JNI 14es Journées Nationales d'Infectiologie
Clermont-Ferrand
et l'interrégion Rhône-Alpes Auvergne
Du mercredi 12 au vendredi 14 juin 2013
Polydome, centre d'expositions et des congrès

Infections sur matériel implanté endocavitaire (pace-makers, cardio-défibrillateurs)

Bruno Hoen
CHU de Besançon – Université de Franche-Comté

Déclarations de liens d'intérêt

- Subvention de recherche pour l'AEPEI : Novartis

- Je n'ai pas de pacemaker
- Je n'ai jamais eu d'endocardite infectieuse
- Il m'est arrivé de consommer des antibiotiques
  - (moins de 10 € par an au cours des 5 dernières années)

Programme des réjouissances

- Remarques préliminaires / Définitions
- Actualités épidémiologiques
  - Incidence
  - Microorganismes responsables
  - Facteurs de risque et pronostic
- Quelques considérations diagnostiques
  - Aspects échocardiographiques
  - Aspects microbiologiques
- Prise en charge thérapeutique
  - Antibiothérapie
  - Explantation
  - Ré-implantation
- Prévention

Remarques préliminaires / Définitions

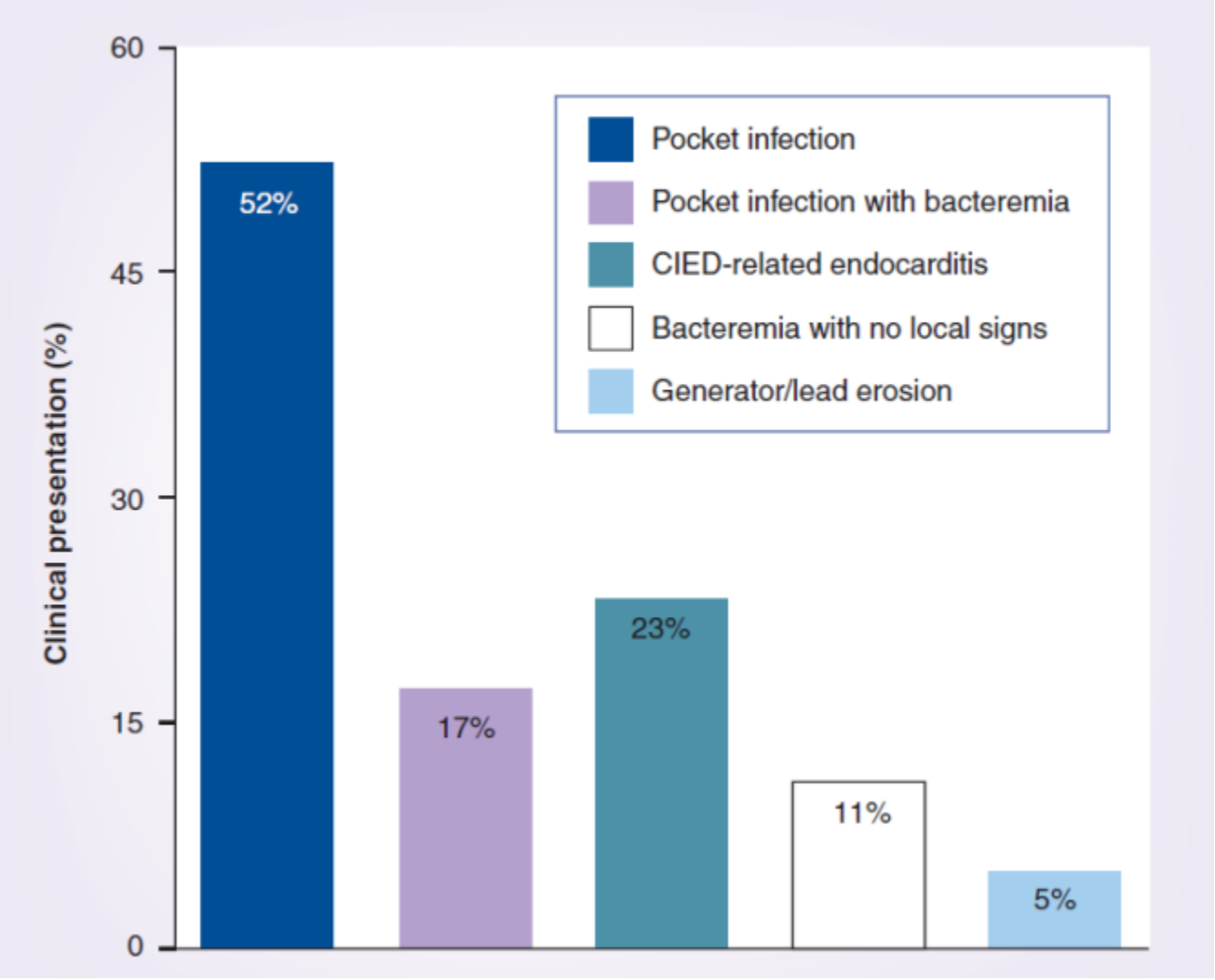
- Infections superficielles/de la loge du boitier
- Infections avec ou sans endocardite infectieuse
- Infections précoces vs tardives



Remarques préliminaires / Définitions

- Infections superficielles/de la loge du boitier
- Infections avec ou sans endocardite infectieuse
- Infections précoces vs tardives

Clinical presentation of CIED infections



Sohail MR, JACC 2007;49:1851

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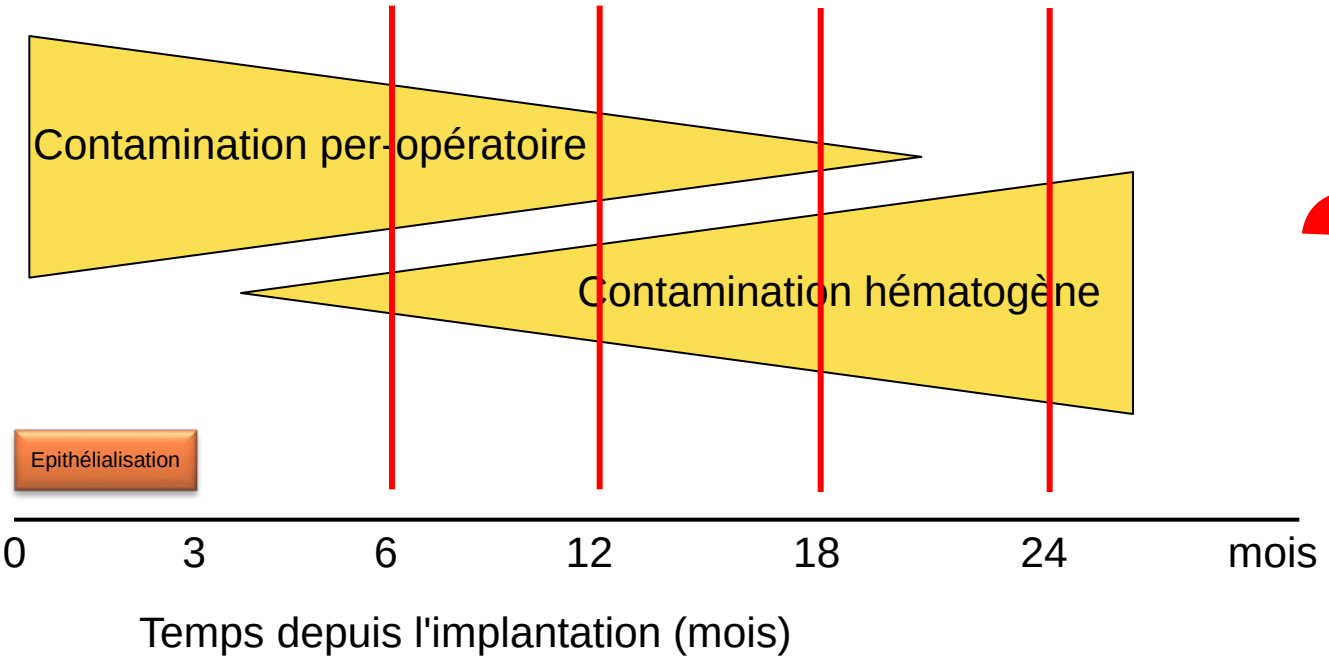

?

