## Conferencia Dr. Juan Gálvez: Lo mejor del año en infección cardiovascular

Noviembre 2022



Servicio de Enfermedades Infecciosas **Hospital Clínic - IDIBAPS** Universidad de Barcelona





**Contacto**: glcuervo@clinic.cat



## Metodología

- Revisión NO sistemática
- Términos de búsqueda: Endocarditis, Infective endocarditis, cardiac electronic devices infection, vascular graft infection.
- Restricciones:
  - Revistas más relevantes
  - Período: 15/09/2021 → 02/11/2022
- Criterios de selección:
  - Relevancia clínica
  - Ensayos clínicos
  - Estudios de cohortes multicéntricos



## Metodología

- Títulos revisados: 3038
  - Abstracts revisados: 84
    - Artículos seleccionados: 10



#### **Endocarditis infecciosa:**

- Epidemiología (1)
- Diagnóstico (1)



- Poblaciones especiales
  - TAVI (1)
  - **DECs** (1)
  - Pacientes ADVP (1)
- Complicaciones (1)
- Prevención (1)
- Tratamiento quirúrgico (1)





























## Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

THE LANCET Global Health

- Systematic review and meta-analysis of studies reporting primary data for the epidemiology of IE in Africa
- **Search terms**: "endocarditis", "Africa", and the name of all African countries
- Inclusion period of participants: 1990 to 2019 (articles published between 1996 and 2020)

2141 records

89 full-texts

42 articles

42 cross-sectional studies (mostly retrospective)

**Total population: 15097 patients** 



## Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

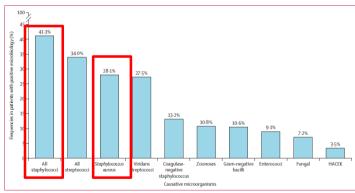
## THE LANCET Global Health

#### Risk factors

	Number of events	Total sample size	Number of studies		l <sup>2</sup>	Prevalence (95% CI)
Rheumatic heart disease	1112	2351	19		0.94	52.0% (42.4-61.5
Congenital heart disease	161	1941	15	+	0.57	7.2% (5.3-9.4)
Degenerative heart disease	90	1511	7	+	0.73	6.2% (4.1-8.6)
Previous infective endocarditis	56	1052	7	+	0.12	5.2% (3.9-6.7)
Prosthetic valve	438	1992	13	<u> </u>	0.74	20-3% (16-9-24-0
Diabetes	56	697	6	+	0.50	7-9% (5-3-10-8)
Intravenous drug use	75	983	5	<del></del>	0.86	7.9% (4.1-12.9)
Haemodialysis	31	748	3	+	0.00	4-1% (2-8-5-6)
Pacemaker	7	504	5	+	0.00	1.3% (0.5-2.4)
				0 10 20 30 40 50 60 Events per 100 observations		

Pooled prevalence of risk factors for infective endocarditis

#### Microbiology

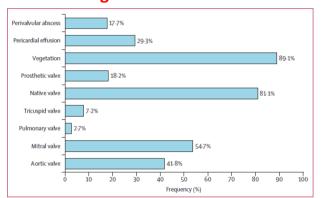


Pooled prevalence of microorganisms in positive blood cultures in infective endocarditis

## Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis

## THE LANCET Global Health

#### **Echocardiogram**



Pooled distribution of echocardiographic features of infective endocarditis

#### **Complications**

	Number of events	Total sample size	Number of studies		Incidence (95% CI)	I <sup>2</sup>
Death	441	1869	13	+	22.6% (19.5–25.9)	0.60
Heart failure	727	1674	10		47.0% (38.2-56.0)	0.87
Embolic events	378	1064	7		31.1% (22.2-40.8)	0.92
All stroke	222	1372	8	<del></del>	15.1% (11.8-18.8)	0.64
Ischaemic stroke	182	1120	7	<del></del>	14.2% (8.7-20.9)	0.91
Intracranial haemorrhage	52	890	6	+	5.8% (4.3-7.4)	0-00
Acute kidney injury	237	1022	5	<b>—</b>	22.8% (18.8-27.0)	0.66
Mycotic aneurysm	59	888	4	+	6.6% (5.0-8.3)	0-00
Splenic infarction	86	1364	8	<del></del>	4.6% (2.0-8.0)	0.90
Cerebral abscess	25	650	4	+	3.7% (2.4-5.3)	0-21
Conduction abnormalities	38	299	3		12-2% (2-6-27-5)	0.93
				0 10 20 30 40 50 60 Events per 100 observations		

Pooled incidence proportions of complications from infective endocarditis

Pooled rate of surgical treatment → 49.1%

Primer resumen exhaustivo de la epidemiología de la endocarditis en África

#### Take-home messages:

- La cardiopatía reumática es el FR más frecuente de El en adultos (y la C. congénita en niños)
- Los estafilococos son los microorganismos causantes más comunes
- La proporción de pacientes que reciben tratamiento quirúrgico por El, la frecuencia de complicaciones y las tasas de mortalidad son similares a las reportadas en países de ingresos altos (sesgo de referencia)

Articles

#### Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis



U.E.Nicoca MCIII. Shecamatologi

Jean Jacques Noubiap, Jan René Nikeck, Beckly Shu Kwondorn, Ulrich Flore Nyaqo

Background The epidemiology of infective endocarditis in Africa is inadequately characterised. We therefore aimed to comprehensively summarise the available data for the incidence, risk factors, clinical pattern, microbiology, and outcomes of infective endocarditis in Africa

Methods We did a systematic review and meta-analysis. We searched PubMed. Embase. African Index Medicus, and African Journals Online for all studies reporting primary data for the epidemiology of infective endocarditis in nonulations within Africa, published from incention to lan 14, 2021, irrespective of the language. We used the search terms "endocarditis", "Africa", and the name of all African countries in the search strategy. We excluded articles that Australia (I) Noobiap MO) did not include primary data, primary studies with a small sample size (<30 participants), and those that report findings from before 1990. We recorded data for study characteristics, sample size, criteria used to define infective endocarditis, risk factors, potential entry site, clinical patterns, microbiology profile, outcomes including complications such as embolic events, heart failure, acute kidney injury, and death, and predictors of death. We used random-effects Compresson (12 Nicork MD) meta-analysis method to pool estimates. This study is registered with PROSPERO, CRD42021243842.

Findings We retrieved 2141 records from the database and bibliographic searches, of which a total of 42 studies were obtain. France IV Steets included in this systematic review. Rheumatic heart disease was the most common risk factor for infective endocarditis in adults (52-0% 195% CI 42-4-61-51), whereas congenital heart disease was the most common risk factor for infective. for Heart Blochen Disorders, endocarditis in children (44-7% [29-5-60-5]), Microbiological testing (mostly blood cultures) was positive in 48-6% (95% CI 42 · 2-51 · 1) of patients with infective endocarditis, with Stuphylococcus species (41 · 3% [95% CI 36 · 2-46 · 5]) and Streptococcus species (34-0% [29-0-39-3]) the most commonly identified microorganisms. The pooled rate of surgical treatment of infective endocarditis was 49 · 1% (95% CI 43 · 2-55 · I). The pooled in-hospital mortality rate was 22.6% (95% CI 19.5-25.9). Other frequent complications included heart failure (47.0% [95% CI 38.2-56.0]), acute kidney injury (22 · 8% [18 · 8-27 · 0]), and embolic events (31 · 1% [22 · 2-40 · 7]).

