
Cardiovascular infections

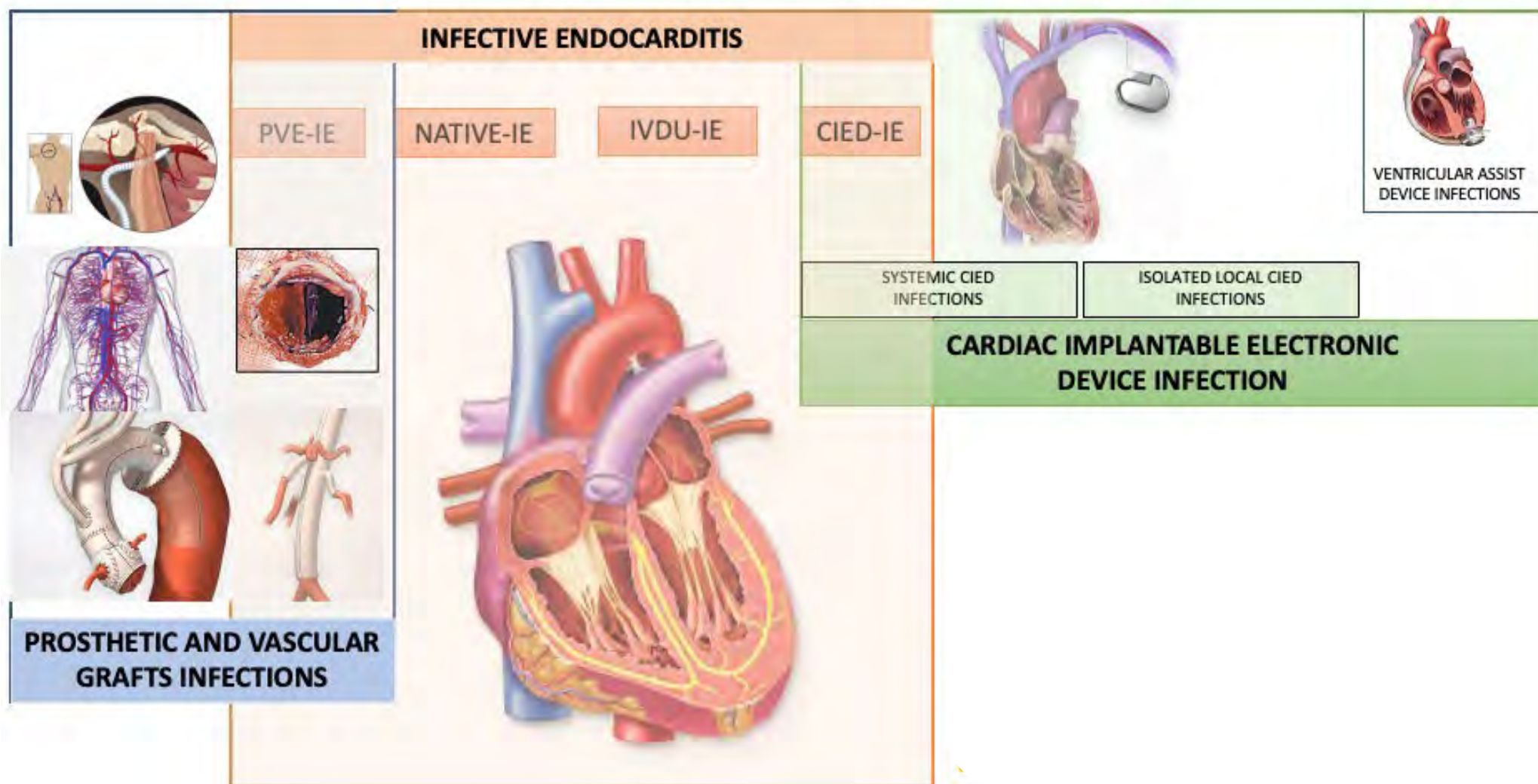
Marta Hernández-Meneses

Infectious diseases Department

Hospital Clínic Barcelona



CARDIOVASCULAR INFECTIONS

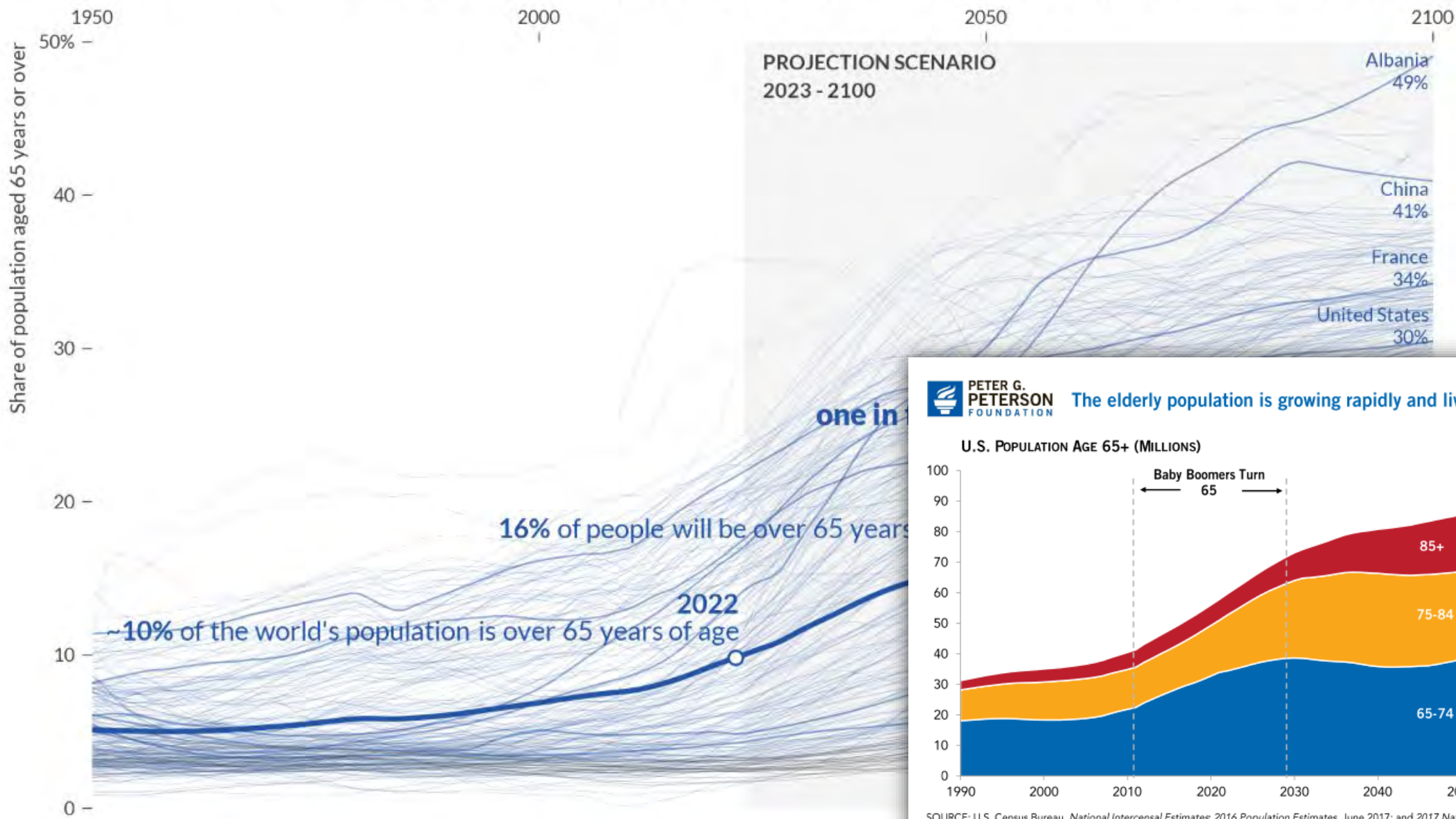


Abbreviations: PVE: prosthetic valve endocarditis; IVDU-IE: intravenous drug use related infective endocarditis; CIED IE: cardiac implantable electronic device infective endocarditis.

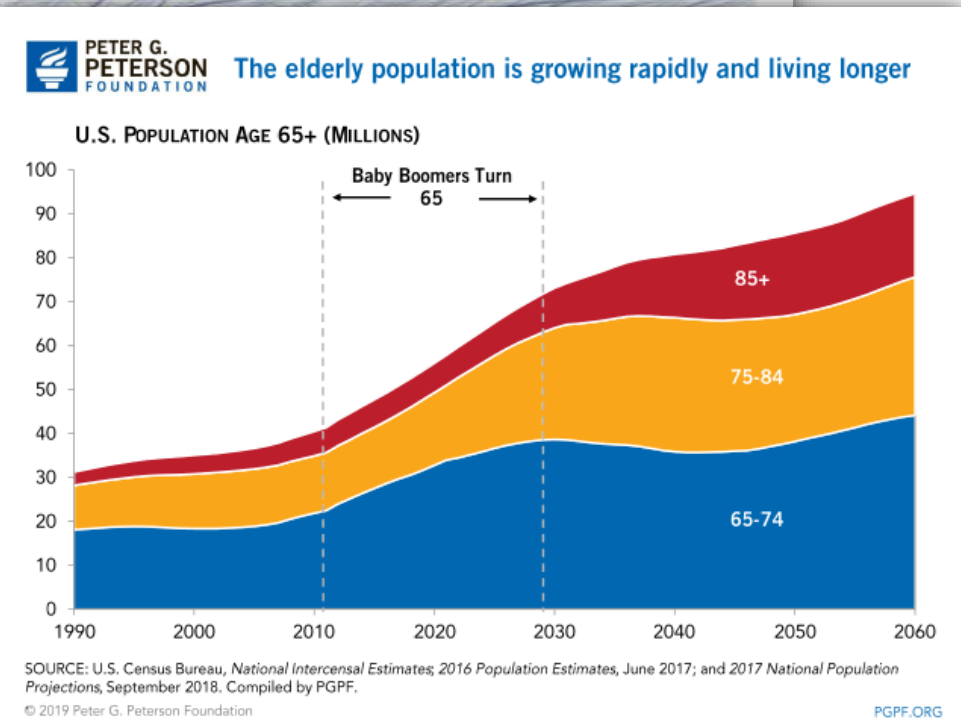
Infeccions dels dispositius d'electroestimulació cardíaca. A on estem?

The world's population is aging

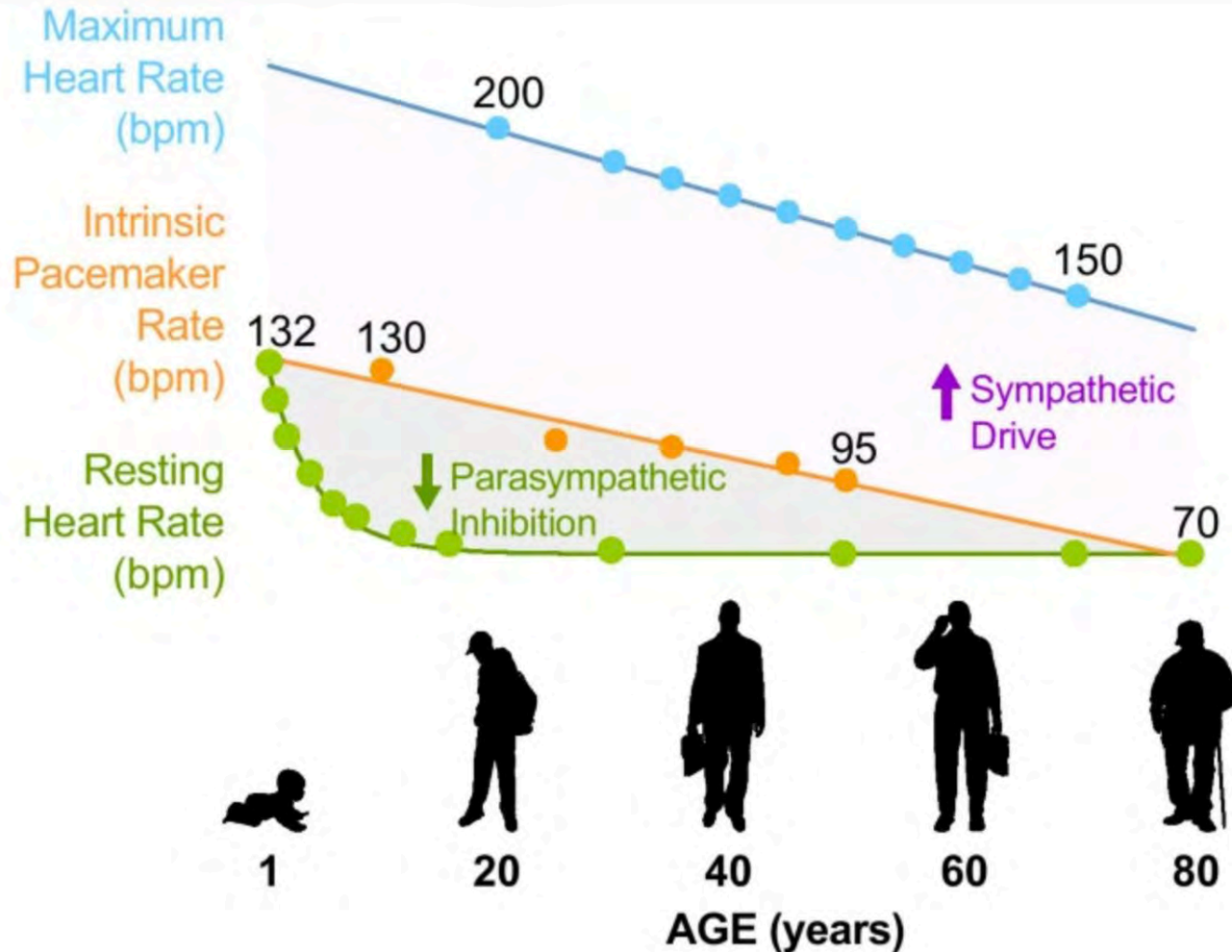
The population of people aged 65 and above is rising in every country, and will continue to do so in the future



Visualization: Pablo Alvarez | Source: United Nations World Population Prospects (2022) (vi



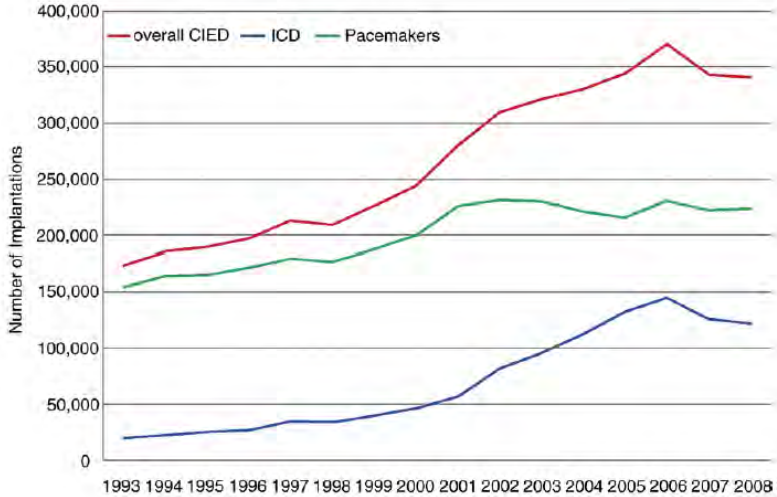
The world's population is aging



The burden of rising life expectancy is the growth in **comorbidities**, primarily **cardiovascular diseases**; therefore, the number of people requiring cardiac implantable electronic devices (CIEDs) has increased.

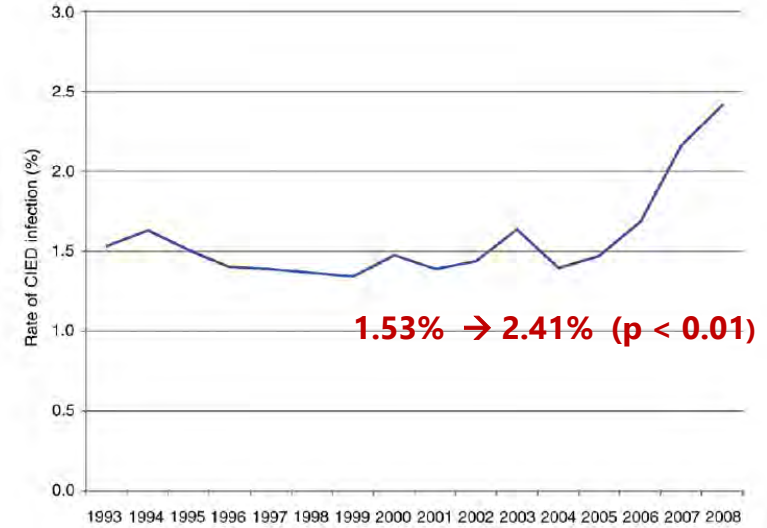
Trends in CIED infections

Number CIED implants

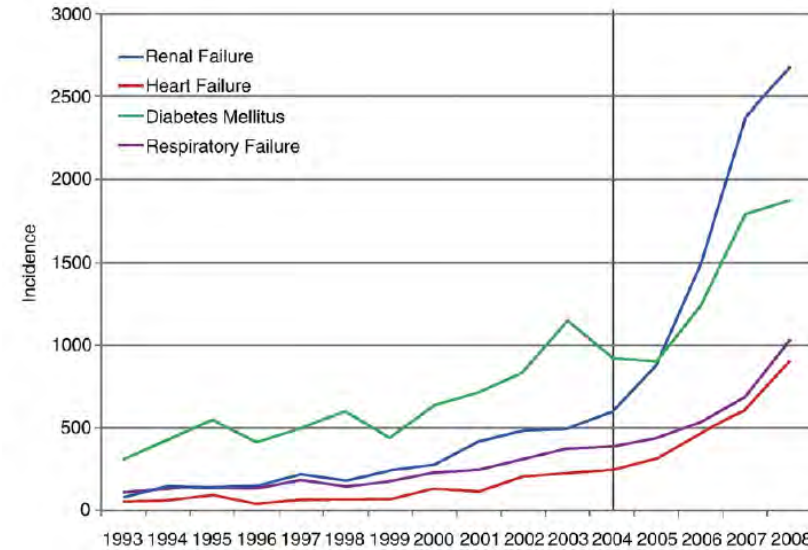


***CIED
implantation
increased by
96% from
1993 to 2008**

Rate of CIED infection

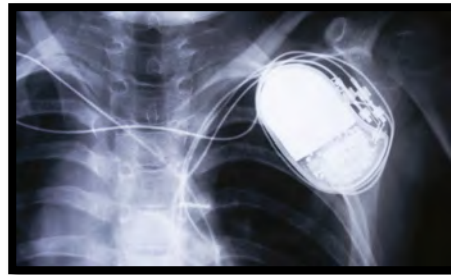


Comorbidities in CIED infections



R
I
S
K

- Device complexity
- Widening indications
- Age / comorbidities
- PPM > ICD > CRT



First-year post-implantation

Trends in CIED Infective endocarditis

Comparison between ICE and EUROENDO cohorts



	ICE (2000-2006) N=2781/3284 (85%)	EURO-ENDO (2016-2018) N=3116
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IE Type