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Des informations épidémiologiques très disparates

Source d'information	Numérateur	Dénominateur	Ratio
Bases de données - Type PMSI - Assurance maladie	N infections	N dispositifs implantés	Taux d'infection
Cohortes de patients implantés	N infections	N patients et durée de suivi	Incidence N/an, N/années-pt
Etudes observationnelles d'infections sur PM/ICD (Registres, cohortes)	N infections	Aucun N dispositifs implantés	- ?
Etudes observationnelles d'EI	N EI sur PM	N EI	% d'EI sur PM *

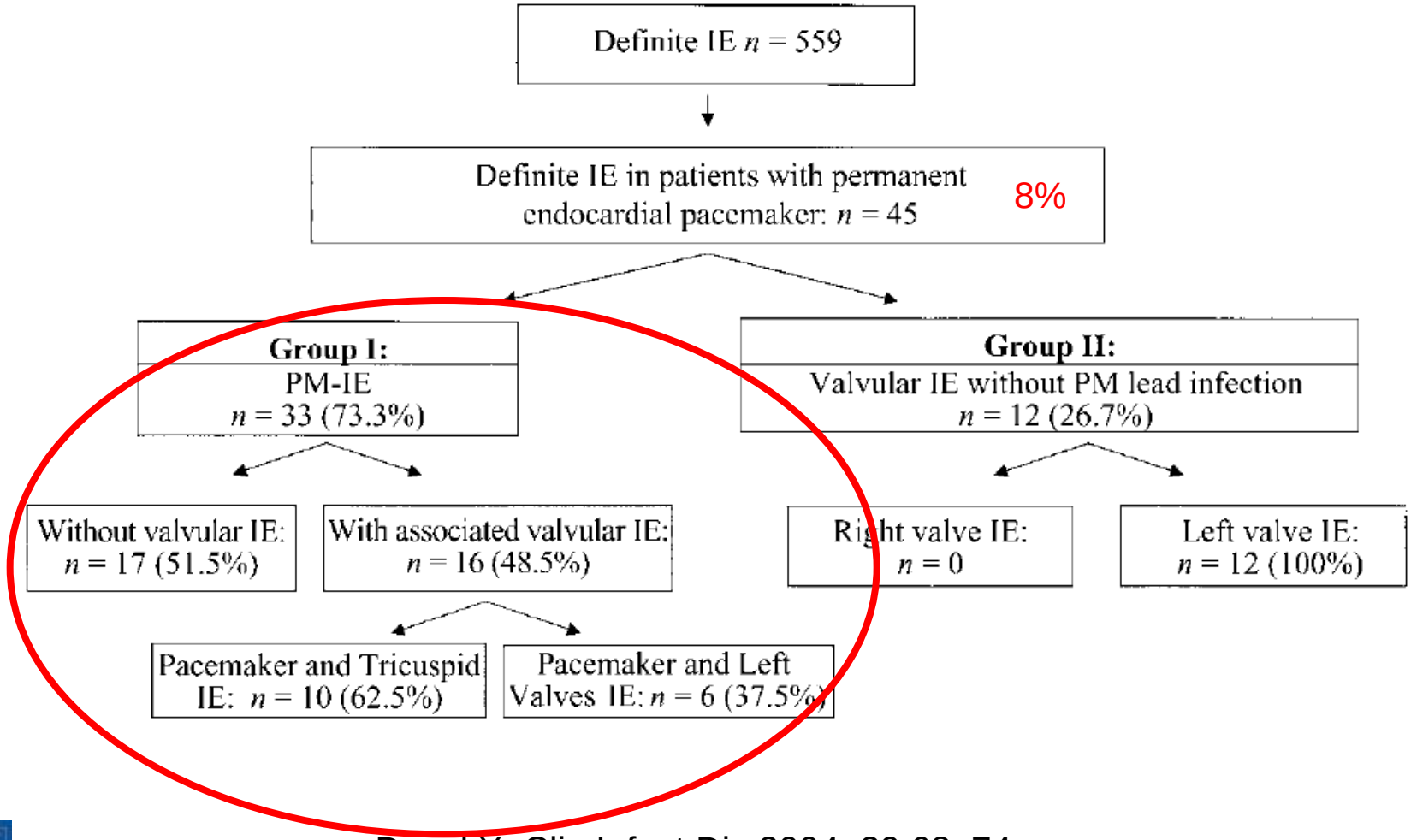
* : Estimation incidence si étude populationnelle

Endocarditis in Patients with a Permanent PM

- EI 1999
  - Overall incidence of IE $30/10^6$
  - Incidence of IE in patients with a PPM: $550/10^6$
  - Incidence of IE in patients with a PV: $3000/10^6$

Hoen B, JAMA 2002;288:75 – Duval X, Clin Infect Dis 2004; 39:68–74

Endocarditis in Patients with a Permanent PM



Duval X, Clin Infect Dis 2004; 39:68–74

The MEDIC (Multicenter Electrophysiologic Device Infection Cohort) study

Early LAE
(< 6 months from insertion)

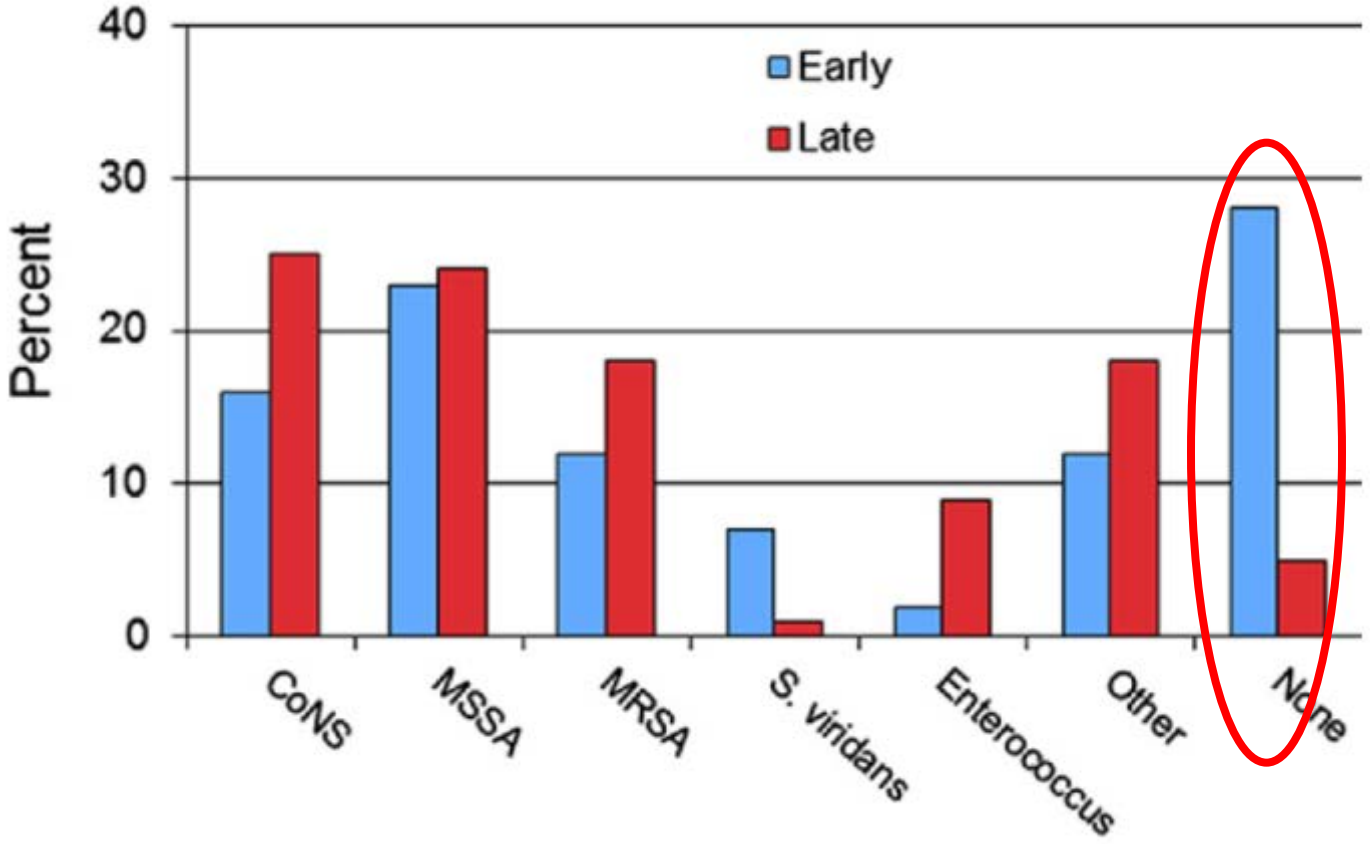
- Local pocket infection
- 54% source identified on local wound device
- 63% vegetations on TEE
- 72% BC positive

