UNIVERSITÄTS KLINIKUM jena

UpDate: Endokarditis

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ESC European Society of Cardiology
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ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM)

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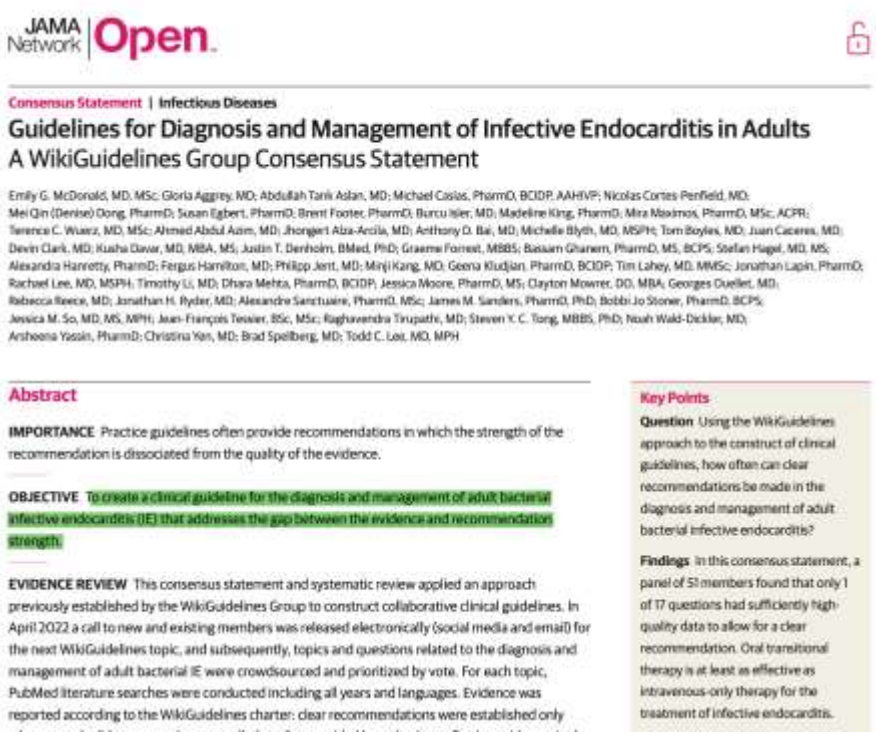

JAMA Network Open.

Consensus Statement | Infectious Diseases

Guidelines for Diagnosis and Management of Infective Endocarditis in Adults
A WikiGuidelines Group Consensus Statement

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Abstract

IMPORTANCE Practice guidelines often provide recommendations in which the strength of the recommendation is dissociated from the quality of the evidence.

OBJECTIVE To create a clinical guideline for the diagnosis and management of adult bacterial infective endocarditis (IE) that addresses the gap between the evidence and recommendation strength.

EVIDENCE REVIEW This consensus statement and systematic review applied an approach previously established by the WikiGuidelines Group to construct collaborative clinical guidelines. In April 2022 a call to new and existing members was released electronically (social media and email) for the next WikiGuidelines topic, and subsequently, topics and questions related to the diagnosis and management of adult bacterial IE were crowdsourced and prioritized by vote. For each topic, PubMed literature searches were conducted including all years and languages. Evidence was reported according to the WikiGuidelines charter: clear recommendations were established only

Key Points

Question Using the WikiGuidelines approach to the construct of clinical guidelines, how often can clear recommendations be made in the diagnosis and management of adult bacterial infective endocarditis?

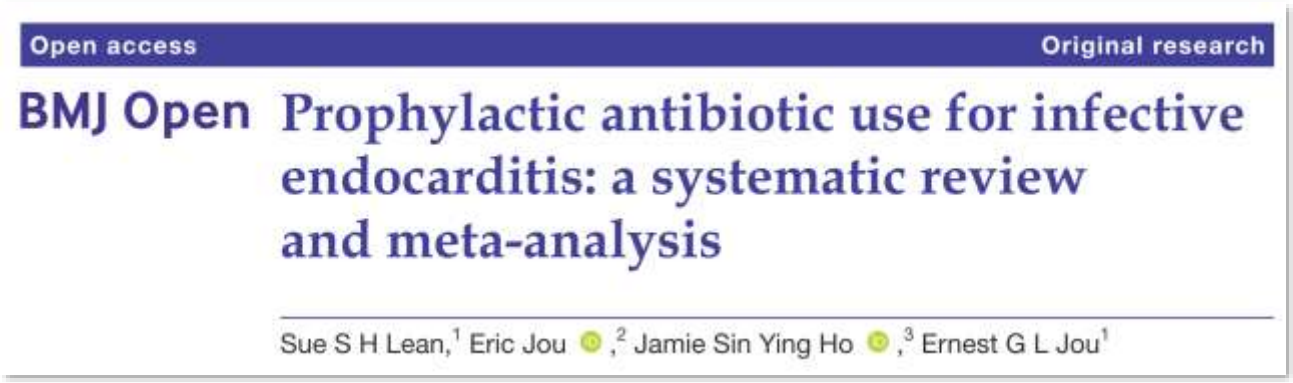
Findings In this consensus statement, a panel of 51 members found that only 1 of 17 questions had sufficiently high-quality data to allow for a clear recommendation. Oral transitional therapy is at least as effective as intravenous-only therapy for the treatment of infective endocarditis.

