27%)	27 (31%)	21 (27%)
BMI, kg/m²	27·6 (6·7)	25·6 (5·4)	27·4 (6·5)	26·1 (5·3)
Time in hospital before randomisation, days	10 (7–14)	11 (7–15)	10 (7–13)	10 (7–13)
Intervention to remove or drain infective focus	9 (8%)	14 (13%)	5 (6%)	10 (13%)
Echocardiography (TTE or TEE, or both) performed within 7 days before or after randomisation	69 (64%)	60 (57%); 1	55 (64%)	46 (58%)
CRP at baseline visit, mg/L*	35 (13–70); 13	23 (10–59); 15	35 (14–64); 11	20 (11–52); 13
Resistance of *Staphylococcus aureus* isolate				
Meticillin	6 (6%)	10 (10%)	4 (5%)	5 (6%)
Clindamycin	12 (12%); 4	11 (11%); 5	10 (12%); 4	7 (10%); 5
Co-trimoxazole	1 (1%); 2	3 (3%); 1	0 (0%); 2	2 (3%)

	Intention-to-treat population		Clinically evaluable population	
	Oral switch group (n=108)	Intravenous group (n=105)	Oral switch group (n=86)	Intravenous group (n=79)
Focus of infection				
Peripheral venous catheter	47 (44%)	46 (44%)	41 (48%)	35 (44%)
Central venous catheter	24 (22%)	25 (24%)	18 (21%)	16 (20%)
Skin and soft-tissue infection	26 (24%)	22 (21%)	19 (22%)	19 (24%)
Other†	5 (5%)	4 (4%)	4 (5%)	3 (4%)
Not identified	6 (6%)	8 (8%)	4 (5%)	6 (8%)
Comorbidities				
Moderate or severe liver disease	11 (10%)	4 (4%)	8 (10%)	2 (3%)
Chronic renal failure	17 (16%); 1	18 (17%)	10 (12%); 1	12 (15%)
End-stage renal disease	9 (8%); 1	5 (5%)	5 (6%); 1	4 (5%)
Chronic lung disease	14 (13%); 1	17 (16%)	10 (12%)	11 (14%)
Diabetes without end-organ damage	25 (23%)	18 (17%)	21 (24%)	11 (14%)
Diabetes with end-organ damage	19 (18%)	10 (10%)	13 (15%)	9 (11%)
Any immunosuppression‡	16 (15%)	16 (15%); 1	12 (14%)	14 (18%); 1
Charlson Comorbidity Index	3 (1–5)	3 (1–4)	2 (1–4)	3 (1–4)
Intravenous antimicrobials before randomisation, days	6 (6–7)	6 (5–7)	7 (6–7)	6 (5–7)

Kaasch AJ, et al SABATO study group. 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;24(5):523-534.

Zgodnji prehod na per os zdravljenje

- Predvidena terapija
  - MSSA
    - Parenteralno
      - flucloksacilin 2 g / 6 ur (kloksacilin 2 g / 6 ur v Španiji in Franciji), cefazolin 2 g / 8 ur, vankomicin 1g /12 ur
    - Per os
      - TMP/SMX (160 mg trimetoprim / 800 mg sulfametoksazol) / 12 ur
      - klindamicin 600 mg /8 ur
  - MRSA
    - Parenteralno
      - vankomicin 1g /12 ur ali daptomicin 6-10mg/kg / 24 ur
    - Per os
      - TMP/SMX (160 mg trimetoprim / 800 mg sulfametoksazol) / 12 ur
      - linezolid 600 mg / 12 ur

Kaasch AJ, et al SABATO study group. 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;24(5):523-534.

Zgodnji prehod na per os zdravljenje

	Intention-to-treat population			Clinically evaluable population		
	Oral switch group (n=108)	Intravenous group (n=105)	Percentage-point difference (95% CI)	Oral switch group (n=86)	Intravenous group (n=79)	Percentage-point difference (95% CI)
Primary endpoint						
SAB-related complication within 90 days	14 (13%)	13 (12%)	0·7 (–7·8 to 9·1)	3 (4%)	4 (5%)	–2·9 (–9·6 to 3·9)
Reason primary outcome was met						
SAB-related complication	6 (6%)	8 (8%)	–2·1 (–9·7 to 5·5)	3 (4%)	4 (5%)	–1·6 (–9·0 to 5·8)
Relapsing SAB	3 (3%)	4 (4%)	–1·0 (–6·8 to 4·7)	2 (2%)	2 (3%)	–0·2 (–5·1 to 4·7)
Deep-seated infection with *S aureus*	5 (5%)	8 (8%)	–3·0 (–10·4 to 4·4)	3 (4%)	4 (5%)	–1·6 (–9·0 to 5·8)
Death attributable to SAB	2 (2%)	0	1·9 (–1·6 to 5·3)	1 (1%)	0	1·2 (–2·3 to 4·6)
Missing outcome data	8 (7%)	5 (5%)	2·7 (–4·7 to 10·0)	..	..	..
Attributability of death non-evaluable	3 (3%)	1 (1%)	1·8 (–2·7 to 6·4)	..	..	..
Secondary endpoints						
Length of hospital stay from SAB onset, days	12 (9–19)	16 (10–19)	–2 (–4 to 0); p=0·043*	11 (9–16)	15 (10–18)	–2 (–5 to 0); p=0·020*
Participants with complications of intravenous administration†						
Any complication	9 (9%); 11	17 (17%); 5	–7·9 (–17·6 to 1·9)	6 (7%); 3	13 (17%); 2	–9·5 (–20·5 to 1·5)
Chemical phlebitis	7	9	–2·1 (–10·1 to 5·9)	5	8	–4·3 (–13·8 to 5·2)
Infectious thrombophlebitis or phlebitis	0	2	–1·9 (–5·5 to 1·7)	0	2	–2·5 (–7·2 to 2·2)
Other‡	2	6	–3·9 (–9·9 to 2·2)	1	3	–2·6 (–8·6 to 3·4)
Participants with *Clostridium difficile* infection§	2 (2%); 8	2 (2%); 7	–0·1 (–3·8 to 3·6)	2 (2%); 7	1 (1%); 5	1·1 (–4·0 to 6·1)
Survival						
14 days	98·1% (1·3); 2	100·0% (0); 0	–1·9 (–4·5 to 0·7)	98·8% (1·2); 1	100·0% (0); 0	–1·2 (–3·4 to 1·1)
30 days	94·3% (2·3); 6	96·0% (2·0); 4	–1·7 (–7·6 to 4·2)	98·8% (1·2); 1	98·7% (1·3); 1	0·1 (–3·3 to 3·5)
90 days	83·6% (3·6); 17	89·0% (3·1); 11	–5·4 (–14·8 to 4·0)	92·9% (2·8); 6	94·8% (2·5); 4	–1·9 (–9·3 to 5·5)

Kaasch AJ, et al SABATO study group. 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;24(5):523-534.

