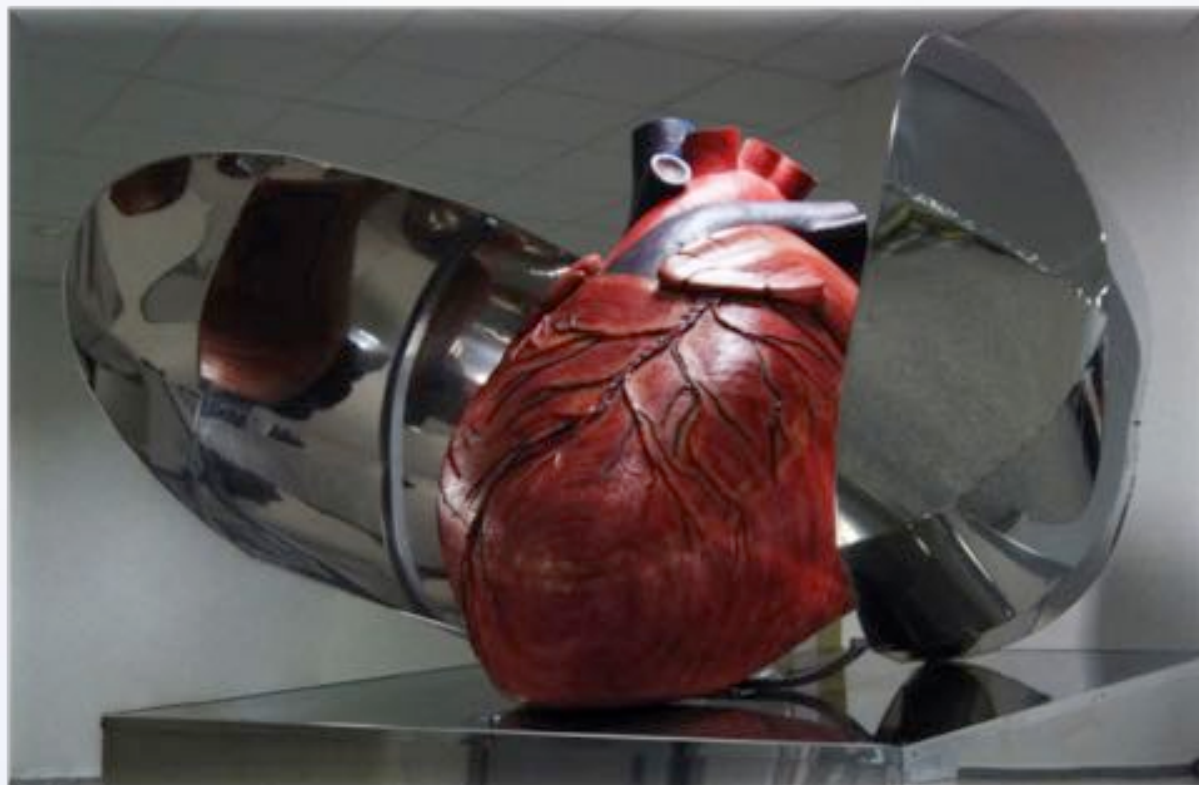


Implantable device infection



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INSTITUT KLINICKÉ A EXPERIMENTÁLNÍ MEDICÍNY
IKEM
KLINIKA KARDIOLOGIE



My Disclosures - 2014

- **Advisory Board member**
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Agenda

- Classification
- Epidemiology
- Risk factors
- Diagnostics
- Microbiology
- Management
- Prognosis
- Prevention