→ 3/79 Schlüsselempfehlungen Level A
→ Oralisierung, PAP, prä-OP Screening

→ 1/17 Fragen ausreichend Evidenz
→ Oralisierung

European Heart Journal (2023) 00, 1–95

JAMA Network Open. 2023;6(7):e2326366.



Open access Original research

BMJ Open

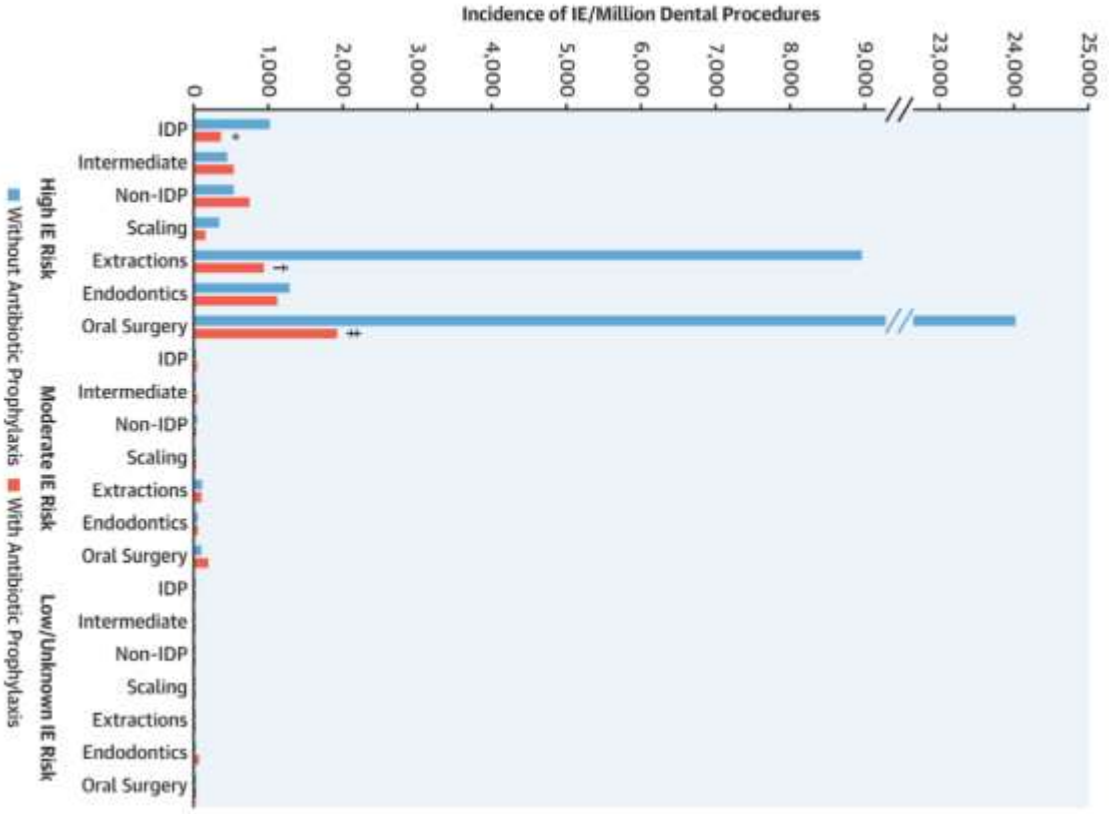
Prophylactic antibiotic use for infective endocarditis: a systematic review and meta-analysis

Sue S H Lean,[1] Eric Jou ,[2] Jamie Sin Ying Ho ,[3] Ernest G L Jou[1]

- 38 Beobachtungsstudien, >> 150.000 Patienten
- Endokarditisfälle < 3 Monate nach Zahnarztbesuch
- 11% (95% CI 0.08 - 0.16) aller Endokarditisfälle
- Erreger (Zahnarzt-assoz. vs. no-Zahnarzt):
  - S. viridans 69% vs. 21%, p=0.003
  - HACEK 13% vs. 5%, p=0.38
  - Staphylococcus 3% vs. 29%, p=0.002
  - Enterokokken 0.3% vs. 8%, p=0.35

Lean SSH, et al. BMJ Open 2023;13:e077026.