Interpretation As the most prevalent risk factor in Africa, rheumatic heart disease should be central in interventions to reduce the burden of infective endocarditis on the continent. In tertiary hospitals with good access to cardiac surgery, the outcomes of infective endocarditis seem relatively similar to what has been reported in other parts of the world, especially in high-income countries.

#### **Funding None**

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Infective endocarditis is defined by infection of a native or regions and socioeconomic status. In high-income prosthetic cardiac valve, the endocardial surface, or an countries, the cardiac conditions predisposing to indwelling cardiac device.' Although infrequent, with an infective endocarditis have shifted from rheumatic heart annual incidence of about 2-12 cases per 100000 people,11 disease and congenital heart disease to a preponderance infective endocarditis is a life-threatening disease with of degenerative valve disease, prosthetic valves, and substantial mortality and disability. The mortality intracardiac devices. The spectrum of causative associated with infective endocarditis is estimated at about microorganisms has also changed, now dominated by 20% in hospital, increasing up to 30% at 6 months and Staphylococcus species compared with Streptococcus 40% at 5 years.12 This mortality varies substantially species a few decades ago.13 Furthermore, early treatment depending on the causative microorganism, underlying and widespread availability of cardiac surgery have cardiac conditions and comorbidities, and the earliness substantially improved the outcomes of infective and appropriateness of treatment, both medical and endocarditis in high-income countries. In Africa, as surgical.1 Infective endocarditis is commonly associated in most low-income and middle-income countries. with severe complications, such as heart failure, embolic rheumatic heart disease remains a major public health events including stroke, and renal failure, which con- problem,44 and access to cardiac services is inadequate tributes to increased mortality and long-term disability.11 for a large proportion of the population despite some

The pattern of infective endocarditis varies across

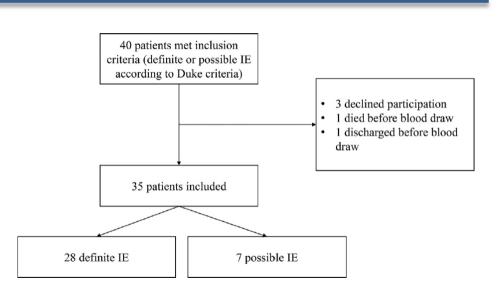
www.thelancet.com/lancetch Vol 10 January 2022

## Pathogen Detection in Infective Endocarditis Using Targeted Metagenomics on Whole Blood and Plasma: a Prospective Pilot Study



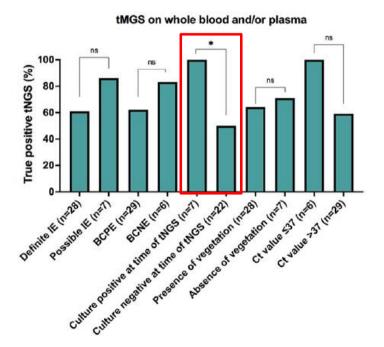
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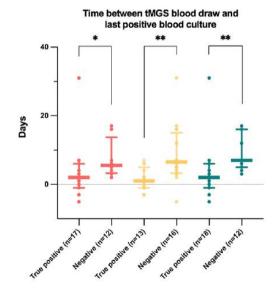
- Single center (Mayo Clinic)
- Prospective pilot study evaluating targeted metagenomic sequencing (tMGS)
- Target: V1-V3 region of the 16S ribosomal RNA gene
- Next-generation sequencing (Illumina MiSeqTM platform)



Flurin L, et al. J Clin Microbiol. 2022

	Positive tMGS test		
Subjects	Whole blood $n = 34$	Plasma n = 34	Combined $n = 35$
All infective endocarditis, n positive/n total (%)	20/34 (59%)	16/34 (47%)	23/35 (66%)
Blood culture positive infective endocarditis, n positive/n total BCPE (%)	17/28 (61%)	13/29 (45%)	18/29 (62%)
Blood culture positive on day tMGS collected, n positive/subgroup total (%)	7/7 (100%)	6/7 (86%)	7/7 (100%)
Blood culture negative on day tMGS collected, n positive/subgroup total (%)	10/21 (48%)	7/22 (32%)	11/22 (50%)
Blood culture negative infective endocarditis, n positive/n total BCNE (%)	3/6 (50%)	3/5 (60%)	5/6 (83%)



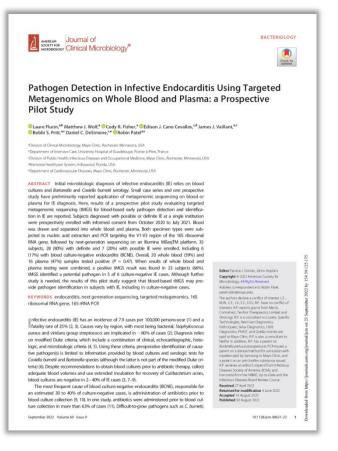


Flurin L, et al. J Clin Microbiol. 2022

 Uno de los primeros estudios prospectivos de cohortes que ha evaluado la utilidad de la tMGS en pacientes con El

#### **Take-home messages:**

- tMGS podría mejorar el diagnóstico de EI:
  - Identificando patógenos en BCN-IE (positividad influenciada por el tiempo transcurrido desde el último cultivo positivo)
  - Proporcionando un diagnóstico más rápido que el hemocultivo para patógenos de crecimiento lento



Flurin L, et al. J Clin Microbiol. 2022

#### Para leer más...



## 



Thomas Olsen, MD, PhD,\*† Ulrik Stenz Justesen, MD, DMSc,†‡
Jens Cosedis Nielsen, MD, PhD, DMSc,§¶ Ole Dan Jørgensen, MD, PhD,||\*\*
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Olsen T, et al. Heart Rhythm. 2022

Para leer más...



## Clinical Infectious Diseases



JOURNAL ARTICLE

ACCEPTED MANUSCRIPT

New perspectives for prosthetic valve endocarditis - impact of molecular imaging by FISHseq diagnostics 3

Maria M Hajduczenia, Frank R Klefisch, Alexander G M Hopf, Herko Grubitzsch, Miriam S Stegemann, Frieder Pfäfflin, Birgit Puhlmann, Michele Ocken, Lucie Kretzler, Dinah von Schöning ... Show more

Hajduczenia M, et al. Clin Infect Dis. 2022

### Sign of the Times: Updating Infective Endocarditis Diagnostic Criteria to Recognize *Enterococcus faecalis* as a Typical Endocarditis Bacterium



## Box 1. The modified Duke criteria (adapted from Li et al [1])

#### Major criteria

- · Blood culture positive for IE
- Typical microorganisms consistent with IE from 2 separate blood cultures:
  - Viridans streptococci, Streptococcus bovis, HACEK group, Staphylococcus aureus; or community-acquired enterococci, in the absence of a primary focus; or



Box 2. The proposed update to the "enterococcal adjusted Duke criteria" with modification shown in hold

#### Major criteria

- · Blood culture positive for IE
- Typical microorganisms consistent with IE from 2 separate blood cultures:
  - Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*, *Enterococcus faecalis*; or