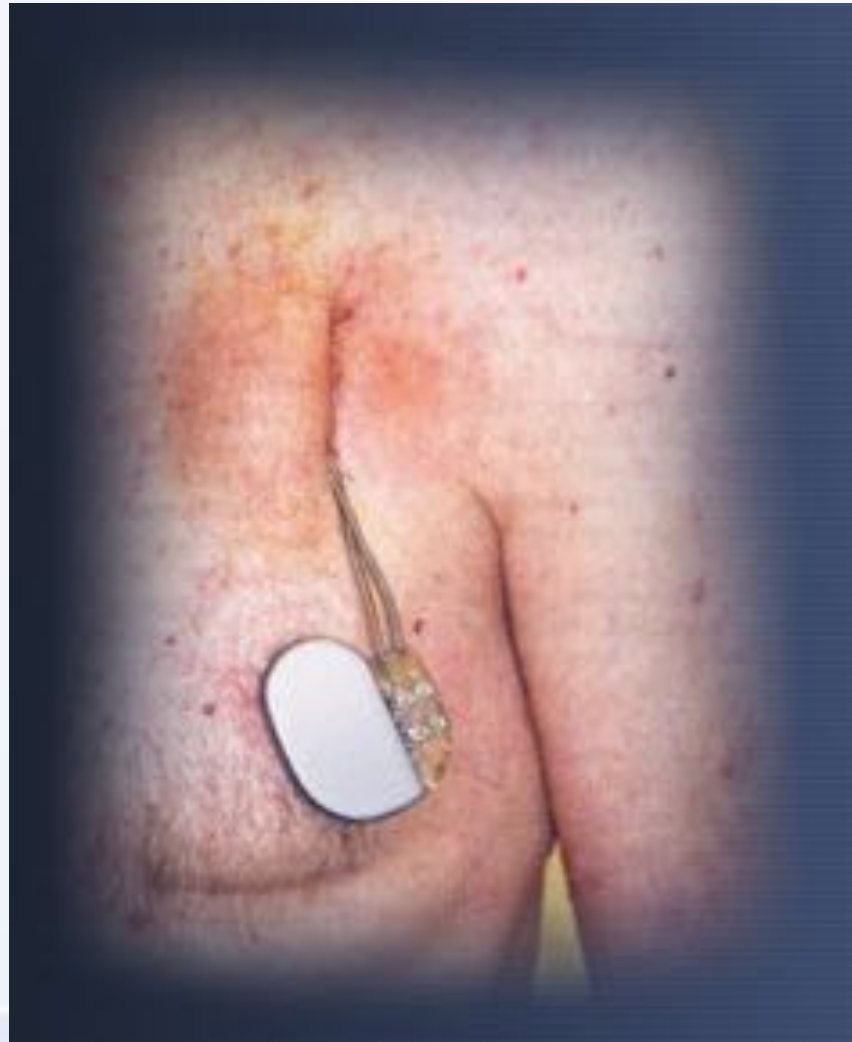
Cardiac Device Infections

- **Pocket infection:**
 - Localized changes at site with swelling, erythema, pain, warmth, fluctuance, drainage, erosion, dehiscence of overlying skin
 - Blood cx are positive ~50%
- **PPM or ICD related Endocarditis:**
 - Oscillating intra-cardiac mass on the electrode leads, valves or endocardial surface by echo
- **Occult bacteremia /fungemia** with no local signs at pocket site

ICD Pocket Infection



Infection/Erosion



CDI: Detailed Classification

- Mode of infection
 - Primary (device or pocket are the sources of infection – usually due to contamination at the implant)
 - Secondary (lead implanted due to bacteremia from different source)
- Time of onset
 - Early infection (within one month from index procedure)
 - Late infection

Epidemiology

Incidence of CIED Infection

- Analysis of 22 studies (at least 1000 pts each)
- Overall incidence of CIED infections: 0.5-2.2 %
- Infections more frequent in ICD pts vs PM pts (8.9 vs 1 per 1000 pt years)
- Less frequent in primary implants (0.5-0.8 % vs 1-4 %)

Danish Registry

2010-2011: 5918 consecutive patients, 562-9.5 % - major complication)