Late LAE
(> 6 months from insertion)

- 38% remote source of bacteremia
- 47% presented with sepsis
- 82% vegetations on TEE
- 93% BC positive

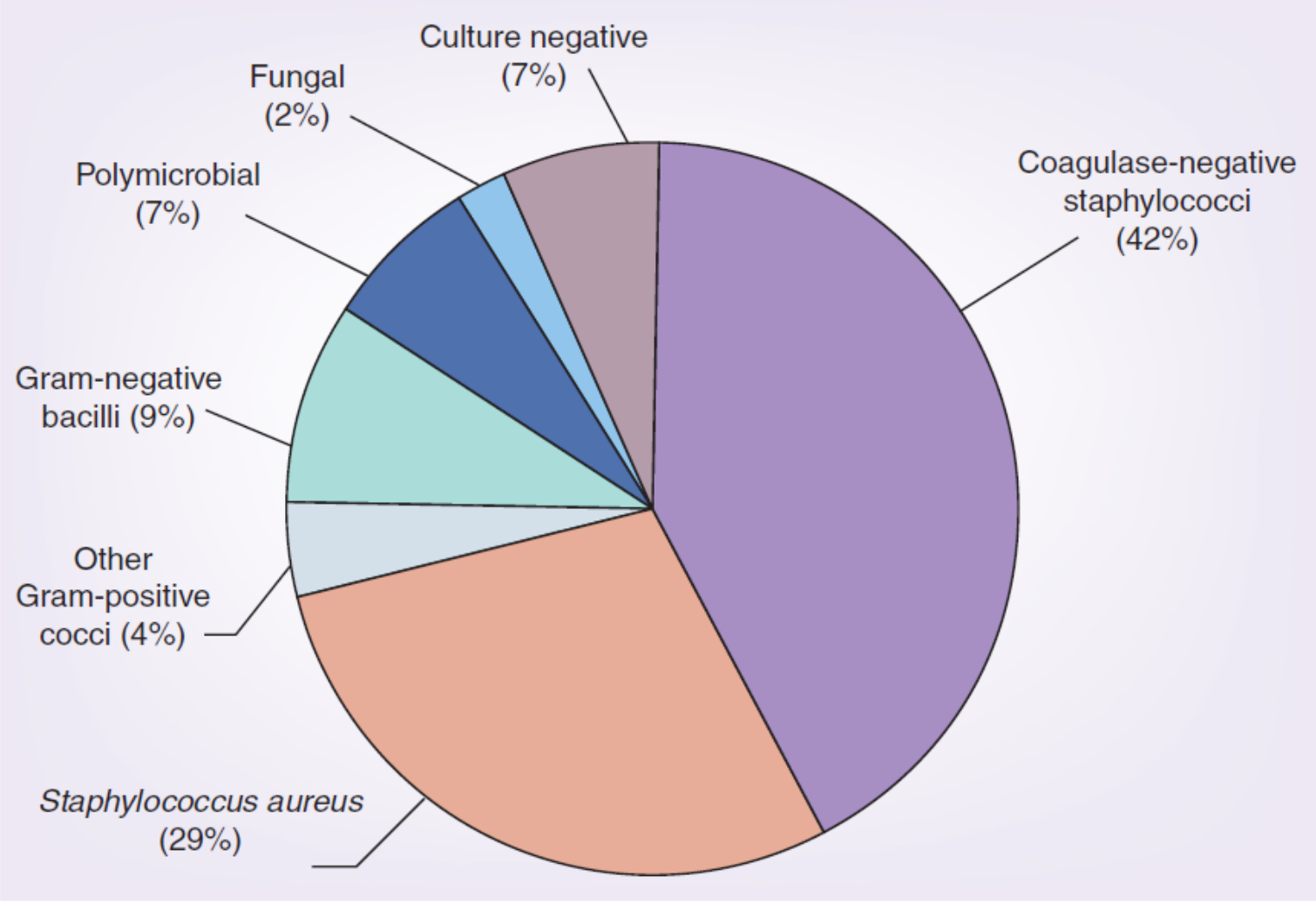
Greenspon AJ, J Am Coll Cardiol 2012;59:681–7

The MEDIC (Multicenter Electrophysiologic Device Infection Cohort) study



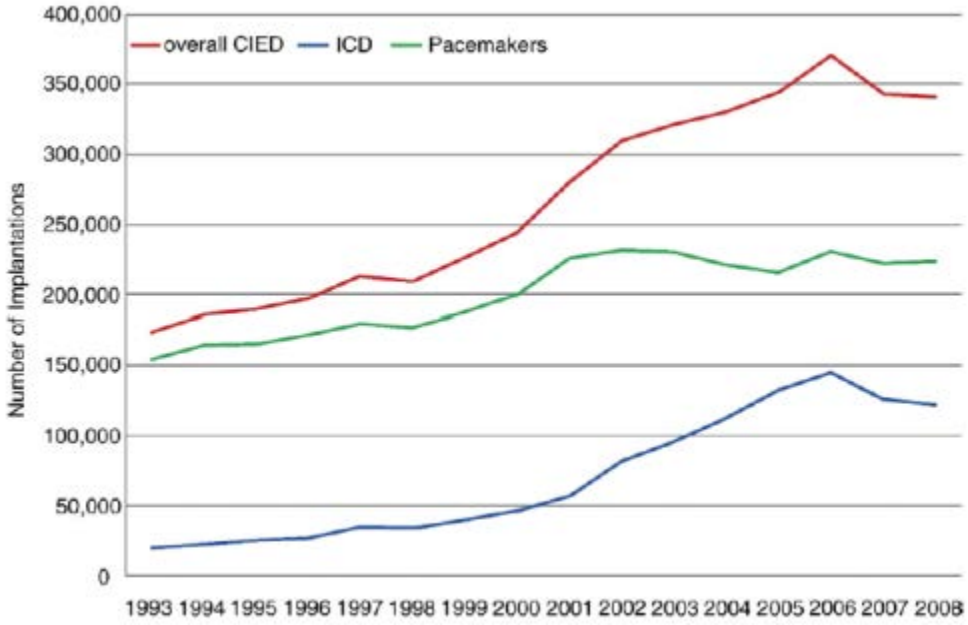
Greenspon AJ, J Am Coll Cardiol 2012;59:681–7