- Native-IE	72%	59%
-	21%	31%
Prosthetic-IE		
- CIED-IE	7%	10%

¹Murdoch DR. Arch Intern Med 2009;169:463-73

²Habib G. EHJ 2019;5:202-207

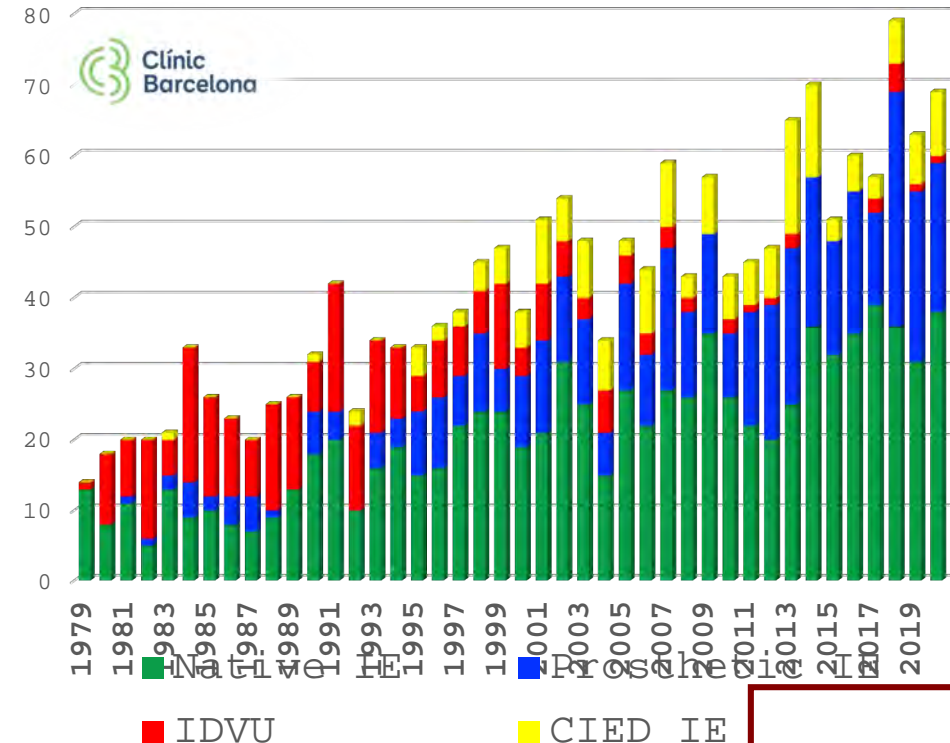
H. Clínic de Barcelona
(1980-2020)

N=1605

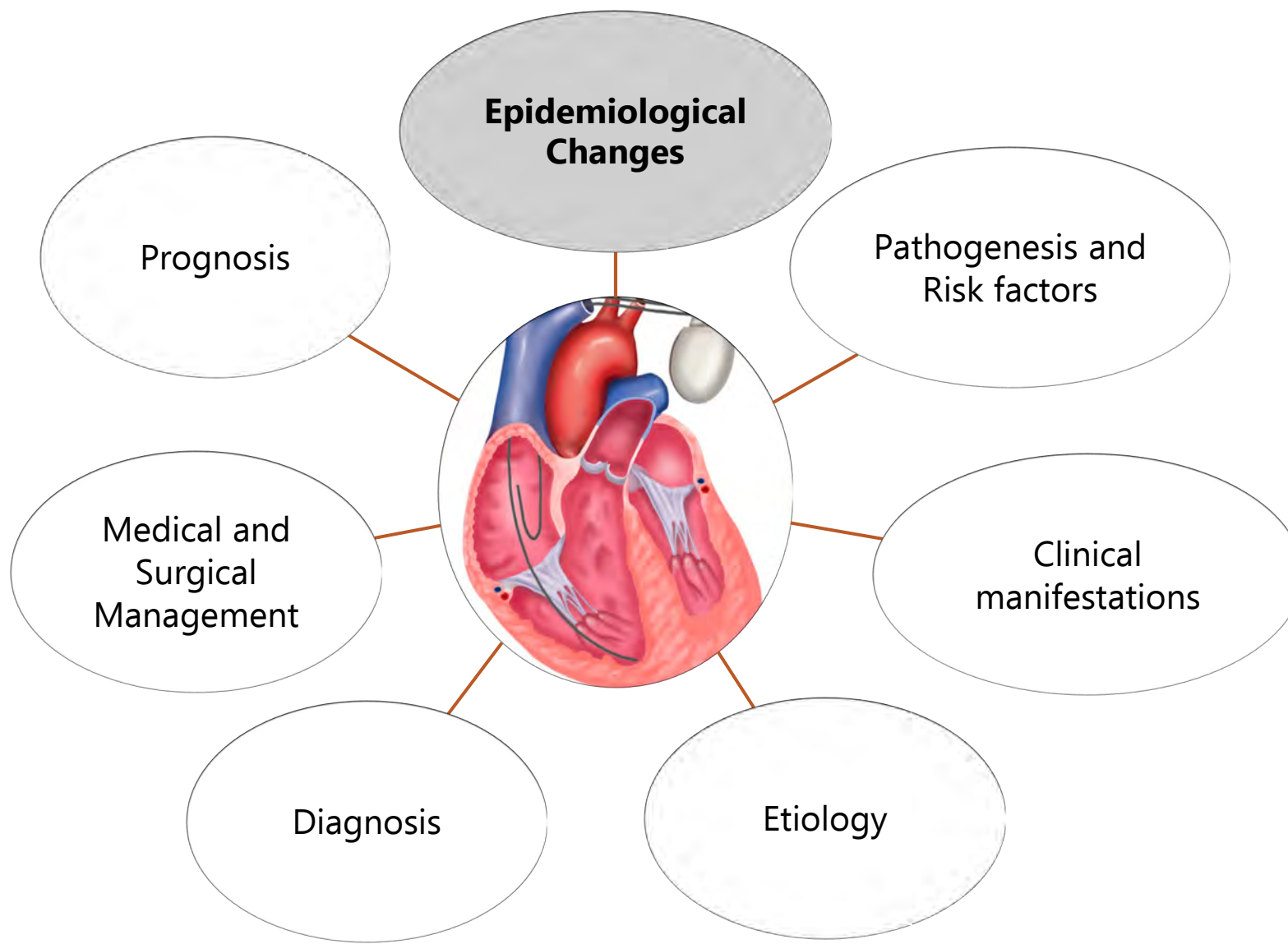
0.8 cases/1,000 admissions
6.3 cases/100,000 hab.



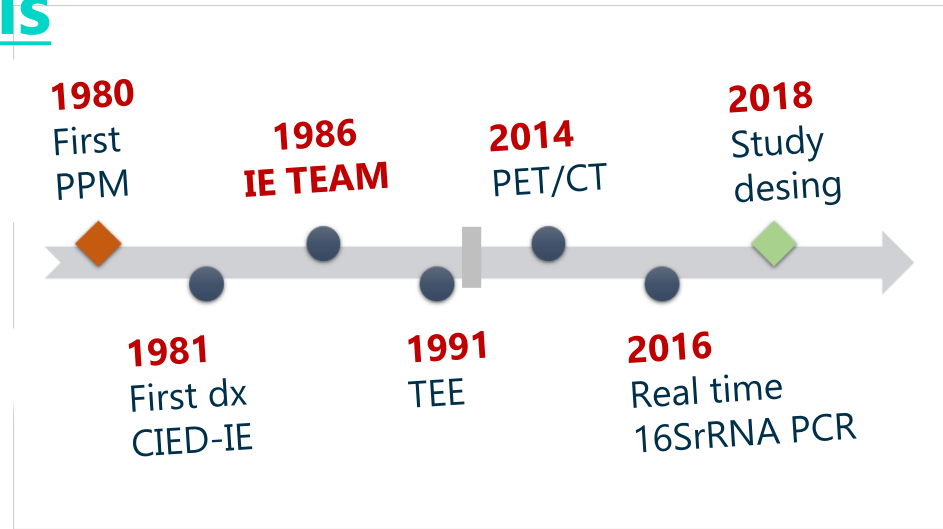
10%
of all IE



CIED INFECTIONS



Trends in CIED Infective endocarditis



Global analysis 40-year CIED-IE HCB cohort



Comparison between periods: **1981-2000** vs. **2001-2020**

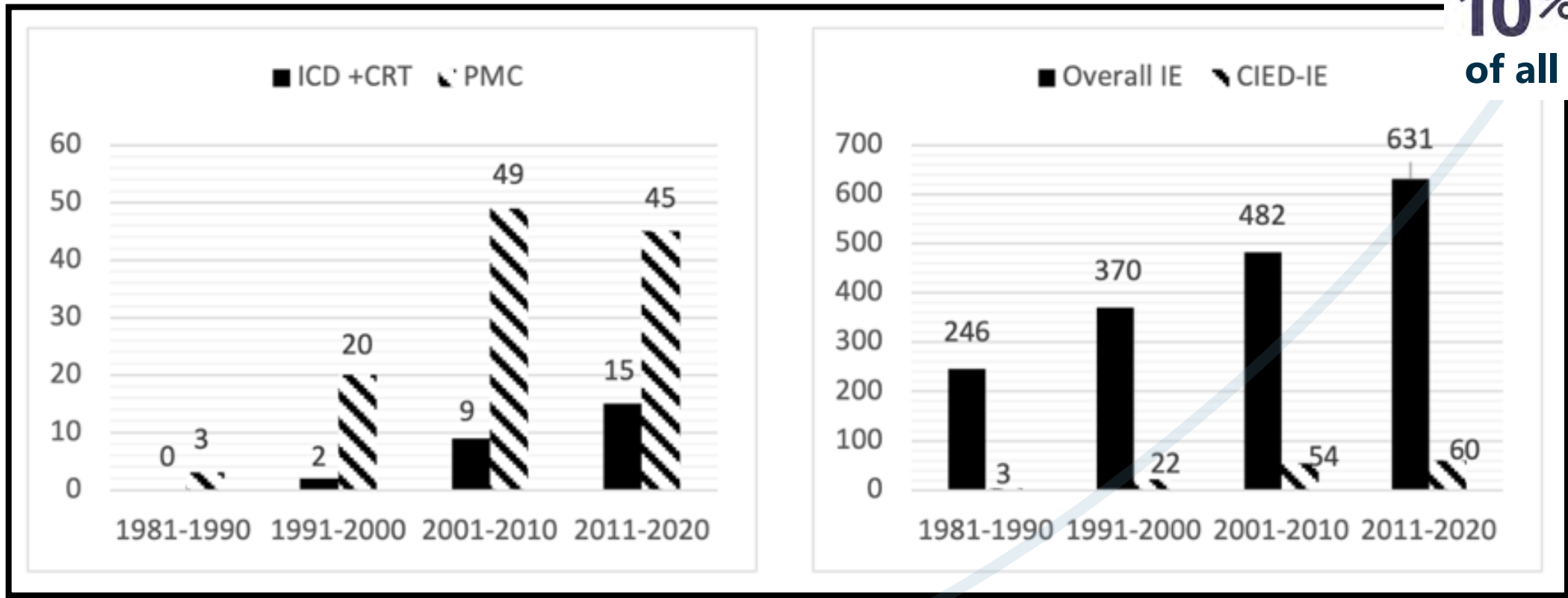
Comparison between the time presenting symptoms: **early** vs. **late CIED-IE**

Differences of CIED-IE depending on the **type of the device**

Survival analysis and **predictors factors of one-year mortality**

Trends in CIED Infective endocarditis

Proportion of CIED IE by type of CIED and compared with overall IE



10%
of all IE

TIME

Trends in CIED Infective endocarditis

40-year CIED IE cohort: comparison between periods

138 consecutive definite CIED IE

**Nosocomial and
HA infections
Transfers
MR- CONS
*E. faecalis***

Variable	Total (N=138)	1981-2000 (N=25)	2001-2020 (N=113)	P value
Age, years (median, IQR)	70 (60-76)	63 (53-71)	71 (63-76)	<0.01
Nosocomial	19 (13.8%)	1 (4%)	18 (15.9%)	0.02
Transferred from other hospital	49 (35.5%)	2 (8%)	47 (41.6%)	<0.01
Charlson comorbidity index (Median IQR)	4.0 (3.0 – 6.0)	3.0 (2.0 – 4.0)	4.5 (3.0 – 6.0)	<0.01
Echocardiography				
Vegetation on device	138 (100%)	25 (100%)	113 (100%)	NA
Tricuspid valve vegetation	31 (22.5%)	7 (28%)	24 (21.2%)	0.49
¹⁸ FDG-PET/CT	29 (21%)	0	29 (25.7%)	<0.01
Microbiology				
S. aureus	46 (33.3%)	7 (28%)	39 (34.5%)	0.52
- MRSA	13 (9.4%)	1 (4%)	12 (10.6%)	0.18
Coagulase-negative Staphylococcus	62 (44.9%)	12 (48%)	50 (44.2%)	0.32
- MR-CoNS	15 (10.9%)	0	15 (13.3%)	<0.01
Enterococcus spp.	6 (4.3%)	0	6 (5.3%)	0.01

Trends in CIED Infective endocarditis

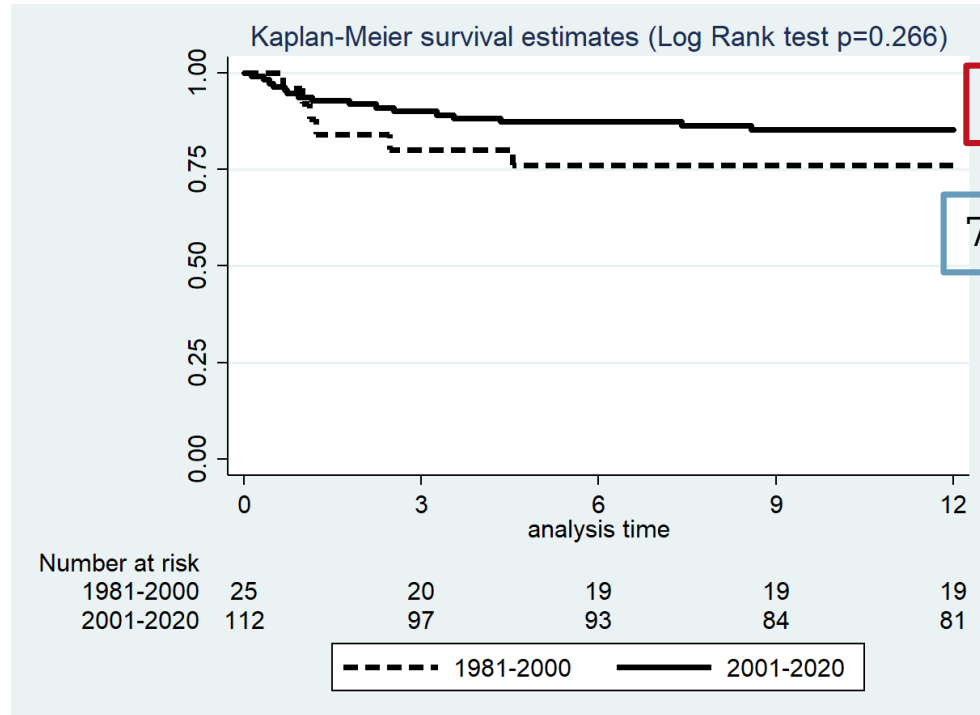
40-year CIED IE cohort: comparison between periods

More
complex
infections

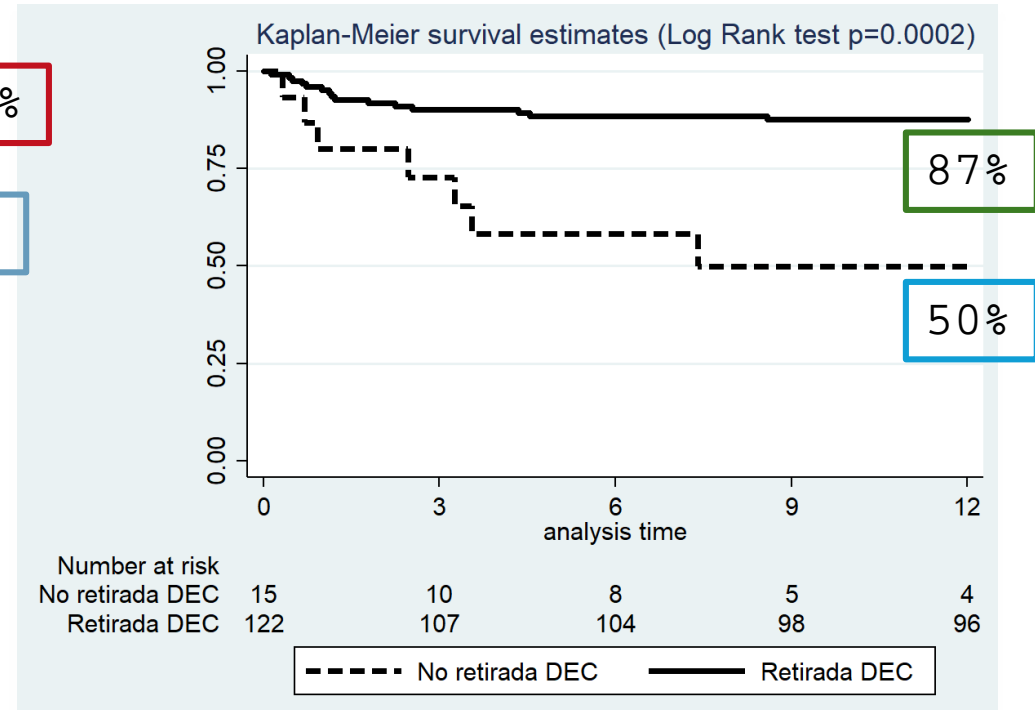
Variable	Total (N=138)	1981-2000 (N=25)	2001-2020 (N=113)	P value
Complications	75 (54.3%)	7 (28%)	68 (60.2%)	<0.01
Pulmonary embolism	12 (8.7%)	0	12 (10.6%)	<0.01
Treatment				
Removal of cardiac device system	123 (89.1%)	24 (96%)	99 (87.6%)	0.09
Interval diagnosis-removal (median, IQR)	29.0 (20.0 – 42.0)	21.5 (18 – 46)	29.5 (23.0 – 42.0)	0.35
Type of removal				
Traction	95 (77.2%)	19 (79.2%)	76 (76.8%)	0.79
Open surgery	28 (22.8%)	5 (20.8%)	23 (23.2%)	0.88
Reimplant	84 (68.3%)	16 (66.7%)	68 (68.7%)	0.85
In-hospital mortality	18 (13%)	5 (20%)	13 (11.5%)	0.32
One-year follow up				
Surgery	8 (5.8%)	3 (12%)	5 (4.4%)	0.26
Mortality	23 (16.7%)	6 (24%)	17 (15%)	0.33
Relapses	8 (5.8%)	2 (8%)	6 (5.3%)	0.65

Trends in CIED Infective endocarditis

CIED-IE comparative survival between period 1981-2000 vs. 2001-2020



Differences in survival between removal or not of the device



Predictors factors for one-year mortality

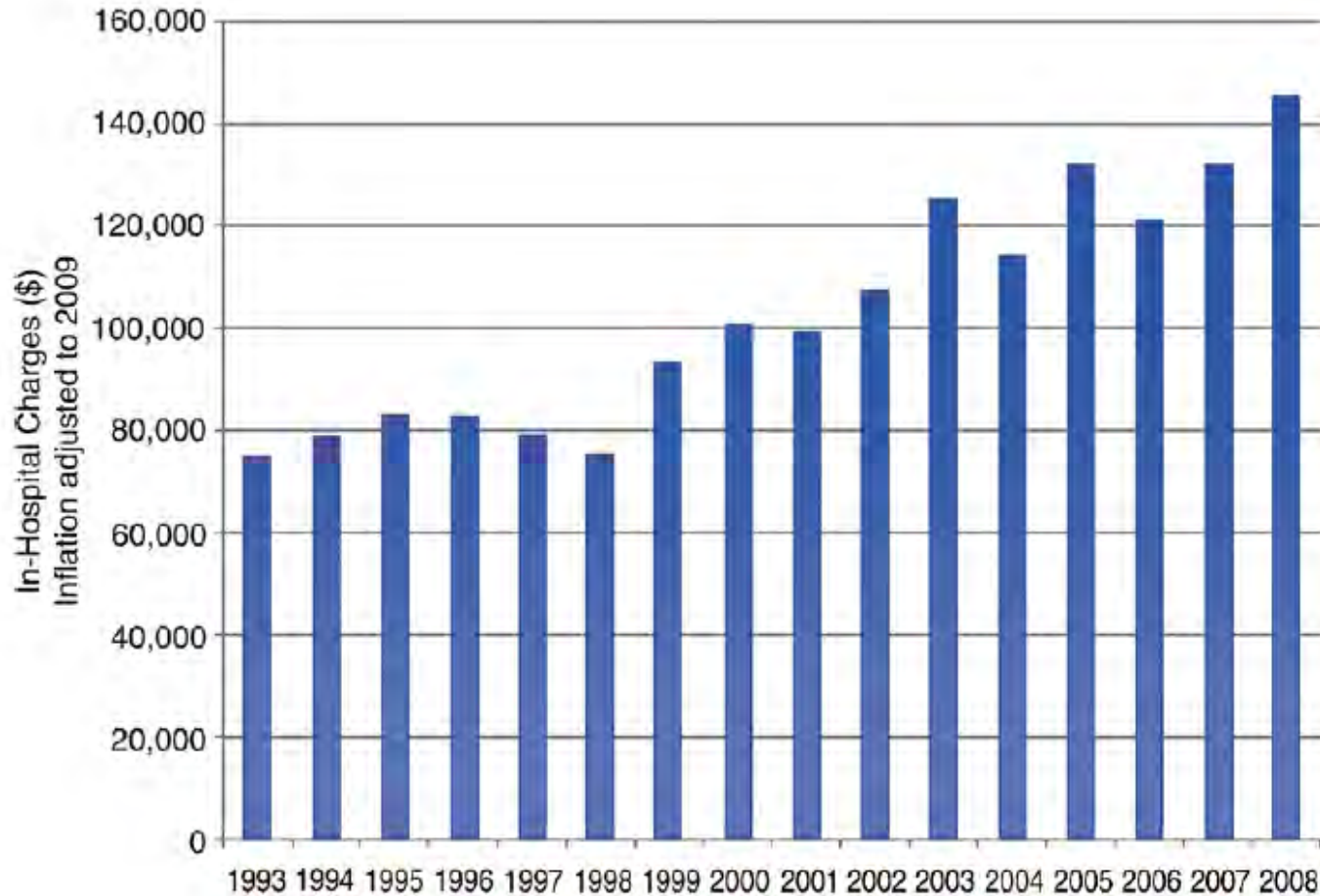
Charlson index and septic shock
Transfers, device removal, and second-period

Increase in
the **CIED**
implantation
and **CIED**
infection
prevalence
impact the
Health-care
system?