Endokarditisrisiko nach Zahnarztbesuch



- 8 Mio US-Bürger
- Endokarditisprophylaxe

  OR 0.49 (0.29-0.85; sig)

<u>Moderates Risiko:</u>
erworbene Herzklappen-fehlfunktion, azyanotische angeborene Herzfehler (nicht als Hochrisiko spezifiziert), HCM, Mitralklappenprolaps oder Regurgitation

mit Prophylaxe ohne Prophylaxe

Scaling: Zahnsteinentfernung, Endodontics: Wurzelbehandlung

Thornhill et al., Journal of the American College of Cardiology, Vol 80, Sept 2022

Endokarditisprophylaxe

(1) Patienten mit überstandener Endokarditis (I, B)

(2) Patienten mit Klappenersatz od. rekonstruierten Klappen (I, C)

(3) Patienten mit TAVI oder TPVI (I, C)

(4) Patienten mit unbehandelten zyanotischen angeborenen Herzfehlern und solche, die mit chirurgischen oder Transkatheterverfahren behandelt wurden, jedoch post-operative Shunts verbleiben oder Conduits bzw. andere Prothesen verwendet wurden. Nach chirurgischer Reparatur, wenn keine Restdefekte oder Klappenprothesen vorhanden sind, wird eine Prophylaxe nur für die ersten 6 Mon empfohlen. (I, C)

(5) Ventrikuläre Herzunterstützungssysteme (LVAD) (I, C)

Eine Antibiotikaprophylaxe sollte erwogen werden (should be considered) bei:

(5) Patienten mit kathetergestützter Reparatur der Mitral- und Trikuspidalklappe (IIa, C)

Eine Antibiotikaprophylaxe kann erwogen werden (maybe be considered) bei:

(6) Patienten nach einer Herztransplantation (III, C)

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Endokarditisprophylaxe

	Substanz*	Erwachsene	Kinder
Keine Allergie	Amoxicillin	2g p.o	50 mg/kg p.o
	Ampicillin	2g i.m. od. i.v.	50 mg/kg i.v. od. i.m.
	Cefazolin od. Ceftriaxon	1g i.m. od. i.v.	50 mg/kg i.v. od. i.m.
Ampicillin oder Penicillin Allergie	Cephalexin	2g p.o	50 mg/kg p.o
	Azithromycin Clarithromycin	500mg p.o	15 mg/kg p.o
	Doxycyclin	100mg p.o	<45 kg, 2.2 mg/kg p.o >45 kg, 100 mg p.o
	Cefazolin od. Ceftriaxon	1g i.m. od. i.v.	50 mg/kg i.v. od. i.m.

*Einmalgabe, 30-60 min vor Eingriff

Delgado V et al, European Heart Journal (2023) 00, 1–95

Contents lists available at ScienceDirect

Infectious Diseases Now

journal homepage: www.sciencedirect.com/journal/infectious-diseases-now

Guidelines

Antibiotic therapy and prophylaxis of infective endocarditis – A SPILF-AEPEI position statement on the ESC 2023 guidelines

Antibiotic prophylaxis regimens in patients at high risk of IE undergoing an at-risk dental procedure.

Situation	Antibiotic	Dose in adults	Dose in children
No allergy to penicillin	Amoxicillin IV or oral	2 g	50 mg/kg
Allergy to penicillin	Azithromycin*	500 mg	20 mg/kg
	Pristinamycin**	1000 mg	25 mg/kg*
	Cefazolin IV***	1 g	50 mg/kg

* Pristinamycin is contraindicated in children younger than 6 years.
** The paediatric dose of azithromycin has been adapted to the graduation system used for dispensing the product in children.
*** Contraindicated in case of allergy to cephalosporins or late severe allergy to penicillin; in this case, vancomycin may be used (15 mg/kg, 2 g maximum).

- TAVI / MitraClip PAP:
  → Ampicillin/Sulbactam

Infectious diseases now 55 (2025) 105011

Endokarditisprophylaxe

Recommendations	Class[a]	Level[b]
Antibiotic prophylaxis is recommended in dental extractions, oral surgery procedures, and procedures requiring manipulation of the gingival or periapical region of the teeth.[11,49,51,108]	I	B
Systemic antibiotic prophylaxis may be considered for high-risk[c] patients undergoing an invasive diagnostic or therapeutic procedure of the respiratory, gastrointestinal, genitourinary tract, skin, or musculoskeletal systems.[6,11]	IIb	C