Zgodnji prehod na per os zdravljenje

- Dokazali ne-inferiornost
- Majhen delež primernih bolnikov
- Krajša hospitalizacija
- Manj zapletov parenteralnega zdravljenja
- 2 smrti v per os skupini
  - Oba okužba povezana z OŽK
  - Ponovitev v 3. tednu od uvedbe zdravljenja
    - Eden ni želel ponovnega zdravljenja
- Manj zapletov (ponovitev, IE, oddaljene okužbe) v per os skupini – ni statistično značilno

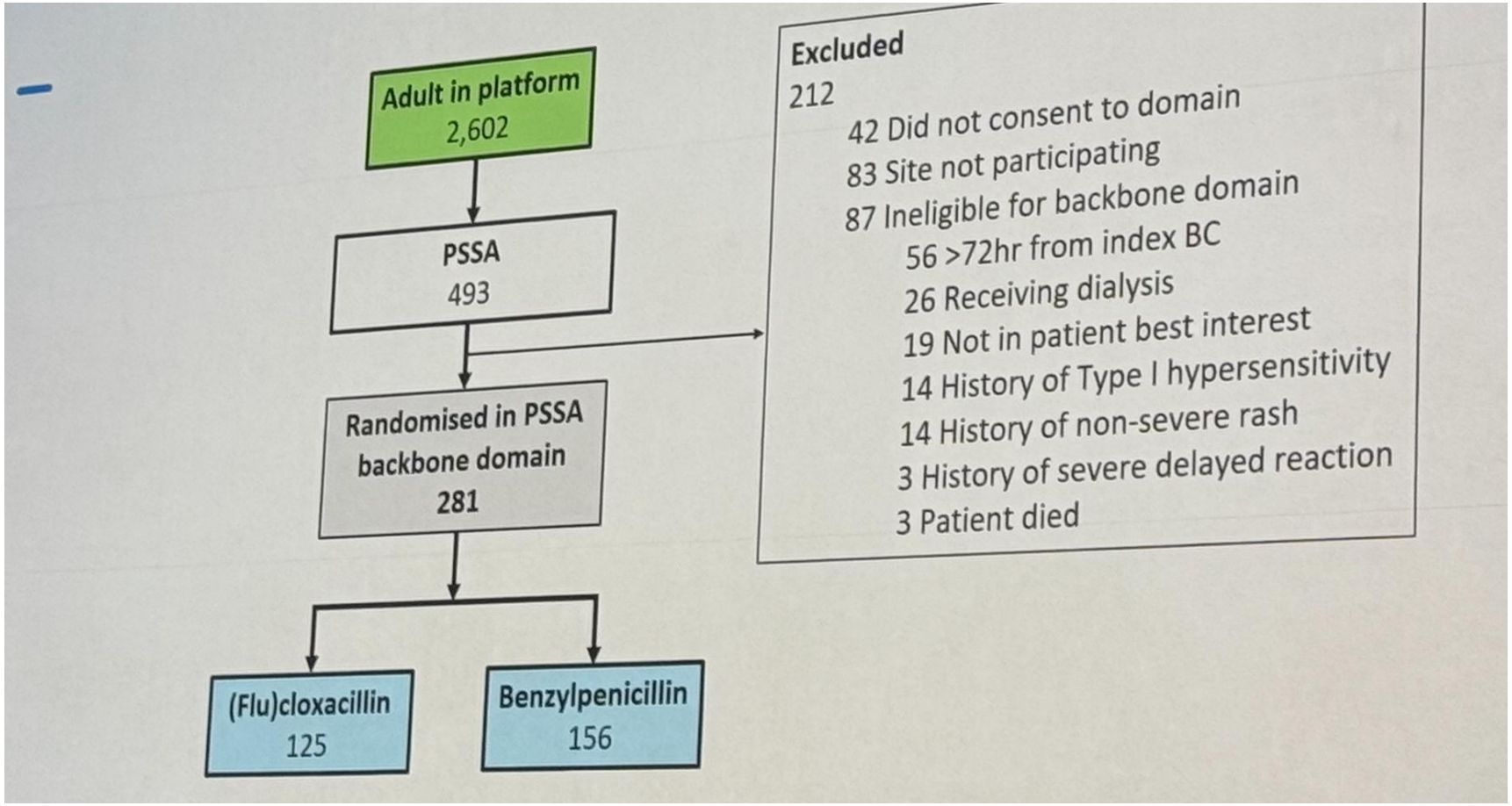
Kaasch AJ, et al SABATO study group. Efficacy and safety of an early oral switch in low-risk Staphylococcus aureus bloodstream infection (SABATO): an international, open-label, parallel-group, randomised, controlled, non-inferiority trial. Lancet Infect Dis. 2024;24(5):523-534.

SNAP platforma

- Mednarodna prospektivna raziskava
- Začetek vključevanja 02/2022
- Zdravljenje PSSA s penicilinom v primerjavi s (flu)kloksacilinom
  - Ustavitev vključevanja 07/24
- Cefazolin vs oksacilin/flukloksacilin za MSSA
  - Ustavitev vključevanja 08/24
- Zgodnji prehod na per os zdravljenje za *S. aureus* bakterimeijo

https://www.snaptrial.com.au/

Penicilin vs (flu)kloksacilin za PSSA



https://www.snaptrial.com.au/

Penicilin vs (flu)kloksacilin za PSSA

Baseline characteristics

Variable	(Flu)cloxacillin (n=125)	Benzylpenicillin (n=156)
Age (median, IQR))	69.0 (57.0, 79.0)	65.5 (55.8, 75.2)
Sex at birth (female)	41 (32.8%)	46 (29.5%)
Weight (kg, median, IQR)	82.0 (70.0, 95.0)	80.0 (70.0, 97.0)
Country		
Australia	47 (37.6)	66 (42.3)
NZ	29 (23.2)	30 (19.2)
Canada	24 (19.2)	29 (18.6)
Israel	14 (11.2)	15 (9.6)
Netherlands	7 (5.6)	5 (3.2)
UK	3 (2.4)	4 (2.6)
Singapore	0 (0.0)	6 (3.8)
South Africa	1 (0.8)	1 (0.6)