Update on the CIED infection burden

16-Year Trends in the Infection Burden for PM and ICD in the US: 1993 to 2008



Increase of 47% per decade

In-Hospital Charges Associated With CIED Infection (Inflation Adjusted to 2009)

Update on the CIED infection burden

Costs of CIED Infections According to the Therapeutic Approach



380 CIED-I

Local infections Systemic infections

	Local CIED I	Systemic CIED I
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Mortality	2.5%	10.8%
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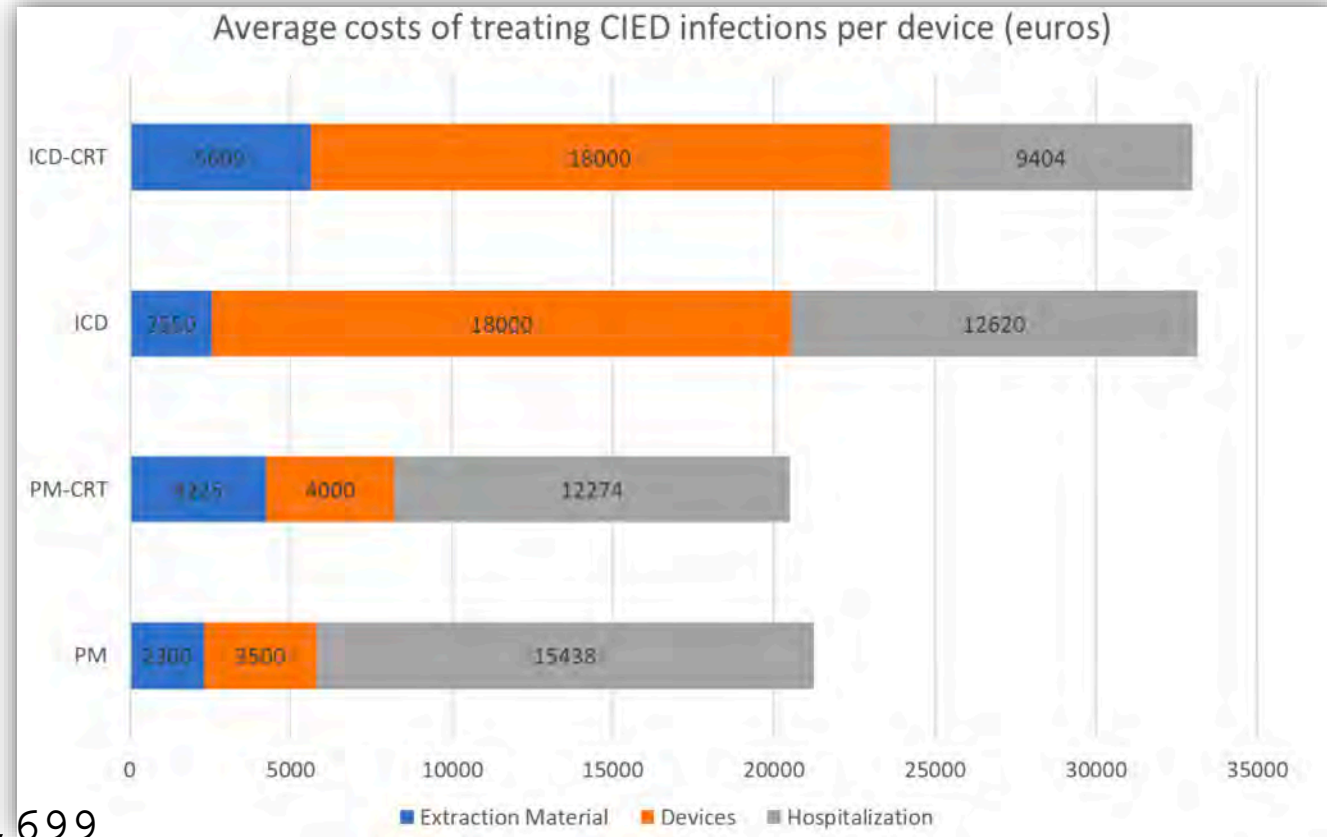
Costs	21,970€	34,086€
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Pocket-only surgery → Recurrence: **87%**
 Progression to systemic infections: **48 patients**

Higher cost than TLE 42,978 vs. EUR 24,699

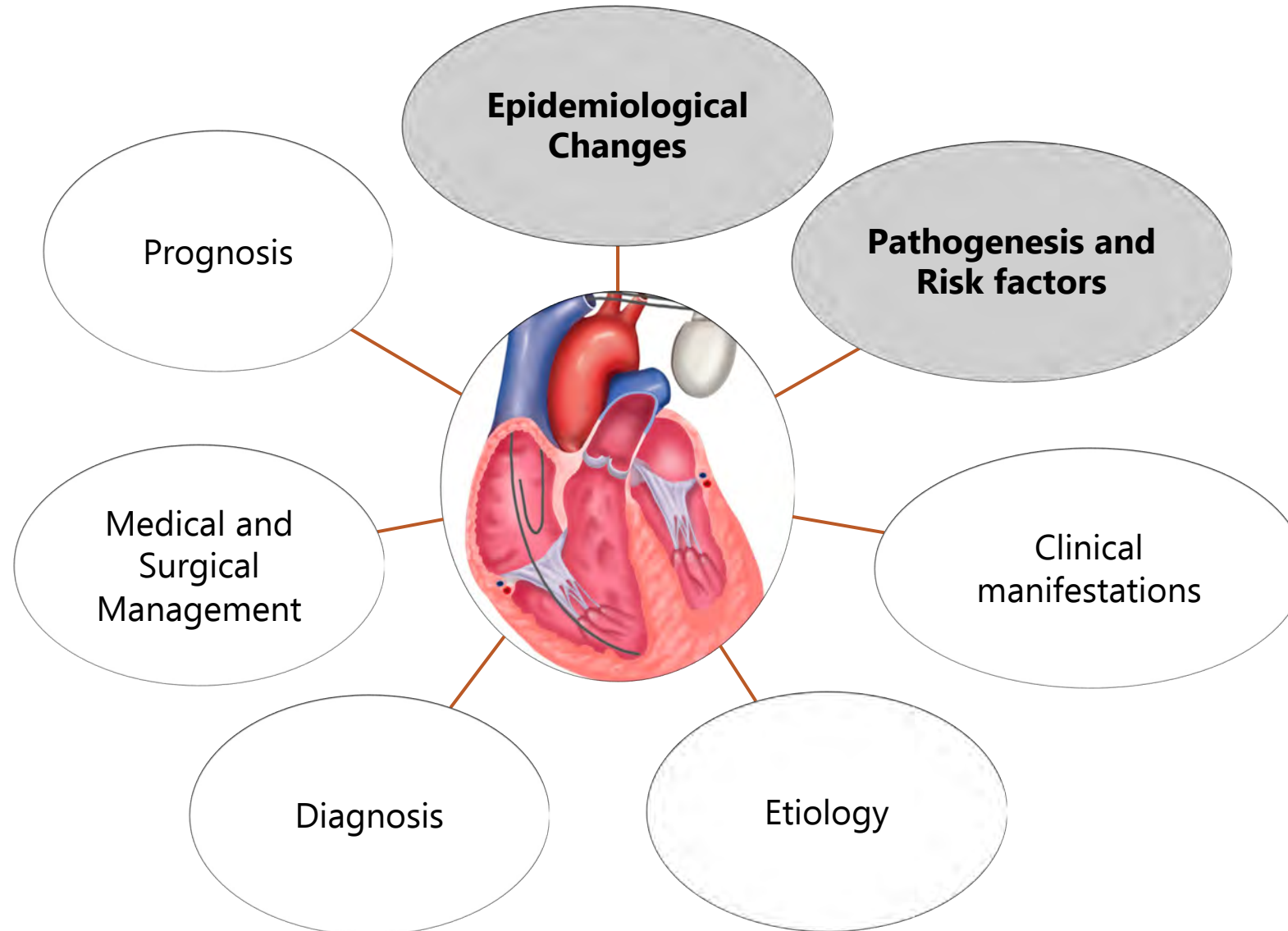
(p < 0.01)

Costs  depends on type of treatment and length of hospitalization.



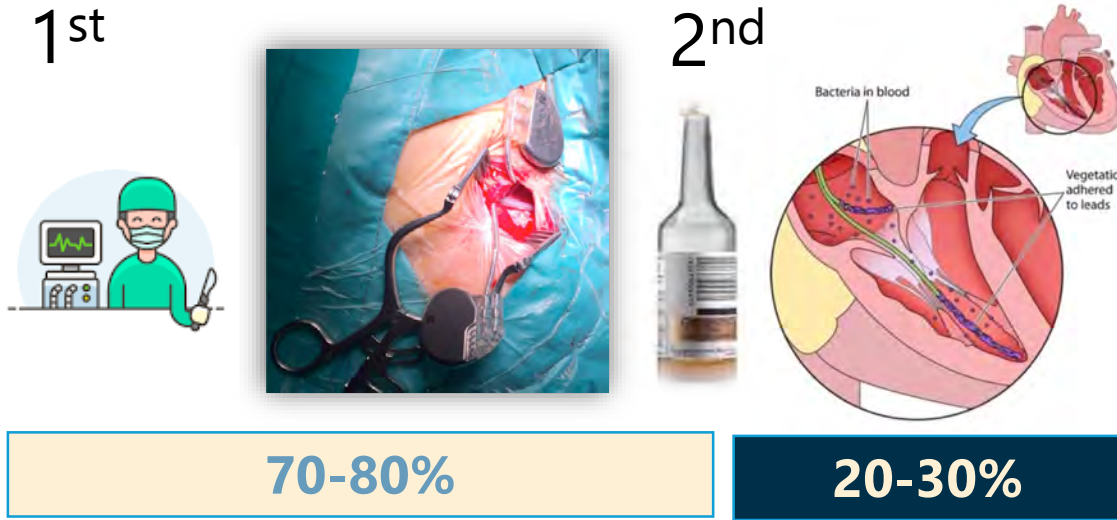
Complete device removal is always the most effective and cost-saving strategy

