2017 HRS Expert Consensus Statement on CIED Lead Management and Extraction

Summary, Discussion, and Perspectives

Bruno Hoen

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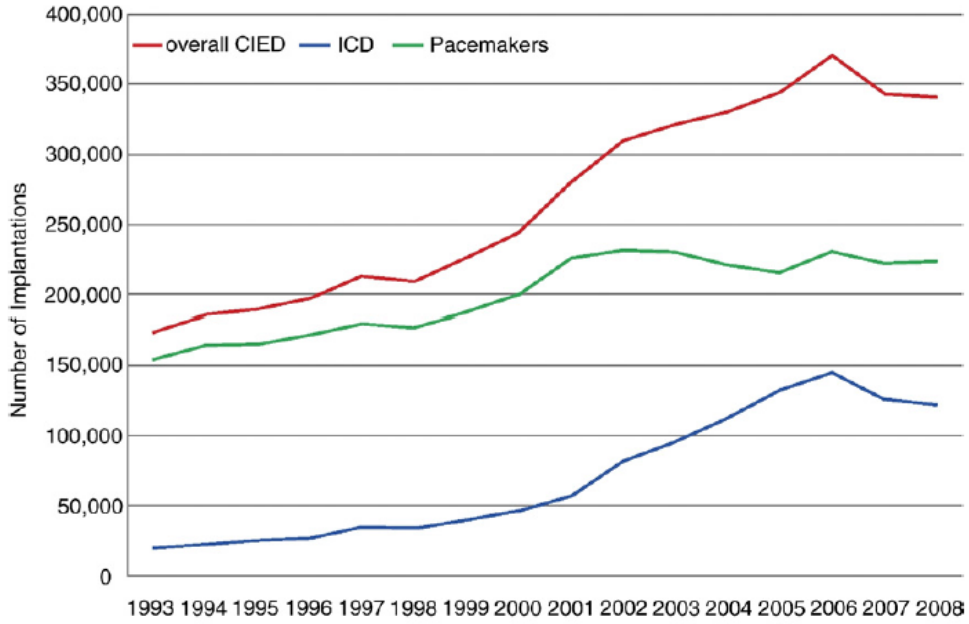
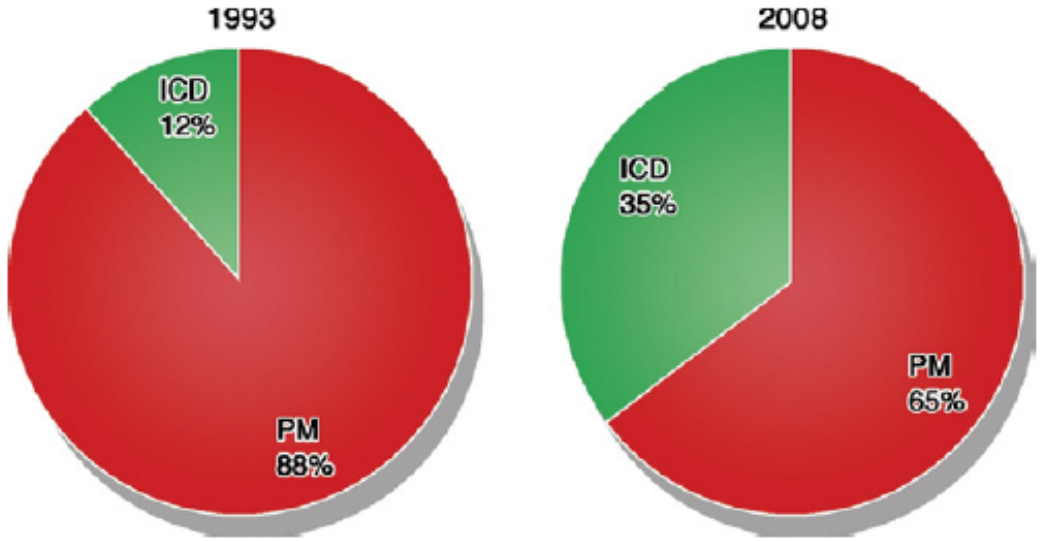
16-Year Trends in the Infection Burden for PM and ICD in the US: 1993 to 2008



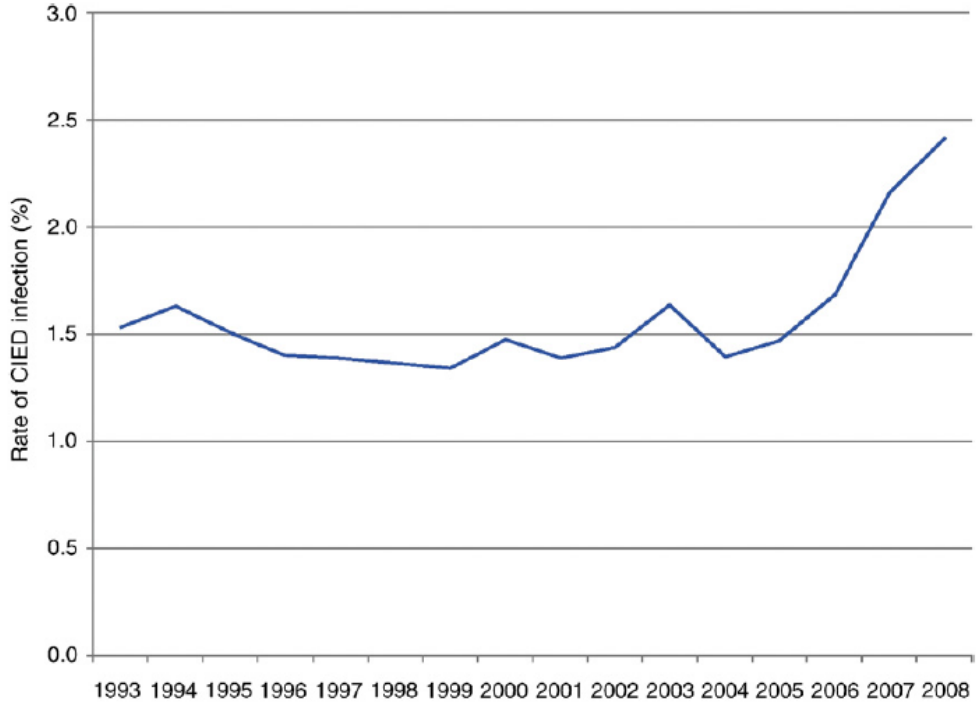
Annual number of PM and ICD implantations: 1993 to 2008



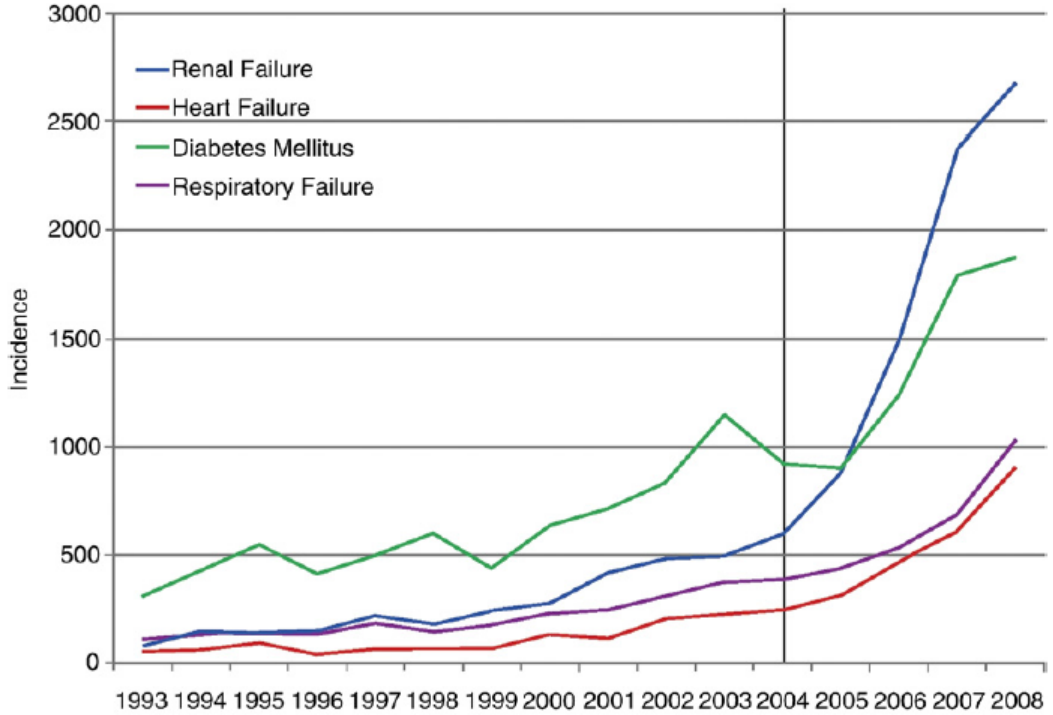
PM vs ICD in % of all CIED implantations: 1993 vs 2008