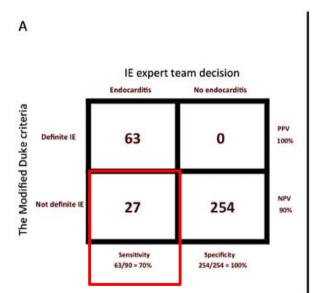
Dahl A, et al. Clin Infect Dis. 2022

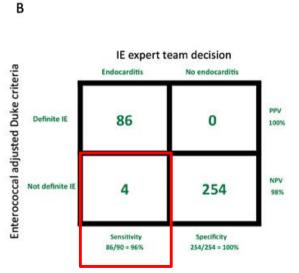
# Sign of the Times: Updating Infective Endocarditis Diagnostic Criteria to Recognize *Enterococcus faecalis* as a Typical Endocarditis Bacterium





- 344 patients with EF bacteremia
- All underwent Echo (74% TEE)





Dahl A, et al. Clin Infect Dis. 2022

 Paso importante para mejorar la concordancia entre la realidad clínica y los criterios diagnósticos de El

#### **Take-home messages:**

 Designar a Enterococcus faecalis como un patógeno de endocarditis "típico" (independientemente del lugar de adquisición o de la puerta de entrada), mejoró la sensibilidad para identificar correctamente la endocarditis definitiva Clinical Infectious Diseases









#### Sign of the Times: Updating Infective Endocarditis Diagnostic Criteria to Recognize *Enterococcus faecalis* as a Typical Endocarditis Bacterium

Anders Dahl, 12 Vance G. Fowler, José M. Miro, 24 and Niels E. Bruun 16

Department of Cardiology, Herier-Gentofte University Hospital Coperhagen, Dermark, "Department of Infectious Diseases, Hispital Clini-SIBAYS, University of Barcelone, Spain," Department of Infectious Diseases, Date University Hospital, Duham, North Cardina, USA, "Sector de Insectaçuois Biomédica en Red de Effermédide Infecciosas (EREINETS, Instituto de Salud Carlos III, Market Spain," Department of Cardiology, September 10, Cardiology, September 11, Cardio

The modified Duke criteria requires that Enterocoxas facults bacteremia must be both community-acquired and without known focus in order to be considered a microbiological "Major" diagnostic criterion in the diagnossis of infective endocarditis. We be-lieve that the microbiological diagnostic criteria should be updated to regard E. faccalis as a "typical" endocarditis bacterium as is currently the case, for example, viridans group streptococci and Staphylococcus aureus. Using data from a prospective study of 344 patients with E. faccalis bacterium exaulated with echocardingraphy, we demonstrate that designating E. faccalis as a "typical" endocarditis pathogen, regardless the place of acquisition or the portal of entry, improved the sensitivity to correctly identify definite endocarditis from 70% (modified Duke criteria) to 80% tenerococcal adultated Duke criteria.

Keywords. modified duke criteria; enterococcal adjusted duke criteria; sensitivity; community acquired; microbiological.

Since published in 2000, the modified Duke criteria [1] has been the internationally accepted basis [2, 3] for diagnosing, investigating, and classifying infective endocarditis (IE). Since the update of these criteria 2 decades ago, the characteristics of IE populations have evolved, with increasing rates of healthcare contact and more patients with implanted endovascular devices [4-6]. These demographic shifts have been accompanied by an increase in IE caused by Enterococcus faecalis [6-10]. Our understanding of bacteremia has also evolved, with the recognition of community-acquired, healthcare-associated, and nosocomial routes of acquisition [11]. However, the modified Duke criteria has not evolved accordingly. These criteria define clinically definite IE based on the presence of either: (a) 2 major criteria; (b) 1 major criterion and 3 minor criteria; or (c) 5 minor criteria (Box 1). The microbiological major criterion requires 2 separate blood cultures (BCs) positive for a "typical" IE microorganism or persistent bacteremia with a microorganism consistent with IE. The "typical" IE microorganisms are defined as viridans group streptococci (VGS), Streptococcus bovis, HACEK (Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, Kingella) group, Staphylococcus aureus, or community-acquired enterococci in the absence of

Received 30 August 2021; editorial decision 24 February 2022; published online 9 March 2022.

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Clinical Infectious Diseases® 2022;XX(XX):1-6

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a primary focus [1–3]. As a result, the current iteration of the modified Duke criteria only considers enterooccal bacteria entrooccal bacteria (anduding that caused by E. facealis! to be a major microbiological criterion when It is either (a) persistent or (b) community acquired and associated with an unknown primary focus. This interpretation contrasts with E. facealis! It have community acquired and sociated with a primary contrast of the properties of the of the prop

The purpose of this article was to investigate the diagnostic performance of the modified Duke criteria compared to an updated version that considered E, foreasis as a "typical" IE bacterium (enterococcal adjusted Duke criteria), using a prospective cohort of E. faecalis bacterenia patients all investigated by echocardiography.

#### **CLINICAL VIGNETTE**

A 73-year-old male, known with diabetes, atrial fibrillation, and benign prostate hyperplass, underwent transurethral resection of the prostate. Two weeks later the patient was treated with oral antibiotics for a culture positive urinary infection with E-facults (no fever and therefore no blood cultures performed. Furthermore, 2 weeks later the patient was admitted with fever, daynes, and symptoms or urinary infection. Urinary culture and blood cultures taken at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 at admission were positive for E-facults (a 54 Pect Justice 14 At admission were positive for E-facults (a 54 Pect Justice 14 Pe

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Dahl A, et al. *Clin Infect Dis*. 2022

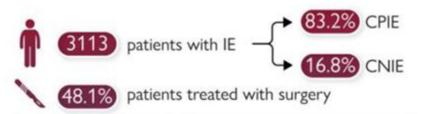
## Outcomes of culture-negative vs. culturepositive infective endocarditis: the ESC-EORP EURO-ENDO registry



European Heart Journal

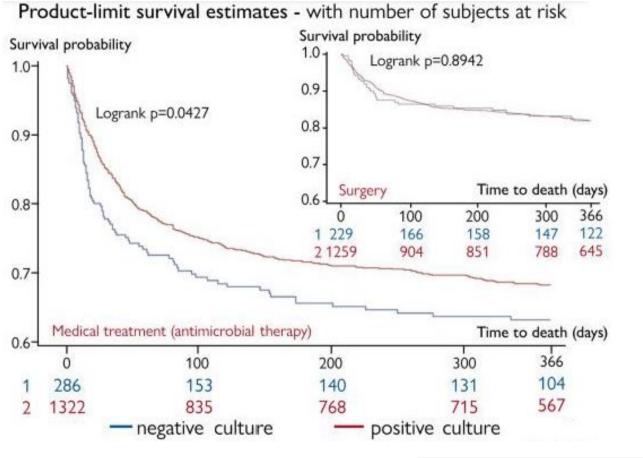


156 centres from 40 countries (2016-2019)