Distribution of causative microorganisms isolated from CIED infections

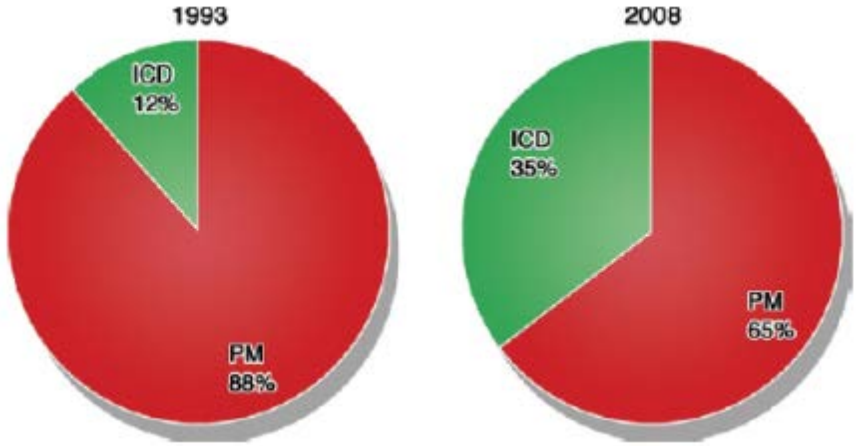


Sohail MR, JACC 2007;49:1851

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



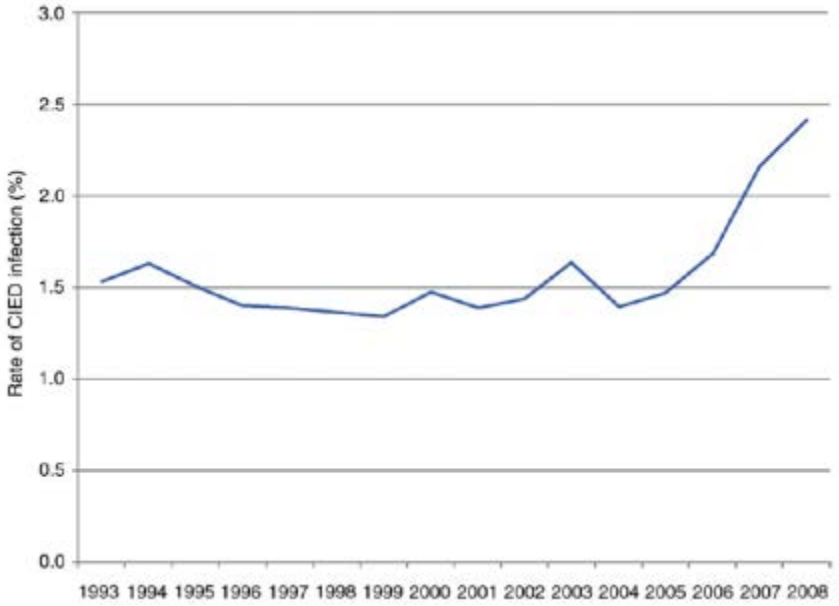
Annual number of PM and ICD implantations 1993 to 2008



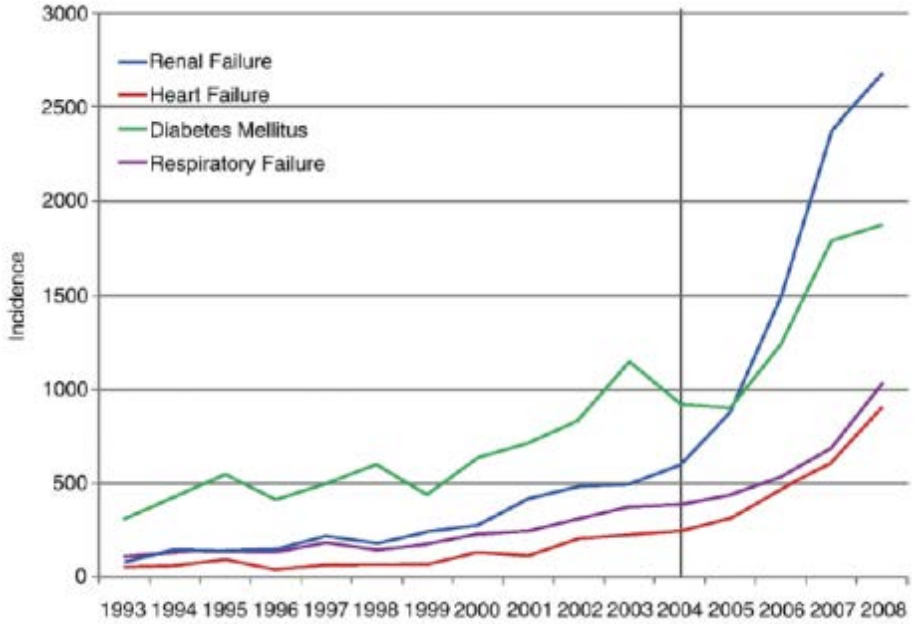
PM vs ICD in % of all CIED implantations: 1993 vs 2008

Greenspon AJ, JACC 2011;58:1001

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



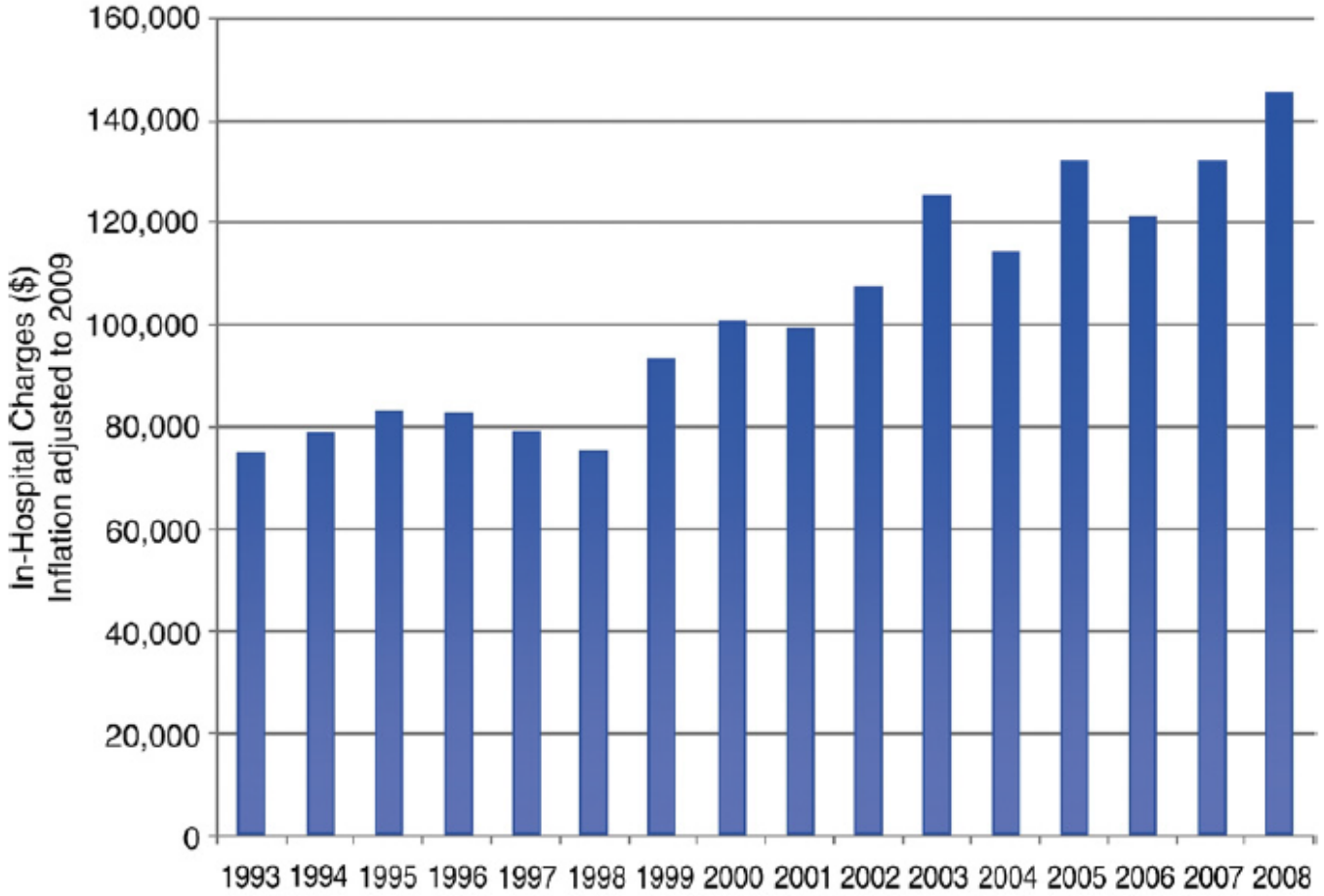
Annual rate of CIED infections



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

ICD Registry – Methods and incidence

- **Patients identified using Medicare claims data**
- **Infectious outcomes with administrative data (ICD-9)**
- **200 909 patients in 1348 hospitals (2006-2009)**