Greenspon AJ, JACC 2011;58:1001

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



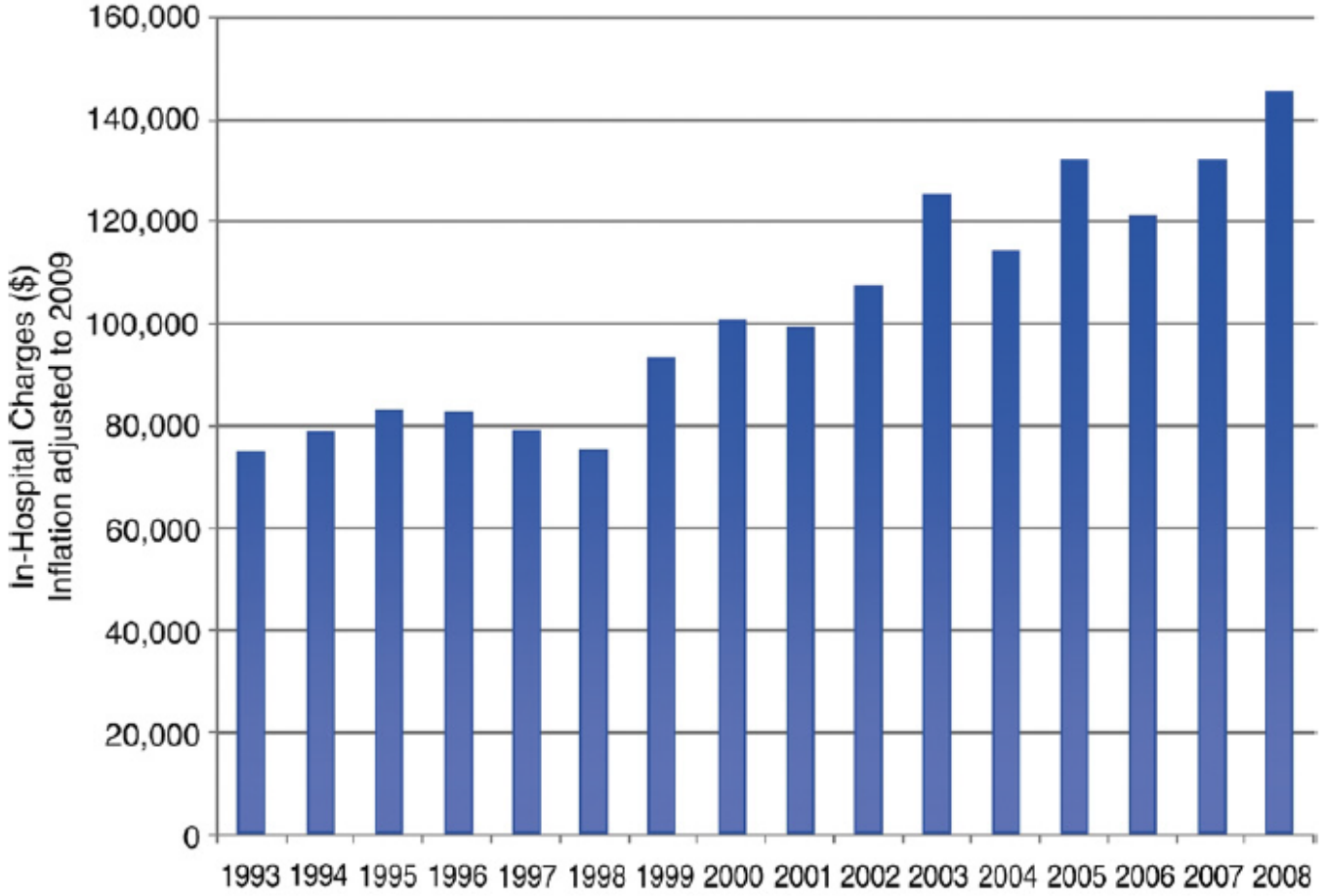
Annual rate of CIED infections



Incidence of comorbidities in patients with CIED infection

Greenspon AJ, JACC 2011;58:1001

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



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

Greenspon AJ, JACC 2011;58:1001

ACC/AHA Task Force Statement

Further Evolution of the ACC/AHA Clinical Practice Guideline Recommendation Classification System

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Class (strength) of recommendation

COR

- I – Benefit >>> Risk STRONG
- IIA – Benefit >> Risk MODERATE
- IIB – Benefit ≥ Risk WEAK
- III – Benefit = Risk NO BENEFIT
- III – Risk > Benefit HARM

Level (quality) of evidence

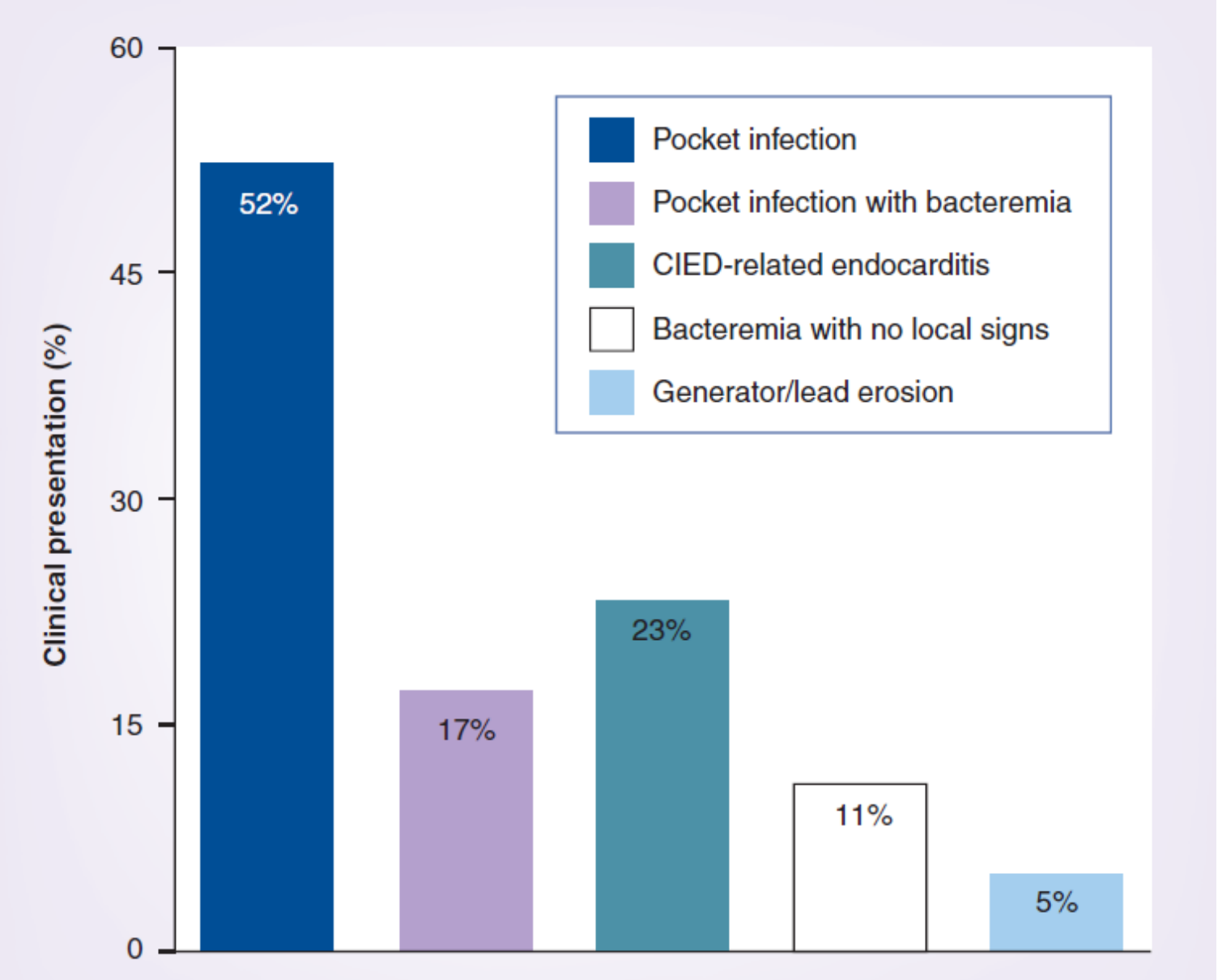
LOE

- A – high quality evidence from more than 1 RCT
- B-R – moderate quality evidence from 1 or more RCT
- B-NR – moderate quality evidence from observational study
- C-LD – Limited data
- C-EO – Expert opinion