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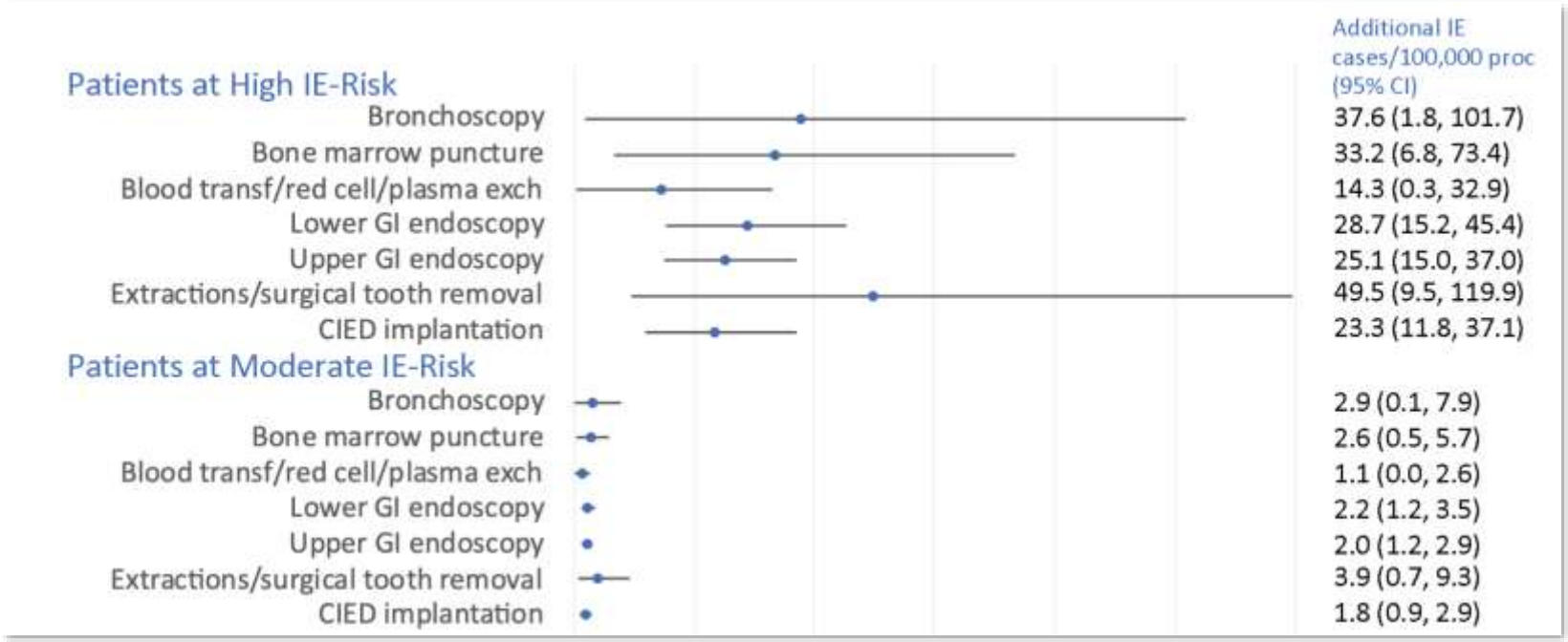
Endokarditisprophylaxe