Table 2 Cumulative incidence of complications at six months*

	All (n = 5918)	New Implant (n = 4333)	Generator replacement (n = 1136)	Upgrade/ lead revision (n = 427)
Any complication	562 (9.5; 8.7–10.2)	432 (9.9; 9.0–10.8)	67 (5.9; 4.5–7.3)	63 (14.8; 11.4–18.1)
Any major complication	329 (5.6; 5.0–6.1)	253 (5.8; 5.1–6.5)	40 (3.5; 2.4–4.6)	36 (8.4; 5.8–11.1)
Any minor complication	250 (4.2; 3.7–4.7)	189 (4.3; 3.7–4.9)	30 (2.6; 1.7–3.6)	31 (7.3; 4.8–9.7)
Major complications				
Lead related re-intervention	143 (2.4; 2.0–2.8)	120 (2.8; 2.3–3.2)	10 (0.9; 0.3–1.4)	13 (3.0; 1.4–4.7)
Infection	49 (0.8; 0.6–1.1)	24 (0.6; 0.3–0.8)	17 (1.5; 0.8–2.2)	8 (1.9; 0.6–3.2)
Local infection	22 (0.4; 0.2–0.5)	10 (0.2; 0.1–0.4)	8 (0.7; 0.2–1.1)	4 (1.0; 0.0–1.9)
Systemic infection/endocarditis	27 (0.5; 0.3–0.6)	14 (0.3; 0.2–0.5)	9 (0.8; 0.3–1.3)	4 (0.9; 0.0–1.9)
Pneumothorax requiring drainage	21 (0.4; 0.2–0.5)	13 (0.3; 0.2–0.4)	0	8 (1.9; 0.3–2.5)
Cardiac perforation	38 (0.6; 0.4–0.8)	35 (0.8; 0.5–1.1)	0	3 (0.7; 0.0–1.5)
No intervention	21 (0.4; 0.2–0.5)	18 (0.4; 0.2–0.6)	0	3 (0.7; 0.0–1.5)
Intervention [†]	17 (0.3; 0.2–0.4)	17 (0.4; 0.2–0.6)	0	0
Pocket revision because of pain	25 (0.4; 0.3–0.6)	10 (0.2; 0.1–0.4)	9 (0.8; 0.3–1.3)	6 (1.4; 0.3–2.5)
Generator-lead interface problem with re-intervention	7 (0.1; 0.0–0.2)	3 (0.1; 0.0–0.1)	4 (0.4; 0.0–0.7)	0
Haematoma requiring re-intervention	10 (0.2; 0.1–0.3)	9 (0.2; 0.1–0.3)	1 (0.1; 0.0–0.3)	0
Other [‡]	16 (0.3; 0.1–0.4)	16 (0.4; 0.2–0.5)	0	0
Minor complications				
Haematoma [§]	138 (2.3; 1.9–2.7)	104 (2.4; 1.9–2.8)	20 (1.8; 1.0–2.5)	14 (3.3; 1.6–5.0)
Wound infection treated with antibiotics	69 (1.2; 0.9–1.4)	47 (1.1; 0.8–1.4)	12 (1.0; 0.5–1.7)	10 (2.3; 0.9–3.8)
Pneumothorax conservatively treated	39 (0.7; 0.5–0.9)	32 (0.7; 0.5–1.0)	0	7 (1.6; 0.4–2.8)
Lead dislodgement without re-intervention	10 (0.2; 0.1–0.3)	9 (0.2; 0.1–0.3)	0	1 (0.2; 0.0–0.7)

*Reported as absolute frequencies and percentages with 95% CIs in parenthesis.

[†]Lead revision, pericardiocentesis, or both.

[‡]Deep venous thrombosis (n = 8), Twiddler's syndrome (n = 3), wound revision (n = 3), stroke (n = 1), myocardial infarction (n = 1)

[§]Resulting in prolonged hospital stay, hospital re-admission, or additional out-patient visit.

Complications of implantable devices

IKEM Prague

	2014	2013	2012	2011
Late dislocations	6 (0.7%)	12 (1.4%)	9 (1.1 %)	2 (0.2 %)
Wound infection without explantation	4 (0.4%)	14 (1.7 %)	8 (1 %)	n.a.
Infection with explantation	11 (1.2%)	7 (0.8 %)	7 (0.9%)	n.a.
Fatal endocarditis	2 (0.2%)	0	1 (0.1%)	1 (0.1%)
Life-threatening endocarditis	0	2 (0.2 %)	1 (0.1 %)	2 (0.2 %)
Endocarditis well treated by ATB	3 (0.2%)	0	3 (0.5%)	2 (0.2%)
System failure or dysfunction of components	0	0	4 (0,5%)	n.a.
Others	5 (untightened screw, change of ports, etc).	0	Vena cava superior syndrome	

Comparison

Complications (%)	Danish pacemaker and ICD register (n=5918)	IKEM (n=910)
Any complication	9.5	9.1
Lead related re-intervention	2.4	2.6
Wound infection treated with antibiotics	1.2	0.4
Local infection	0.4	1.2
Systemic infection/endocarditis	0.5	0.4
Pneumothorax requiring drainage	0.9	0.5
Cardiac perforation	0.6	0.7
Haematoma requiring re-intervention	0.2	0.4