Variable	CPIE N=2590	CNIE N=523	P-value
Malesex	70%	64%	.01
Age (years)	60	54	<.001
Ischemic heart disease	22.3%	17.5%	.02
Diabetes mellitus	23.5%	18.4%	.01
HTA	49.4%	42.6%	.005
Congenital disease	10.9%	15.7%	.002
Embolic events	21.7%	15.3%	.001
Spondylitis	5.3%	1.3%	<.001
Acute renal failure	17%	20.5%	.06
New abscess	6.7%	3.6%	.008
Heart Failure	13.7%	17.9%	.02
Valve or prosthetic dysfunction	16.3%	20.8%	.02
30-day mortality	10.2%	14.9%	.001
1-year mortality	22.5%	25.8%	.04

Kong W, et al. Eur Heart J. 2022

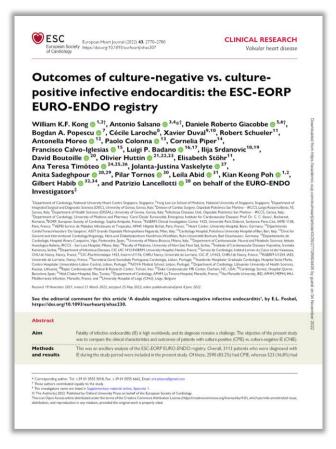


Kong W, et al. Eur Heart J. 2022

 El estudio más grande que compara CN-IE y CP-IE hasta la fecha

#### **Take-home messages:**

- Aumento de la mortalidad a corto (30 días) y largo plazo (1 año) en pacientes con CN-IE
- Esta diferencia estuvo presente en los pacientes que recibieron tratamiento médico exclusivo y NO en los que se sometieron a cirugía, asociándose la cirugía con una menor mortalidad



### 5

# Surgical Treatment of Patients With Infective Endocarditis After Transcatheter Aortic Valve Implantation

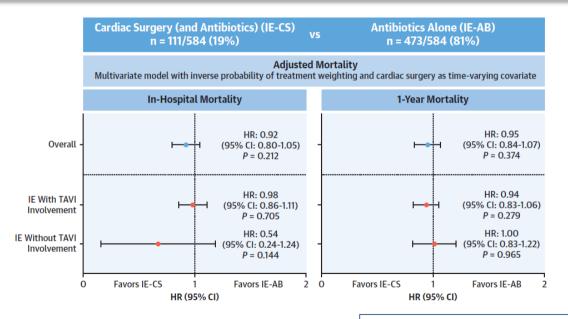


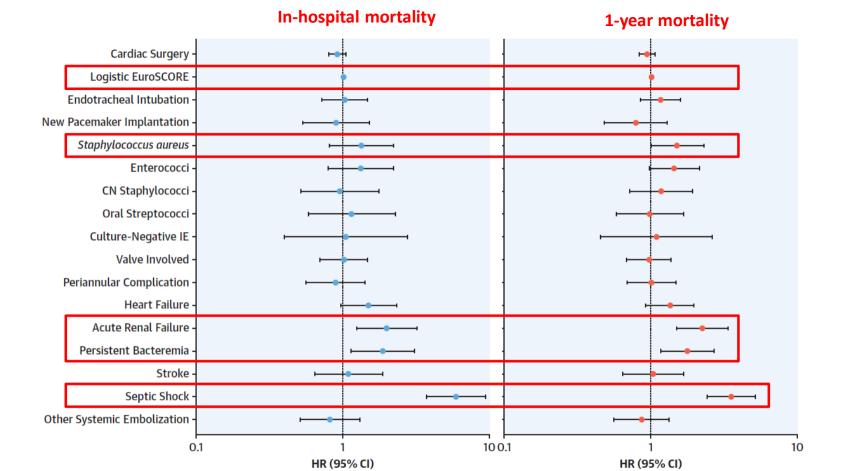
	IE-AB (n = 473)	IE-CS (n = 111)	Unadjusted P Value <sup>a</sup>
Early IE (within 1 y)	330 (69.8)	72 (64.9)	0.316
Late IE (>1 y)	143 (30.2)	39 (35.1)	
Initial symptoms			
Fever	375 (79.3)	85 (76.6)	0.531
New-onset heart failure	194 (41.0)	49 (44.1)	0.547
Neurological	99 (20.9)	10 (9.0)	0.004
Echocardiographic findings			
Vegetation	287 (60.7)	84 (75.7)	0.003
Vegetation size, mm	10 (6-15)	11 (8-20)	0.016
TAVI platform involvement	268 (56.7)	82 (73.9)	0.001
Periannular complication	78 (16.5)	39 (35.1)	< 0.001
Valves involved			
Isolated TAVI prosthesis	222 (46.9)	62 (55.9)	< 0.001
Mitral (native/prosthetic valve)	80 (16.9)	6 (5.4)	
Cardiac device	8 (1.7)	15 (13.5)	
Right-sided IE	6 (1.3)	2 (1.8)	
Other <sup>d</sup>	157 (33.2)	26 (23.4)	
IE complication			
Any complication	327 (69.1)	92 (82.9)	0.004
Heart failure	180 (38.1)	63 (56.8)	< 0.001
Other systemic embolization	38 (8.0)	21 (18.9)	< 0.001
Persistent bacteremia	122 (25.8)	49 (44.1)	< 0.001

- 59 centers in 11 countries (2005-2020)
- 604 patients with definite IE <u>after TAVI</u>
  - 473 (81%) antibiotics alone (IE-AB)
  - 111 (19%) antibiotics and surgery (IE-CS)

## Surgical Treatment of Patients With Infective Endocarditis After Transcatheter Aortic Valve Implantation







 Evaluación metodológicamente apropiada de las estrategias terapéuticas (médica vs. quirúrgica) en una gran cohorte de pacientes con endocarditis después de TAVI

#### **Take-home messages:**

- 1/5 pacientes desarrollaron El después de TAVI recibieron cirugía
- La mortalidad intrahospitalaria y por todas las causas a 1 año fue alta
- Las tasas de mortalidad para ambas estrategias no fueron significativamente diferentes (ni en la cohorte cruda y ni en la ajustada)
- Fueron predictores de mortalidad las comorbilidad/gravedad de los pacientes, los patógenos y las complicaciones relacionadas con la El



#### Para leer más...

Clinical Infectious Diseases

#### MAJOR ARTICLE









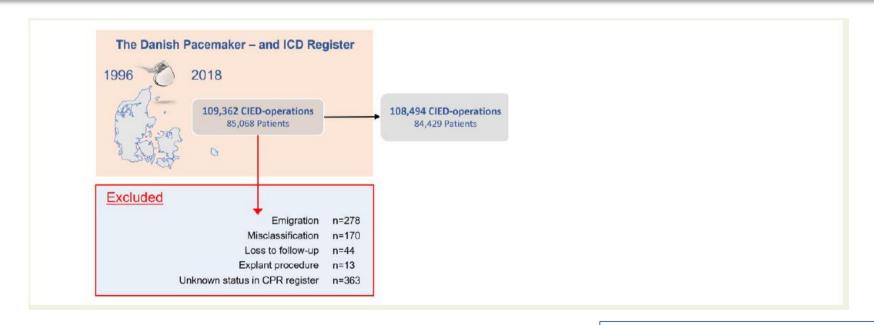
## Perivalvular Extension of Infective Endocarditis After Transcatheter Aortic Valve Replacement