	Infection (N=3390)	P value
Overall	3390 (1.7%)	
ICD Type		<0.0001
Single Chamber	450 (1.4%)	
Dual Chamber	1,079 (1.5%)	
Biventricular	1,860 (2.0%)	
Initial ICD implant		
No (Gen Change)	1,084 (1.9%)	<0.0001
Yes	2,306 (1.6%)	

Sohail MR, et al. Arch Intern Med 2011;171:1821-8

REPLACE Registry – Patients & Methods

- Prospective, observational multicenter registry
- Purpose: Procedure-related complication rates for PPM/ICD generator replacement
- 1744 patients, 6 months of follow-up
- 61 enrolling sites (US only)
- Complications:
  - Pre-defined
    - Major (severity, procedure, re-admission, explantation)
    - Minor (superficial inflammation, treatment on an outpatient basis)
  - Reviewed by blinded CEC (EP and ID)

Uslan D., PACE 2012; 35:81–87

REPLACE Registry – Main results

- Infections were infrequent
  - 100% of patients received preoperative antibiotic prophylaxis
  - Infection developed in 22 patients (1.3%)
- Infected patients were more likely to have postoperative hematoma (22.7% vs 0.98%)
- Sites with high infection rates (> 5%):
  - Use povidone-iodine (Betadine)
  - Lower implantation volume (< 250/year)
  - Patients with higher Charlson Comorbidity Index

Uslan D., PACE 2012; 35:81–87

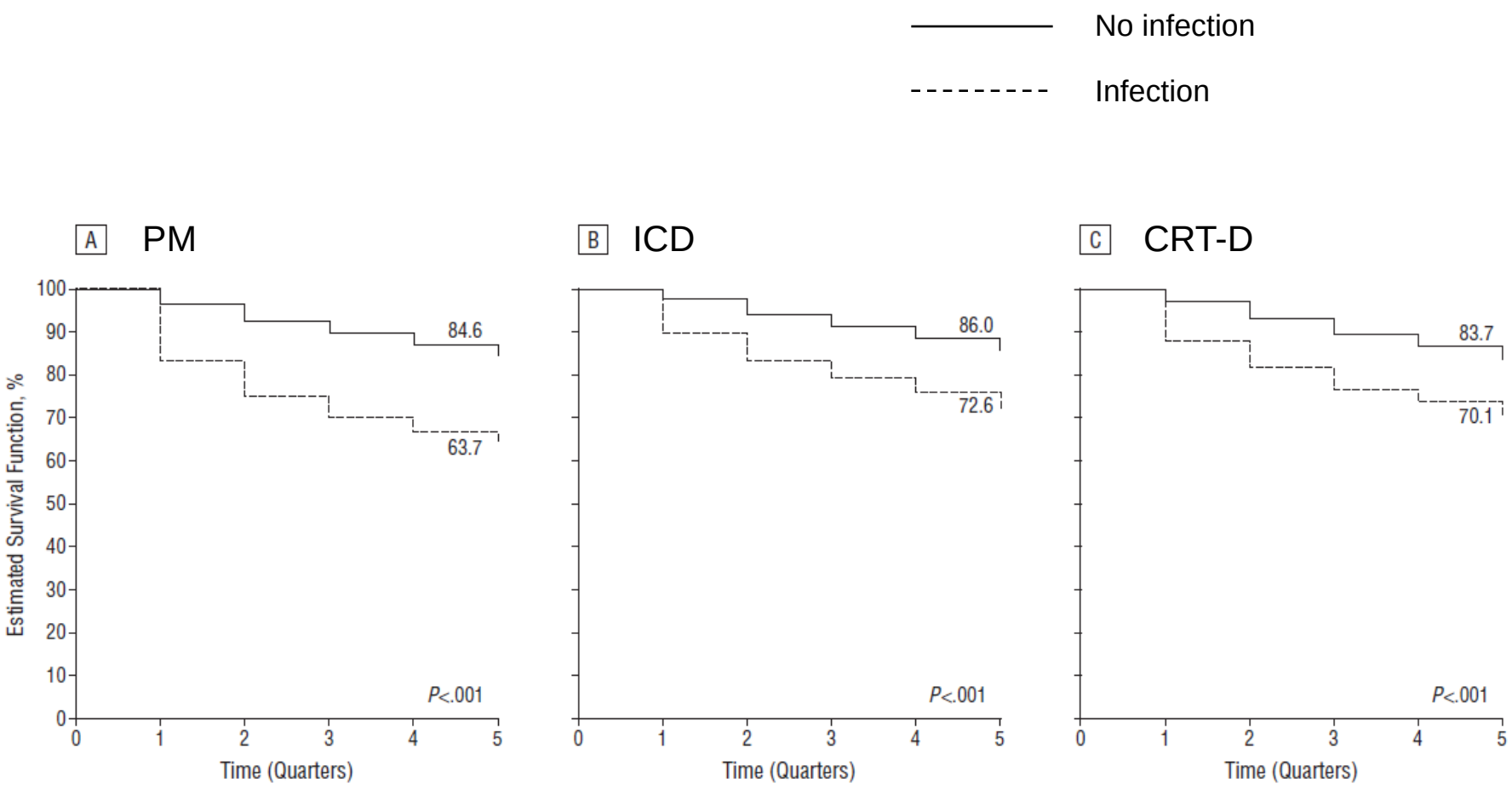
Risk factors for PM/ICD infection

- Device-related factors
  - Abdominal generator
  - Presence of more than two electrode leads
  - Multiple device revisions in the past
  - Previous history of CIED infection
- Procedure-related factors
  - Operator inexperience

Healthcare associated ≈ 50%

  - Post-operative hematoma at pocket site
- Host-related factors
  - Presence of tunneled central venous catheter (such as hemodialysis catheter)
  - Long-term corticosteroid therapy
  - Oral anticoagulation
  - Comorbid conditions (e.g., diabetes mellitus, heart failure, renal failure or malignancy)

ICD Registry – impact of infection on survivaal



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Guidelines for diagnosis of CIED infections

- Class I (benefit >>>risk, should be done)
  - All patients with suspected CIED infection should have at least two sets of blood cultures before initiation of antibiotics
  - Pocket tissue and lead-tip cultures should be obtained if the device is explanted
  - Patients with positive blood cultures (or negative cultures who were treated with antibiotics) should undergo TTE and a TEE to rule out endocarditis
  - Adult patients with suspected CIED endocarditis should undergo TEE even if the transthoracic echo is negative
- Class IIa (benefit >> risk, reasonable to be done
  - Patients with CIEDs who develop fever or bloodstream infection should seek CIED infection evaluation by a cardiologist or infectious disease specialist
- Class III (risk > benefit, should not be done)
  - Percutaneous aspiration of the pulse generator pocket should not be performed as part of diagnostic evaluation of CIED infection

Baddour L, Circulation 2010;121:458

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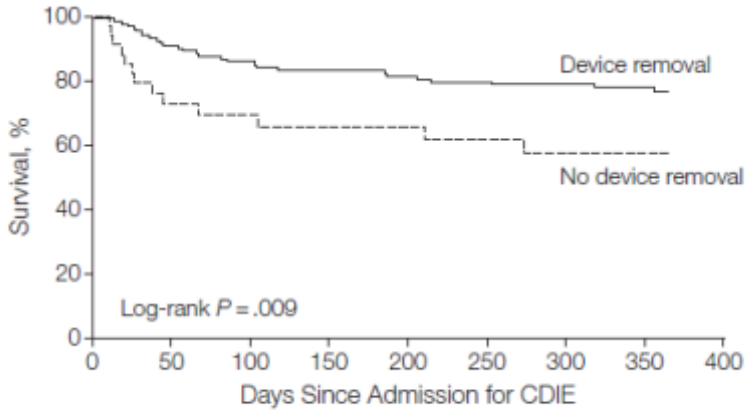
Endocarditis in patients with IECD (PPM & ICD)