https://www.snaptrial.com.au/
ESCMID Global 2025

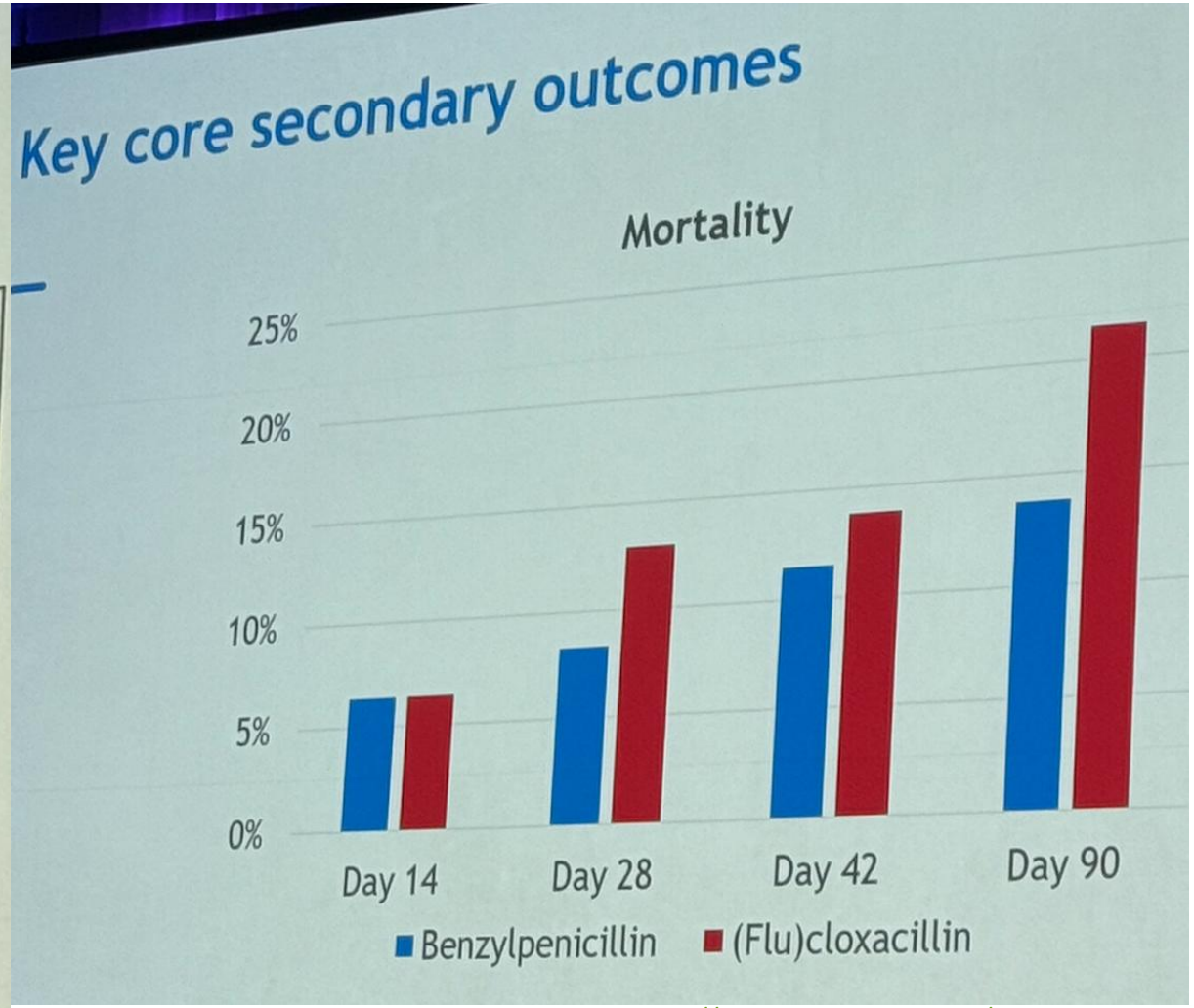
Penicilin vs (flu)kloksacilin za PSSA

Primary outcome - Intention to treat

	(Flu)cloxacillin (n=125)	Benzylpenicillin (n=156)
All-cause mortality at 90 days		
Yes	26 (21.5)	21 (13.8)
Missing	4 (3.2)	4 (2.6)

Adjusted odds ratio (median, 95% CrI)	0.67 (0.35, 1.28)
Non-inferiority, Pr(OR<1.2):	0.9611
Superiority, Pr(OR<1.0):	0.8887

Key core secondary outcomes



https://www.snaptrial.com.au/

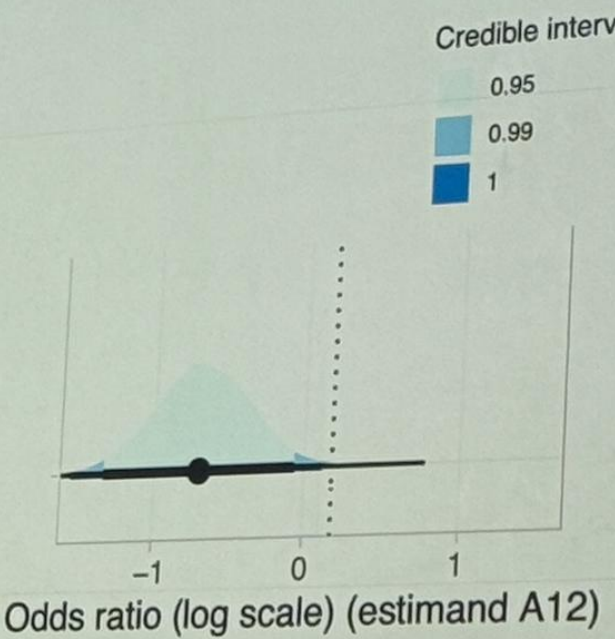
ESCMID Global 2025

Penicilin vs (flu)kloksacilin za PSSA

Key domain secondary outcomes

	(Flu)cloxacillin (n=125)	Benzylpenicillin (n=156)
Acute kidney injury		
Yes	27 (21.6)	17 (10.9)
Missing	1 (0.8)	3 (1.9)