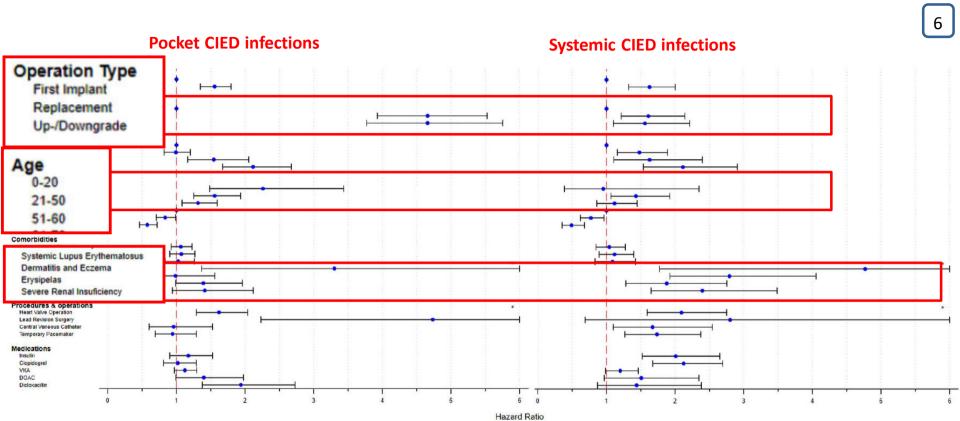
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Panagides V, et al. Clin Infect Dis. 2022

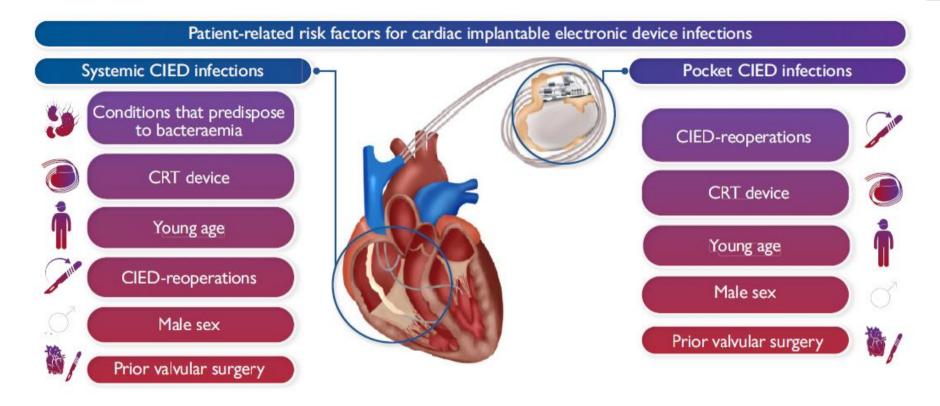
## Risk factors for cardiac implantable electronic device infections: a nationwide Danish study







Olsen T, et al. Eur Heart J. 2022

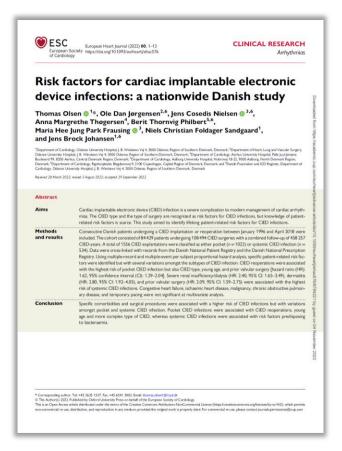


Olsen T, et al. Eur Heart J. 2022

- Cohorte nacional de 84.429 pacientes consecutivos de CIED con <u>seguimiento de por vida</u>
- Mayor análisis multivariado de factores de riesgo para infecciones por CIED

#### **Take-home messages:**

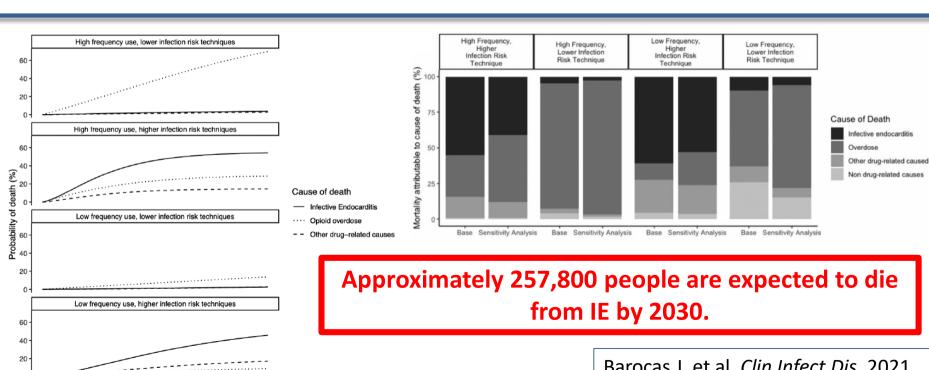
- Las infecciones de bolsillo se asociaron principalmente con reoperaciones, menor edad y tipo más complejo de CIED
- Las infecciones sistémicas se correlacionaron con <u>factores</u> de riesgo que predisponen a la bacteriemia



### Long-term Infective Endocarditis Mortality Associated With Injection Opioid Use in the United States: A Modeling Study

Age





Barocas J, et al. Clin Infect Dis. 2021

Estimación de la tasa de mortalidad por El a nivel poblacional entre las personas que se invectan opioides utilizando un nuevo modelo de microsimulación

#### Take-home messages:

- Durante los próximos 10 años, se estima que la El representará una quinta parte de todas las muertes en esta población
- El riesgo de muerte por El fue más pronunciado entre aquellos con prácticas de mayor riesgo de infección
- La frecuencia de inyección tuvo poco efecto sobre el riesgo de muerte por El

Clinical Infectious Diseases









#### Long-term Infective Endocarditis Mortality Associated With Injection Opioid Use in the United States: A Modeling Study

Joshua A. Barocas, <sup>12</sup> Golnaz Eftekhari Yazdi, <sup>1</sup> Alexandra Savinkina, <sup>1</sup> Shayla Nolen, <sup>1</sup> Caroline Savitzky, <sup>1</sup> Jeffrey H. Samet, <sup>3</sup> Honora Englander, <sup>4</sup> and

Education Unit, Section of General Internal Medicine, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, USA, and "Division of Hospital Medicine, Oregon Hoolth Sciences University Portland Oronne USA

Background. The expansion of the US opioid epidemic has led to significant increases in infections, such as infective endocarditis (IE), which is tied to injection behaviors. We aimed to estimate the population-level IE mortality rate among people who inject opioids and compare the risk of IE death against the risks of death from other causes.

Methods. We developed a microsimulation model of the natural history of injection opioid use. We defined injection behavior profiles by both injection frequency and injection techniques. We accounted for competing risks of death and populated the model with primary and published data. We modeled cohorts of 1 million individuals with different injection behavior profiles until age 60 years. We combined model-generated estimates with published data to project the total expected number of IE deaths in the United States by 2030.

Results. The probabilities of death from IE by age 60 years for 20-, 30-, and 40-year-old men with high-frequency use with higher infection risk techniques compared to lower risk techniques for IE were 53.8% versus 3.7%, 51.4% versus 3.1%, and 44.5% versus 2.2%, respectively. The predicted population-level attributable fraction of 10-year mortality from IE among all risk groups was 20%. We estimated that approximately 257 800 people are expected to die from IE by 2030.