Rising Rates of Device Infections

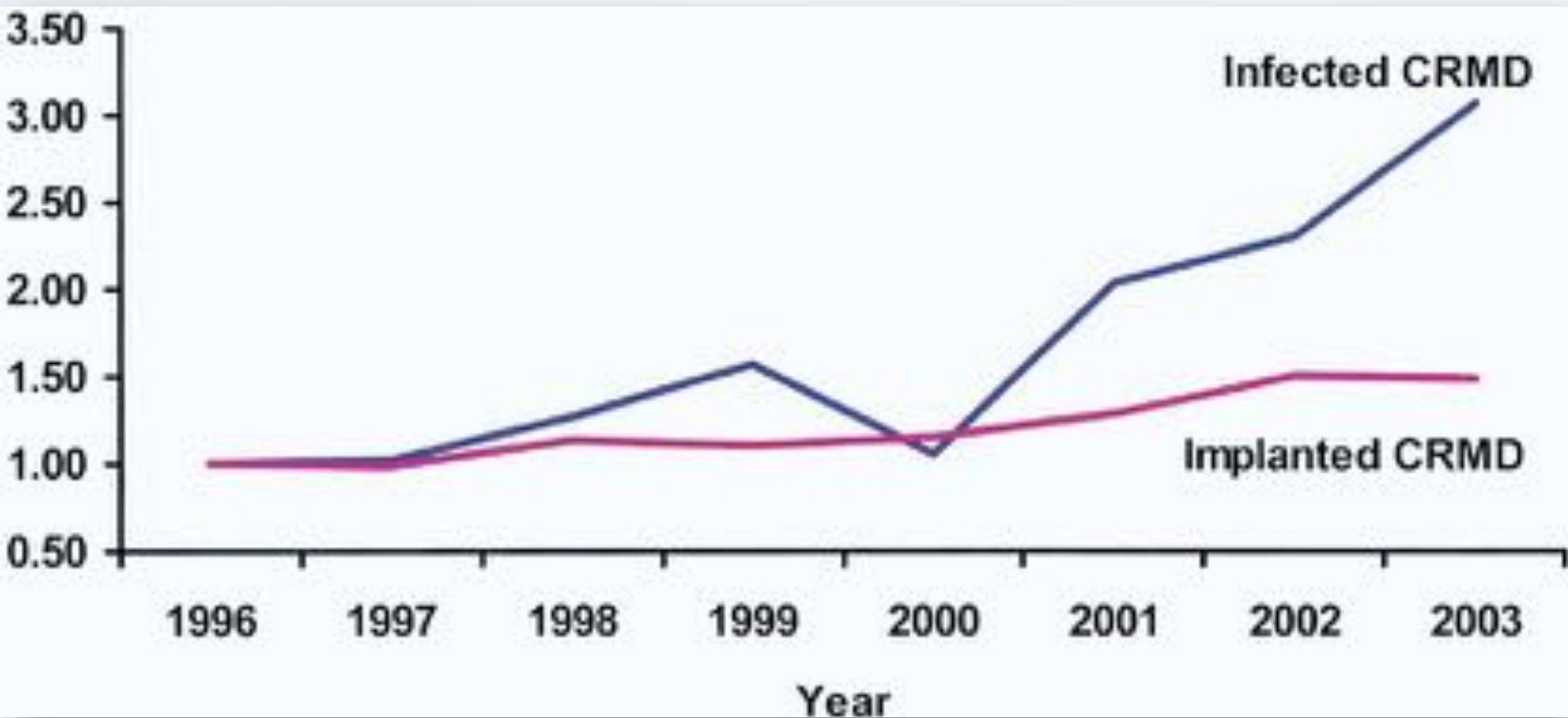
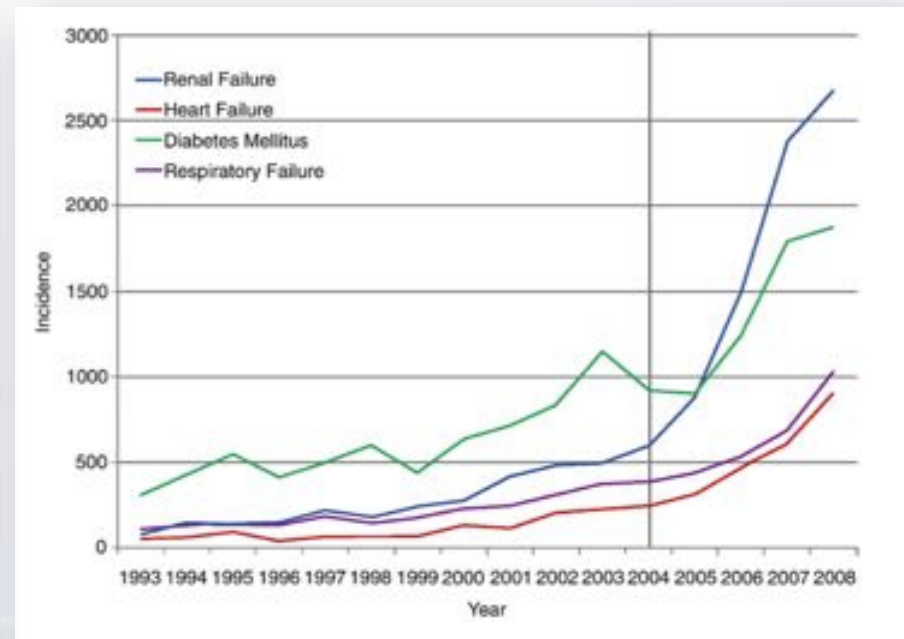
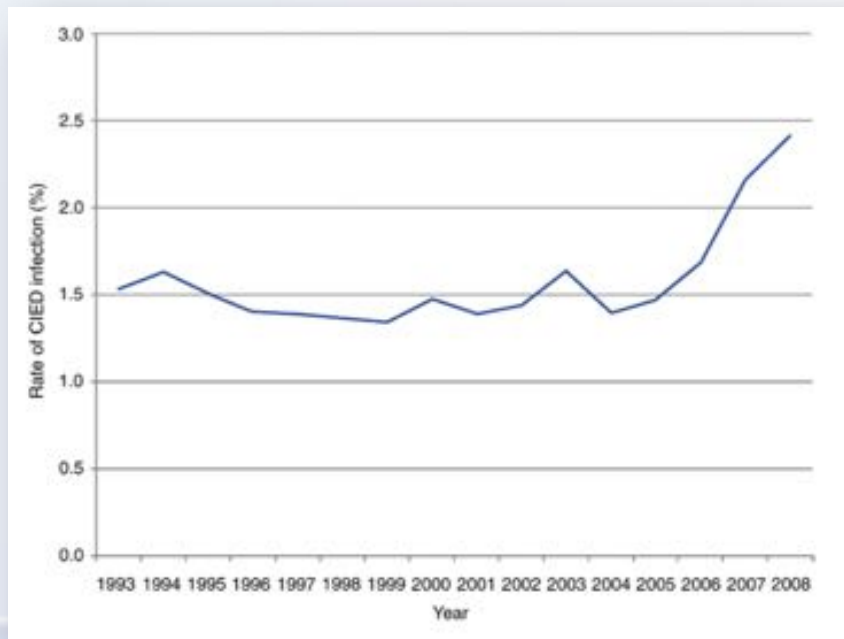