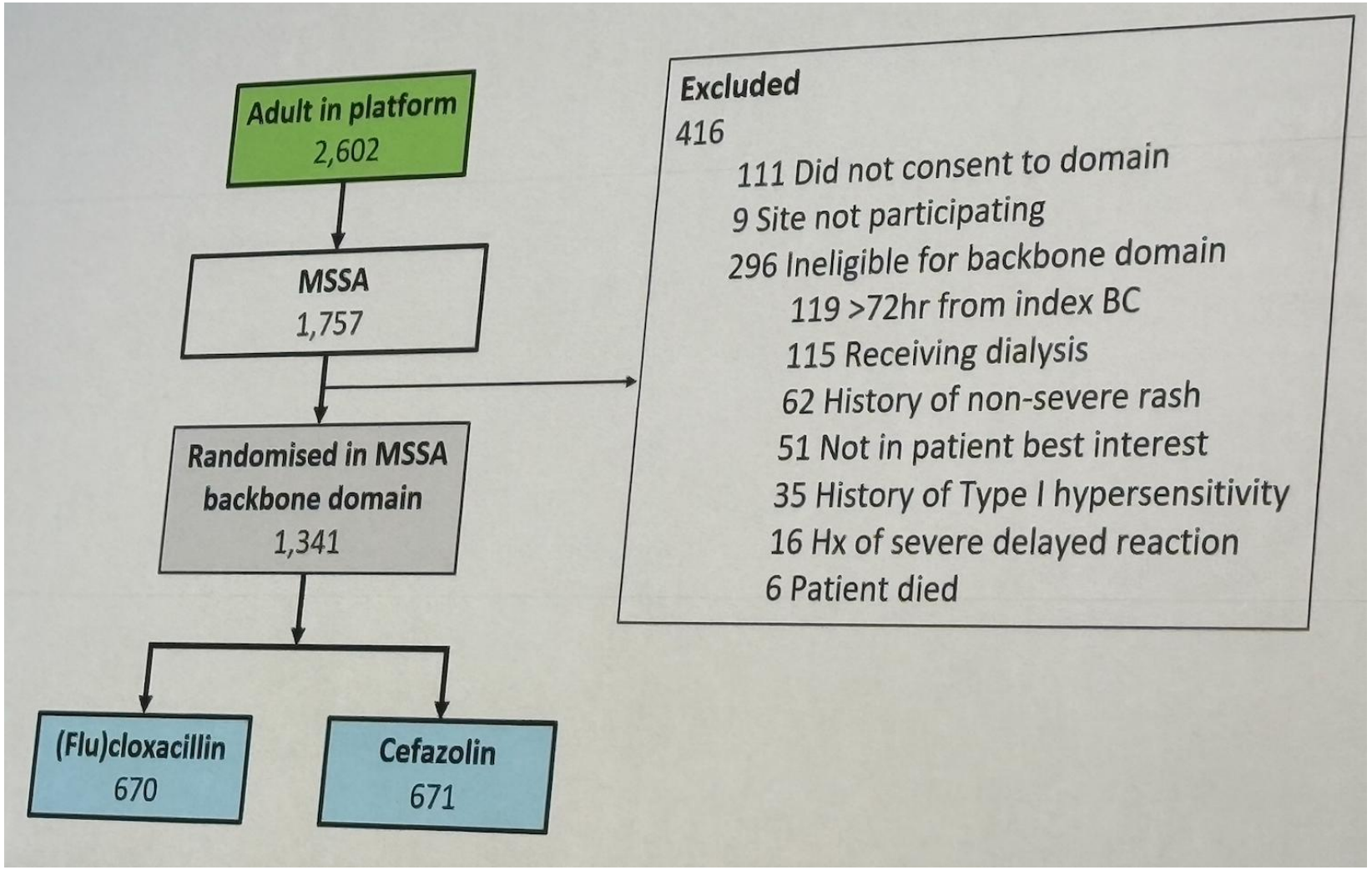
Adjusted odds ratio (median, 95% CrI)	0.50 (0.26, 0.94)
Non-inferiority, Pr(OR<1.2):	0.9975
Superiority, Pr(OR<1.0):	0.9843



https://www.snaptrial.com.au/

ESCMID Global 2025

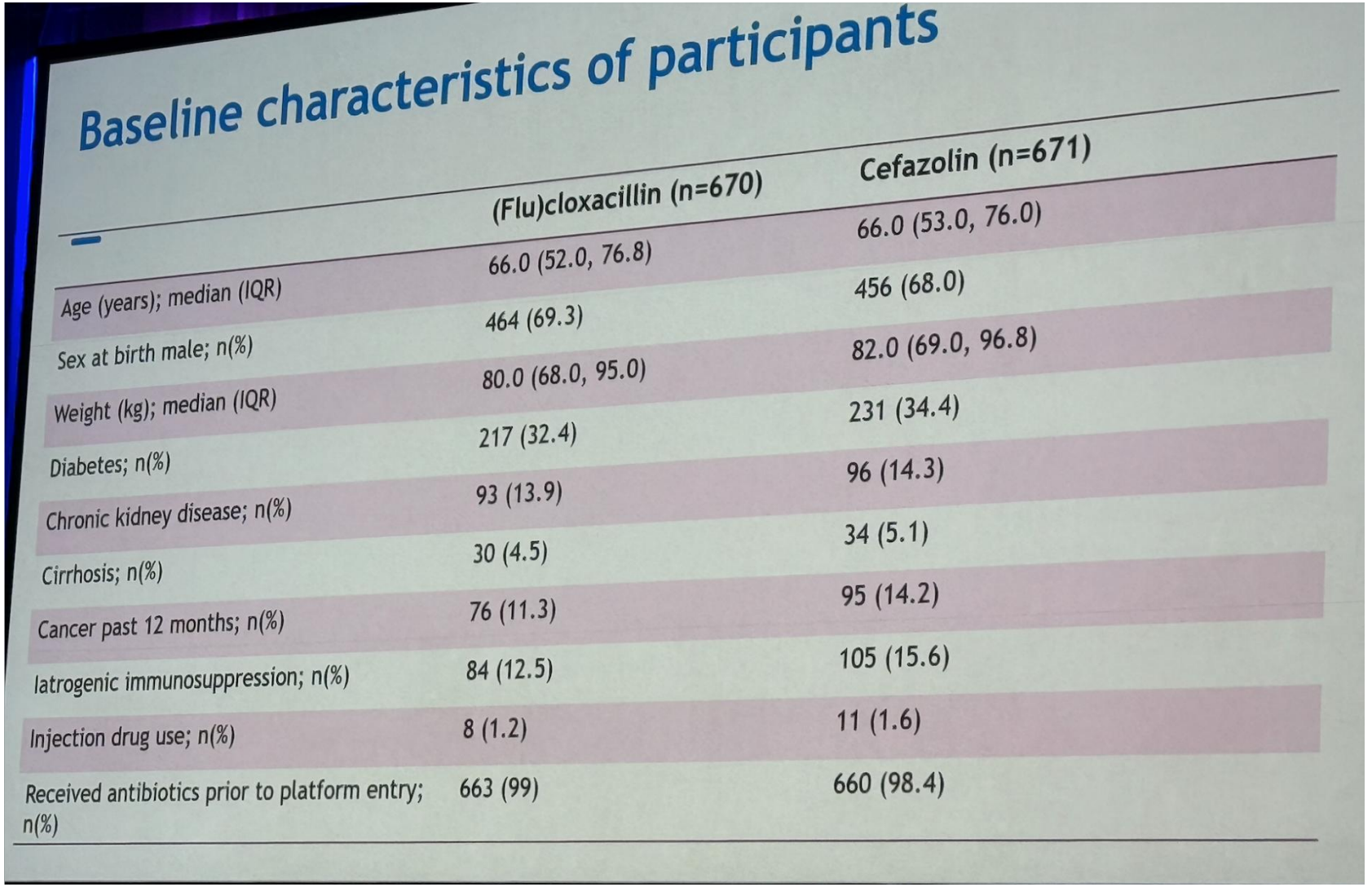
Cefazolin vs (flu)kloksacilin za MSSA



https://www.snaptrial.com.au/

ESCMID Global 2025

Cefazolin vs (flu)kloksacilin za MSSA



Baseline characteristics of participants

	(Flu)cloxacillin (n=670)	Cefazolin (n=671)
Age (years); median (IQR)	66.0 (52.0, 76.8)	66.0 (53.0, 76.0)
Sex at birth male; n(%)	464 (69.3)	456 (68.0)
Weight (kg); median (IQR)	80.0 (68.0, 95.0)	82.0 (69.0, 96.8)
Diabetes; n(%)	217 (32.4)	231 (34.4)
Chronic kidney disease; n(%)	93 (13.9)	96 (14.3)
Cirrhosis; n(%)	30 (4.5)	34 (5.1)
Cancer past 12 months; n(%)	76 (11.3)	95 (14.2)
Iatrogenic immunosuppression; n(%)	84 (12.5)	105 (15.6)
Injection drug use; n(%)	8 (1.2)	11 (1.6)
Received antibiotics prior to platform entry; n(%)	663 (99)	660 (98.4)