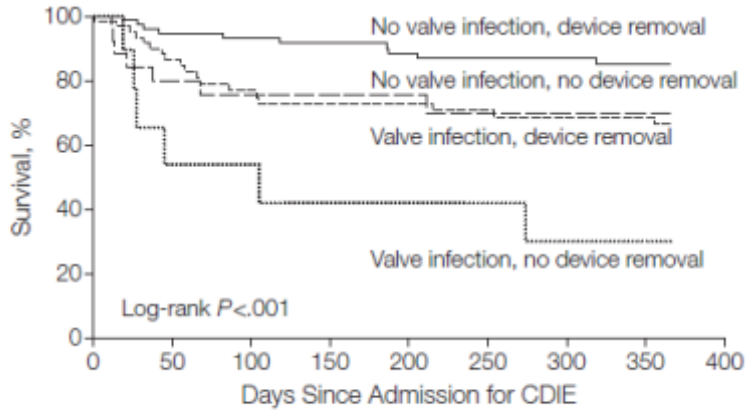
One-year survival

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

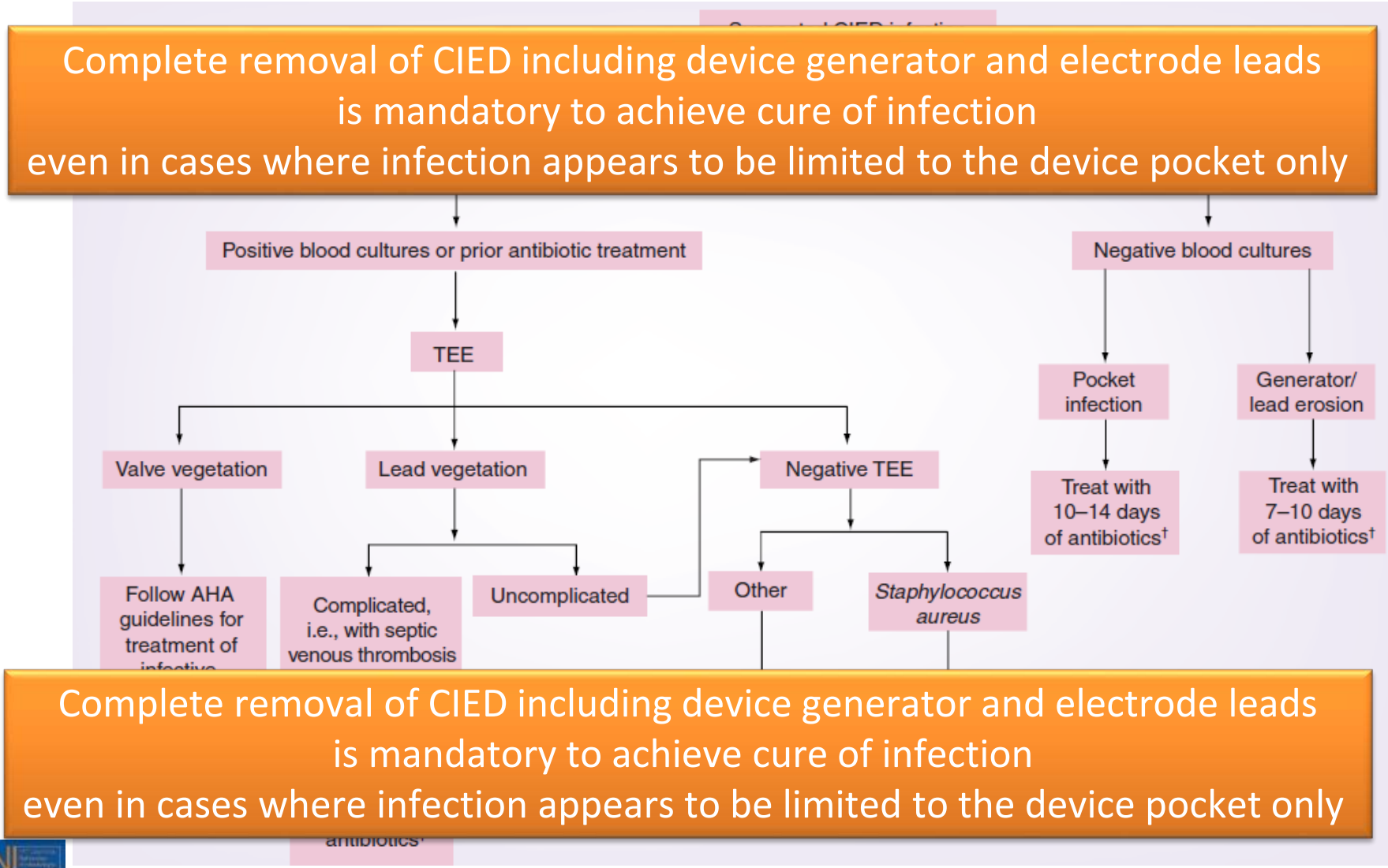
By concomitant valve infection and device removal