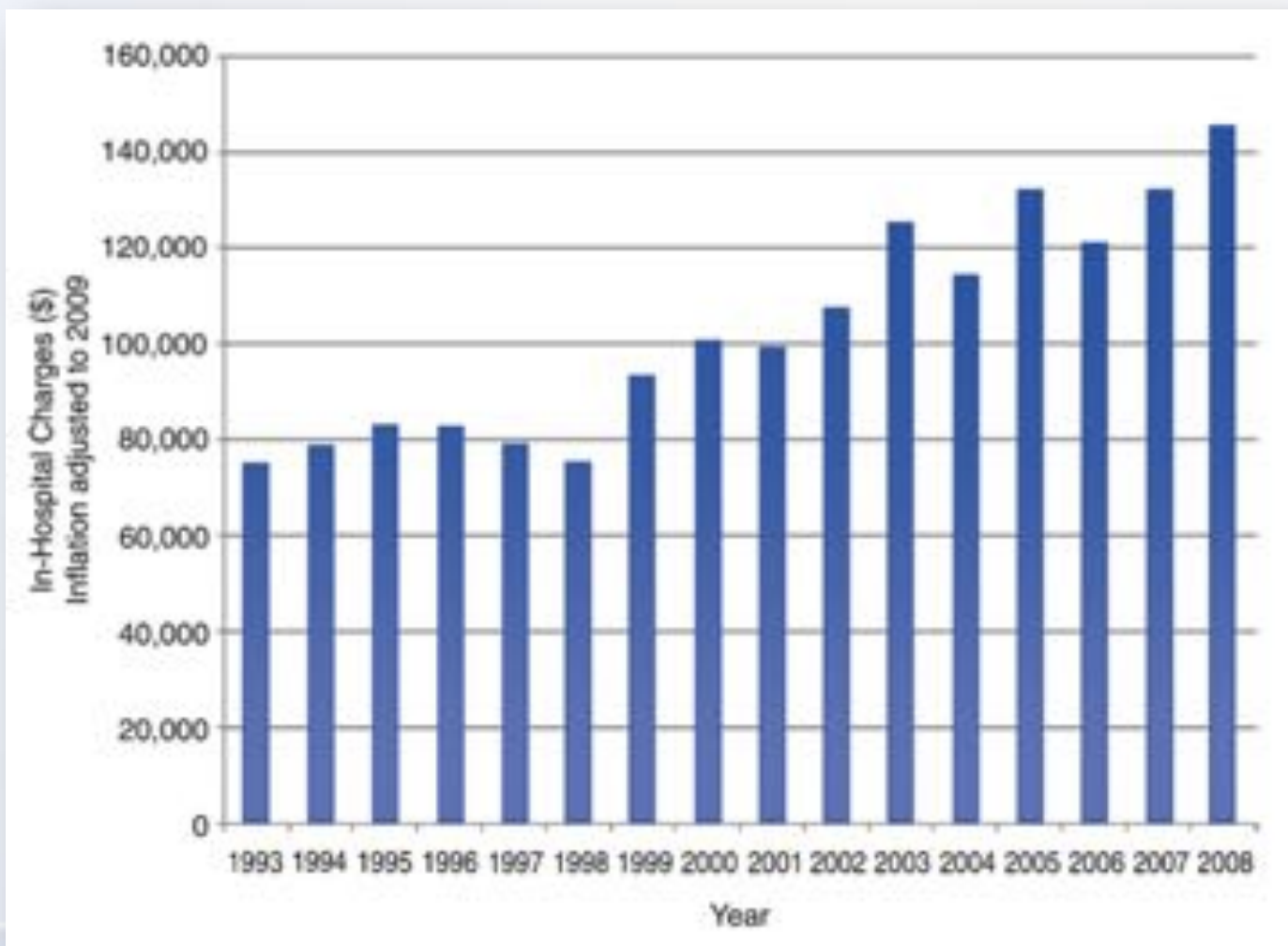
Figure 1. Proportional increase in cardiac devices implanted and those infected by year of hospitalization, normalized to the number of devices implanted and infected in 1996, respectively. Note the dramatic increase in device infections compared with device implantations, after 2000.