Definitions

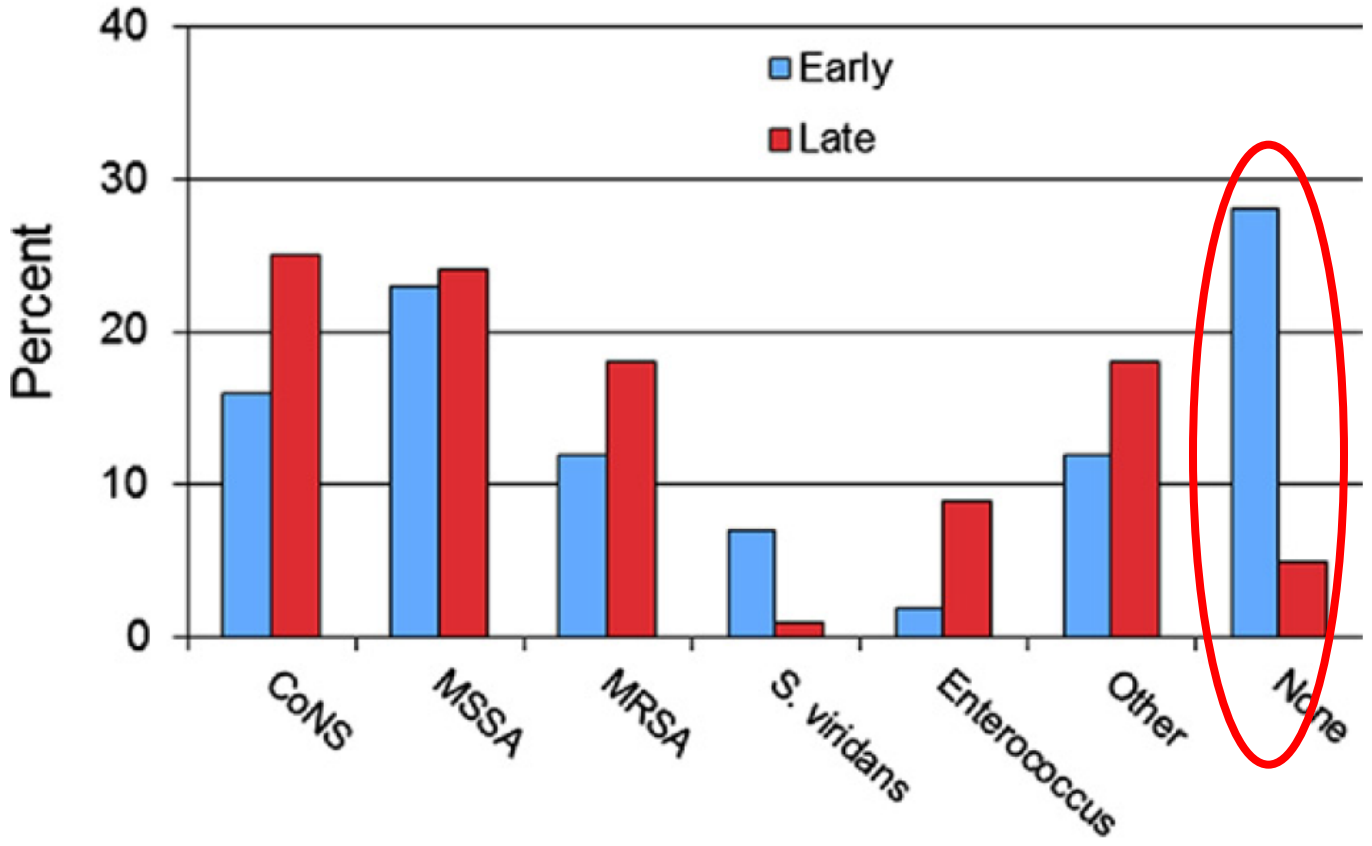
- Isolated generator pocket infection: localized erythema, swelling, pain, tenderness, warmth, or drainage with negative blood cultures
- Isolated pocket erosion: device and/or lead(s) are through the skin, with exposure of the generator or leads, with or without local signs of infection
- Bacteremia: positive blood cultures with or without systemic infection symptoms and signs
- Pocket site infection with bacteremia: local infection signs and positive blood cultures
- Lead infection: lead vegetation and positive blood cultures
- Pocket site infection with lead/valvular endocarditis: local signs and positive blood cultures and lead or valvular vegetation(s)
- CIED endocarditis without pocket infection: positive blood cultures and lead or valvular vegetation(s)
- Occult bacteremia with probable CIED infection: absence of alternative source, resolves after CIED extraction
- Situations in which CIED infection is not certain: impending exteriorization, isolated left heart valvular endocarditis in a patient with a CIED
- Superficial incisional infection: involves only skin and subcutaneous tissue of the incision, not the deep soft tissues (eg, fascia and/or muscle) of the incision

Clinical presentation of CIED infections



Sohail MR, JACC 2007;49:1851

The Multicenter Electrophysiologic Device Infection Cohort (MEDIC) study



Greenspon AJ, J Am Coll Cardiol 2012;59:681–7

Risk factors for CIED infection

Patient-related factors	Procedure-related factors	Microbe-related factors
Age	Pocket reintervention (generator change, upgrade, lead or pocket revision)	Highly virulent microbes (eg, staphylococci)
Chronic kidney disease	Pocket hematoma	
Hemodialysis	Longer procedure duration	
Diabetes mellitus	Inexperienced operator	
Heart failure	ICD (compared with PM)	
Chronic obstructive pulmonary disease	Lack of use of prophylactic antibiotics	
Preprocedure fever		
Malignancy		
Skin disorder		
Immunosuppressive drug		
Prior CIED infection		
Anticoagulation		

CIED = cardiovascular implantable electronic device; ICD = implantable cardioverter defibrillator; PM = pacemaker.

Diagnosis - Summary of recommendations (1)

COR	LOE	Recommendations
I	C-LD	If antibiotics are going to be prescribed, drawing at least two sets of blood cultures before starting antibiotic therapy is recommended for all patients with suspected CIED infection to improve the precision and minimize the duration of antibiotic therapy.
I	C-LD	• The sensitivity of tissue culture (69%) is higher than that of the swab culture (31%) of the pocket • A connector culture provides a more than 90% positive yield
I	B-NR	• TEE should be considered for all patients who have documented/suspected BSI or CIED pocket infection
I	C-EO	Evaluation by physicians with specific expertise in CIED infection and lead extraction is recommended for patients with documented CIED infection.

Diagnosis - Summary of recommendations (2)

COR	LOE	Recommendations
IIa	B-NR	TEE can be useful for patients with CIED pocket infection with and without positive blood cultures to evaluate the absence or size, character, and potential embolic risk of identified vegetations.
IIa	C-EO	Evaluation by physicians with specific expertise in CIED infection and lead extraction can be useful for patients with suspected CIED infection.
IIb	C-LD	Additional imaging may be considered to facilitate the diagnosis of CIED pocket or lead infection when it cannot be confirmed by other methods.

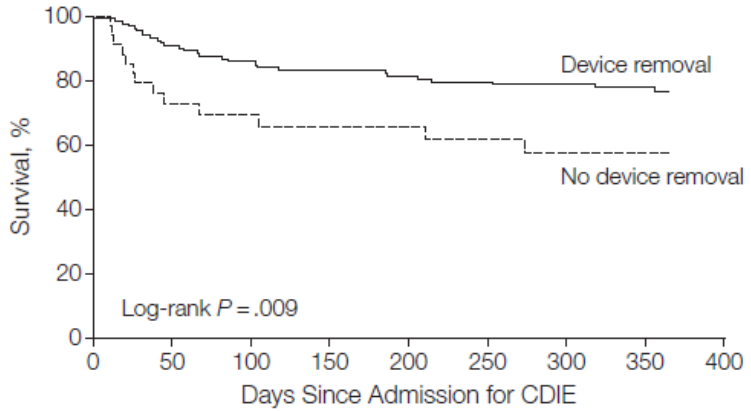
Management- Summary of recommendations

COR	LOE	Recommendations
I		Early diagnosis of CIED infection and performing lead extraction within 3 days of diagnosis is associated with lower in-hospital mortality A multivariate analysis found a 7-fold increase in 30-day mortality if the CIED was not removed
I	C-EO	Complete removal of epicardial leads and patches is recommended for all patients with confirmed infected fluid (purulence) surrounding the intrathoracic portion of the lead.
I	B-NR	Complete device and lead removal is recommended for all patients with valvular endocarditis without definite involvement of the lead(s) and/or device.
I	B-NR	Complete device and lead removal is recommended for patients with persistent or recurrent bacteremia or fungemia, despite appropriate antibiotic therapy and no other identifiable source for relapse or continued infection.
I	C-EO	Careful consideration of the implications of other implanted devices and hardware is recommended when deciding on the appropriateness of CIED removal and for planning treatment strategy and goals.