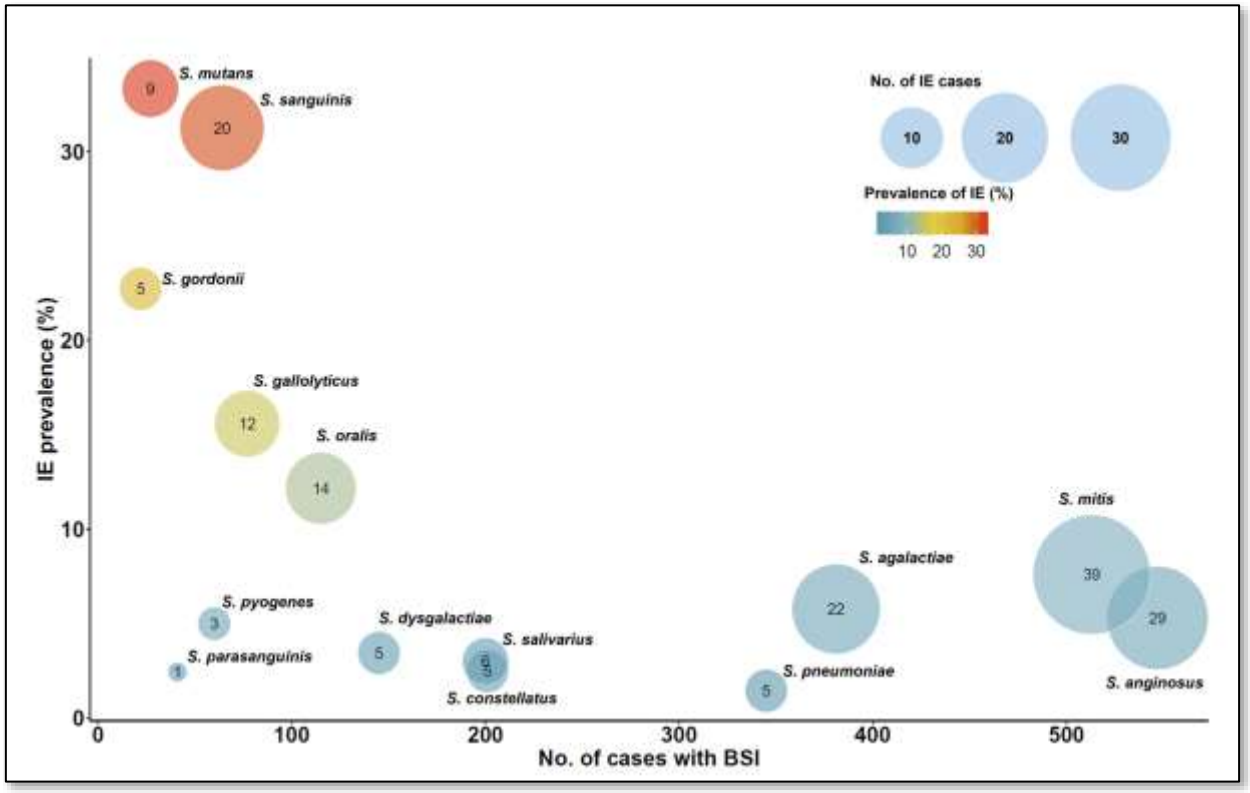
For these reasons, this Task Force no longer felt that a class III recommendation for antibiotic prophylaxis in high-risk patients undergoing non-dental medical procedures was appropriate, despite the limitations of observational data used to support this class IIb recommendation.

Thornhill MA et al, Heart 2022,0: 1-9

Majorkriterium: Mikrobiologie

Endokarditis-typische Mikroorganismen in 2 unabhängigen Blutkulturen:

- Orale Streptokokken (S. *mitis*, *sanguinis*, *anginosus*, *salivarius*, *downei*, and *mutans)*
- Streptococcus gallolyticus (früher S. bovis), HACEK-Gruppe, S. aureus, **E. faecalis**



Delgado V et al, European Heart Journal (2023) 00, 1–95
Seo H et al., Microbiol Spectr. 2023;11:e01049-23

Bildgebung

→ TEE: bei allen Patienten (außer Re-NVE)

→ Kardio CT: besser als TEE bei perivalvulären und periprosthetischen Komplikationen (Abszess, Pseudoaneurysma, Fisteln)

→ [18F]FDG-PET/CT:

- → PVE: 86% Sensitivität, 84% Spezifität
- → V.a. Pt. mit hohem klin. Verdacht für **PVE-IE aber nicht eindeutigem TEE**
  - → **hoher PPV**
- → **NVE: 31% Sensitivität**, 98% Spezifität
- → CIED-IE: 70% Sensitivität
- → Eine NV-IE oder CIED-IE, kann mittels PET/CT NICHT ausgeschlossen werden

Recommendations	Class[a]	Level[b]
Cardiac CTA is recommended in patients with possible NVE to detect valvular lesions and confirm the diagnosis of IE.[33,168,169]	I	B
[18F]FDG-PET/CT(A) and cardiac CTA are recommended in possible PVE to detect valvular lesions and confirm the diagnosis of IE.[22,129,209,210,237–239]	I	B
Cardiac CTA is recommended in NVE and PVE to diagnose paravalvular or periprosthetic complications if echocardiography is inconclusive.[20,168,169,185,186]	I	B
Brain and whole-body imaging (CT, [18F]FDG-PET/CT, and/or MRI) are recommended in symptomatic[c] patients with NVE and PVE to detect peripheral lesions or add minor diagnostic criteria.[22,197–200,210,213,240,241]	I	B
WBC SPECT/CT should be considered in patients with high clinical suspicion of PVE when echocardiography is negative or inconclusive and when PET/CT is unavailable.[213–216]	IIa	C
[18F]FDG-PET/CT(A) may be considered in possible CIED-related IE to confirm the diagnosis of IE.[22,129,209,210,237,238]	IIb	B
Brain and whole-body imaging (CT, [18F]FDG-PET/CT, and MRI) in NVE and PVE may be considered for screening of peripheral lesions in asymptomatic patients.[188,197–201]	IIb	B

TAVI-IE

- keine Vegetationen im TEE → 38-60%
- Vegetationen im Stent-Rahmen → 12-19%
- Vegetationen in 1/3 der Fälle außerhalb der Transkatheter-klappe (oft Mitralebene)
- FDG/PET*:
- 1 Mon post-Implant:
- → in 22% d. Fälle FDG-Signal um Klappe, meist >50% des Umfang
- Infektion: eher fokal, < 25% d. U.