Conclusions. The expected burden of IE among people who inject opioids in the United States is large. Adopting a harm reduction approach, including through expansion of syringe service programs, to address injection behaviors could have a major impact on decreasing the mortality rate associated with the opioid epidemic.

Keywords. simulation modeling; injection drug use; opioids; endocarditis; serious infections

The epidemiology of the United States opioid epidemic has ex- frequency, sterile injection practices, and sharing injection panded from oral ingestion of prescription opioids to injection equipment—which are important, potentially modifiable facof illicitly produced opioids, such as heroin and fentanyl [1], tors that can impact outcomes [9-11]. As the US opioid epi-As a result, serious bacterial infections, such as infective endo- demic continues to evolve, with an increased availability of carditis (IE) and skin and soft tissue infections (SSTIs), have high-potency, short-acting synthetic opioids, estimates of probecome among the most common medical complications in jected complications of injection opioid use can help guide serpersons who inject drugs (PWID) [2, 3]. In recent years, hospitalizations for injection-related IE have increased significantly. the contributions of injection frequency and injection techup 12-fold in some states [4]. As such, costs of these infections have grown and may be as high as \$400 000 000 per year for in the United States and to compare the risk of death from IE individual states [5]

Many individuals, even those on medications for opioid use disorder (MOUD), do not always completely abstain from drug use for sustained periods [6-8]. Therefore, greater attention needs to be paid to the details of injection opioid use—injection

Received 15 June 2020: editorial decision 24 August 2020: accepted 7 September 2020: Comesonodence: J. A. Ramcas. Roston University Medical Campus. 901 Massachusetts Ave.

2<sup>nd</sup> Floor, Boston, MA, 02131 (Joshua Barocas@BMC.org). Clinical Infectious Diseases® 2021;73(11):e3661-9

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niques to IE mortality risks among people who inject opioids against the risks of death from other causes as a function of in-

We developed, validated, and calibrated the Reducing Infections Related to Drug Use Cost-Effectiveness Model, a Monte Carlo microsimulation model that simulates the natural history of injection opioid use. We then projected IE mortality and competing risks of death according to injection behavior profiles. We defined injection behavior profiles by both injection frequency (high, low, and no current) and, for those with current use, injection practices (sharing injection equipment and using sterile injection

Long-term Endocarditis Mortality • CID 2021:73 (1 December) • e3661



# Management of Infective Endocarditis in People Who Inject Drugs: A Scientific Statement From the American Heart Association

Larry M. Baddour, MD, FAHA; Melissa B. Weimer, DO, MCR; Alysse G. Wurcel, MD, MS; Doff B. McElhinney, MD, Vice Chair; Laura R. Marks, MD, PhD; Laura C. Fanucchi, MD, MPH; Zerelda Esquer Garrigos, MD; Gosta B. Pettersson, MD; Daniel C. DeSimone, MD, Chair; on behalf of the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee of the Council on Lifelong Congenital Heart Disease and Heart Health in the Young; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Council on Peripheral Vascular Disease

Baddour L, et al. Circulation. 2022

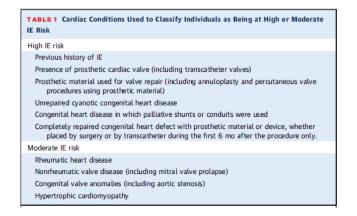
## Antibiotic Prophylaxis Against Infective Endocarditis Before Invasive Dental Procedures



**OBJECTIVES**: To investigate any association between invasive dental procedures (IDPs) and IE, and the effectiveness of antibiotic prophylaxis (AP)

**METHODS**: Case-crossover analysis and cohort study of the association between IDPs and IE, and AP efficacy in 7,951,972 U.S. subjects

3774 IE-admissions



#### TABLE 2 Examples of IDP, Intermediate Dental Procedures, and Non-IDP

IDP-procedures that should be covered by AP

Dental extractions (including surgical removal of impacted teeth and residual tooth roots)

Oral surgery procedures (including biopsies, periodontal surgery, implant surgery, and other oral surgery and maxillofacial procedures involving oral soft tissues or bone)

Scaling procedures (including dental prophylaxis, periodontal scaling and root planning, periodontal maintenance and gingival irrigation, or delivery of antimicrobial agents into the diseased gingival crevice)

Endodontic treatment (including pulpal debridement, endodontic treatment and retreatment, apexification/recalcification, apicectomy, and peri-radicular procedures)

Intermediate dental procedures-procedures that may or may not require AP cover

Restorative dental procedures (fillings, inlays, crowns and bridges) and oral examination procedures that may on occasion involve gingival manipulation (when AP cover should be provided), but on other occasions do not involve gingival manipulation (when AP should not be provided).

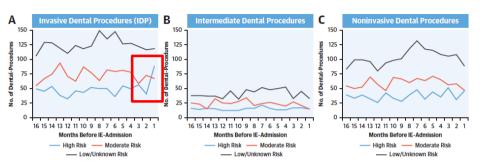
Non-IDP

Oral examinations not involving manipulation of the gingival or apical tissues Dental radiographs

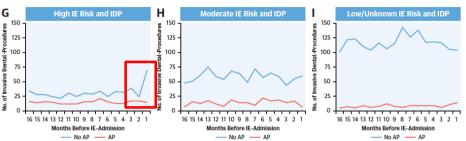
Placement of removable prosthodontic or orthodontic appliances

Adjustment of orthodontic appliances and placement of orthodontic brackets

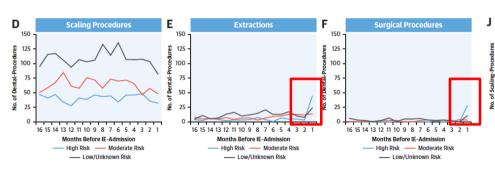
#### Incidencia de procedimientos dentales antes del ingreso por IE (según grupo de riesgo de EI)



#### Incidencia de procedimientos dentales antes del ingreso por IE (según uso de profilaxis)



#### Incidencia de procedimientos dentales INVASIVOS antes del ingreso por IE (según grupo de riesgo de EI)



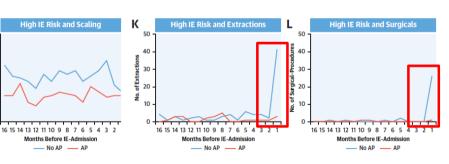
#### Incidencia de procedimientos dentales INVASIVOS antes del ingreso por IE (según uso de profilaxis)

**High IE Risk and Scaling** 

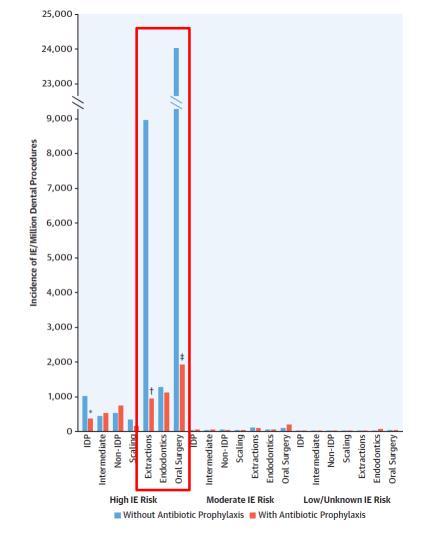
Months Before IE-Admission

— No AP — AP

20



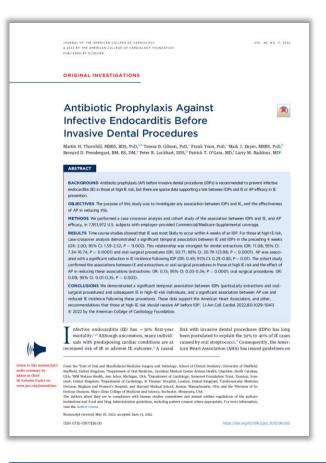
Infective Endocarditis Incidence Within 1 Month of Dental Procedures Performed With or Without Antibiotic Prophylaxis