Infective Endocarditis in Patients with CIED

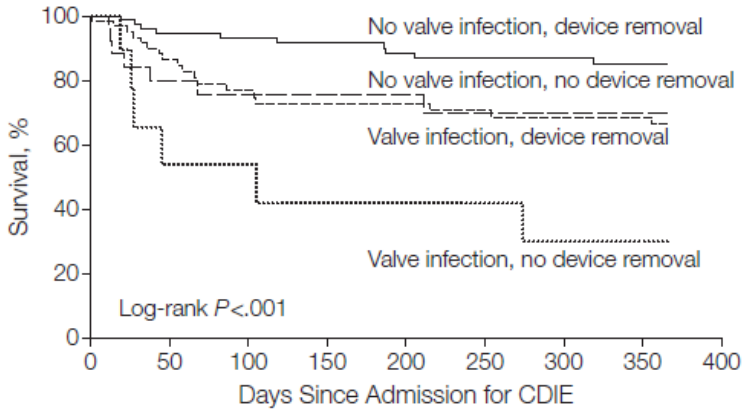
One-year survival

By device removal



No. at risk								
Device removal	141	112	98	94	92	87	84	80
No device removal	34	22	19	17	16	14	13	12

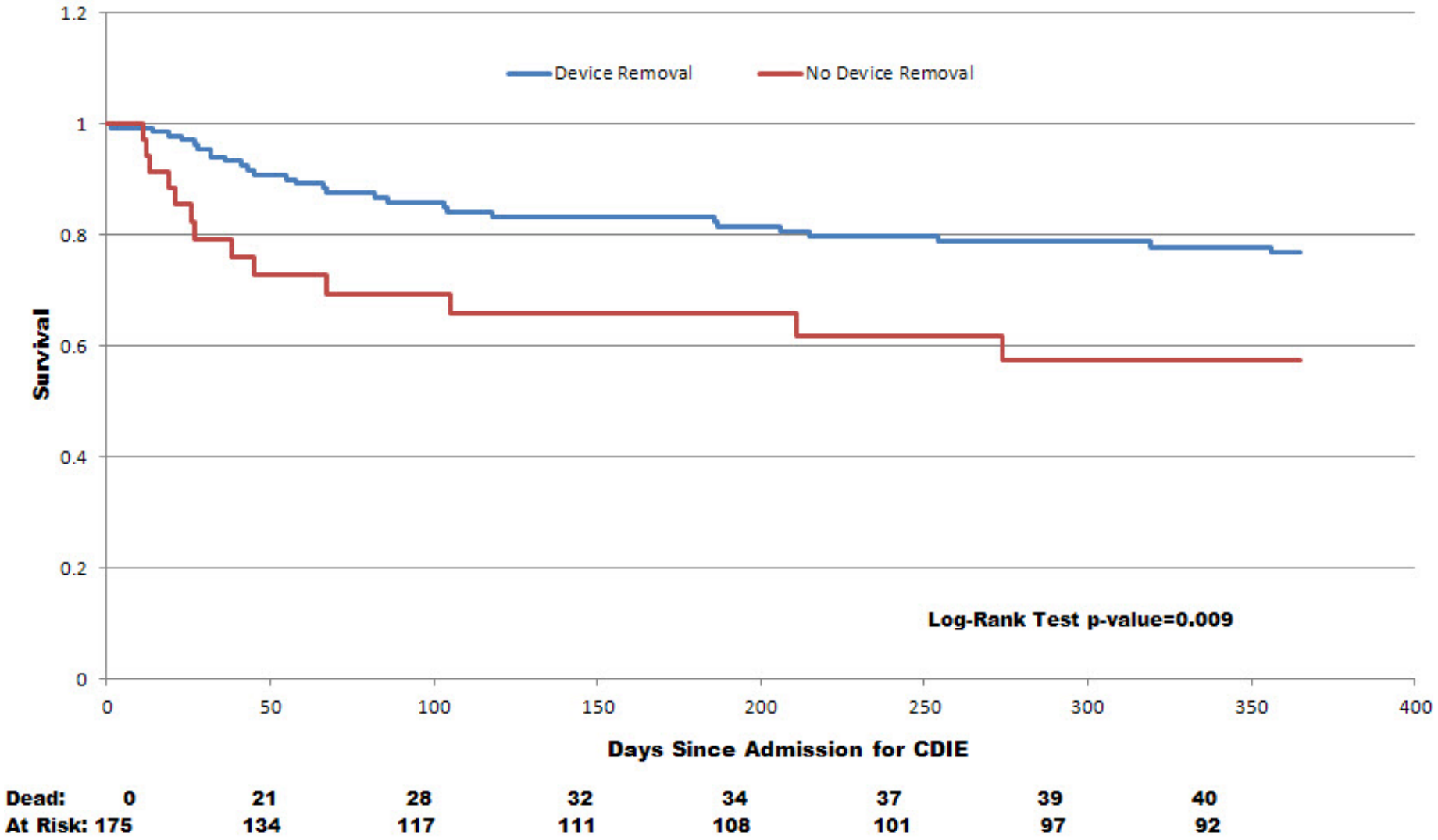
By concomitant valve infection and device removal



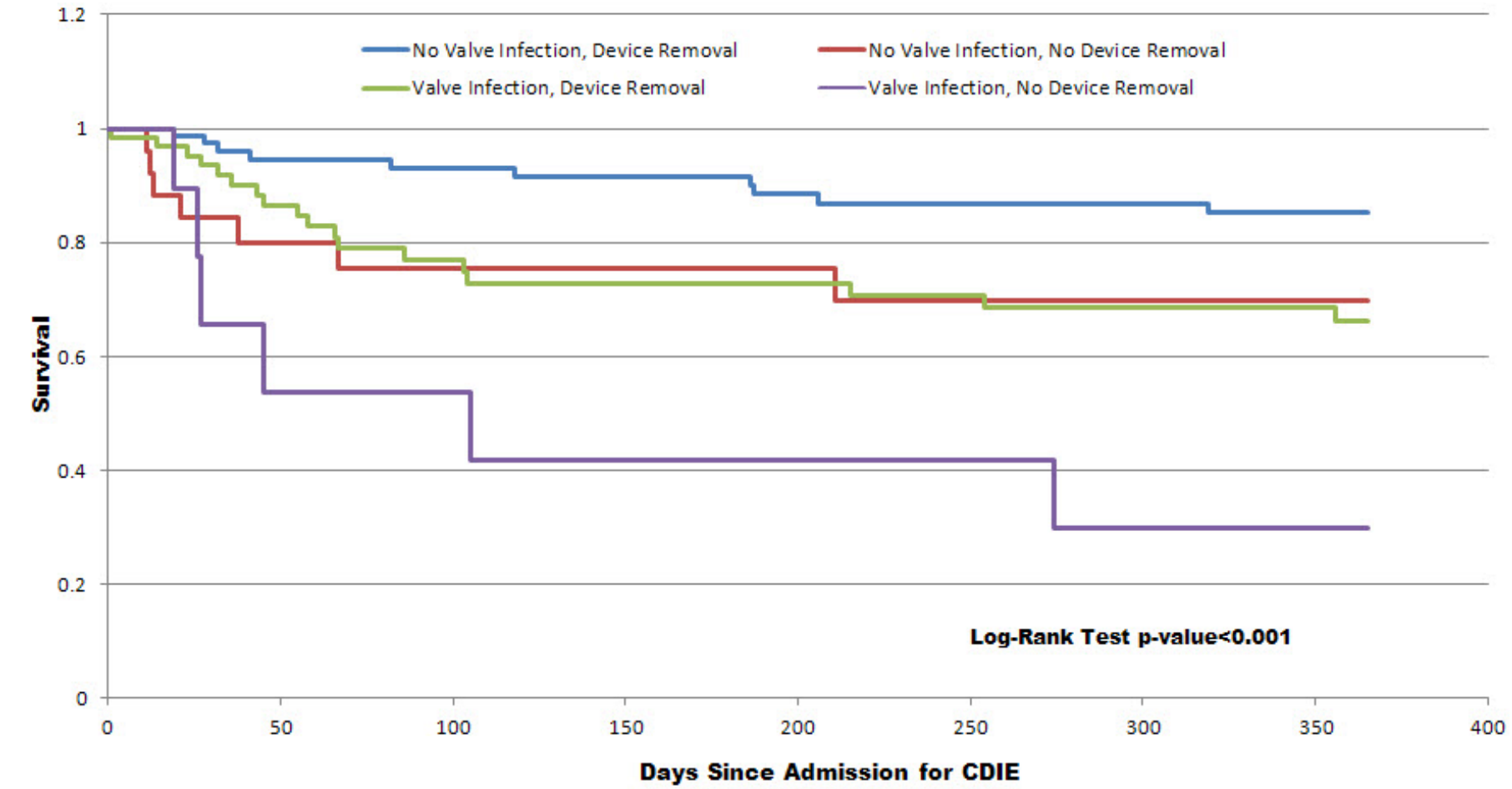
No. at risk								
No valve infection								
Device removal	79	66	61	59	57	54	53	50
No device removal	25	18	15	14	13	11	11	10
Valve infection								
Device removal	62	46	37	35	35	33	31	30
No device removal	9	4	4	3	3	3	2	2

Athan E, JAMA 2012;307:1727

Infective Endocarditis in Patients with CIED



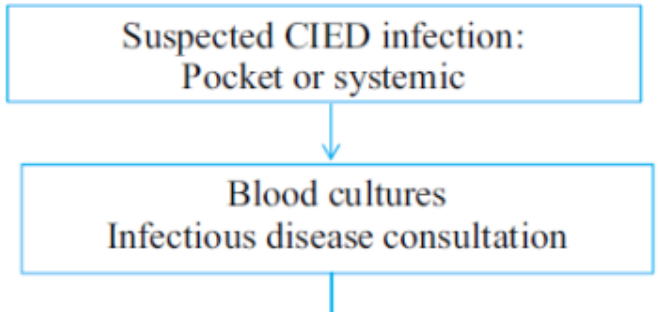
Infective Endocarditis in Patients with CIED