https://www.snaptrial.com.au/

ESCMID Global 2025

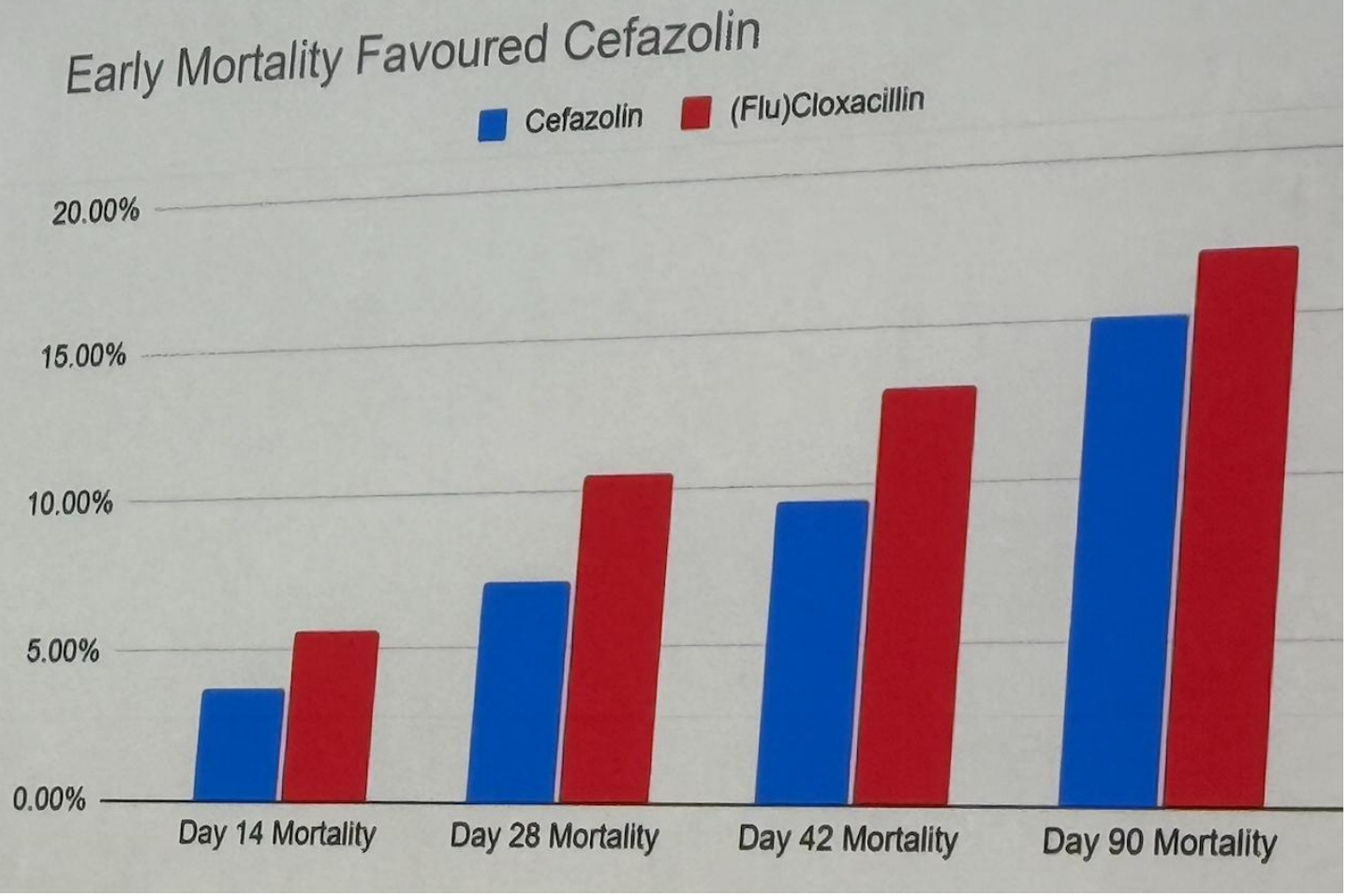
Cefazolin vs (flu)kloksacilin za MSSA

	(Flu)cloxacillin (n=670)	Cefazolin (n=671)
All-cause mortality at 90 days		
Yes	109 (17.0)	97 (15.0)
Missing	28 (4.2)	26 (3.9)
Adjusted odds ratio (median, 95% CrI)		0.81 (0.59, 1.12)
Non-inferiority, Pr(OR<1.2):		0.9922
Superiority, Pr(OR<1.0):		0.8978