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

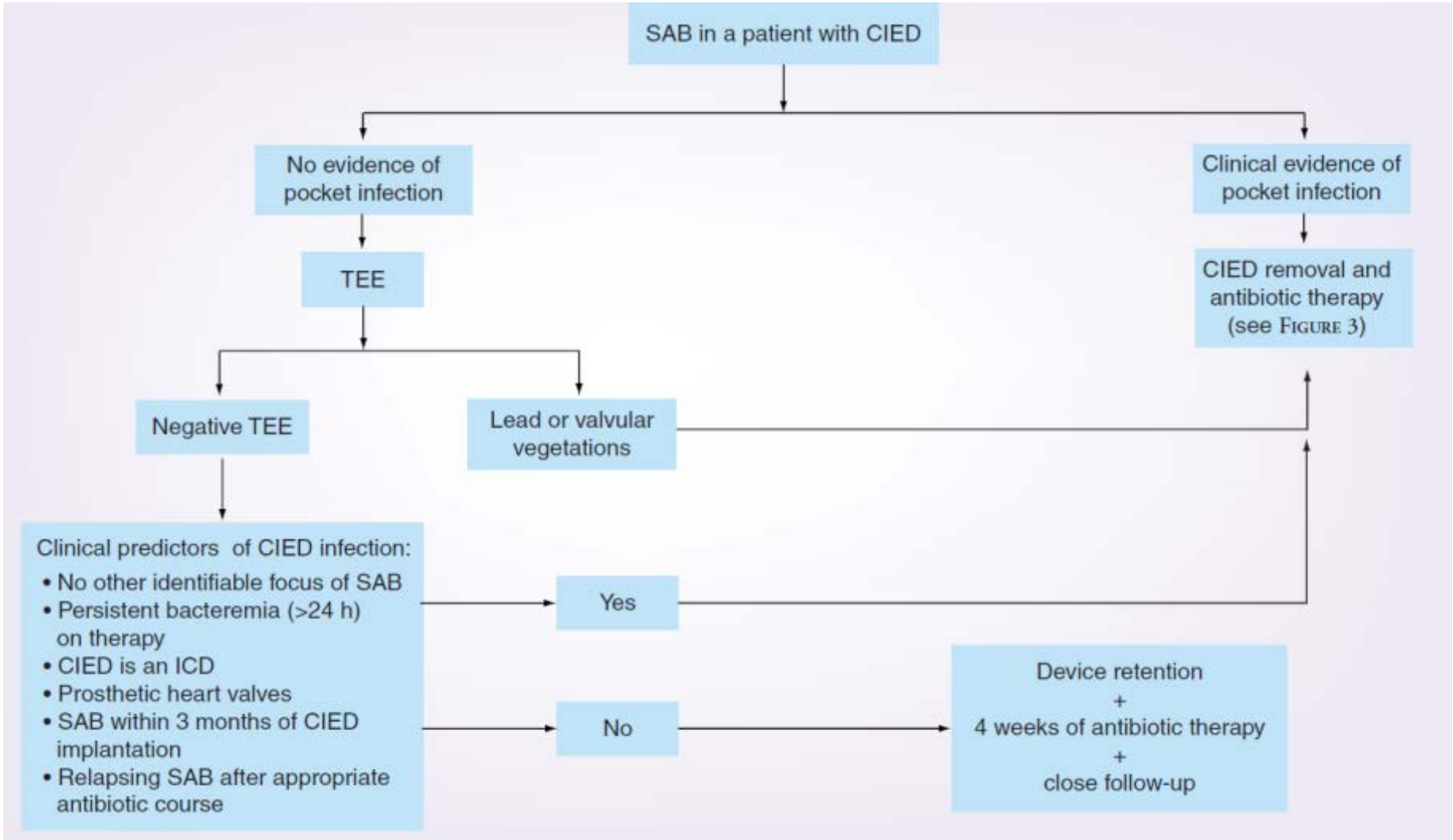
Athan E, JAMA 2012;307:1727

Management of CIED infections – Statement of the AHA



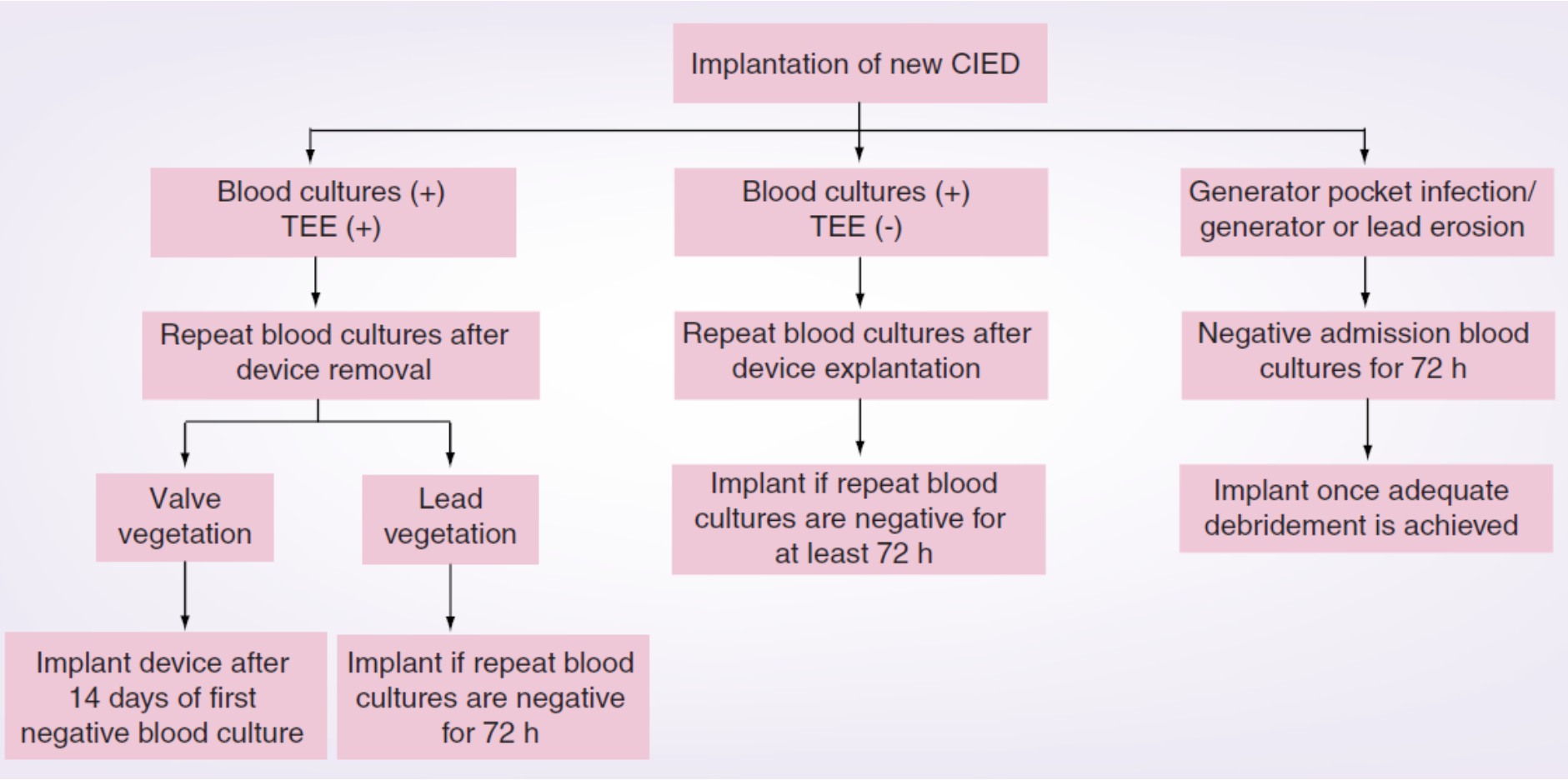
Sohail MR, Expert Rev Anti Infect Ther 2010;8:831
Baddour L, Circulation 2010;121:458

Management of adults with SAB and CIED



Sohail MR, Expert Rev Anti Infect Ther 2010;8:831
Baddour L, Circulation 2010;121:458

Guidelines for implantation of a new device in patients with CIED infection



Sohail MR, Expert Rev Anti Infect Ther 2010;8:831
Baddour L, Circulation 2010;121:458

Clinical Infectious Diseases Advance Access published November 18, 2011

MAJOR ARTICLE

High-Dose Daptomycin for Cardiac Implantable Electronic Device–Related Infective Endocarditis

Emanuele Durante-Mangoni, Roberta Casillo, Mariano Bernardo, Cristina Caianiello, Irene Mattucci, Daniela Pinto, Federica Agrusta, Roberta Caprioli, Rosina Albisinni, Enrico Ragone, and Riccardo Utili

Department of Internal Medicine, University of Naples S.U.N., and Unit of Infectious and Transplant Medicine, A.O.R.N. "V. Monaldi," Naples, Italy

Background. Cardiac implantable electronic device (CIED)–related endocarditis is a growing challenge because of increasing incidence and significant mortality. Current treatment is based on complete hardware removal coupled with long-term administration of effective and safe antimicrobials. Daptomycin at the dose of 6 mg/kg/day has been found to be effective in staphylococcal endocarditis, but limited data exist on CIED endocarditis. Moreover, whether higher doses could be more effective but equally safe in this setting is currently unknown.

Methods. We report here our experience with high-dose daptomycin in the treatment of 25 cases of CIED endocarditis due to staphylococci.

Results. Patients were mostly elderly and male, with large lead vegetations and severe comorbidities. Pathogens were *Staphylococcus epidermidis* (56%), *Staphylococcus aureus* (28%), and other coagulase-negative staphylococci (16%). Only 4 patients (16%) had a normal pretreatment renal function. The median daptomycin daily dose was 8.3 mg/kg (range, 6.4–10.7). Daptomycin was administered for a median of 20 days (range, 8–52). Percutaneous lead extraction was performed in 88% of patients. Two patients (8%) failed to clear bacteremia. The overall clinical success of treatment was 80%, whereas a complete microbiological success was observed in 92% of patients. Creatine phosphokinase values were monitored and increased above normal in 5 cases (20%). No serious adverse event related to high-dose daptomycin was observed and no patient required discontinuation because of muscle toxicity.

Conclusions. Our experience suggests that high-dose daptomycin may be a safe therapeutic option in staphylococcal CIED endocarditis and may be associated with high microbiological responses and clinical success.

The MEDIC (Multicenter Electrophysiologic Device Infection Cohort) study

- The CIED device and leads were removed in all cases.
  - A laser sheath was required for lead removal in 56% of early LAE patients and 64% of late LAE patients.
- The entire system was successfully removed in all but 2 of 43 (5%) early LAE patients and 4 of 102 late LAE patients (4%)
- Some residual lead material remained in the 2 early LAE patients and 4 late LAE patients
- No patient required conversion to open thoracotomy
- Pulmonary emboli after CIED removal occurred in 1 early LAE patient (2.3%) and 6 late LAE patients (6%)

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

Questions sans réponses

- La taille des végétations a un impact sur le pronostic ?
- La décision de retrait du dispositif par voie chirurgicale doit-elle être prise en fonction de la taille des végétations ?
- Quels sont les indications d'extraction par thoracotomie ?