CIED INFECTIONS



Pathogenesis

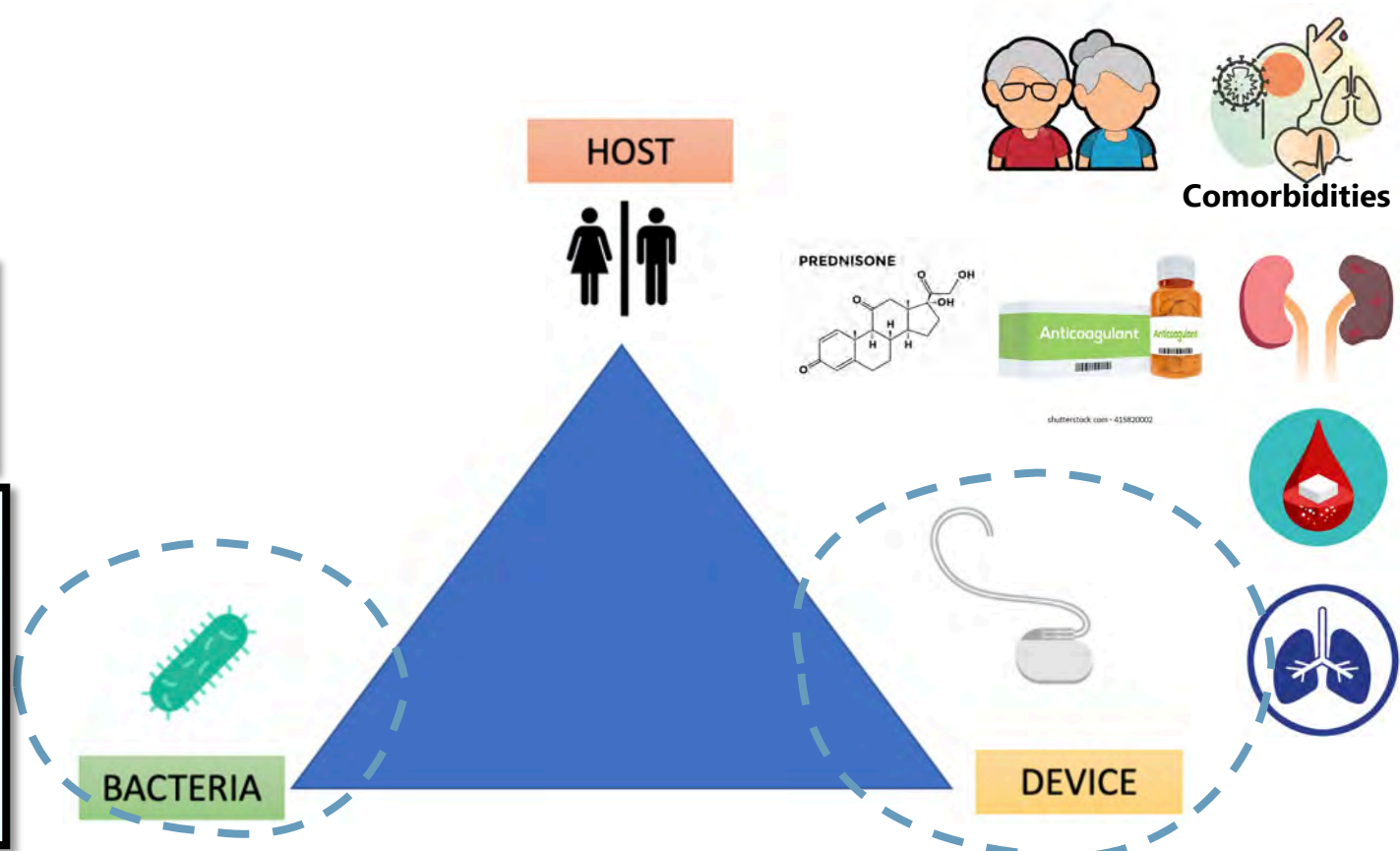
Two major mechanisms



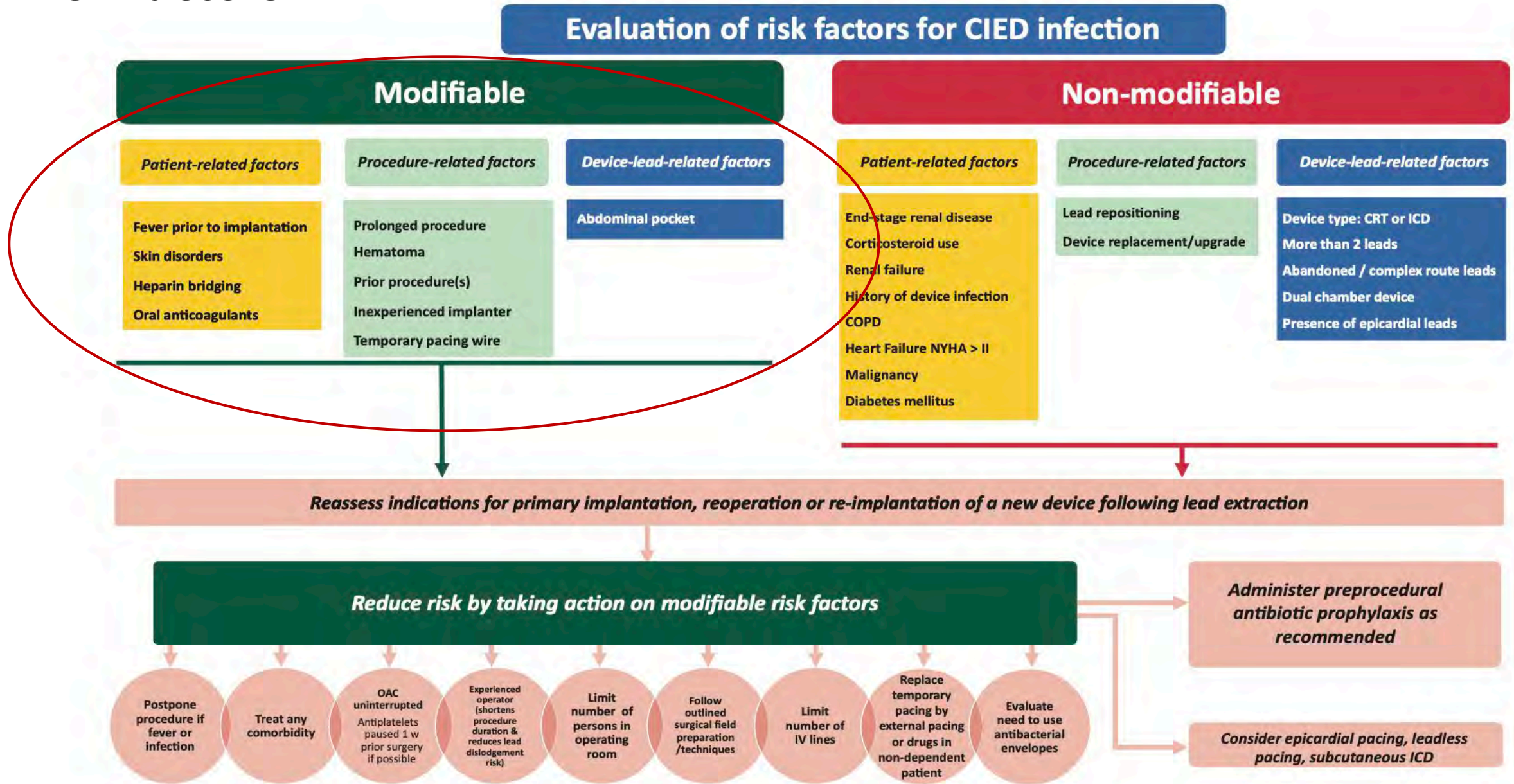
Risk factors

- Device factors**
- >2 leads
 - ICD/CRT
 - Heart disease/dysfunction

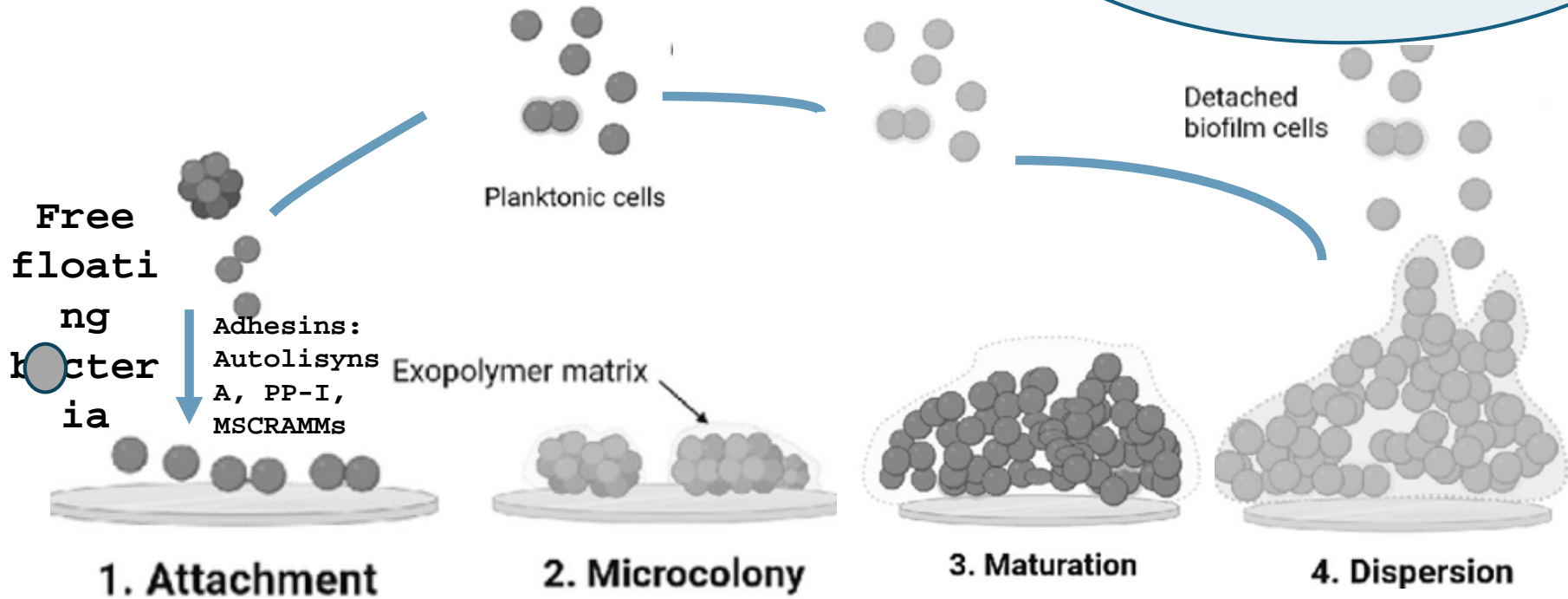
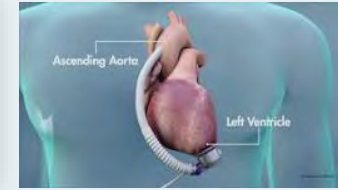
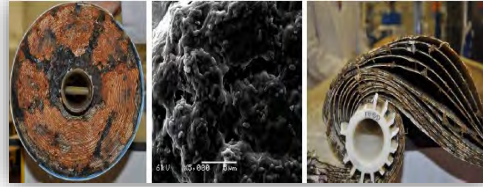
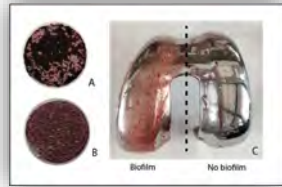
- Procedural factors**
- Early reintervention
 - Temporary pacing
 - Fever \leq 24 hours before implantation
 - Unrecognized bacteremia or focus of infection
 - Prolonged procedure duration



Risk factors



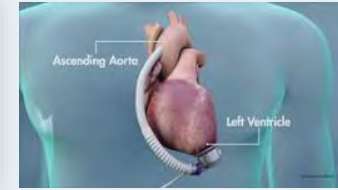
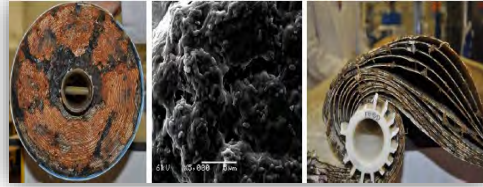
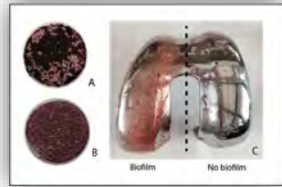
Biofilm: the major cause of medical device-associated infections



Cardiac implantable electronic device

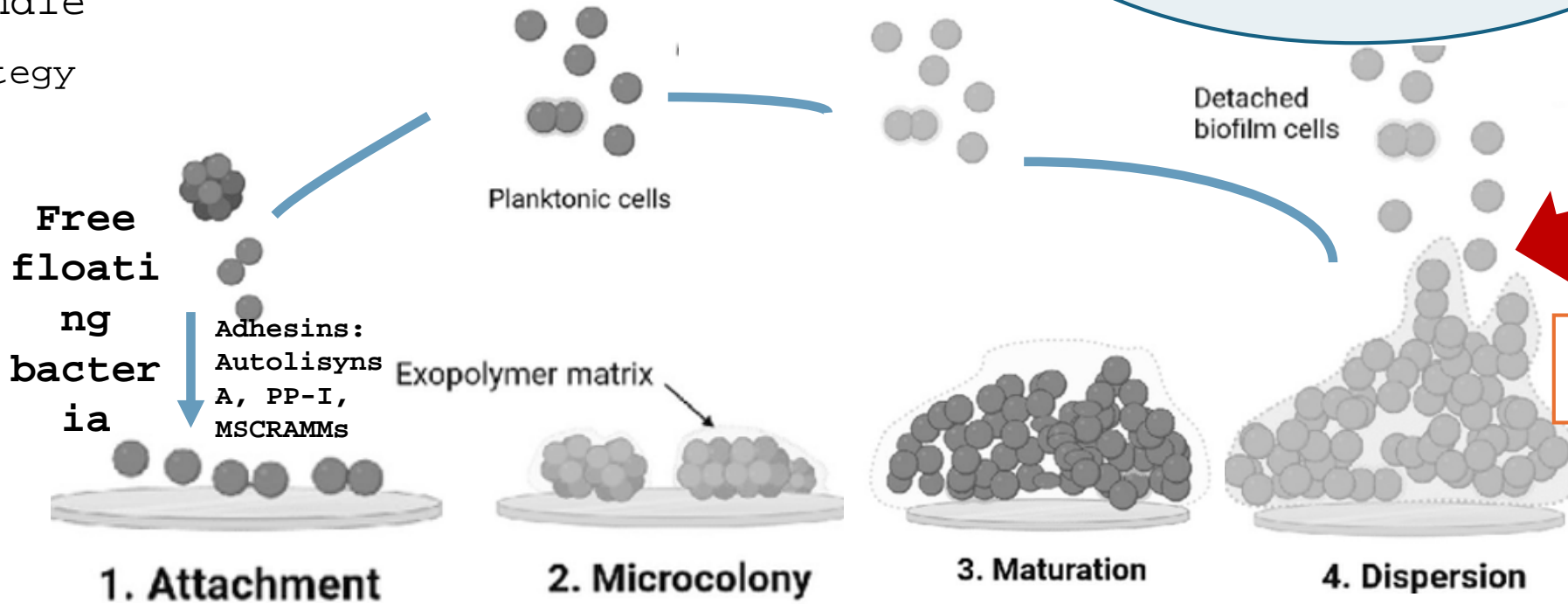


Biofilm: the major cause of medical device-associated infections



Prevention bundle

The better strategy for cure!

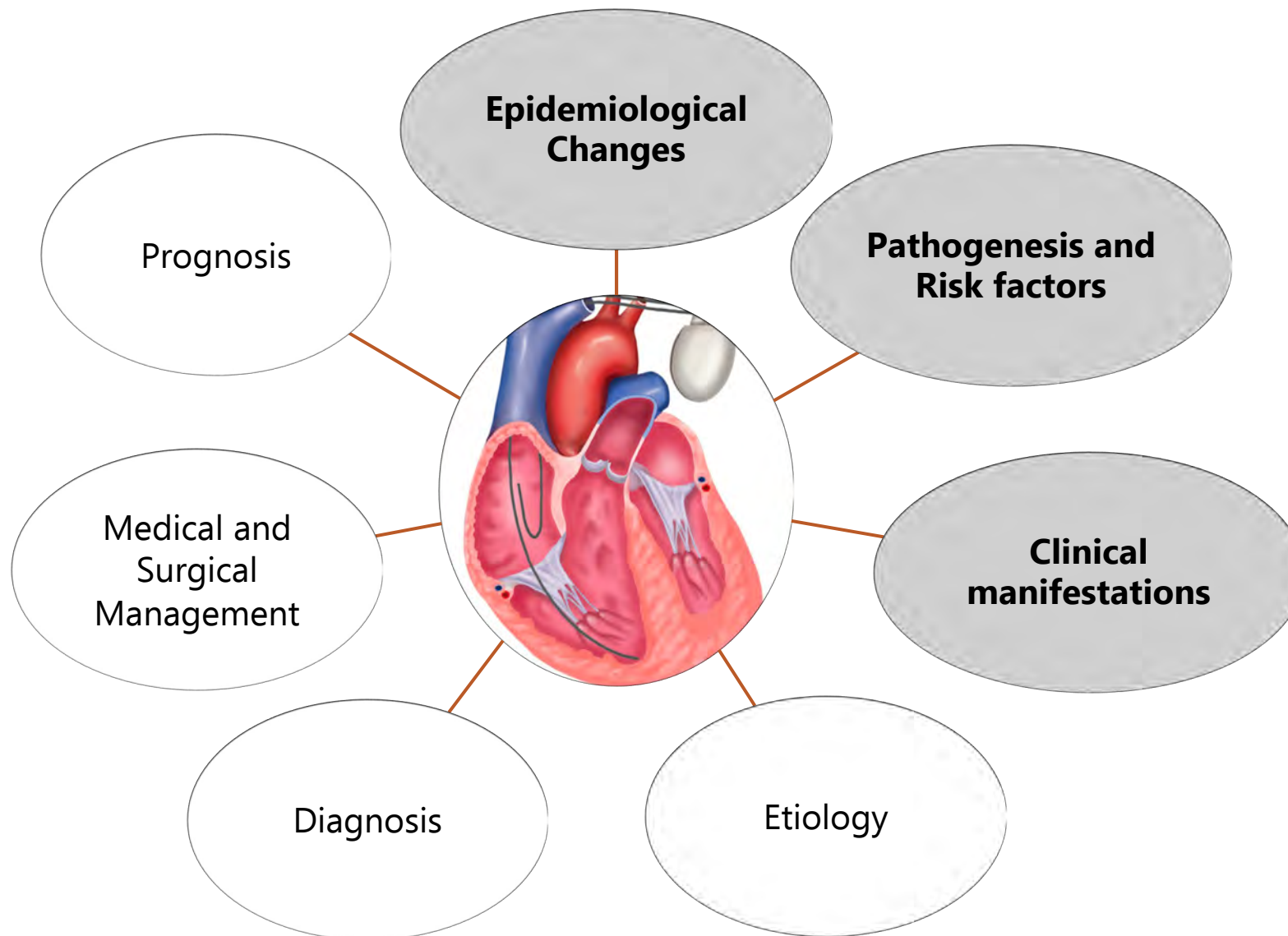


Antimicrobial

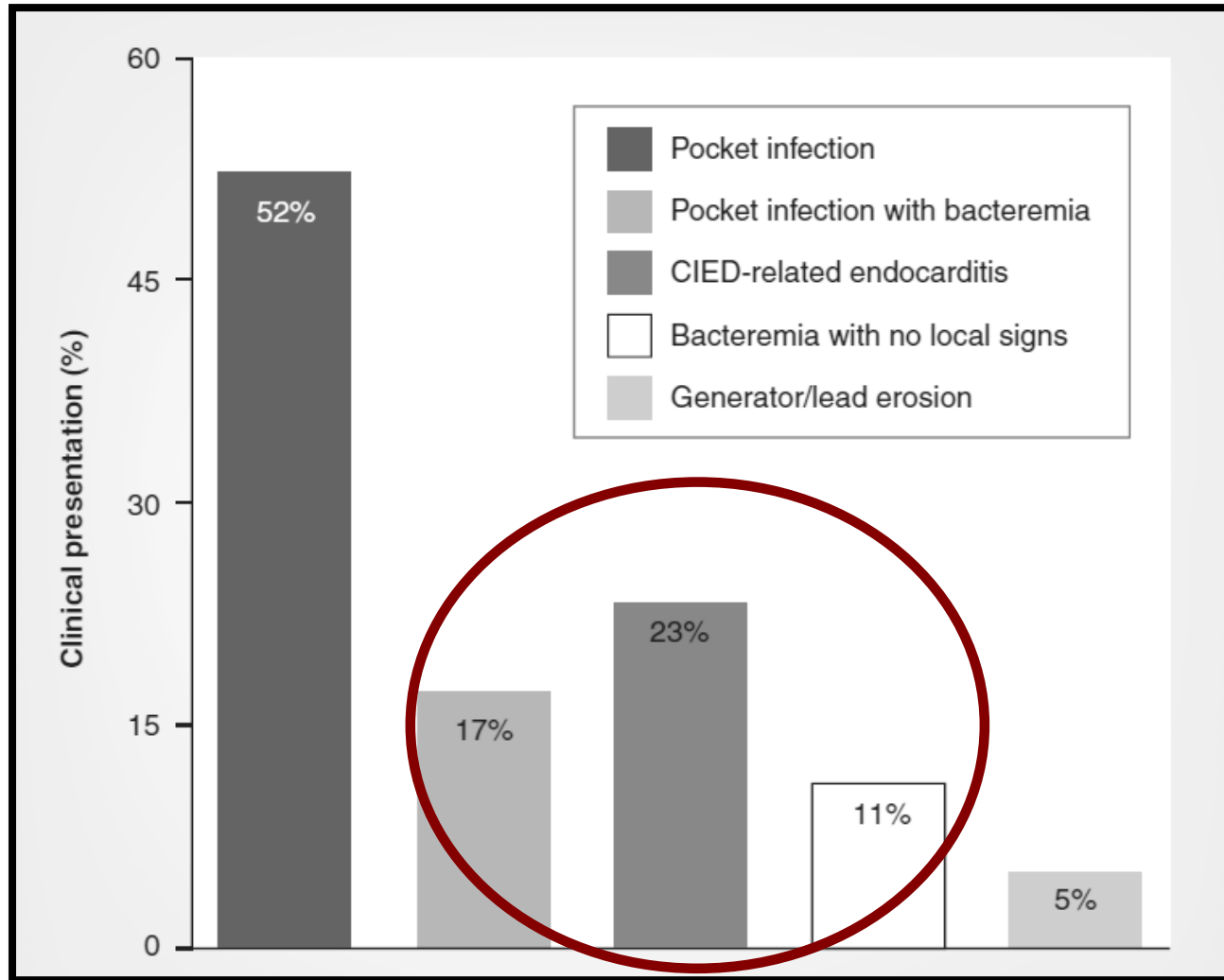
Treatment
Avoid the spread of infection.
Prevent complications



CIED INFECTIONS

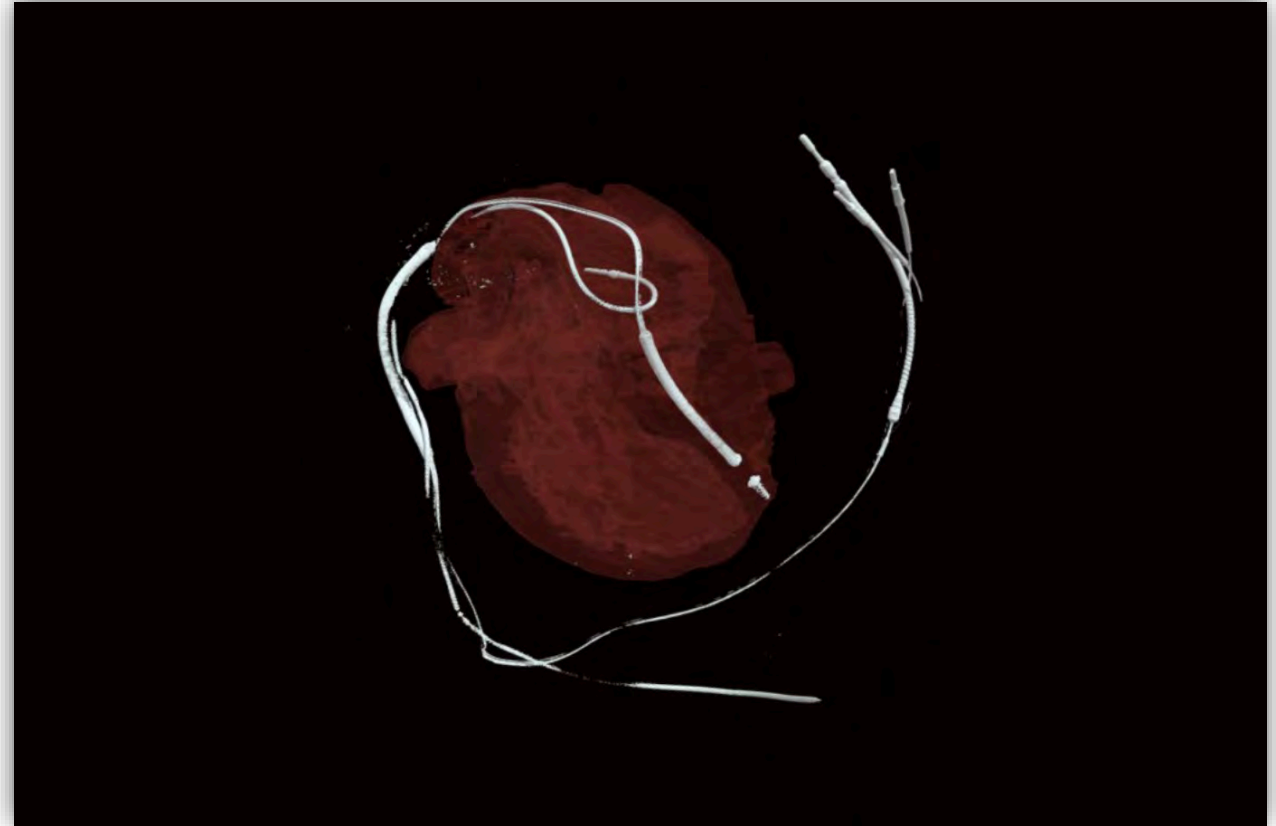
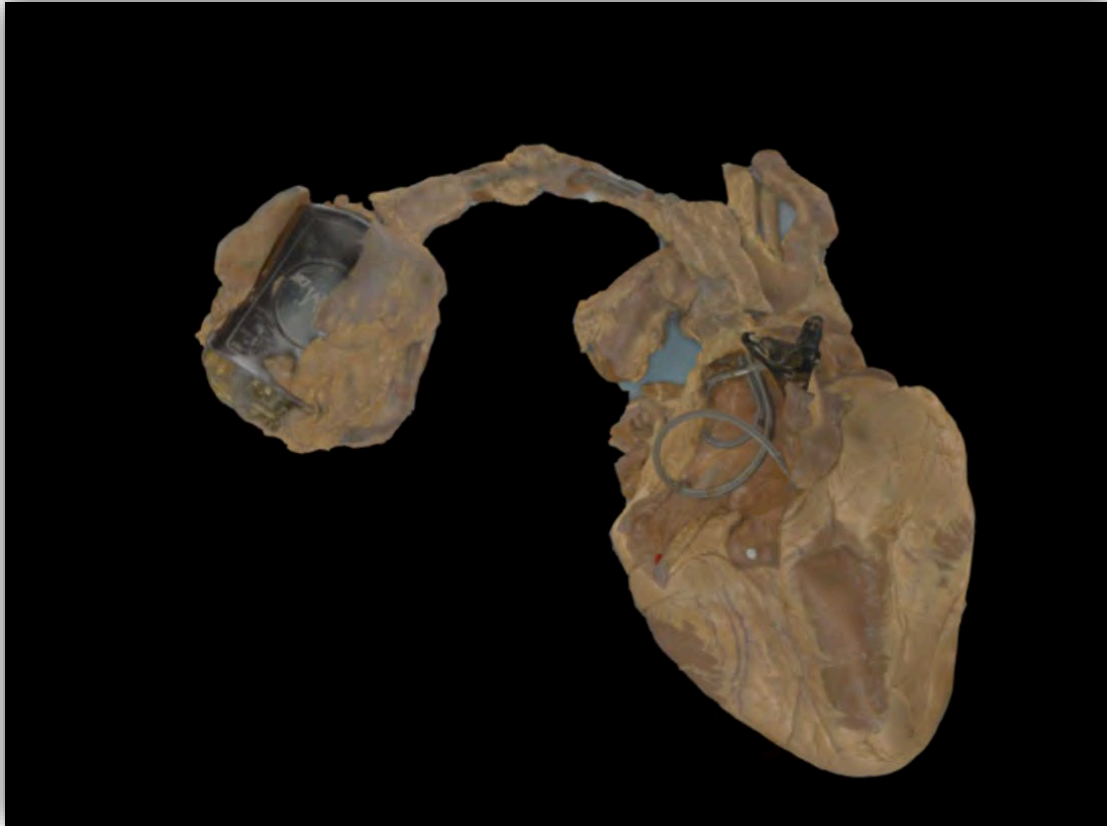


Clinical presentation of CIED infections



>50% CIED infections are high risk infections!