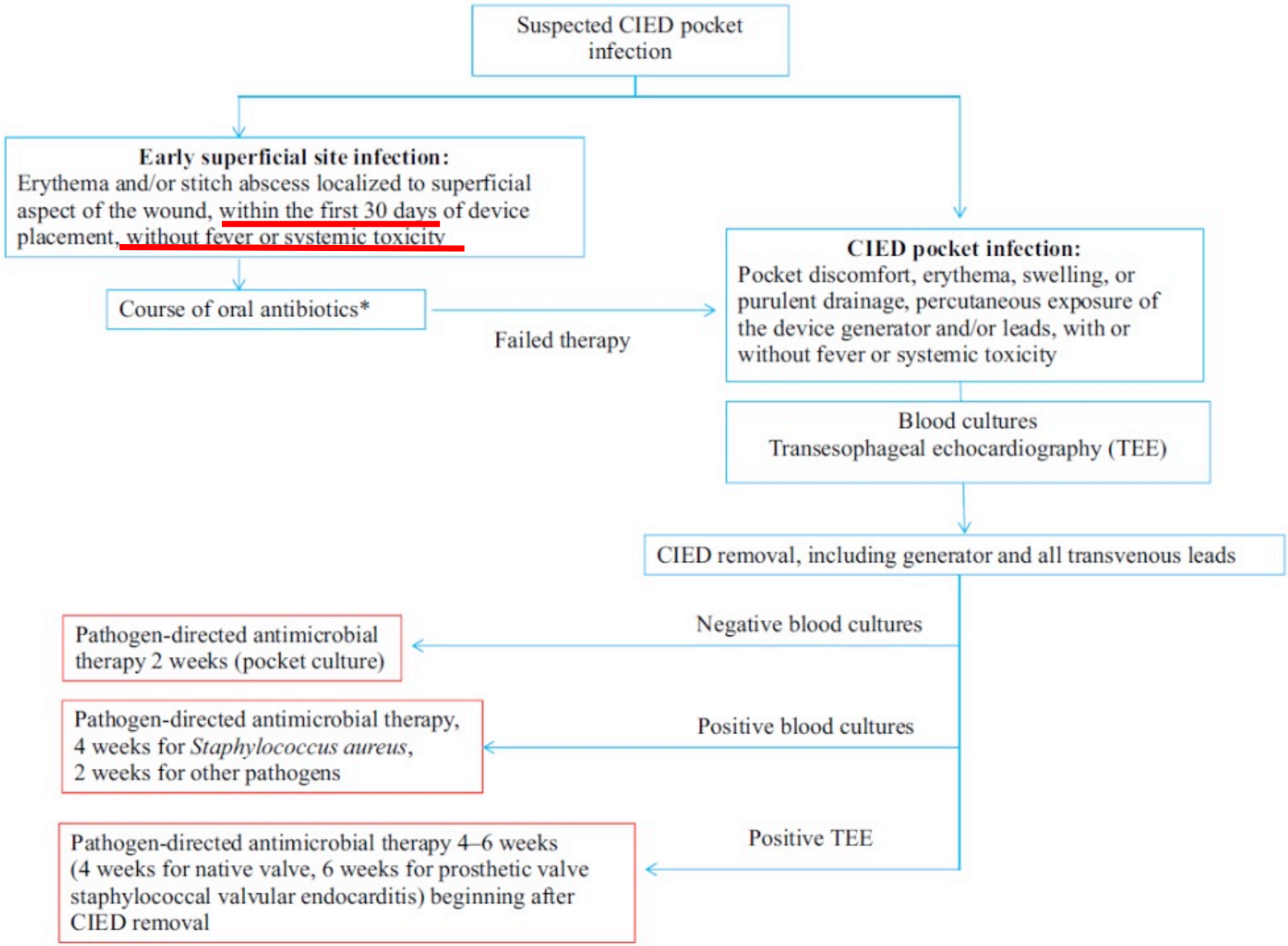
Considerations for reimplantation

- Reassessment of the need for a new CIED is imperative after removal of an infected CIED
- The optimal timing of device replacement is unknown: there are no prospective trial data on the timing of new device replacement and risk of relapsing infection
- A new implantation can reasonably be postponed until blood cultures are negative for 72 hours, although implantation should be delayed if the patient has another undrained source of infection
- Replacement device implantation should be performed in an alternative location such as the contralateral side, the iliac vein, or using epicardial or subcutaneous implantation
- Single-center studies have suggested that same-day implantation is feasible for patients with isolated pocket infections and is not associated with adverse outcomes

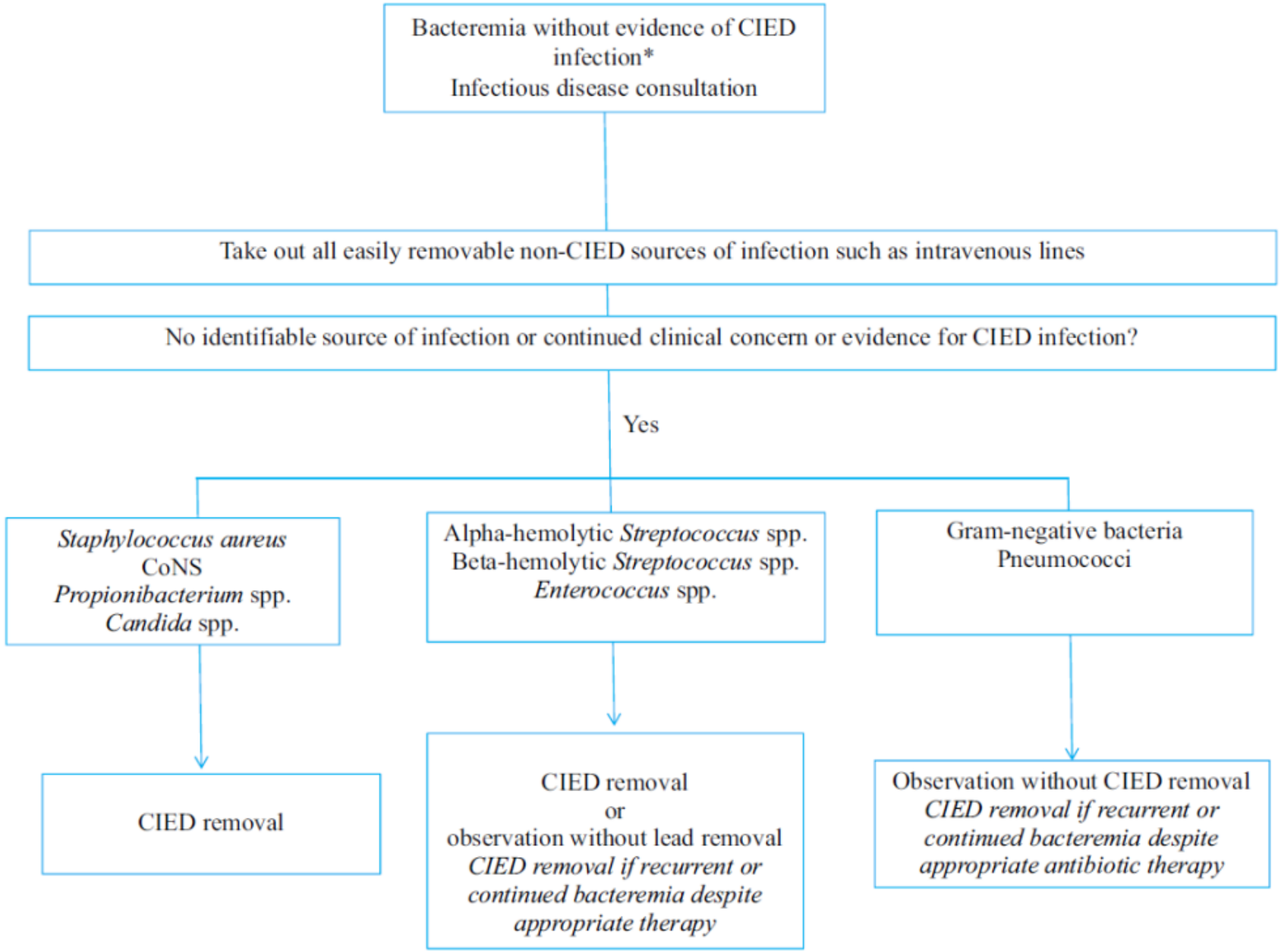
Management of suspected CIED infection



Management of suspected pocket infection



Management of bacteremia without evidence of CIED infection



First-line, empirical Ab Rx

Drug	Dosing and route	Duration	Comments
Early isolated pocket infection			
Pristinamycin or Clindamycin	1gx3/d oral 600 mgx3/d oral	10 days	 If body weight > 100kg: 600 mgx4/d
Suspected CIED infection			
Sepsis (Quick sofa ≥ 2)			Alternative choice
Vancomycin + Cefotaxime	40 mg/kg/d, continuous IV infusion, after a loading dose of 30mg/kg IVL 150 mg/kg/d	Until culture results	Daptomycin 10 mg/kg/d, qd IV β-lactam allergy: Aztreonam 100 mg/kg/d tid IV
No sepsis: initiation of Ab Rx immediately after device removal and microbiology sampling			
Vancomycin	40 mg/kg/d, continuous IV infusion, after a loading dose of 30mg/kg IVL	Until culture results	Daptomycin 10 mg/kg/d, qd IV