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Intranasal mupirocin prevents postoperative *Staphylococcus aureus* infections: RCT

	Mupirocin group		Placebo group	
	Total	*S. aureus* carriers	Total	*S. aureus* carriers
Pre-op. carriage	23.0%	100%	23.1%	100%
Post-op. carriage	4.6%	16.6%	21.3%	72.2%
Nosocomial infection	11.3%	12.8%	11.4%	16.1%
S. aureus infection	2.4%	4.0%*	2.9%	7.7%*
SSI	7.9%	9.9%	8.5%	11.6%
S. aureus SSI	2.3%**	3.7%	2.4%**	5.9%

*p<0.05; **p=NS

Perl TM et al. N Engl J Med. 2002. 346:1871-7.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 28, 2006 VOL. 355 NO. 26

An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU

Peter Pronovost, M.D., Ph.D., Dale Needham, M.D., Ph.D., Sean Berenholtz, M.D., David Sinopoli, M.P.H., M.B.A., Haitao Chu, M.D., Ph.D., Sara Cosgrove, M.D., Bryan Sexton, Ph.D., Robert Hyzy, M.D., Robert Welsh, M.D., Gary Roth, M.D., Joseph Bander, M.D., John Kepros, M.D., and Christine Goeschel, R.N., M.P.A.

ABSTRACT

BACKGROUND

Catheter-related bloodstream infections occurring in the intensive care unit (ICU) are common, costly, and potentially lethal.

From the School of Medicine (P.P., D.N., S.B., S.C., B.S.), the School of Professional Studies in Business and Education (D.S.),

The Intervention

The recommended procedures were:

1) Hand washing,
2) Using full-barrier precautions during the insertion of central venous catheters,
3) Cleaning the skin with chlorhexidine,
4) Avoiding the femoral site if possible, and
5) Removing unnecessary catheters.

Provonost P et al. N Engl J Med 2006;355:2725-32.

Rates of Catheter-Related Bloodstream Infection from Baseline (before Implementation of the Study Intervention) to 18 Months of Follow-up

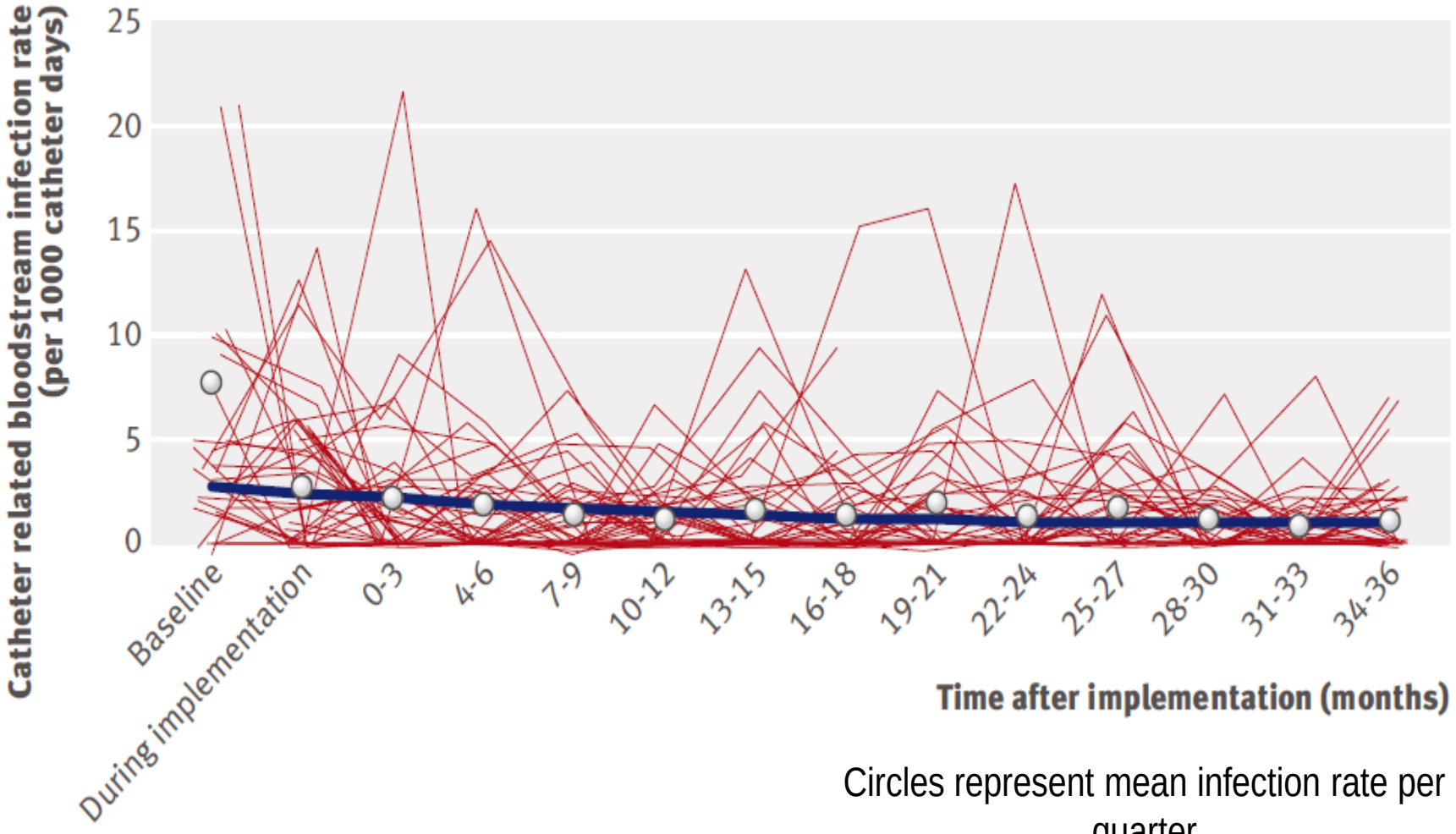
Study Period	No. of ICUs	No. of Bloodstream Infections per 1000 Catheter-Days				
		Overall	Teaching Hospital	Nonteaching Hospital	<200 Beds	≥200 Beds
		median (interquartile range)				
Baseline	55	2.7 (0.6–4.8)	2.7 (1.3–4.7)	2.6 (0–4.9)	2.1 (0–3.0)	2.7 (1.3–4.8)
During implementation	96	1.6 (0–4.4)†	1.7 (0–4.5)	0 (0–3.5)	0 (0–5.8)	1.7 (0–4.3)†
After implementation						
0– 3 mo	96	0 (0–3.0)‡	1.3 (0–3.1)†	0 (0–1.6)†	0 (0–2.7)	1.1 (0–3.1)‡
4–6 mo	96	0 (0–2.7)‡	1.1 (0–3.6)†	0 (0–0)‡	0 (0–0)†	0 (0–3.2)‡
7–9 mo	95	0 (0–2.1)‡	0.8 (0–2.4)‡	0 (0–0)‡	0 (0–0)†	0 (0–2.2)‡
10–12 mo	90	0 (0–1.9)‡	0 (0–2.3)‡	0 (0–1.5)‡	0 (0–0)†	0.2 (0–2.3)‡
13–15 mo	85	0 (0–1.6)‡	0 (0–2.2)‡	0 (0–0)‡	0 (0–0)†	0 (0–2.0)‡
16–18 mo	70	0 (0–2.4)‡	0 (0–2.7)‡	0 (0–1.2)†	0 (0–0)†	0 (0–2.6)‡

Conclusions: An evidence-based intervention resulted in a large and sustained reduction (up to 66%) in rates of catheter-related bloodstream infection that was maintained throughout the 18-month study period.

Provonost P et al. N Engl J Med 2006;355:2725-32.

† P≤0.05.
‡ P≤0.002.

The Reduced Rates of Catheter-Related Bloodstream Infection were Sustained up to 36 Months after Implementation



Circles represent mean infection rate per quarter

Provonost P et al. BMJ. 2010; 340:c309.

Messages à emporter à la maison

- La moitié des infections sur PPM/ICD sont liées aux soins
- Deux tiers des infections sur PPM/ICD sont dues à des staphylocoques
- Le diagnostic des infections sur PPM/ICD repose sur les hémocultures et l'ETO
- Une "infection de la loge" est une infection du dispositif
- Le traitement d'une infection sur PPM/ICD associe antibiothérapie ET extraction du matériel
- La réduction du risque infectieux passe par
  - éradication du portage nasal de staphylocoques
  - Antibioprophylaxie
  - protocole "0 bactériémie" (Keystone)
  - Réduction du risque de saignement du site opératoire
  - Expérience de l'opérateur