Clinical presentation of CIED infections



70-80% from local source -
pocket
20-30% hematogenous spread

Staphylococcus aureus bacteriemia in CIED patients

3m - early infecti

Population: 87 257 Danish patients (18-99) y/o undergoing first cardiac implantable electronic device (CIED) implantation between 2000 and 2020
 Pacemaker n= 66 180; ICD n= 13 504; CRT-P/D 7573.
 Median age 75 [IQR 66-82], 62.6 % male sex

METHODS

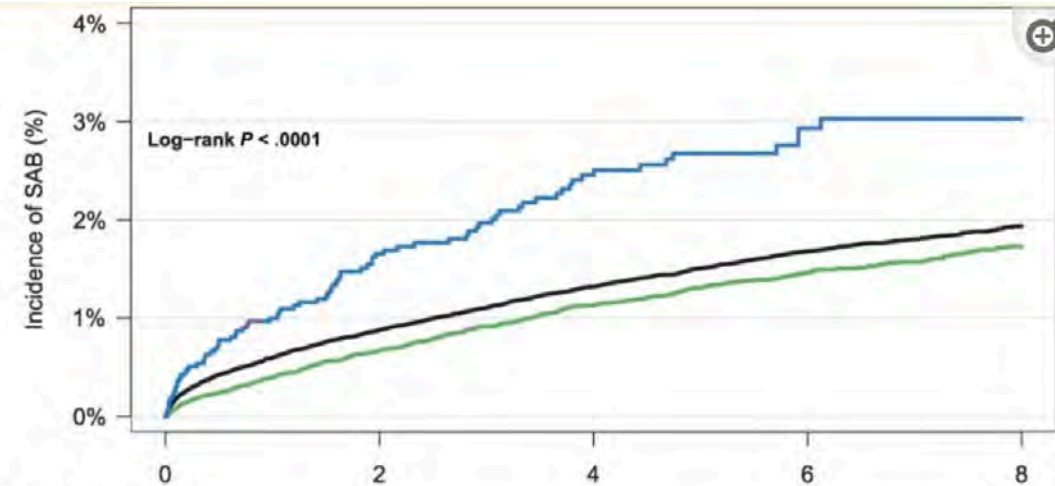
Nationwide Danish register study, cross-linking administrative registers and clinical quality databases. Study cohort obtained from *The Danish Pacemaker and ICD Register*. Primary outcome identified from *The National Danish Staphylococcus aureus Bacteraemia Database*



Primary Outcome Measure: First-time *Staphylococcus aureus* bacteremia after CIED implantation

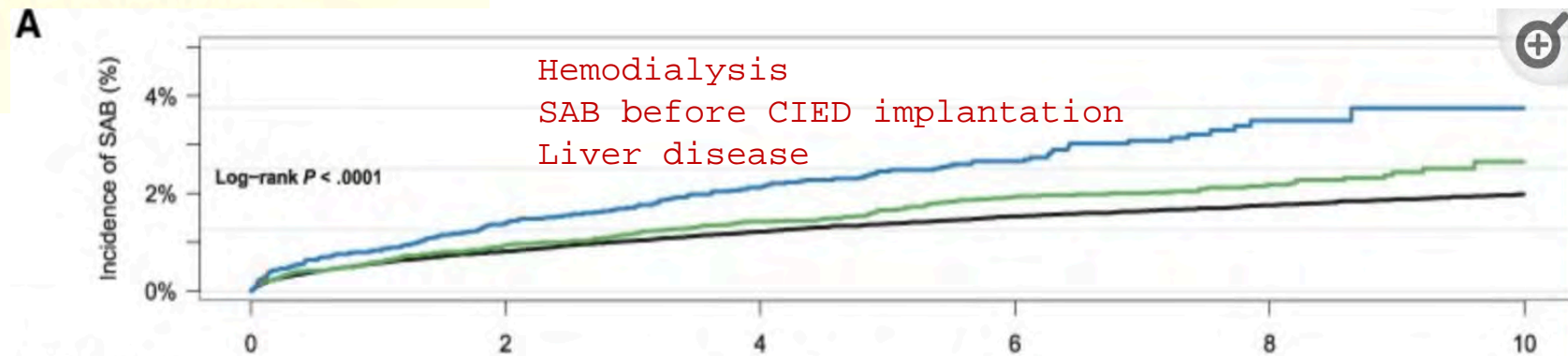


Secondary Outcome Measure: Identification of risk factors associated with SAB



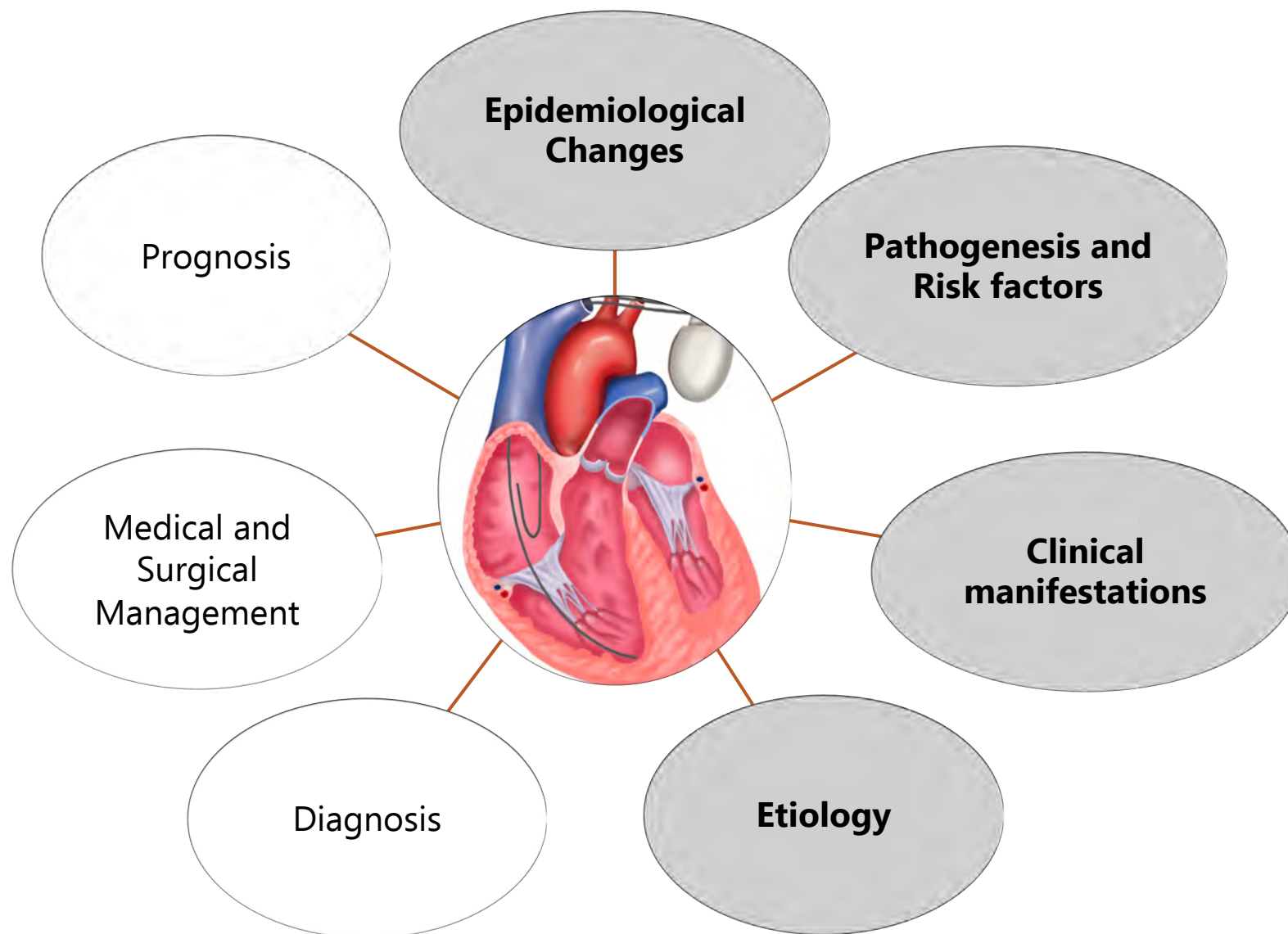
	First	2	4	6	8
Number of patients (Risk of event,%)	87 257 (0.0)	59 986 (0.9)	41 770 (1.3)	26 972 (1.7)	13 562 (1.9)
Exchange	27 959 (0.0)	19 216 (0.7)	13 106 (1.1)	8 185 (1.5)	3 932 (1.7)
Up-/downgrade	3 638 (0.0)	2 242 (1.7)	1 340 (2.5)	575 (2.9)	141 (3.0)

1,366 patients (1.6%) developed SAB
 10-year absolute risk of SAB: **PM**: 2.0% (1.9%-2.1%)
ICD: 2.6% (2.2%-3.1%)
CRT: 3.7% (3.0%-4.5%)

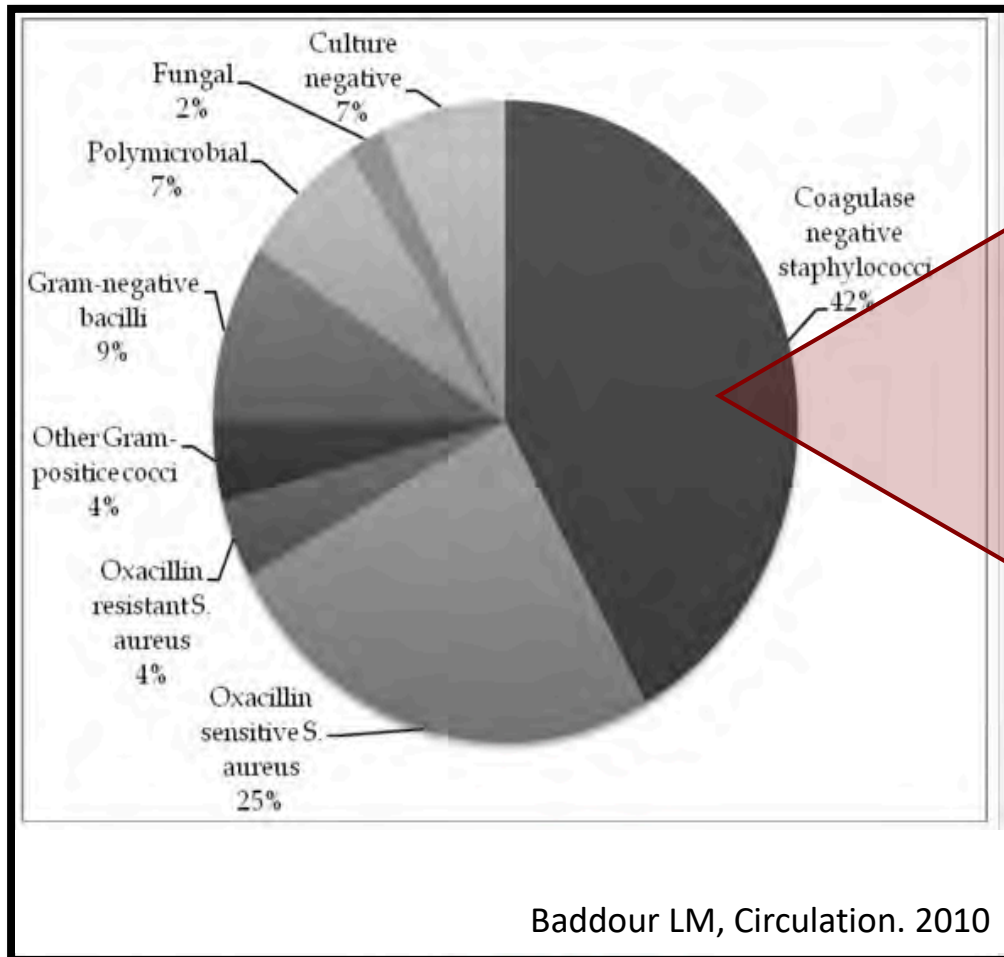


	First	2	4	6	8	10
Number of patients (Risk of event,%)	66 180 (0.0)	44 903 (0.8)	31 120 (1.2)	20 622 (1.5)	11 003 (1.8)	4 141 (2.0)
PM	66 180 (0.0)	44 903 (0.8)	31 120 (1.2)	20 622 (1.5)	11 003 (1.8)	4 141 (2.0)
ICD	13 504 (0.0)	10 050 (0.9)	7 261 (1.4)	4 623 (1.9)	2 162 (2.2)	244 (2.6)
CRT	7 573 (0.0)	5 033 (1.4)	3 389 (2.1)	1 727 (2.7)	397 (3.5)	38 (3.7)

CIED INFECTIONS



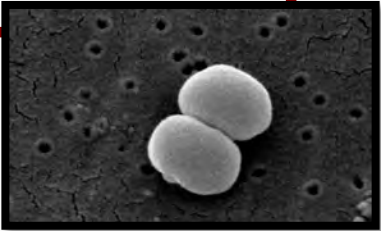
Etiology of CIED infections



Skin flora

>2/3
Staphylococcus spp.

> 50% of CoNS may present resistance to methicillin



S. epidermidis

Etiology of CIED Infective endocarditis

TABLE 2. Etiology, Diagnosis, and Outcome of 1804 Episodes of Infective Endocarditis Prospectively Collected in Spain

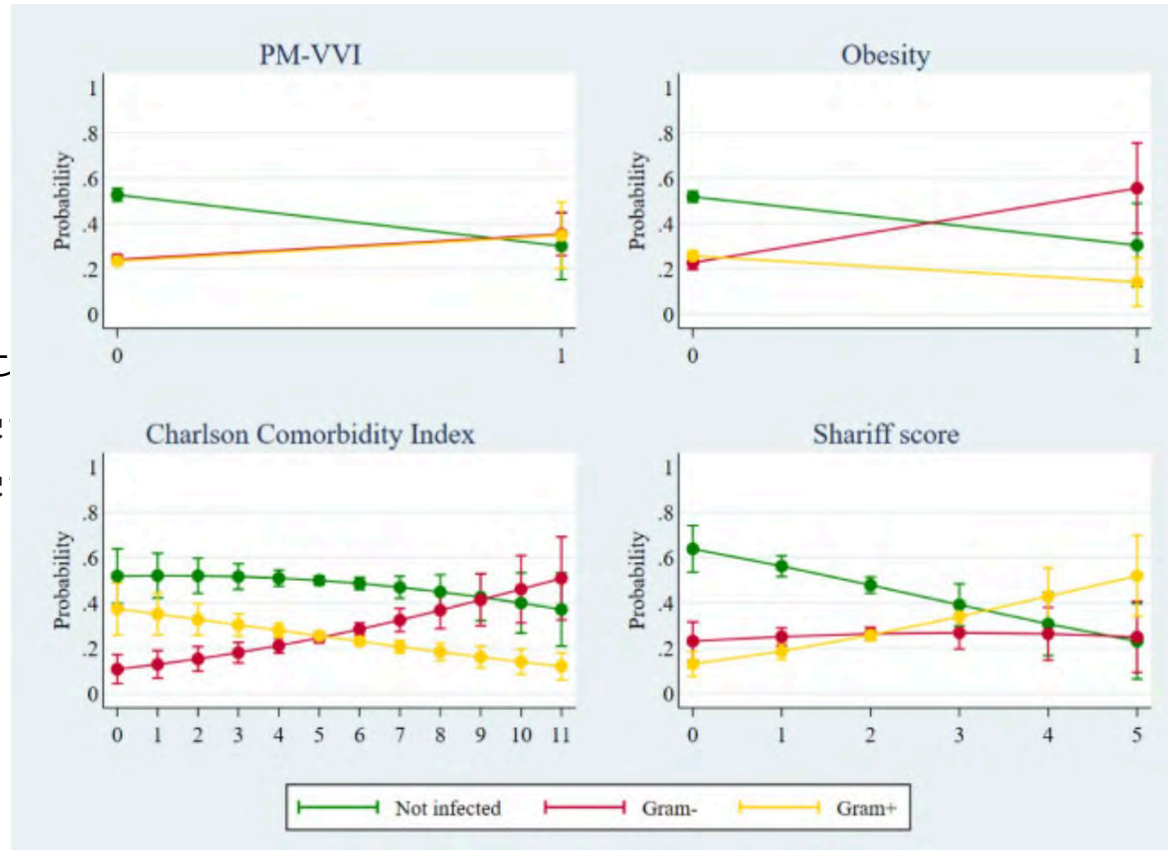
	Total N=1804	Native Non-IVDU N=1079	Native IVDU N=52	Prosthetic N=504	Device N=169	P
Definite IE	1498 (83.0)	919 (85.6)	48 (92.3)	409 (81.3)	122 (72.2)	<0.01
Possible IE	300 (16.6)	155 (14.4)	4 (7.7)	94 (18.7)	47 (27.8)	<0.01
Etiology						
<i>Staphylococcus</i> spp.	728 (40.3)	382 (35.3)	30 (55.8)	218 (43.2)	98 (58.0)	<0.01
<i>S. aureus</i>	426 (23.6)	278 (25.8)	26 (50.0)	77 (15.3)	45 (26.6)	<0.01
MSSA	360 (84.5)	235 (84.5)	24 (92.3)	64 (83.2)	37 (82.3)	0.46
MRSA	66 (15.5)	43 (15.5)	2 (7.7)	13 (16.8)	8 (17.7)	
CoNS	302 (16.7)	104 (9.7)	4 (7.7)	141 (28.0)	53 (31.5)	<0.01
<i>Streptococcus</i> spp.	440 (24.4)	329 (30.5)	8 (15.4)	86 (17.1)	17 (10.1)	<0.01
<i>S. bovis</i>	117 (6.4)	80 (7.4)	0	32 (6.5)	5 (3.0)	0.036
<i>S. viridans</i> group	223 (12.3)	171 (16.0)	7 (13.5)	38 (7.5)	7 (4.1)	<0.01
Others	100 (5.5)	79 (7.3)	1 (1.9)	15 (3.0)	5 (5.3)	0.001
<i>Enterococcus</i> spp.	230 (12.7)	142 (13.2)	5 (9.6)	77 (15.3)	6 (3.6)	0.001
Other Gram-positives*	26 (1.4)	14 (1.3)	2 (3.8)	8 (1.5)	2 (1.1)	0.48
Gram-negatives**	93 (5.2)	53 (4.9)	—	25 (5.0)	15 (8.9)	0.05
Fungi***	44 (2.4)	21 (1.9)	2 (3.8)	15 (3.0)	6 (3.6)	0.38
Negative BC	264 (14.7)	152 (14.0)	5 (9.6)	75 (14.8)	32 (18.9)	0.67
Echocardiogram						