Delgado V et al, European Heart Journal (2023) 00, 1–95
**Ghanem-Zoubi, Infect Dis Ther (2022) 11:1769–1777*

Gezielte Therapie

Streptokokken „S“*	**NV (4 Wo), PV (6 Wo):** Penicillin 12-18 Mio IU, Ampicillin od. Ceftriaxon 2g 1x tgl, (Verkürzung der Therapie auf 2 Wochen in Kombination mit Gentamicin bei NVE möglich)
Streptokokken „I“ oder „R“ *	**NV (4 Wo), PV (6 Wo):** Penicillin 24 Mio IU, Ampicillin od. Ceftriaxon 2g 1x tgl jeweils PLUS Gentamicin für 2 Wochen

Delgado V et al, European Heart Journal (2023) 00, 1–95

* früher MHK basierte Empfehlungen


EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

EUCAST guidance document on Infective Endocarditis:

Reporting of antimicrobial susceptibility testing results

December 2024

→ <u>bis 31.12.24; S viridians</u>: MHK ≤ 0,25 mg/l = S, 0,5 - 2mg/l = I, >2 mg/l = R

→ <u>ab 1.1.25, S. viridans</u>: MHK ≤ 0,25 mg/l = S, >0.25 mg/l = R

→ <u>Argumentation</u>:

1) hohe Penicillin-Dosis bei EUCAST (=12 Mio IU/24h) entspricht sowieso ESC-Standarddosis bei Endokarditis mit "S" Streptokokken (12-18 Mio IU/24h)
2) *Pilmis, B et al, 2019*: 414 Pt. mit Viridans-Streptokokken-IE:
   → Sterblichkeit höher bei Amox-MIC 0,25 - 2mg/l vs. ≤ 0,125 mg/l, AG kein Benefelt
3) *Escrihuela-Vidal, Francesc et al., 2023*: 914 Pt. mit Viridans-Streptokokken-IE**:**
   → n=688, PEN-S (MIC ≤0.125 mg/L) vs. 226. Pt. PEN-I (MIC 0,25–1 mg/L)
   → PEN-I: 21% Pen+AG,, 30% Cephalo+AG, 32% Cephalo-Mono
   <u>MV-Analyse</u>: Cephalo Mono nicht mit erhöhter Sterblichkeit assoziiert

Clinical Microbiology and Infection 25 (2019) 518–520

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Third-generation cephalosporin and carbapenem resistance in *Streptococcus mitis/oralis*. Results from a nationwide registry in the Netherlands

J. van Prehn [1,*], M.I. van Triest [2], W. Altorf-van der Kuil [2], K. van Dijk [1] on behalf of the Dutch National AMR Surveillance Study Group

Penicillin (n=4164):

→ S = 87.2%

→ I = 6.7%

→ R = 6.0% (n=250)

Amoxicillin/ampicillin (n=2019): R= 5.8%

Ceftriaxon (n=2079): R= 7.6%

Penicillin susceptibility	Amoxicillin/ampicillin susceptibility			Cefotaxime/ceftriaxone susceptibility		
	Susceptibility reported	Resistant		Susceptibility reported	Resistant	
	(n)	(n)	%	(n)	(n)	%
Penicillin S	1799	9	0.5	1832	31	1.7
Penicillin I	126	31	24.6	138	53	38.0
Penicillin R	94	77	81.9	109	75	69.0

JAC Antimicrob Resist, 2024

UKJ,2024

Resistenzen für Erreger vergrünende Streptokokken

	Antibiotika/Legende	sensibel	intermediär	resistent	Testungen
1	Penicillin G	88%	10%	2%	240
2	Vancomycin	100%	0%	0%	235
3	Rifampicin	100%	0%	0%	22
4	Clindamycin	84%	0%	16%	229
5	Linezolid	100%	0%	0%	12
6	Erythromycin	50%	0%	50%	18
7	Ampicillin	93%	5%	2%	212
8	Ampicillin/Sulbactam	100%	0%	0%	6
9	Cefotaxim	93%	1%	6%	103
10	Piperacillin/Tazobactan	100%	0%	0%	3
11	Meropenem	100%	0%	0%	2
12	Levofloxacin	68%	11%	21%	28
13	Tigecyclin	96%	0%	4%	23
14	Amoxycillin/Clavulansä	100%	0%	0%	6
15	Ceftriaxon	94%	1%	5%	176
16	Doxycyclin	100%	0%	0%	17
17	Moxifloxacin	92%	0%	8%	171
18	Teicoplanin	100%	0%	0%	232
19	Trimethoprim/Sulfamet	42%	0%	58%	24