 Primera evidencia clínica que respalda las recomendaciones de la AHA y ESC sobre profilaxis antibiótica

#### **Take-home messages:**

- En una población de casi 8 millones de personas, se demostraron asociaciones significativas:
  - Entre procedimientos dentales invasivos (particularmente extracciones y procedimientos quirúrgicos) y El en pacientes con alto riesgo de El
  - Entre uso de profilaxis antibiótica y una menor incidencia de El



Characteristics, management, and outcomes of patients with left-sided infective endocarditis complicated by heart failure: a substudy of the ESC-EORP EURO-ENDO (European infective endocarditis) registry

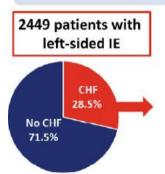
European Journal of

## Heart Failure



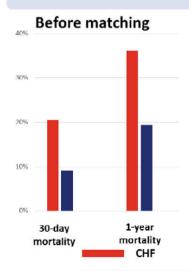


#### **Baseline differences**



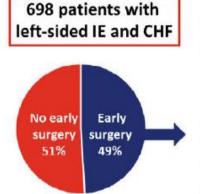
- Older
- More comorbidities
- More severe valvular damage:
- ↑ Vegetation size
- ↑ Severe regurgitations
- ↑Mitro-aortic involvement
- More uncontrolled infection

#### Survival differences



Bohbot Y, et al. Eur J Heart Fail. 2022

#### Early surgery in CHF patients (within 30 days)



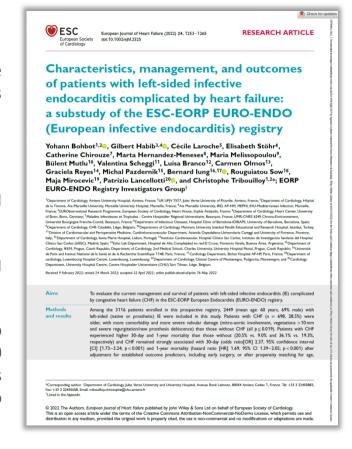
- Younger
- Less comorbidities
- More severe valvular damage:
- ↑ Vegetation size
- ↑ Severe regurgitations
- ↑ Perivalvular complications
- Less uncontrolled infection

Bohbot Y, et al. Eur J Heart Fail. 2022

 Primer estudio sobre una gran cohorte europea que evaluó las características clínicas, tratamiento y outcomes de pacientes con El izquierda complicada con ICC

#### **Take-home messages:**

- La insuficiencia cardiaca congestiva es frecuente en la El izquierda
- Los pacientes con ICC en el momento del diagnóstico de El muestran una mayor mortalidad a los 30 días y al año
- La cirugía precoz en pacientes con ICC se asoció independientemente con una menor mortalidad a los 30 días y al año (aunque se realizó solo en un 50 % de los casos, principalmente debido a un riesgo quirúrgico prohibitivo)



Bohbot Y, et al. Eur J Heart Fail. 2022

### Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial

## Circulation

452 ineligible 127 inclusion criteria not fullfilled:

171 inability to obtain informed consent 94 no Nominated Consultee possible

103 Duke Criteria not fullfilled 24 no surgical indication

29 the legal representative was

48 refused

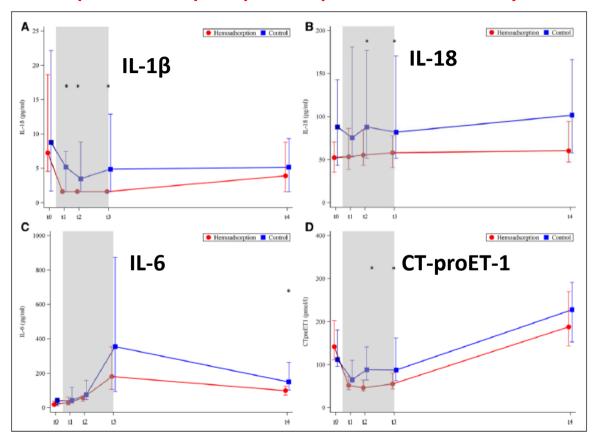
unavailable 109 Exclusion criteria

740 were assessed for eligibility

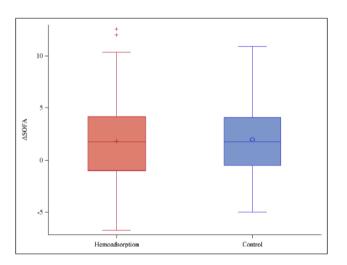
- **REMOVE trial** (Revealing Mechanisms and Investigating Efficacy of Hemoadsorption for Prevention of Vasodilatory Shock in Cardiac Surgery Patients With Infective Endocarditis)
- Multicenter (14 cardiac surgery centers in Germany) randomized, non-blinded, controlled trial with 2 groups designed for assessing superiority
- bypass using CytoSorb or to the control group.
- score [ΔSOFA]

73 had EuroSCORE II < 3 11 immunosuppressive therapy 6 participation in another trial 1 previous participation in current trial 18 unspecified 45 Miscellaneous Patients undergoing cardiac surgery for IE were randomly 288 underwent randomization assigned to receive hemoadsorption during cardiopulmonary 142 assigned to CytoSorb 146 assigned to control **Primary outcome:** change in sequential organ failure assessment 4 did not undergo surgery 2 did not undergo surgery Diab M, et al. Circulation. 2022 138 were included in modified 144 were included in modified intention-to-treat analysis intention-to-treat analysis

#### Intraoperative and postoperative plasma levels of citokynes



#### **Primary Outcome: Δ SOFA**



Diab M, et al. Circulation. 2022

### Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial



Table 2. Secondary Outcomes

Outcomes	Hemoadsorption group (n=138)	Control group (n=144)	P value	Difference (95% CI)*
30-day mortality	29 (21.0)	32 (22.4)	0.782	0.94 (0.60-1.47)
Postoperative stroke	5 (3.6)	3 (2.1)	0.442	1.73 (0.42–7.09)
Hospital stay, d	20 (13–30)	19 (12–29)	0.392	1 (0-2)
ICU stay, d	7 (3–12)	6 (3–10)	0.241	1 (0-2)
Duration of postoperative hemodialysis, d	0 (0-1)	0 (0-2)	0.791	0 (0-0)
Duration of postoperative ventilation, d	1 (0-7)	1 (0-3)	0.165	0.5 (0-1)
Duration of postoperative vasopressors therapy, d	3 (1-8)	3 (1-7)	0.896	0 (-1-1)
Δ SOFA: CVS subscore	1.57±1.52	1.67±1.49	0.841	-0.04 (-0.39 to 0.32)
Δ SOFA: CNS subscore	0.16±0.54	0.19±0.40	0.560	-0.04 (-0.16 to 0.09)
Δ SOFA: coagulation subscore	0.52±0.88	0.50±0.83	0.487	-0.08 (-0.31 to 0.15)
Δ SOFA: hepatic subscore	0.42±0.84	0.46±0.82	0.840	-0.02 (-0.27 to 0.22)
Δ SOFA: renal subscore	-1.86±1.94	-1.93±1.73	0.392	-0.16 (-0.54 to 0.22)
Δ SOFA: respiratory subscore	0.94±1.29	0.85±1.22	0.662	-0.05 (-0.27 to 0.17)