Gram-negative CIED infection: CarDINe Study



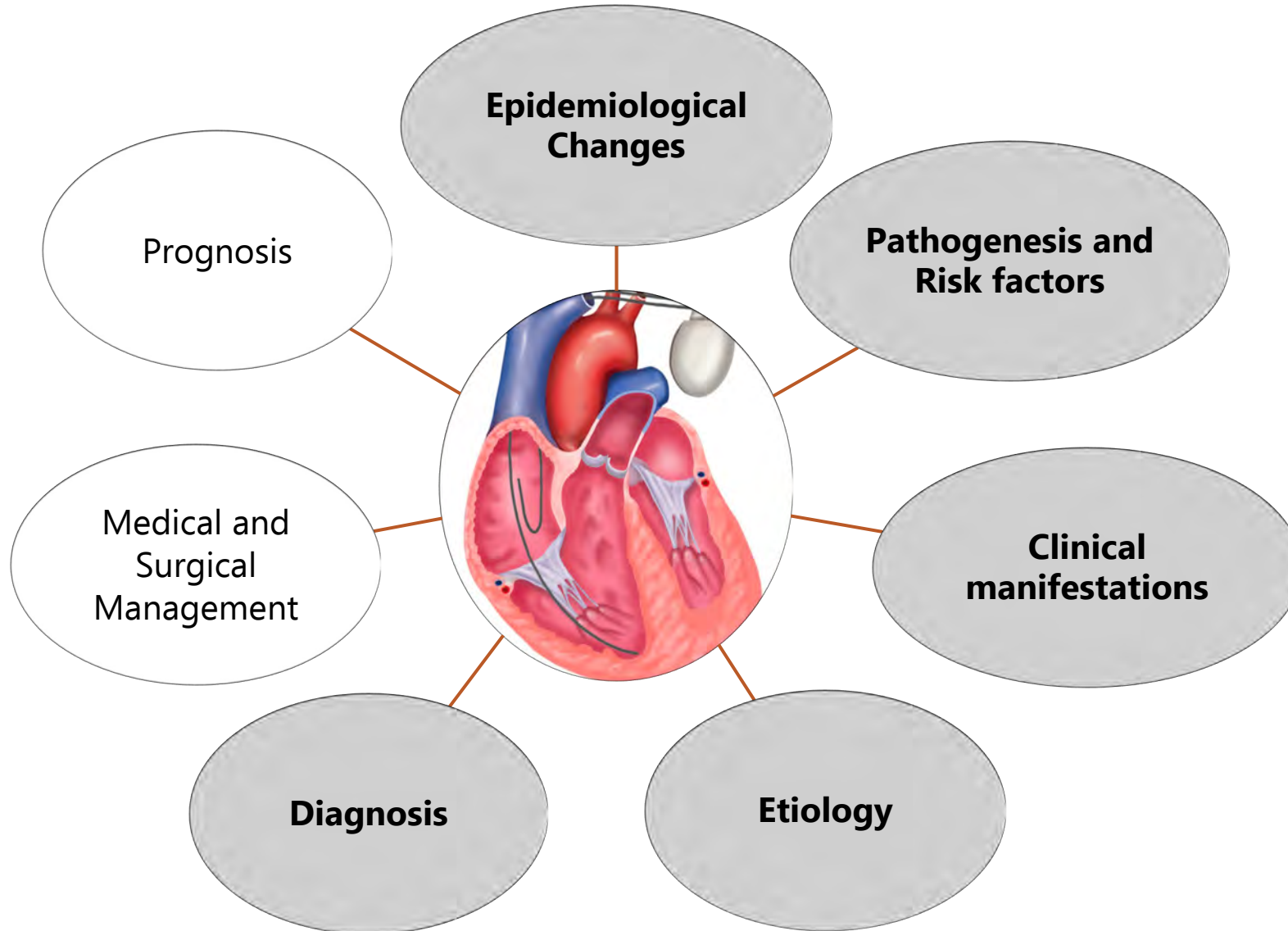
Multicentric observational study
 236 patients with GNB-CIED infection
 59 patients with GPB-CIED infection
 118 patients without infection

Risk factors for GNB-CIED infection



Increased mortality (180 days): HR 1.842 (P = 0.067)

CIED INFECTIONS



AHA SCIENTIFIC STATEMENT

Update on Cardiovascular Implantable Electronic Device Infections and Their Prevention, Diagnosis, and Management: A Scientific Statement From the American Heart Association

Endorsed by the International Society for Cardiovascular Infectious Diseases

Larry M. Baddour, MD, FAHA, Chair; Zerelda Esquer Garrigos, MD; M. Rizwan Sohail, MD; Eva Havers-Borgersen, MD; Andrew D. Krahn, MD; Vivian H. Chu, MD; Connie S. Radke, MSN, NP; Jennifer Avari-Silva, MD, FAHA; Mikhael F. El-Chami, MD; Jose M. Miro, MD, PhD; Daniel C. DeSimone, MD, Vice Chair; on behalf of the American Heart Association Council on Lifelong Congenital Heart Disease and Heart Health in the Young (Young Hearts); and Council on Clinical Cardiology

Baddour LM. Circulation. 2024 Jan 9;149(2):e201-e216.

J Antimicrob Chemother 2015; **70**: 325–359
doi:10.1093/jac/dku383 Advance Access publication 29 October 2014

Journal of Antimicrobial Chemotherapy

Guidelines for the diagnosis, prevention and management of implantable cardiac electronic device infection. Report of a joint Working Party project on behalf of the British Society for Antimicrobial Chemotherapy (BSAC, host organization), British Heart Rhythm Society (BHRS), British Cardiovascular Society (BCS), British Heart Valve Society (BHVS) and British Society for Echocardiography (BSE)

Sandoe JA. *J Antimicrob Chemother*. 2015 Feb;70(2):325-59.



ESC

European Society of Cardiology

European Heart Journal (2023) **00**, 1–95
<https://doi.org/10.1093/eurheartj/ehad193>

ESC GUIDELINES

2023 ESC Guidelines for the management of endocarditis

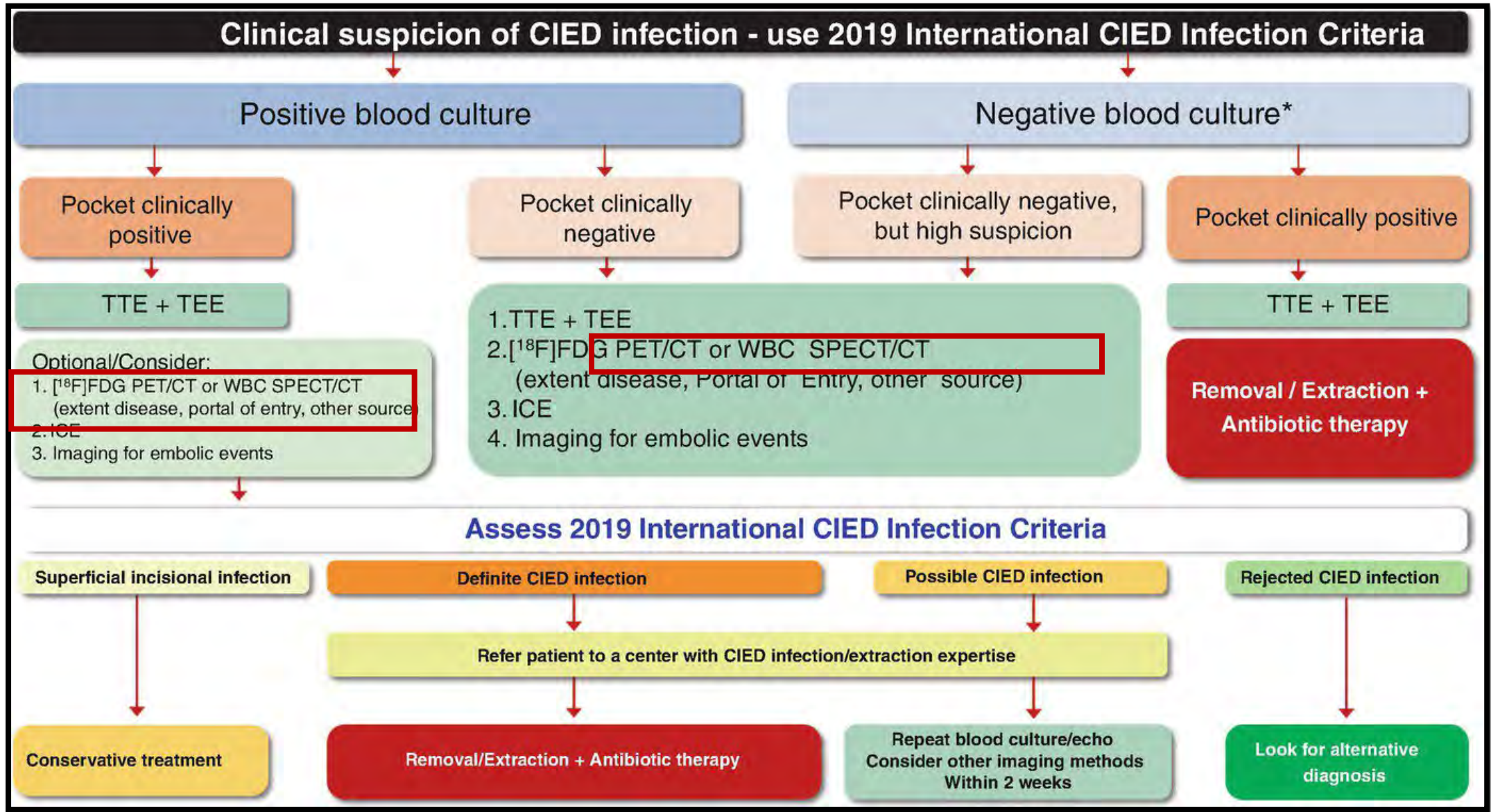
Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC)

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

Authors/Task Force Members: Victoria Delgado *[†], (Chairperson) (Spain), Nina Ajmone Marsan [‡], (Task Force Co-ordinator) (Netherlands), Suzanne de Waha[‡], (Task Force Co-ordinator) (Germany), Nikolaos Bonaros (Austria), Margarita Brida (Croatia), Haran Burri (Switzerland), Stefano Caselli (Switzerland), Torsten Doenst (Germany), Stephane Ederhy (France), Paola Anna Erba ¹ (Italy), Dan Foldager (Denmark), Emil L. Fosbøl (Denmark), Jan Kovac (United Kingdom), Carlos A. Mestres (South Africa), Owen I. Miller (United Kingdom), Jose M. Miro ² (Spain), Michal Pazdernik (Czech Republic), Maria Nazarena Pizzi (Spain), Eduard Quintana ³ (Spain), Trine Bernholdt Rasmussen (Denmark), Arsen D. Ristić (Serbia), Josep Rodés-Cabau (Canada), Alessandro Sionis

Delgado V. *Eur Heart J*. 2023 Oct 14;44(39):3948-4042

What's new in CIED infection diagnostic criteria?



Innovations in Imaging: ¹⁸F-Fluorodeoxyglucose PET/CT for Assessment of Cardiovascular Infection and Inflammation

Pathology			Sensitivity	Specificity	Summary
Cardiac Infection	Infective endocarditis	PVE	86% (7)	84% (7)	Combining ¹⁸ F-FDG PET with CT angiography improves diagnostic performance and helps detect peri-prosthetic and peripheral complications
		NVE	31–36% (7)	98–99% (7)	Emerging use – limited sensitivity due to small vegetations; may have a role in assessing extracardiac infection
		Transcatheter valve infection	83% (34)	–	Increasing utility in TAVI, particularly when combined with CT angiography
	Cardiac implanted electronic device infection		Pocket infection: 96% (38); Lead involvement: 97% (38)	Pocket infection: 97% (38); Lead involvement: 83% (38)	Utility is superior for pocket infection compared to lead involvement
	LVAD infection		95% (50)	91% (50)	Promising role of ¹⁸ F-FDG PET/CT as many components of the LVAD are not assessed by echocardiography
Cardiovascular Inflammation	Cardiac sarcoidosis		84% (62)	83% (62)	Quantification of inflammation may provide added value for diagnosis and monitoring of disease progression and response to therapy
	Large vessel vasculitis		76% (83)	93% (83)	Role in patients with symptoms of large vessel vasculitis or fever/inflammation of unknown origin

Abbreviations: ¹⁸F-FDG, ¹⁸F-Fluorodeoxyglucose; CT, computed tomography; LVAD, left ventricular assist device; NVE, native valve endocarditis; PET, positron emission tomography; PVE, prosthetic valve endocarditis; TAVI, transcatheter-aortic valve implantation

PET's usefulness is not well characterized

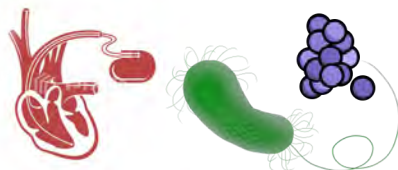
	Local infection	Systemic infection
Mahmood⁵	N=66	N=78
Sensitivity	96%	76%
Specificity	97%	83%
Jerónimo⁶	N=14	N=13
Sensitivity	72%	38.5%
Specificity	95.6%	98%
Bensihmon⁷	N=5	N=10
Sensitivity	100%	60%
Specificity	100%	100%
Cautela⁸	N=15	N=13
Sensitivity	86%	31%
Specificity	100%	62%
	Sn 72-100% Sp 96-100%	Sn 30-60% Sp 62-100%

The topographical lead segment has not been studied.

PROGNOSIS

What's new on CIED infections and PET/CT

Retrospective case-control study (2014 – 2021) → 54 cases and 54 controls*



Cases (definite CIED infection diagnosis)

- Local infection (pocket +/- SC lead) → local signs of infection and/or device positive cultures
- Systemic infection (EV-lead or IE) → positive blood or lead cultures w/wo vegetations on TEE

Controls

(patients without CIED infection)

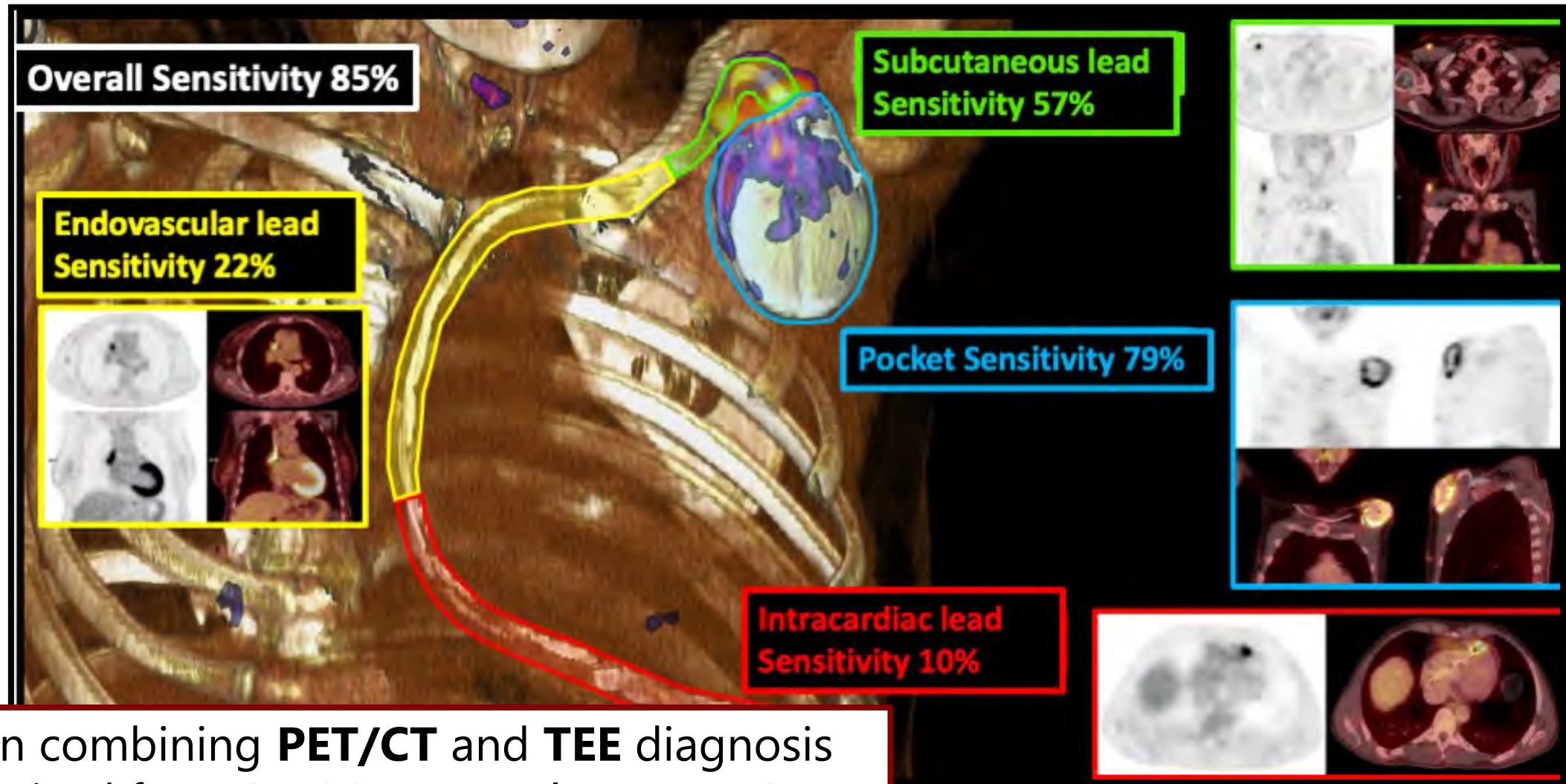
PET done for other reasons (neoplasms)

* Matched by gender, similar age, calendar year and CIED type

Primary endpoint → PET accuracy (Sn, Sp, PPV, NPV) on each topographical region

Secondary endpoints → Comparison with TEE, SUVmax (ROC curve), time between device implantation and PET and time since ATB and PET, bone marrow and spleen uptake, role in the follow up.

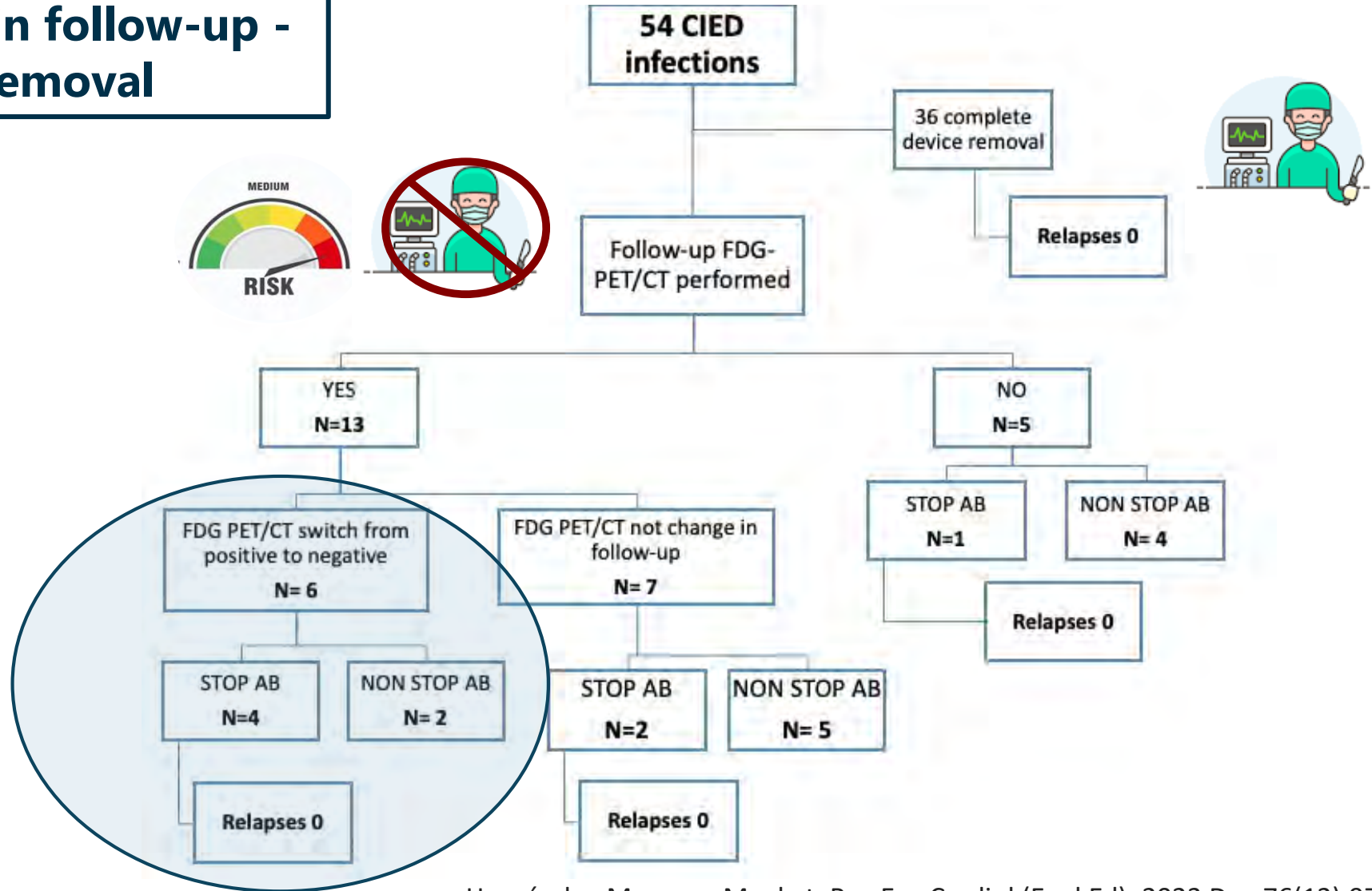
What's new on CIED infections and PET/CT



When combining **PET/CT** and **TEE** diagnosis rate raised from **34-39%** (TEE alone) to **56%-67%** (both).