Ab Rx, after documentation

Drug	Dosing and route	Duration (weeks)
Pocket infection with neither endocarditis nor bacteremia: oral switch after device removal		
Staphylococcus spp.		**2**
Pristinamycin or Clindamycin	1gx3/d 600 mgx3/d (x4/d if body weight > 100 kg)	
Streptococcus spp		
Amoxicillin	50 mg/kg/d tid	
***Streptococcus spp and* β-lactam allergy**		
Pristinamycin	1gx3/d	
Enterococcus spp.		
Amoxicillin	50 mg/kg/d tid	
***Enterococcus spp. and* β-lactam allergy**		
Linezolid	600 mgx2/d	

Ab Rx, after documentation

Drug	Dosing and route	Duration (weeks)	Comments
Bacteremia and no IE			
Streptococcus spp			
Amoxicillin	100 mg/kg/d, IV	2	
***Streptococcus spp and* β-lactam allergy, non anaphylaxis**			
Ceftriaxone or Cefotaxime	2g/d, IV 100 mg/kg/j, IV	2	
***Streptococcus spp and* β-lactam allergy and anaphylaxis or allergy to cephalosporins**			
Vancomycin	40 mg/kg/d, IV	2	Plasma concentration 15-20 mg/l
Enterococcus spp.			
Amoxicillin	200 mg/kg/d, IV	2	
***Enterococcus spp.* Ampi-R or β-lactam allergy**			
Vancomycin	40 mg/kg/d, IV	2	Plasma concentration 15-20 mg/l

Ab Rx, after documentation (Cont')

Drug	Dosing and route	Duration (weeks)	Comments
Bacteremia and no IE			
		MSSA	
(Cl)oxacillin or Cefazolin	150 mg/kg/d, IV 100 mg/kg/d, IV	2-4	Alternative choice: Clindamycin 600 mgx4/d if body weight > 100 kg
		MSSA and* β-lactam allergy (anaphylaxis) *or MRSA	
Vancomycin or Daptomycin	40 mg/kg/d, IV 10 mg/kg/d, IV	2-4	Plasma concentration 15-20 mg/l

Ab Rx, after documentation (Cont')

If IE, follow 2015 ESC guidelines

How to optimize prevention of CIED infections?

Efficacy of Antibiotic Prophylaxis Before the Implantation of Pacemakers and Cardioverter-Defibrillators

Results of a Large, Prospective, Randomized, Double-Blinded, Placebo-Controlled Trial

Julio Cesar de Oliveira, MD; Martino Martinelli, MD; Silvana Angelina D'Orio Nishioka, PhD; Tânia Varejão, PhD; David Uipe, MD; Anísio Alexandre Andrade Pedrosa, PhD; Roberto Costa, MD; Stephan B. Danik, MD

Methods and Results—This double blinded study included 1000 consecutive patients who presented for primary device (Pacemaker and implantable cardioverter-defibrillators) implantation or generator replacement randomized in a 1:1 fashion to prophylactic antibiotics or placebo. Intravenous administration of 1 g of cefazolin (group I) or placebo (group 2) was done immediately before the procedure. Follow-up was performed 10 days, 1, 3, and 6 months after discharge. The primary end point was any evidence of infection at the surgical incision (pulse generator pocket), or systemic infection related to be procedure. The safety committee interrupted the trial after 649 patients were enrolled due to a significant difference in favor of the antibiotic arm (group I: 2 of 314 infected patients—0.63%; group II: 11 of 335 to 3.28%; RR=0.19; P=0.016). The following risk factors were positively correlated with infection by univariate analysis: nonuse of preventive antibiotic (P=0.016); implant procedures (versus generator replacement: P=0.02); presence of postoperative hematoma (P=0.03) and procedure duration (P=0.009). Multivariable analysis identified nonuse of antibiotic (P=0.037) and postoperative hematoma (P=0.023) as independent predictors of infection.

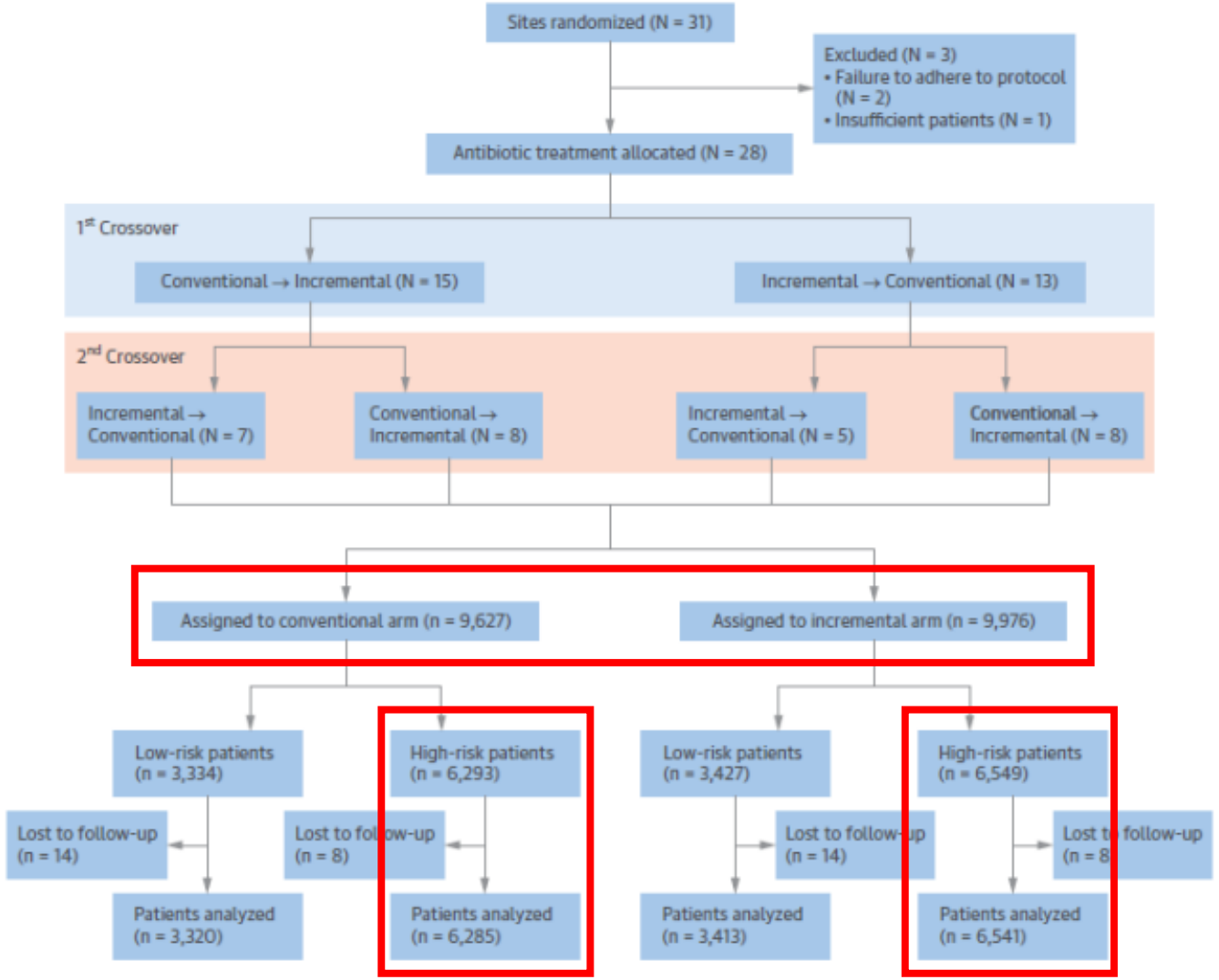
Conclusions—Antibiotic prophylaxis significantly reduces infectious complications in patients undergoing implantation of pacemakers or cardioverter-defibrillators. **(*Circ Arrhythmia Electrophysiol*. 2009;2:29-34.)**

Prevention of Arrhythmia Device Infection Trial
The PADIT Trial

- High-risk patients undergoing a device procedure
- Hypothesis: incremental antimicrobial prophylaxis will reduce the risk of hospitalization for device infection, compared with a conventional strategy of a single dose of preprocedural antibiotic
- 2 interventions
  - Conventional: single dose of pre-operative antibiotics (cefazolin or vancomycin in allergic patients) within 120 min before skin incision
  - Incremental: conventional + intraoperative wound pocket bacitracin wash before skin closure and post-operative oral antibiotics for 2 days (cephalexin or clindamycin in allergic patients)
- Cluster randomized 4-period crossover design: each participating hospital was randomized to one of four 6-month sequences of incremental (I) and conventional (C) strategies (i.e., ICIC, ICCI, CICI, CIIC)
- Primary outcome: 1-year hospitalization for device infection in the high-risk group