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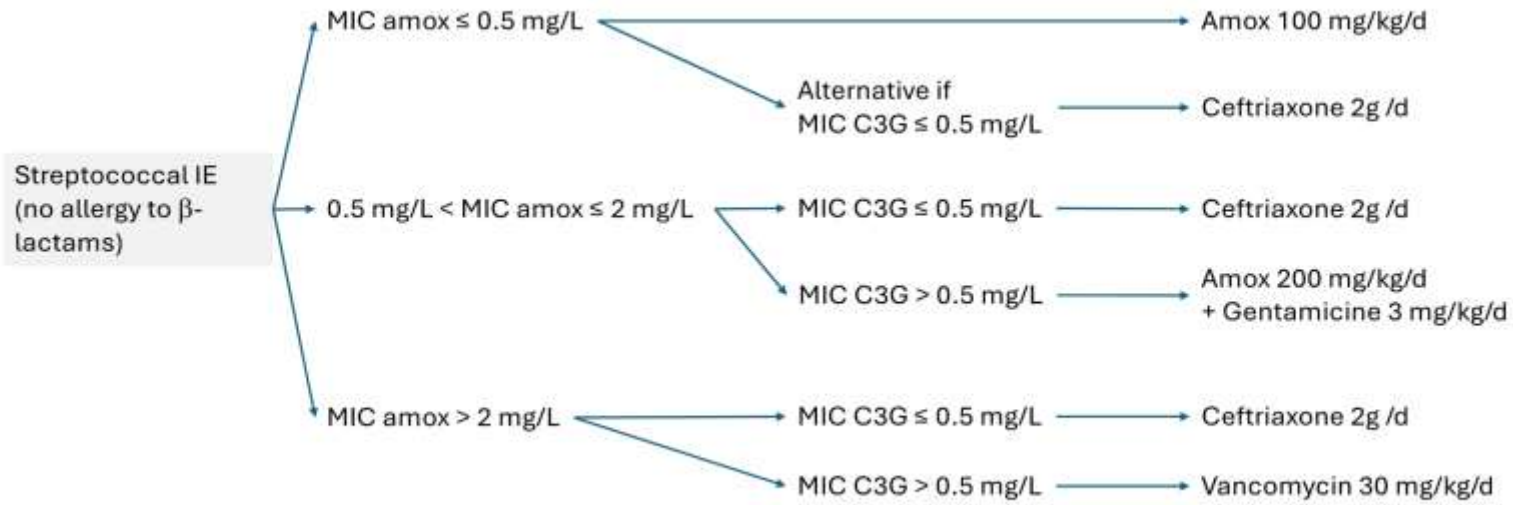


Fig. 1. Algorithm for the choice of antibiotic in streptococcal IE according to the MICs of amoxicillin and ceftriaxone. Abbreviations: MIC: minimal inhibitory concentration, C3G: ceftriaxone, amox: amoxicillin.

Gezielte Therapie

Staphylokokken **→ Oxa sensibel**	**NV (4 Wo)**: Flucloxacillin od. Cefazolin **PV (6 Wo)**: PLUS Rifampicin 6 Wo + Gentamicin 2 Wo **Pen-Allergie**: NV: Dapto + Fosfo (od. Ceftarolin); PV: Dapto + (Fosfo od. Ceftarolin od. Genta) + Rifa
Staphylokokken **→ Oxa resistent**	**NV (4-6 Wo)**: Vancomycin; Alternativ: Daptomycin + (Flucloxacillin od. Fosfomycin od. Ceftarolin) **PV (6 Wo)**: Vanco + Rifa 6 Wo + Gentamicin 2 Wo