https://www.snaptrial.com.au/

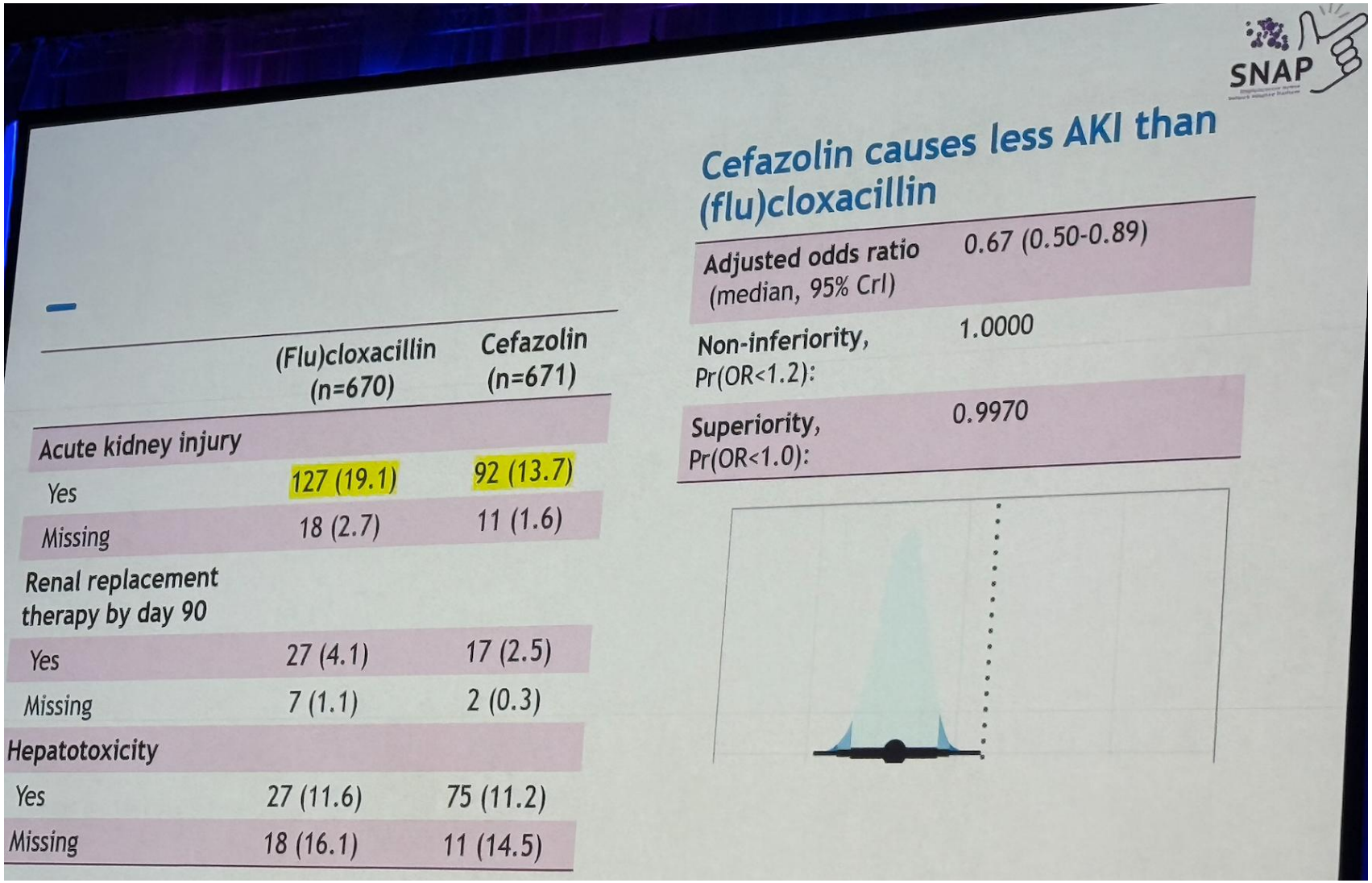
Cefazolin vs (flu)kloksacilin za MSSA

Mortality time point	OR cefazolin vs (flu)cloxacillin	Prob OR<1 (superiority)
14 days	0.67	0.9411
28 days	0.61	0.9919
42 days	0.66	0.9887