Krahn AD, J Am Coll Cardiol 2018;72:3098–109

Prevention of Arrhythmia Device Infection Trial
The PADIT Trial



Krahn AD, J Am Coll Cardiol 2018;72:3098–109

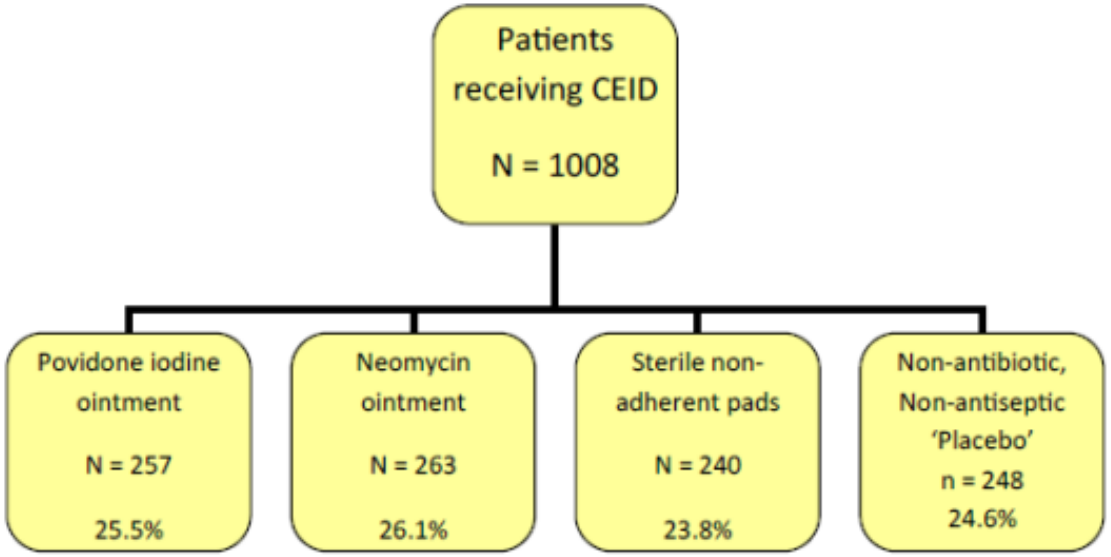
Prevention of Arrhythmia Device Infection Trial
The PADIT Trial

	High-Risk Patients					
	All (N = 12,826)	Conventional (n = 6,285)	Incremental (n = 6,541)	Incremental vs. Conventional OR†	95% CI	p Value
Hospitalization due to device infection	143 (1.11)	77 (1.23)	66 (1.01)	0.82	0.59-1.15	0.26
Subtype						
Skin, subcutaneous/pocket infection	124 (0.97)	67 (1.07)	57 (0.87)	0.82	0.57-1.17	0.27
Bloodstream infection	34 (0.27)	19 (0.30)	15 (0.23)	0.76	0.38-1.49	0.42
Endocarditis	37 (0.29)	22 (0.35)	15 (0.23)	0.66	0.34-1.27	0.21
Erosion of skin with device exposure	3 (0.02)	1 (0.02)	2 (0.03)	1.96	0.18-21.70	0.58
Bloodstream and/or endocarditis	49 (0.38)	28 (0.45)	21 (0.32)	0.72	0.41-1.28	0.26
Pocket infection and/or erosion	94 (0.73)	49 (0.78)	45 (0.69)	0.89	0.58-1.37	0.59
Requiring surgical intervention						
Yes	128 (1.00)	66 (1.05)	62 (0.95)	0.90	0.64-1.28	0.57
No	15 (0.12)	11 (0.18)	4 (0.06)	0.35	0.11-1.10	0.07
Antibiotics treatment for infection	103 (0.80)	57 (0.91)	46 (0.70)	0.79	0.52-1.20	0.27
Composite of primary outcome and any antibiotics treatment for infection	239 (1.86)	130 (2.07)	109 (1.67)	0.81	0.62-1.05	0.11

Krahn AD, J Am Coll Cardiol 2018;72:3098–109

The Role of Prophylaxis Topical Antibiotics in CIED Implantation

- Patients
  - 1008 high-risk patients who underwent transvenous implantation of CIED
  - High-risk: diabetes mellitus, malignancy, advanced age, anticoagulation, corticosteroids use, and chronic renal failure
- Ab prophylaxis with IV gentamicin and cefazolin < 60 min before procedure
- Primary outcome: rate of inflammation and infection at the surgical site during the 12 months following the procedure
- Randomization arms



Khalighi K , PACE 2014; 37:304–311

The Role of Prophylaxis Topical Antibiotics in CIED Implantation

Factors Predictive of CEID Infection

		Variable		Single Variable			Multiple Variables		
	Percent-Age	Present	Absent	aOR	95% CI	P Value*	aOR	95% CI	P Value
Female sex	35.4	0.04	0.07	0.54	0.28–1.01	0.05	0.54	0.28–1.02	0.58
Procedure time (110 minutes and more)	53.7	7.5	3.49	2.30	1.27–4.18	0.006	2.09	1.48–3.81	0.01
Povidone	25.5	0.07	0.04	1.40	0.65–2.99	0.39			
Neomycin	26.1	0.05	0.04	1.03	0.46–2.29	0.95			
Antiseptic	23.7	0.06	0.04	1.23	0.56–2.71	0.61			
Placebo†	24.7	0.05	0.04						
Cephalic pacemaker	15	0.02	0.06	0.31	0.09–1.0	0.05	0.35	0.11–1.16	0.086
Cephalic ICD	23.7	0.06	0.05	1.08	0.58–2.01	0.81			
Subclavian ICD	17.7	0.04	0.06	0.77	0.36–1.65	0.5			
Subclavian pacemaker	25.5	0.06	0.05	1.65	0.96–2.83	0.07			
Diabetes	22.5	0.08	0.05	1.68	0.94–3.01	0.08			
CKD	6.3	0.08	0.05	1.51	0.58–3.93	0.4			
Malignancy	4.1	0.17	0.05	3.86	1.61–9.17	<0.01	3.63	1.51–8.74	0.004
Steroids	2.6	0.04	0.06	0.67	0.09–5.07	0.7			
Anticoagulation	29.3	0.06	0.05	1.25	0.71–2.22	0.43			

	Povidone Iodine Solution (%)	Neomycin Ointment (%)	Antiseptic Pad (%)	Placebo (%)	Total
Erythema	9 (3.5)	10 (3.8)	7 (2.9)	7 (2.8)	33
Erythema and discharge	4 (1.5)	2 (0.7)	3 (1.2)	2 (0.8)	11
Wound culture positive	4 (1.5)	2 (0.7)	4 (1.6)	3 (1.2)	13
Bacteremia/pocket infection	–	–	–	1 (0.4)	1
Total	17/257	14/263	14/240	13/248	58

Khalighi K , PACE 2014; 37:304–311

ORIGINAL ARTICLE

Antibacterial Envelope to Prevent Cardiac Implantable Device Infection

Khaldoun G. Tarakji, M.D., M.P.H., Suneet Mittal, M.D., Charles Kennergren, M.D., Ph.D., Ralph Corey, M.D., Jeanne E. Poole, M.D., Edward Schloss, M.D., Jose Gallastegui, M.D., Robert A. Pickett, M.D., Rudolph Evonich, M.D., François Philippon, M.D., Janet M. McComb, M.D., Steven F. Roark, M.D., Denise Sorrentino, M.D., Darius Sholevar, M.D., Edmond Cronin, M.B., B.Ch., B.A.O., Brett Berman, M.D., David Riggio, M.D., Mauro Biffi, M.D., Hafiza Khan, M.D., Marc T. Silver, M.D., Jack Collier, M.D., Zayd Eldadah, M.D., Ph.D., David J. Wright, M.D., Jeff D. Lande, Ph.D., Daniel R. Lexcen, Ph.D., Alan Cheng, M.D., and Bruce L. Wilkoff, M.D., for the WRAP-IT Investigators*

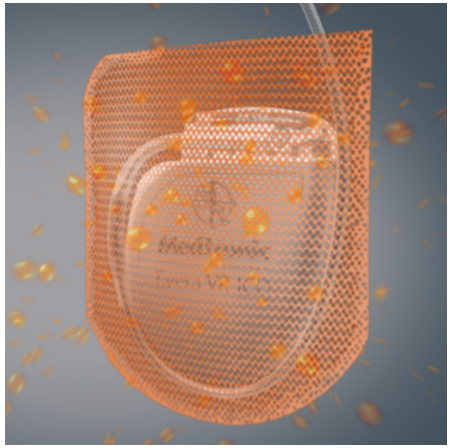
Worldwide Randomized Antibiotic Envelope Infection Prevention Trial (WRAP-IT)

Absorbable, multifilament mesh envelope (TYRX Absorbable Antibacterial Envelope, Medtronic)

Tarakji KG et al. NEJM. 2019 March 17th DOI: 10.1056/NEJMoa1901111

THE TYRX™ ABSORBABLE ANTIBACTERIAL ENVELOPE

TIME SEQUENCE SIMULATION OF ELUTION & ABSORPTION



Envelope after implantation[1]