What's new on CIED infections and PET/CT

[18F]FDG PET/CT role in follow-up - non-complete device removal



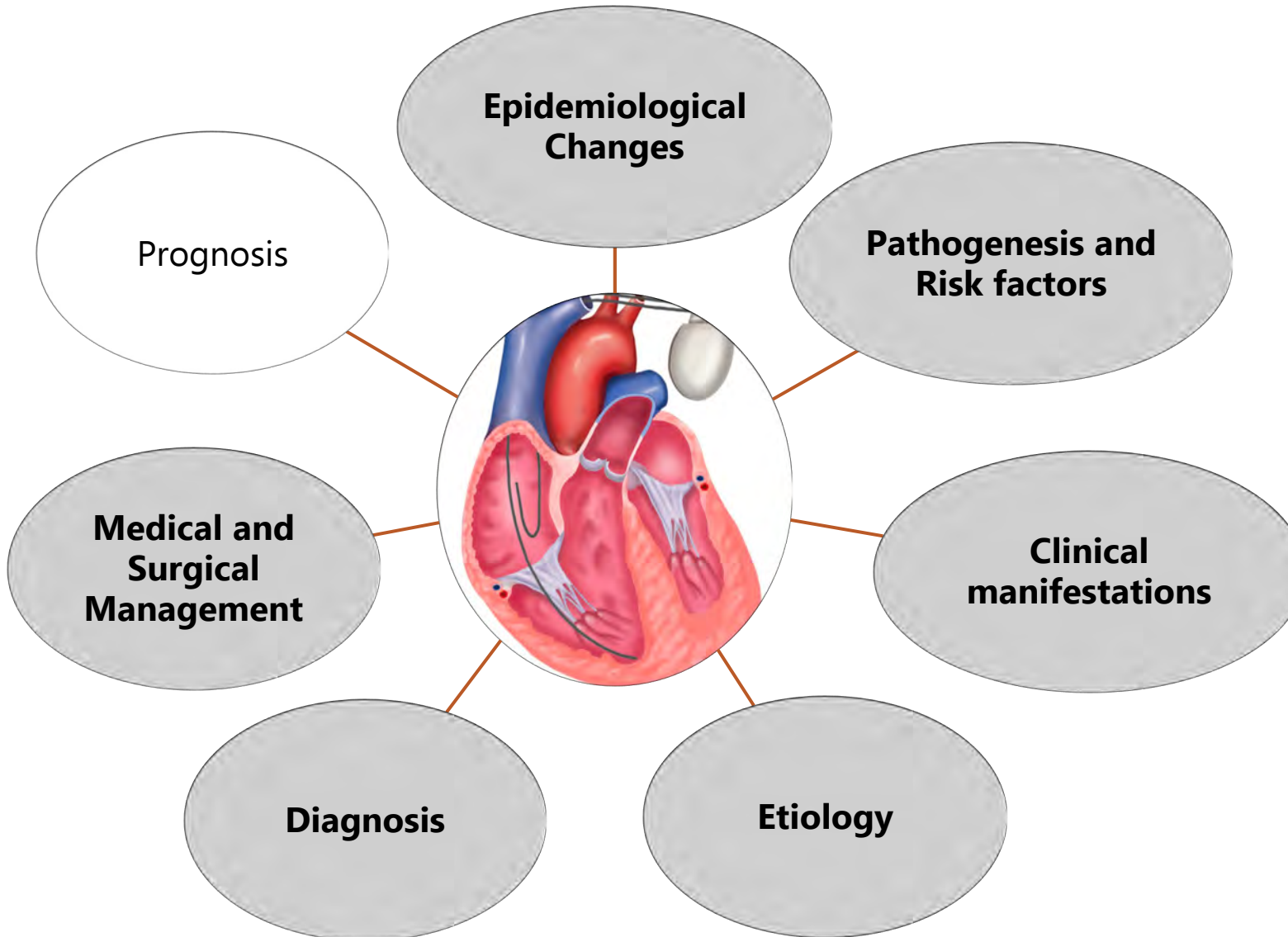
FUTURE DIRECTIONS



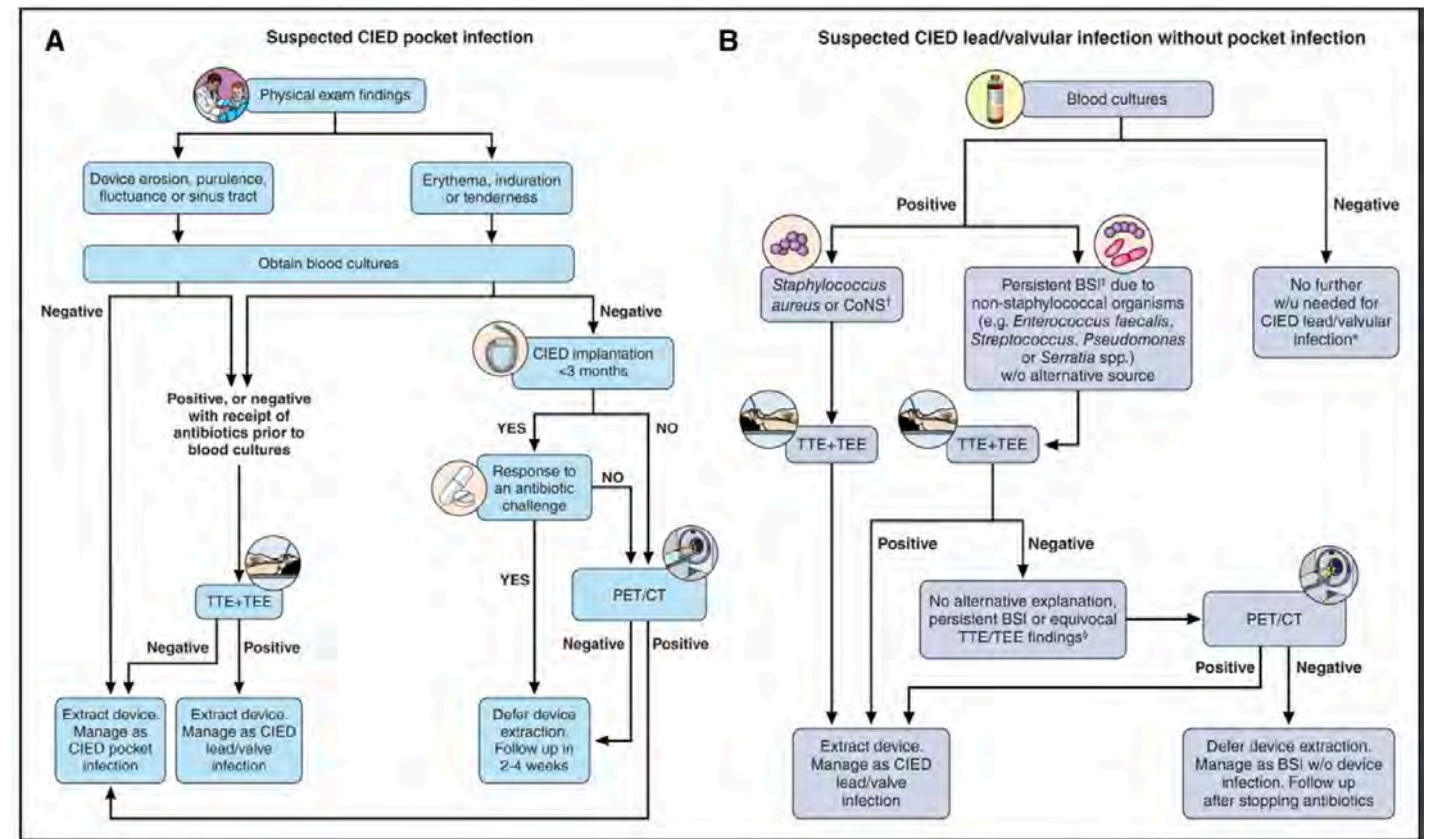
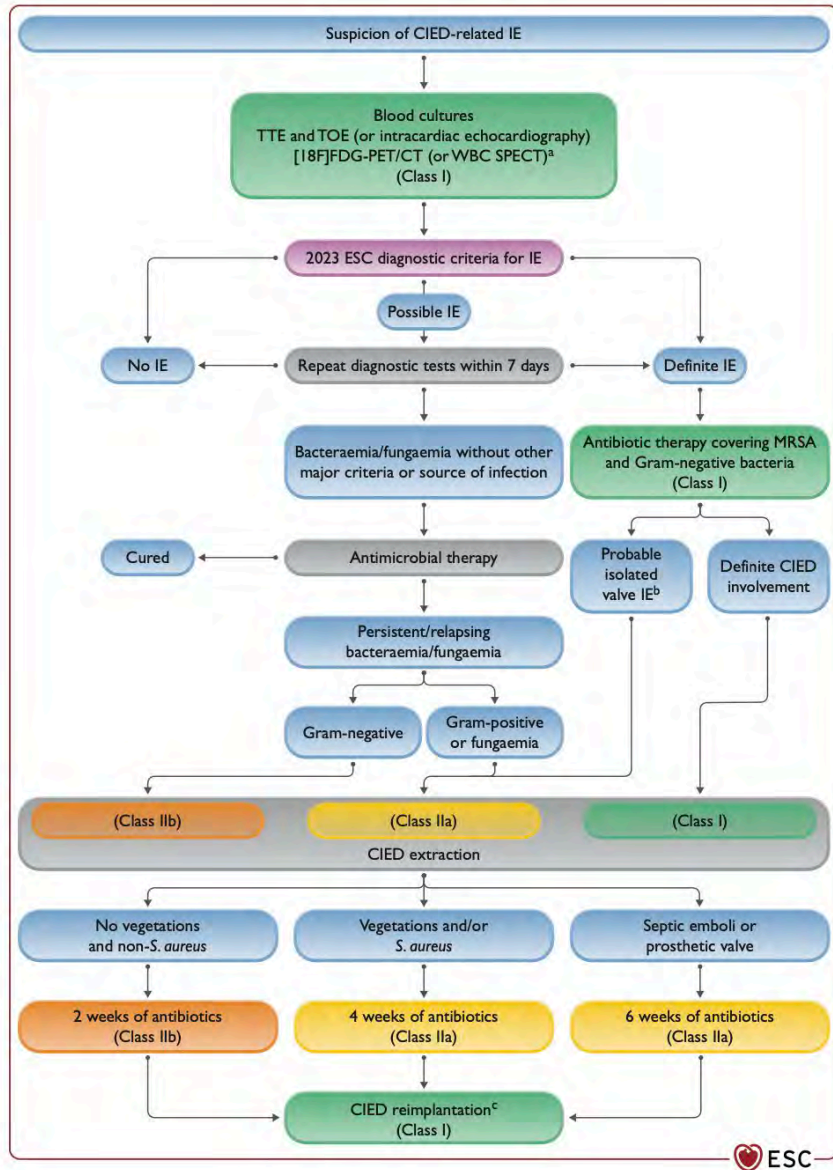
INNOVATION RESEARCH

- GLU LEVELS
- VISUAL ANALYSIS
- INFLUENCE OF AB
- TIMMIG CIED IMPLANT
- LACK OF AVAILABILITY

CIED INFECTIONS

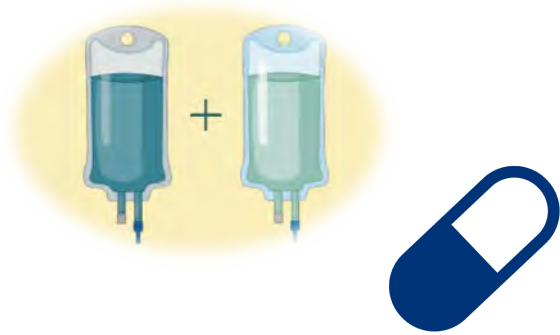


What's new in CIED infection management?



Baddour LM. Circulation. 2024 Jan 9;149(2):e201-e216.

Medical and surgical management



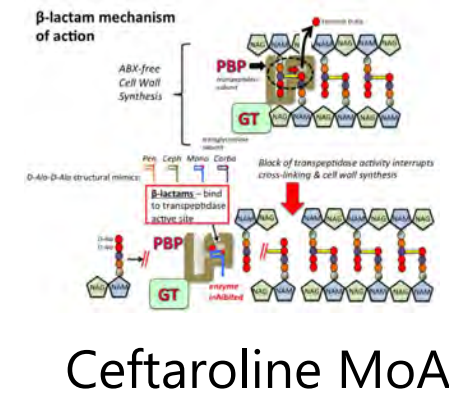
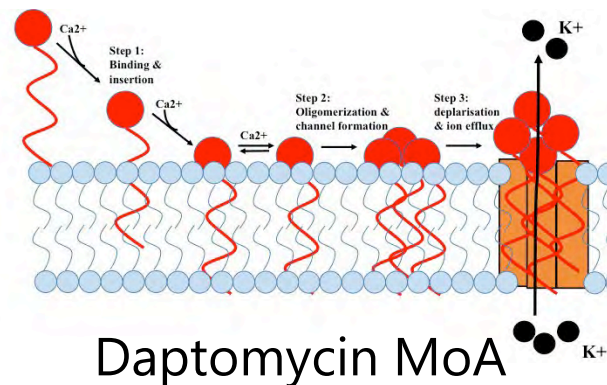
Antibiotics
+
Device Removal



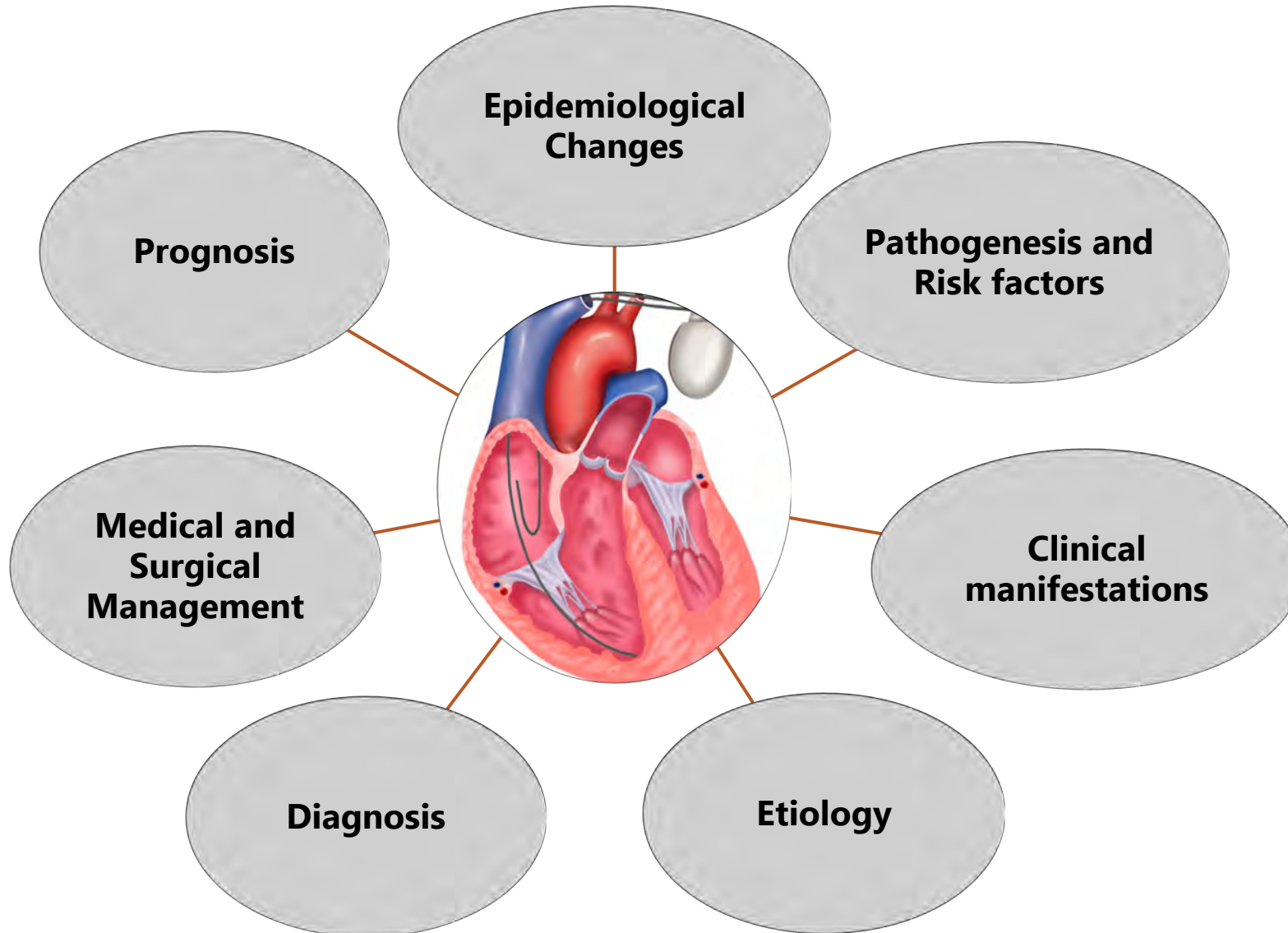
But AB treatments have not changed over 20 years!!

Guidelines AHA, ESC and EHRA consensus
Vancomycin/gentamicin-based AB suboptimal efficacy toxicity.