https://www.snaptrial.com.au/

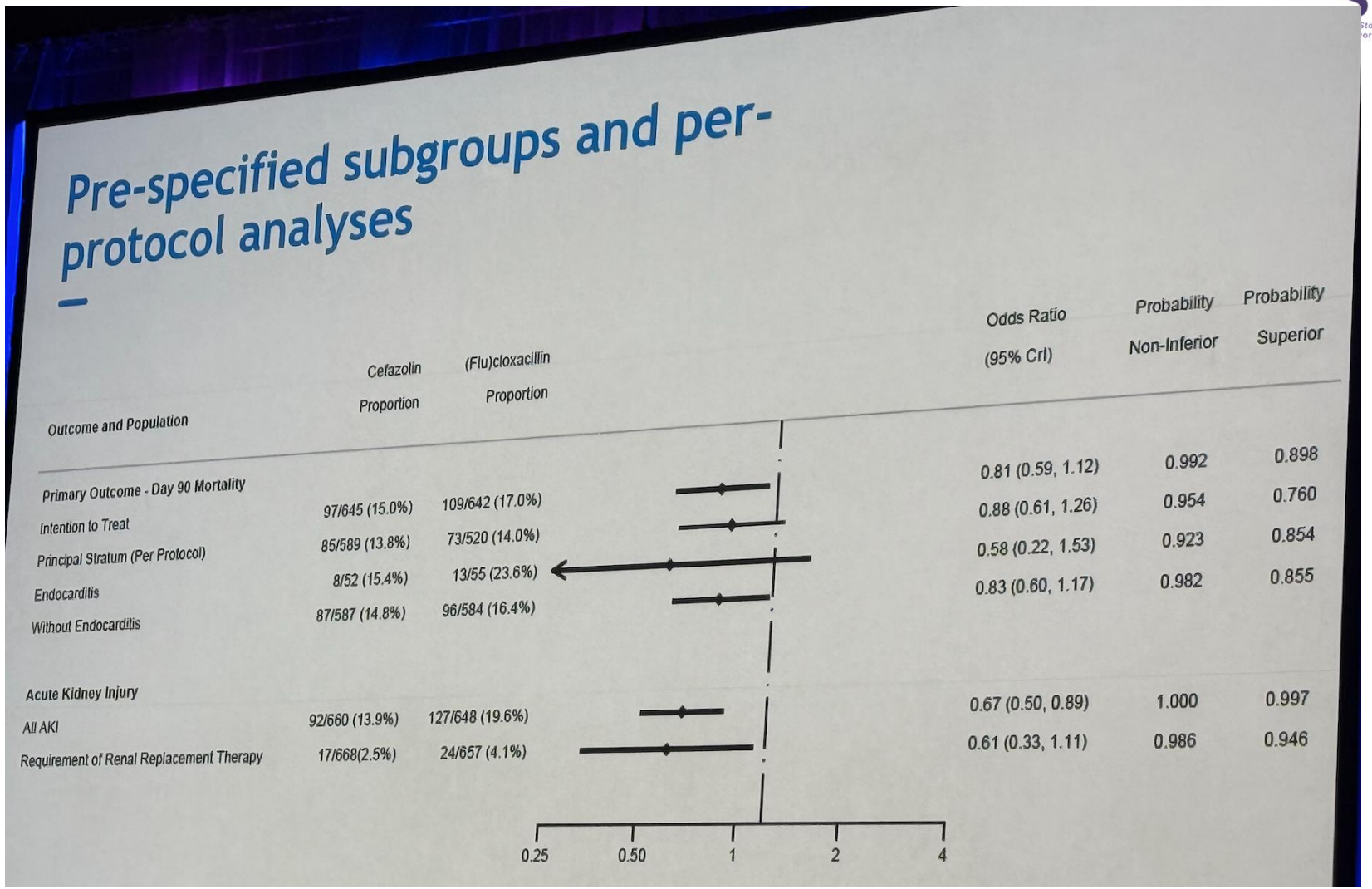
Cefazolin vs (flu)kloksacilin za MSSA



https://www.snaptrial.com.au/

ESCMID Global 2025

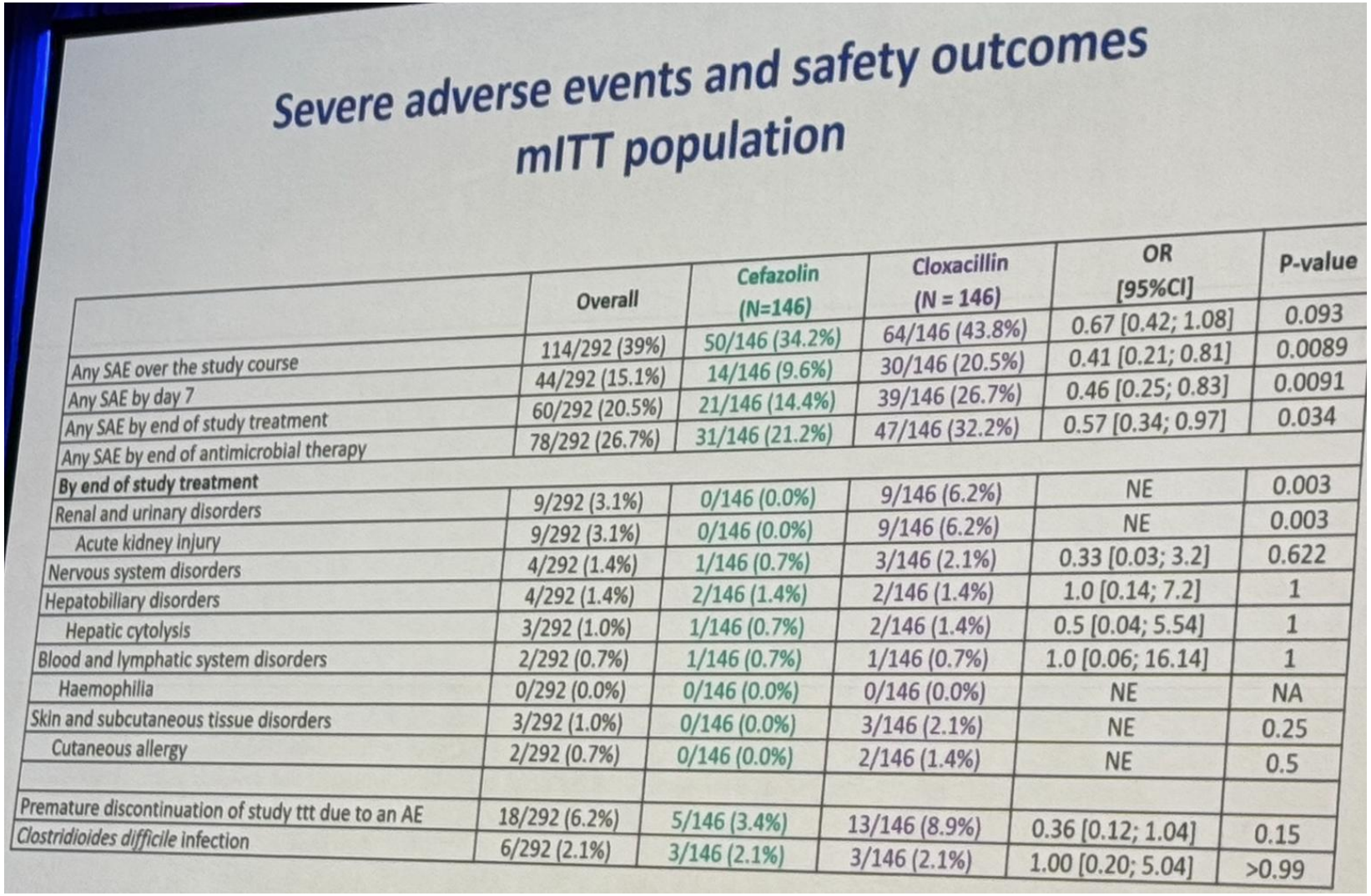
Cefazolin vs (flu)kloksacilin za MSSA



https://www.snaptrial.com.au/

ESCMID Global 2025

Cefazolin vs (flu)kloksacilin za MSSA



Severe adverse events and safety outcomes
mITT population

	Overall	Cefazolin (N=146)	Cloxacillin (N = 146)	OR [95%CI]	P-value
Any SAE over the study course	114/292 (39%)	50/146 (34.2%)	64/146 (43.8%)	0.67 [0.42; 1.08]	0.093
Any SAE by day 7	44/292 (15.1%)	14/146 (9.6%)	30/146 (20.5%)	0.41 [0.21; 0.81]	0.0089
Any SAE by end of study treatment	60/292 (20.5%)	21/146 (14.4%)	39/146 (26.7%)	0.46 [0.25; 0.83]	0.0091
Any SAE by end of antimicrobial therapy	78/292 (26.7%)	31/146 (21.2%)	47/146 (32.2%)	0.57 [0.34; 0.97]	0.034
By end of study treatment					
Renal and urinary disorders	9/292 (3.1%)	0/146 (0.0%)	9/146 (6.2%)	NE	0.003
Acute kidney injury	9/292 (3.1%)	0/146 (0.0%)	9/146 (6.2%)	NE	0.003
Nervous system disorders	4/292 (1.4%)	1/146 (0.7%)	3/146 (2.1%)	0.33 [0.03; 3.2]	0.622
Hepatobiliary disorders	4/292 (1.4%)	2/146 (1.4%)	2/146 (1.4%)	1.0 [0.14; 7.2]	1
Hepatic cytolysis	3/292 (1.0%)	1/146 (0.7%)	2/146 (1.4%)	0.5 [0.04; 5.54]	1
Blood and lymphatic system disorders	2/292 (0.7%)	1/146 (0.7%)	1/146 (0.7%)	1.0 [0.06; 16.14]	1
Haemophilia	0/292 (0.0%)	0/146 (0.0%)	0/146 (0.0%)	NE	NA
Skin and subcutaneous tissue disorders	3/292 (1.0%)	0/146 (0.0%)	3/146 (2.1%)	NE	0.25
Cutaneous allergy	2/292 (0.7%)	0/146 (0.0%)	2/146 (1.4%)	NE	0.5
Premature discontinuation of study ttt due to an AE	18/292 (6.2%)	5/146 (3.4%)	13/146 (8.9%)	0.36 [0.12; 1.04]	0.15
Clostridioides difficile infection	6/292 (2.1%)	3/146 (2.1%)	3/146 (2.1%)	1.00 [0.20; 5.04]	>0.99