- Absorbable Envelope is eluting Minocycline & Rifampin

Envelope at 4 weeks[2]

- Absorbable Envelope is dissolving into fragments

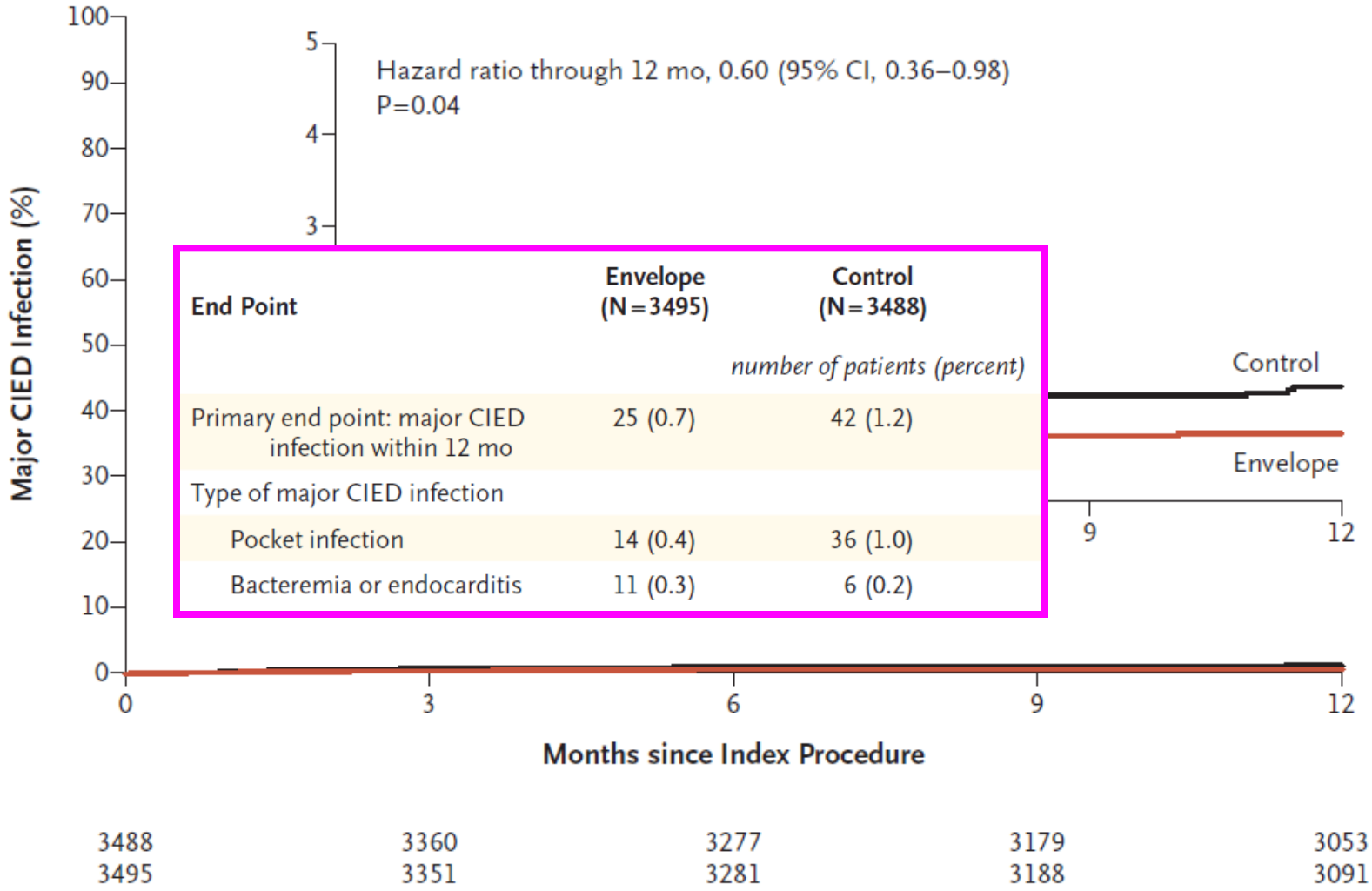
Envelope at ~9 weeks[3]

- Mesh has no physical presence and is fully absorbed

1. Huntingdon Life Sciences Study TR-2013-001. 2. Data on File, 093013-1. 3. Huntingdon Life Sciences Study TR-2011-054.

Adjunctive use of an antibacterial envelope resulted in a 40% reduction of major CIED infections (pocket)

A

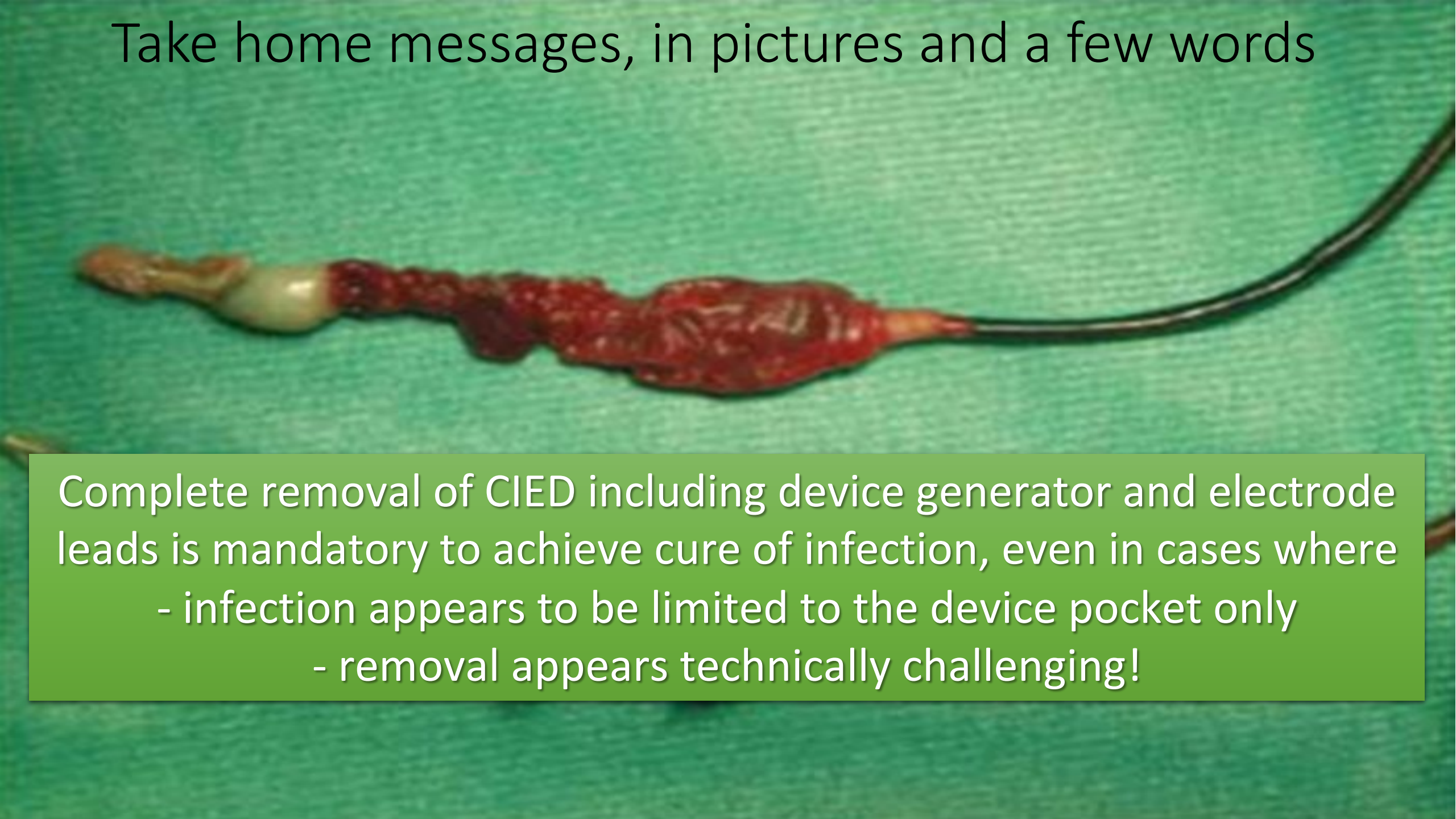


End Point	Envelope (N=3495)	Control (N=3488)
		number of patients (percent)
Primary end point: major CIED infection within 12 mo	25 (0.7)	42 (1.2)
Type of major CIED infection		
Pocket infection	14 (0.4)	36 (1.0)
Bacteremia or endocarditis	11 (0.3)	6 (0.2)

No. at Risk					
Control	3488	3360	3277	3179	3053
Envelope	3495	3351	3281	3188	3091

Tarakji KG et al. NEJM. 2019 March 17th DOI: 10.1056/NEJMoa1901111

Take home messages, in pictures and a few words



Complete removal of CIED including device generator and electrode leads is mandatory to achieve cure of infection, even in cases where

- infection appears to be limited to the device pocket only
- removal appears technically challenging!