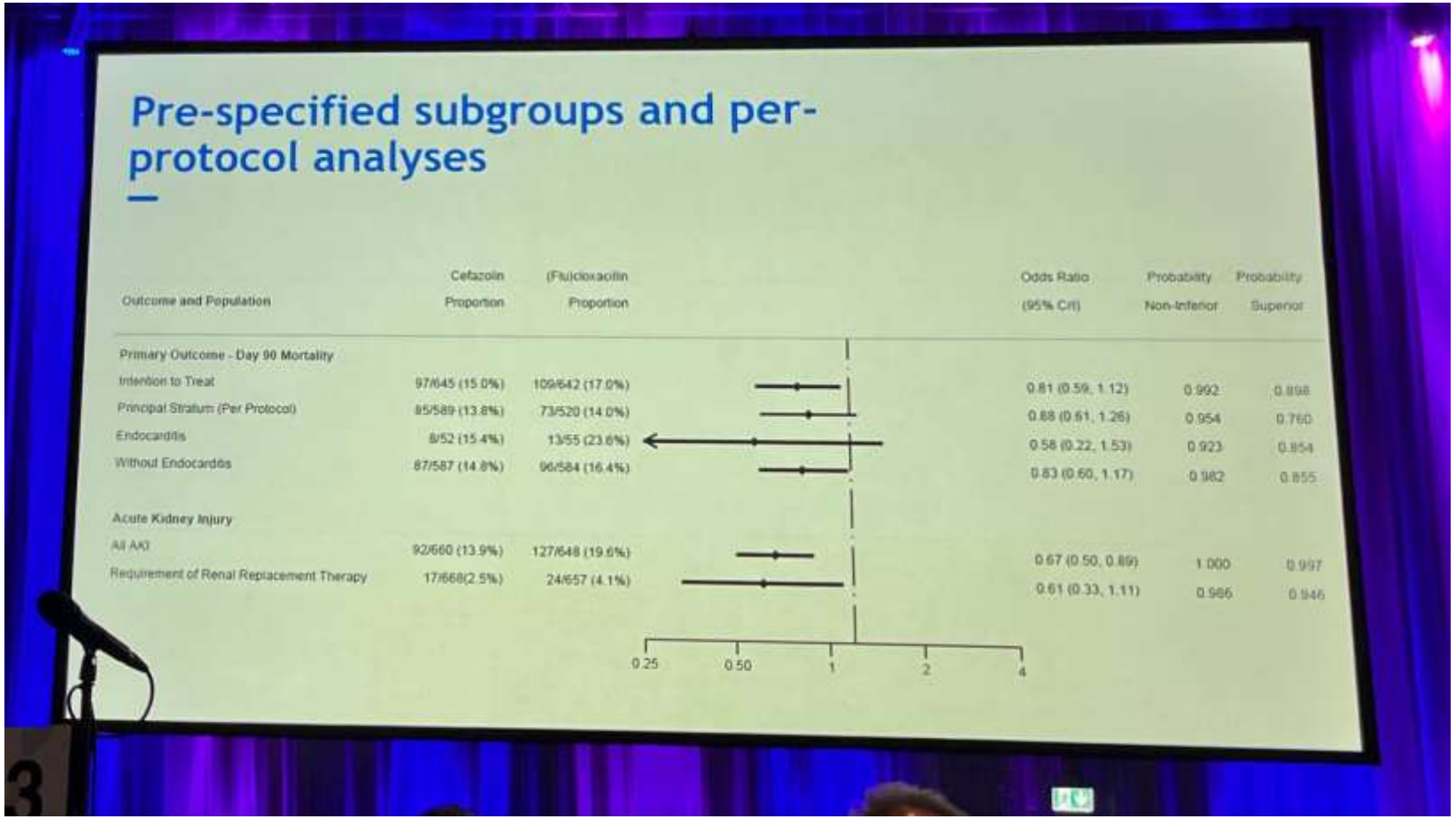
Delgado V et al, European Heart Journal (2023) 00, 1–95

SNAP-Trial

1. Flucloxacillin n=670 vs. Cefazolin n=671
2. Pat. mit Endokarditis n=107 (8.0%)
3. Primary Endpoint (90d Sterblichkeit):
   → Cefazolin 15% vs. Flucloxacillin 17%
   → adj.OR 0.81 (0.59, 1.21), non-inferior
4. Secondary Endpoint AKI/RRT:
   → AKI: Cefazolin 13.9% vs. Flucloxacillin 19.6%, sig
   → RRT: Cefazolin 2.5% vs. Flucloxacillin 4.1%, sig

Davis J, presented at ECCMID Global 2025

SNAP-Trial



Davis J, presented at ECCMID Global 2025

Konsolidierungstherapie

Bei stabilem Pat. ab 10d (od. 7d post-OP):

→Oralisierung (Idem zu POET), APAT od. langwirksame Glykopeptide (z.B. Dalbavancin)

Stabil definiert als:

- *S. aureus*, KNS, Streptokokken, *E. faecalis*
- CRP <25% Max., od. <20mg/L u. Leukos <15GpT/L
- mind. 48h Fieberfrei
- BMI <40, Resorption gewährleistet, Compliance
- TEE ohne Abszess

Delgado V et al, European Heart Journal (2023) 00, 1–95

Fazit für Klinik und Praxis

- Weiterhin eingeschränkte „gute" Evidenz zur optimalen Therapie einer infektiösen Endokarditis
- ESC-LL: alte Konzepte übernommen und um „Baukasten" Kombinationen ergänzt
- Neu: Oralisierung und long-acting Glykopeptide in der Konsolidierungstherapie