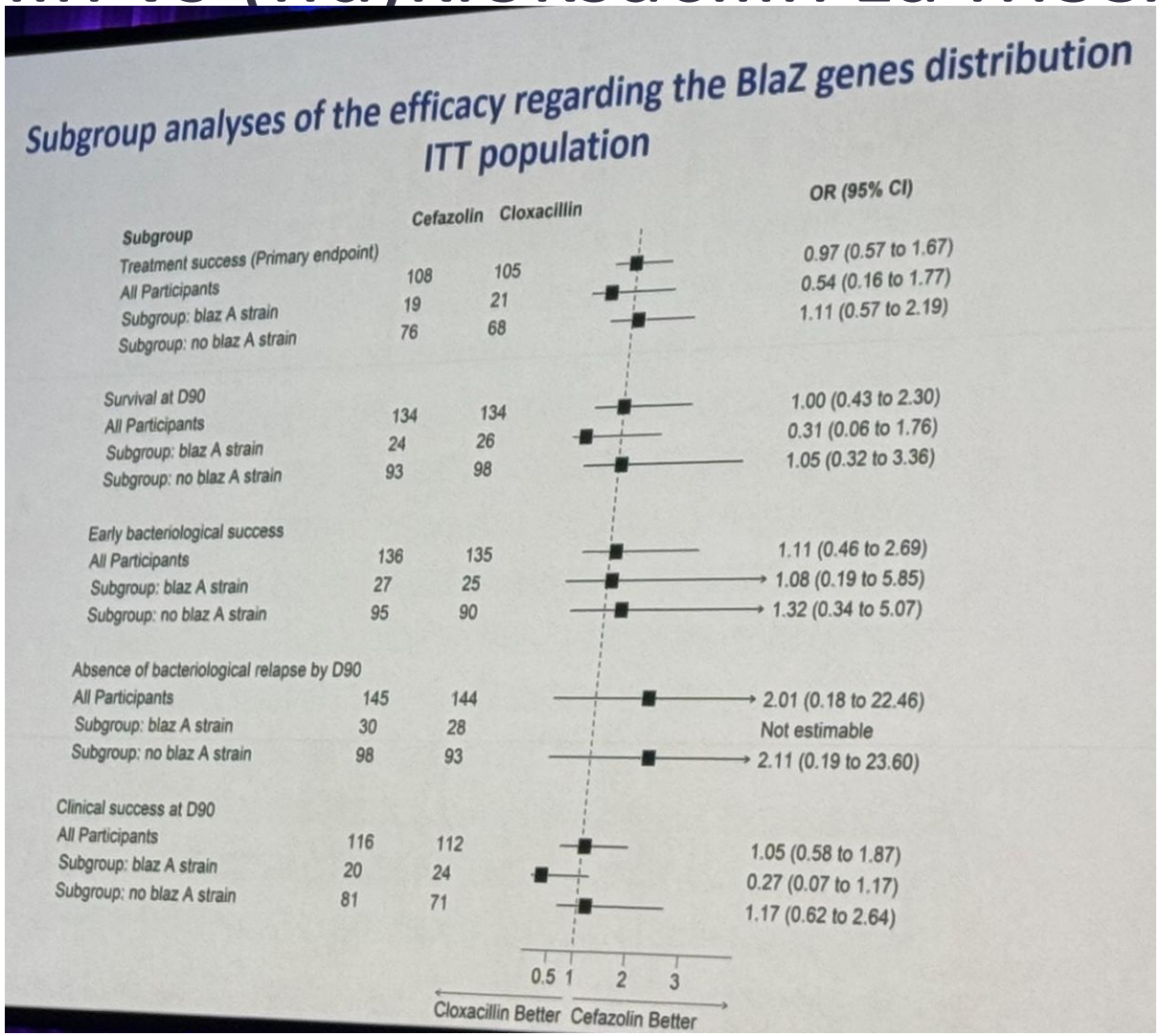
https://www.snaptrial.com.au/

ESCMID Global 2025

Cefazolin vs (flu)kloksacilin za MSSA

- *blazA*
  - gen, ki kodira betalaktamazo →potencialna razgradnja cefazolina
- “inoculum effect”
  - Zmanjšana učinkovitost cefazolina ob večjih koncentracijah bakterij
    - Ni potrjeno v vseh raziskavah

Cefazolin vs (flu)kloksacilin za MSSA



https://www.snaptrial.com.au/

ESCMID Global 2025

https://www.snaptrial.com.au/

SNAP platforma

- Preliminarni rezultati
  - Penicilin vsaj enako učinkovit kot (flu)kloksacilin za zdravljenje PSSA
  - Manj neželeneih učinkov
  - Cefazolin vsaj enako učinkoivt kot (flu)kloksacilin za zdravljenje MSSA
    - Manj neželenih učinkov

- Nerazrešena vprašanja
  - *BlazA*
  - Inoculum effect
  - Cefazolin vs penicilin za PSSA
  - Cefazolin za MSSA okužbe osrednejga živčevja

Sklep

- *S. aureus* sepsa/septični šok
  - Velika pojavnost
  - Velika smrtnost
  - Nerazrešen optimalen način in trajanje zdravljenja
  - Pomembno odstraniti izvor okužbe
  - Ustrezne preiskave za izključitev možnih vnetnih žarišč

Sklep

- Novi trendi v zdravljenju
  - Možnost prehoda na per os zdravljenje
  - Skrajševanje zdravljenja
  - Cefazolin namesto (flu)kloksacilina za MSSA
  - Penicilin namesto (flu)kloksacilina za PSSA

Caravaggio

THE LANCET
Infectious Diseases

CORRESPONDENCE · Volume 18, Issue 11, P1178, November 2018 Download Full Issue

Did Caravaggio die of *Staphylococcus aureus* sepsis?

Michel Drancourt [a] · Rémi Barbieri [a] · Elisabetta Cilli [b] · Giorgio Gruppioni [b] · Alda Bazaj [c] · Giuseppe Cornaglia [c] · et al. Show more

Affiliations & Notes Article Info Linked Articles (2)

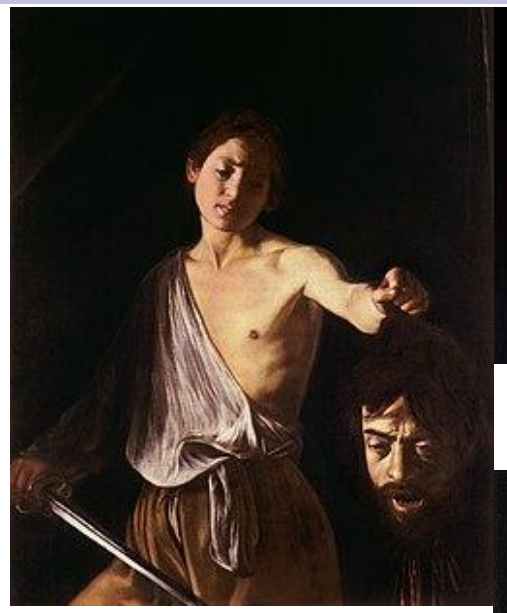
Caravaggio

- Italijanski slikar 1571 – 1610
- Barok
- Zelo vzkipljiv
- Večkrat udeležen v pretepih
  - Udeležen tudi pri ubojih
- Mesec pred smrtjo poškodba v pretepu
- Nenadoma zbolel z visoko vročino in znaki sepse

https://en.wikipedia.org/wiki/Caravaggio

Caravaggion

- Ohranjeno okostje
  - Visoke koncentracije svinca
    - Znano nepazljiv pri uporabi barv s svincem
  - Primerjava DNK z drugimi člani družine Merisi
    - edinstven Y-STR haplotip
  - Analiza zobne pulpe
    - Nespecifična metagenomska analiza - *S. aureus*
    - Specifična kvantitativna PCR preiskava na *S. aureus*
    - Metaproteomična analiza - *S. aureus*
  - Znaki osteomielitisa
  - Zaključek: smrt zaradi *S. aureus* sepse



Drancourt, Michel et al. Did Caravaggio die of Staphylococcus aureus sepsis? The Lancet Infectious Diseases, Volume 18, Issue 11, 1178
https://en.wikipedia.org/wiki/Caravaggio