New antibiotics have not been studied:



CIED INFECTIONS



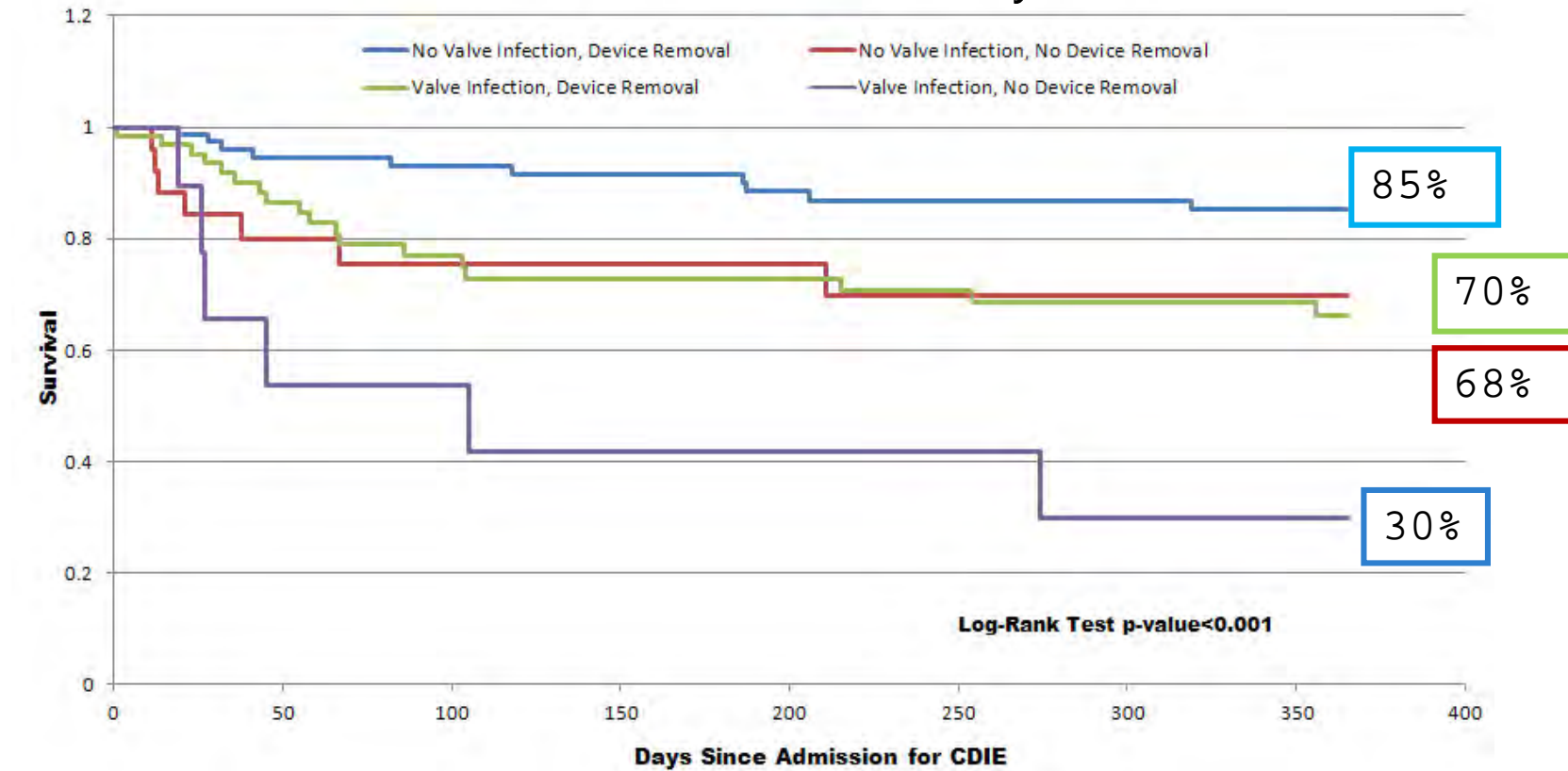
Prognosis in CIED infections

Complete device removal is the key for survival!



ICE-Pro prospective cohort study, 2000-2006

One-year survival



Dead:	0	21	28	32	34	37	39	40
At Risk:	175	134	117	111	108	101	97	92

Non-complete device removal?

Mayo Clinic cohort study, 2005-2015

660 CIED infections
 48 (7%) non-complete removal

Chronic antimicrobial suppression
 (CAS) therapy
 7%

RELAPSES: 18%
 IN-HOSPITAL MORTALITY: 25%
 ONE-YEAR MORTALITY: 44%

CAS-Toxicity (rash 9%, C. diff
 pancreatitis 3%)

- 18% developed CIED relapse:
- 100% → alternative AB therapy
 - 33% → underwent extraction due to relapse
 - 50% → expired due to CIED extraction surgery.

MEDIC cohort study, 2009-2012

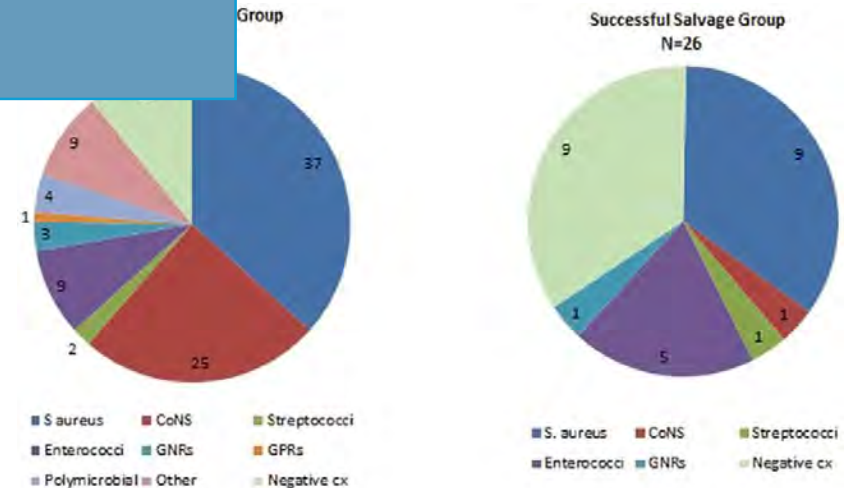
443 CIED infections,
 127 (29%) non-complete removal

Chronic antimicrobial suppression
 (CAS) therapy
 29%

RELAPSES: 22%

MORTALITY: 30%
 ATALITY: -

Antibiotics Duration?
 Follow-up?

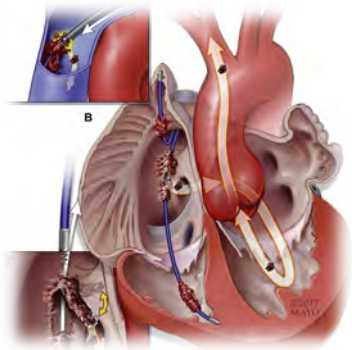


Non-complete device removal cohort



Comparison between complete vs. non-complete device removal

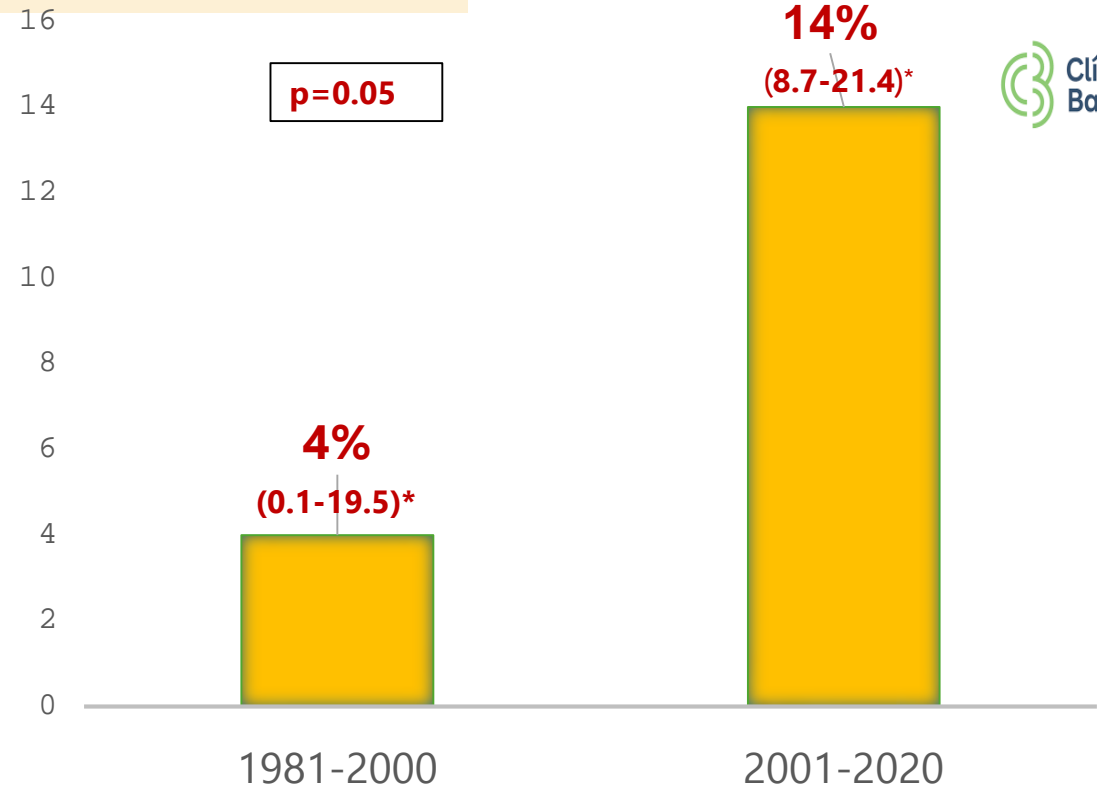
Prevalence of non-complete device removal
Overall cohort **12.14% (6.7-17.5)***



REMOVAL

VS.

**NON-COMPLETE
REMOVAL**



1981-2021



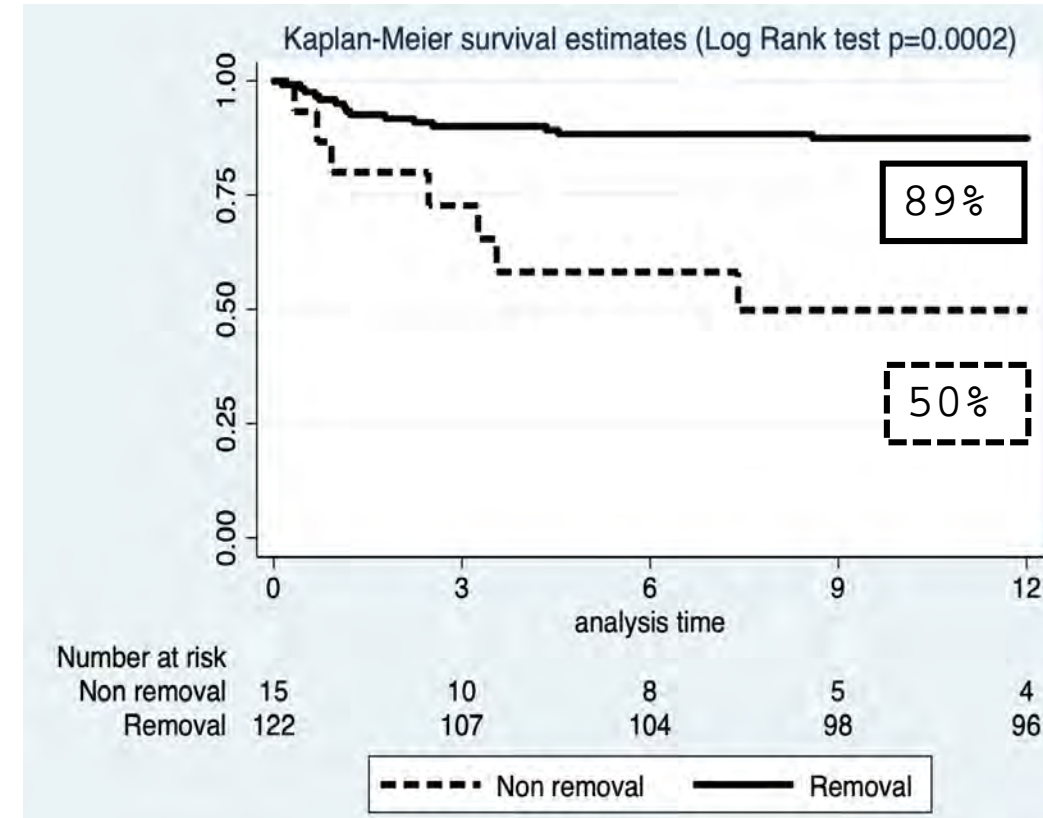
*95% Confidence interval

Non-complete device removal cohort



Predictors factors for non-complete device removal

	Univariate			Multivariate		
	OR	CI 95%	p	OR	CI 95%	p
2001-2020 vs. 1981-2000	0.58	(0.12, 2.71)	0.12	-	-	-
Age	1.12	(1.05, 1.21)	<0.01	1.15	(1.05, 1.25)	<0.01
Charlson index	1.18	(0.99, 1.41)	0.05	1.15	(0.97, 1.39)	0.11
PPM vs ICD+CRT	1.82	(0.39, 8.49)	0.45	-	-	-
Transferred from another hospital	0.72	(0.24, 2.18)	0.56	-	-	-
> 2 leads vs <= 2 leads	0.57	(0.07, 4.66)	0.60	-	-	-
Concomitant pocket infection	0.55	(0.17, 1.81)	0.33	-	-	-
Concomitant tricuspid vegetation	0.19	(0.02, 1.52)	0.12	0.23	(0.03, 2.03)	0.20
CoNS CIED-IE	0.34	(0.11, 1.12)	0.08	0.60	(0.11, 3.15)	0.54
<i>S. aureus</i> CIED-IE	3.32	(1.17, 9.51)	0.02	4.35	(1.93, 9.51)	<0.01



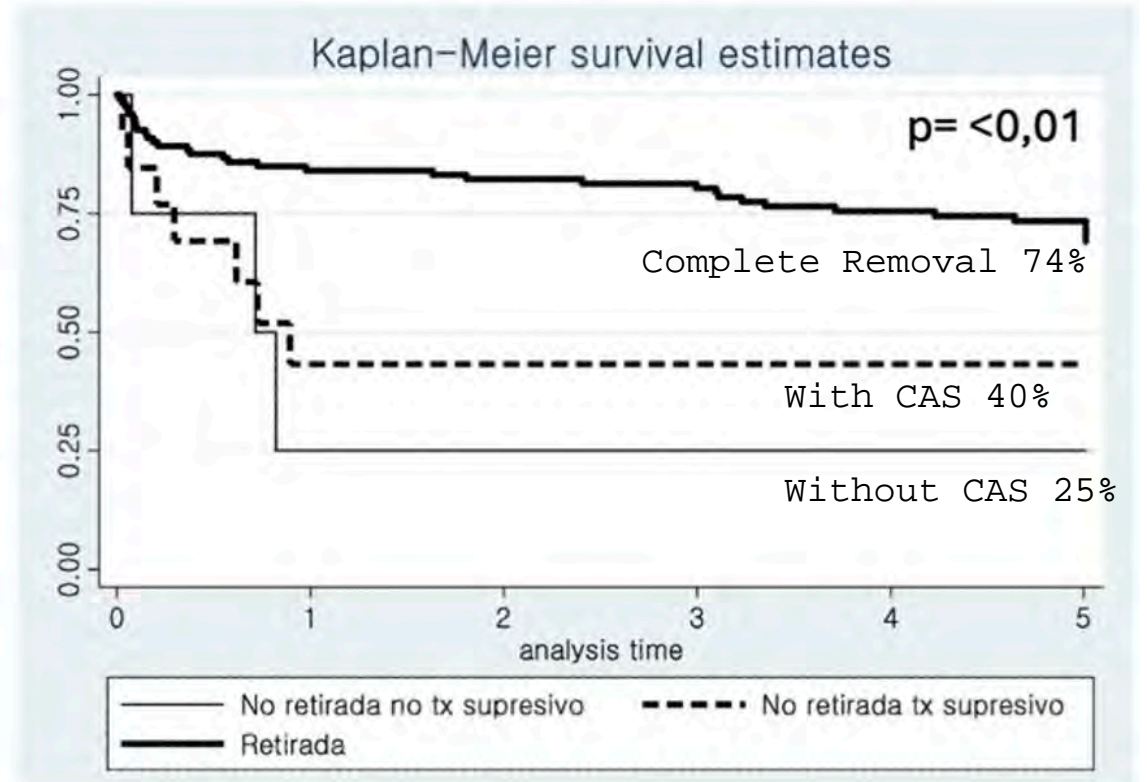
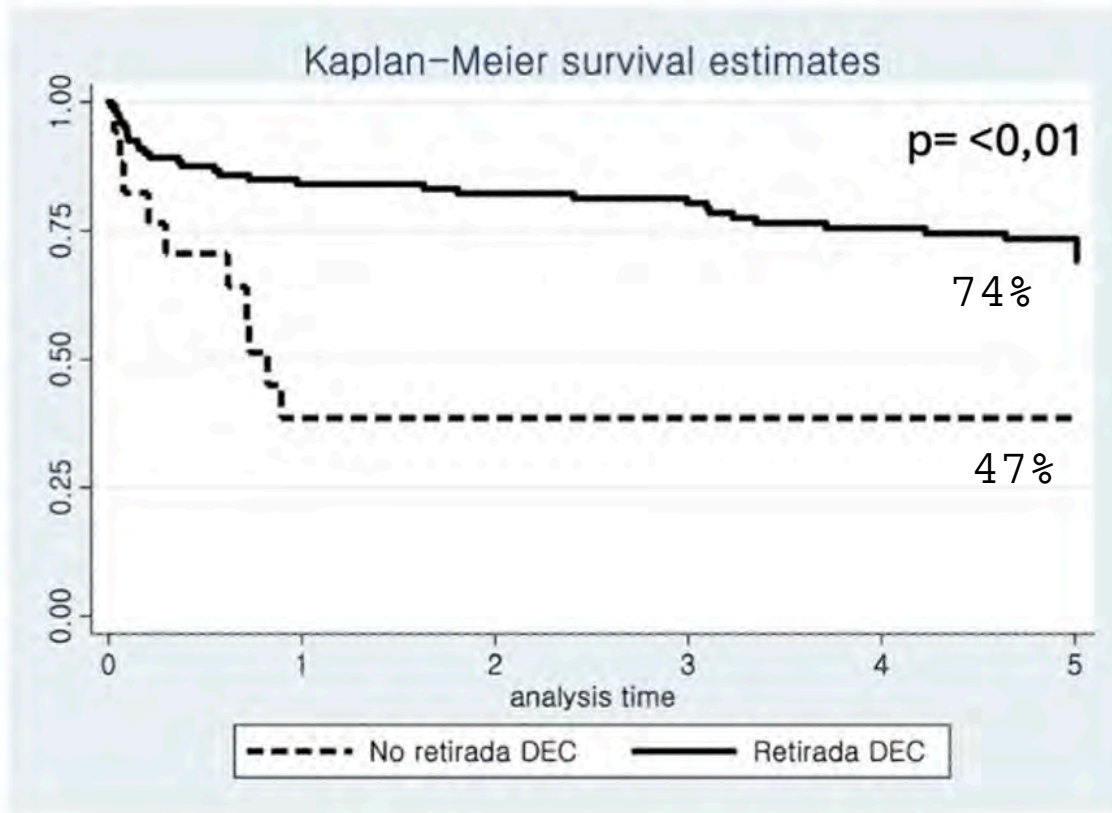
Hernández-Meneses M et al. OFID 2022

Hernandez-Meneses et al. Manuscript on preparation

Non-complete device removal cohort



Five-year survival of non-removal CIED IE



Take home messages

- The **rise in CIED implants** leads to **more infections**, especially in **older, comorbid** populations with longer life expectancy. **CIED IE** also increased. More **healthcare-associated infections**, more **transfers** from other centers, and higher rates of resistant pathogens (**staphylococci, enterococci**). Despite this, **one-year survival has improved.**
- **Staphylococci** (primarily CONS) are the most frequent cause. Obesity, comorbidities, and ventricular stimulation may be risk factors for Gram-negative infections, though this data should be interpreted cautiously.
- **New Guidelines: Limited changes**, but **PET/CT** is highlighted for pocket infections. There is limited published evidence on molecular biology use, but it has proven efficacy. Combining PET/CT with TEE increases the diagnosis of systemic lead infections. **PET/CT is key for local infections, and TEE is crucial for intracardiac leads.** PET/CT disappearance of uptake during follow-up could help safely stop CAS when device removal is incomplete.
- **Complete device removal is critical for survival**, requiring updated guidelines

**Thank
you**

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S O C I E T A T
C A T A L A N A
DE
M A L A L T I E S
I N F E C C I O S E S
|
M I C R O B I O L O G I A
C L Í N I C A