Diab M, et al. Circulation. 2022

 Ensayo clínico que aleatorizó a casi 290 pacientes con El e indicación quirúrgica

#### Take-home messages:

- La hemoadsorción redujo las citocinas plasmáticas al final del bypass cardiopulmonar
- No hubo diferencia en ninguna de las medidas de resultado clínicamente relevantes

#### Circulation ORIGINAL RESEARCH ARTICLE Cytokine Hemoadsorption During Cardiac Surgery Versus Standard Surgical Care for Infective Endocarditis (REMOVE): Results From a Multicenter Randomized Controlled Trial Mahmoud Diable PhD: Thomas Lehmann, PhD: Wolfgang Bothe, PhD: Payam Akhyari, PhD: Stephanie Platzer, PhD: Daniel Wendt, PhD; Antie-Christin Deppe, PhD; Justus Strauch, PhD; Stefan Hagelo, PhD; Albrecht Günthero, MD; Gloria Faerber, PhD: Christoph Sponholzo, PhD: Marcus Franz, PhD: André Scherag, PhD: Ilia Velichkovo, MD: Miriam Silaschi, MD; Jens Fassl, PhD; Britt Hofmann, PhD; Sven Lehmann, PhD; Rene Schramm, PhD; Georg Fritz, MD; Gabor Szabo, PhD: Thorsten Wahlers PhD: Klaus Matschke, PhD: Artur Lichtenberg PhD: Mathias W. Pletz PhD: Jan F. Gummert, PhD; Friedhelm Beyersdort PhD; Christian Hagl, PhD; Michael A. Borger, PhD; Michael Bauer PhD; Frank M. Brunkhorst, PhD: Torsten Doensto, PhD; on behalf of the REMOVE Trial Investigators BACKGROUND: Cardiac surgery often represents the only treatment option in patients with infective endocarditis (IE). However, IE surgery may lead to a sudden release of inflammatory mediators, which is associated with postoperative organ dysfunction. We investigated the effect of hemoadsorption during IE surgery on postoperative organ dysfunction. METHODS: This multicenter, randomized, nonblinded, controlled trial assigned patients undergoing cardiac surgery for IE to hemoadsorption (integration of CytoSorb to cardiopulmonary bypass) or control. The primary outcome (change in sequential organ failure assessment score [ASOFA]) was defined as the difference between the mean total postoperative SOFA score, calculated maximally to the 9th postoperative day, and the basal SOFA score. The analysis was by modified intention to treat. A predefined intergroup comparison was performed using a linear mixed model for ASOFA including surgeon and baseline SOFA score as fixed effect covariates and with the surgical center as random effect. The SOFA score assesses dysfunction in 6 organ systems. each scored from 0 to 4, Higher scores indicate worsening dysfunction, Secondary outcomes were 30-day mortality, duration of mechanical ventilation, and vasopressor and renal replacement therapy. Cytokines were measured in the first 50 patients RESULTS: Between January 17, 2018, and January 31, 2020, a total of 288 patients were randomly assigned to hemoadsorption (n=142) or control (n=146). Four patients in the hemoadsorption and 2 in the control group were excluded because they did not undergo surgery. The primary outcome, ASOFA, did not differ between the hemoadscration and the control group (1.79±3.75 and 1.93±3.53, respectively; 95% CI, -1.30 to 0.83; P=0.6766). Mortality at 30 days (21% hemoadsorption versus 22% control: P=0.782), duration of mechanical ventilation, and vasopressor and renal replacement therapy did not differ between groups. Levels of interleukin-18 and interleukin-18 at the end of integration of hemoadsorption to cardiopulmonary bypass were significantly lower in the hemoadsorption than in the control group. CONCLUSIONS: This randomized trial failed to demonstrate a reduction in postoperative organ dysfunction through intraoperative hemoadsorption in patients undergoing cardiac surgery for IE. Although hemoadsorption reduced plasma cytokines at the end of cardiopulmonary bypass, there was no difference in any of the clinically relevant outcome measures. REGISTRATION: URL: https://www.clinicaltrials.gov: Unique identifier: NCT03266302 Key Words: cardiopulmonary bypass ■ cytokines ■ endocarditis ■ thoracic surgery Correspondence for Torsten Doenst, MD, PhD, Department of Cardiothoracic Surgery, Friedrich-Schiller-University of Jena, Am Klinikum 1, 07747, Jena, German "A list of the REMOVE Trial Investigators is provided in the Supplemental Material. Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.121.056940. For Sources of Funding and Disclosures, see page 967.

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Circulation is available at www.ahajournals.org/journal/circ

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Diab M, et al. Circulation. 2022

March 29, 2022 959

#### Para leer más...



#### ORIGINAL ARTICLE



## Impact of therapeutic drug monitoring of antibiotics in the management of infective endocarditis

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#### Outpatient Parenteral Antibiotic Treatment vs Hospitalization for Infective Endocarditis: Validation of the OPAT-GAMES Criteria

Juan M. Pericàs, <sup>1,2,a</sup> Jaume Llopis, <sup>1,3,a</sup> Patricia Muñoz, <sup>4,e</sup> Victor González-Ramallo, <sup>4</sup> M. Eugenia García-Leoni, <sup>4</sup> Arístides de Alarcón, <sup>5</sup> Rafael Luque, <sup>5</sup> M. Carmen Fariñas, <sup>5</sup> Miguel Á. Goenaga, <sup>7</sup> Marta Hernández-Meneses, <sup>1</sup> David Nicolás, <sup>1</sup> Antonio Ramos-Martínez, <sup>8</sup> M. Ángeles Rodríguez-Esteban, <sup>9</sup> Aroa Villoslada-Gelabert, <sup>10</sup> and José M. Miró, <sup>1,11</sup> on behalf of the GAMES Investigators <sup>b</sup>

#### ORIGINAL RESEARCH

Machine Learning-Based Risk Model for Predicting Early Mortality After Surgery for Infective Endocarditis

Li Luo , MD\*; Sui-qing Huang, MD\*; Chuang Liu, MCS; Quan Liu , MD; Shuohui Dong, MD; Yuan Yue, MD; Kai-zheng Liu, MD; Lin Huang, MD; Shun-jun Wang, MD; Hua-yang Li, MD; Shaoyi Zheng, PhD, MD; Zhong-kai Wu , PhD, MD

Macheda G, et al. Eur J Clin Microbiol Infect Dis. 2022

Pericàs JM, et al. Open For Infect Dis. 2022

Luo L, et al. J Am Heart Assoc. 2022









## ¡Muchas gracias!

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