Increased CIED infection rate reflects more comorbidities

- Nationwide Inpatient Sample (1993-2008)
- Over 4.2 M pacemaker (3.2 M) and ICD (1.1 M) implants
- Incidence CIED infection: 1.61 %



Increased CIED Infection Rate Increases Costs



Risk Factors



Risk Factors for CIED Infection

Case-control study – 29 pts, 58 controls (1991-2003)
83% pocket infection, 10 % endocarditis

Clinical variable	OR (95% CI)	P
Corticosteroid use ^a	13.90 (1.27–151.7)	.03
Received antibiotic prophylaxis prior to implantation procedure	0.087 (0.016–0.48)	.005
No. of leads in place ^b		
>2 leads vs. 1 lead	5.64 (0.76–42.15)	.09
>2 leads vs. 2 leads	5.41 (1.44–20.29)	.01

^a Defined as receipt of ≥ 20 mg of prednisone, or equivalent, for ≥ 1 month during preceding year.
^b Overall P value for this comparison was .04.

Risk Factors for Device Infection

- Patient Factors (Odds Ratios where listed)
 - Immunosuppression
 - Renal dysfunction
 - Corticosteroid use
 - Oral anticoagulant use
 - Coexisting illnesses such as diabetes mellitus
 - Amount of indwelling hardware
- Procedural characteristics
 - Not administering antimicrobial prophylaxis
 - Device revision/replacement (2% vs <1% risk)
 - Physician experience / surgical technique
 - Microbiology if bloodstream infection i.e. *Staph aureus*

Sohail *CID* 2007 45:166.

Klug, *Circulation*;2007116:1349

Bloom *Pac Clin EP* 2006 29;142

Risk Factors for IE (IKEM)

Wound healing problem, re-implant within 6 months	17 (25%)
Adjacent to another surgical procedure	7 (10%)
Infection focus elsewhere	9 (13%)
Immunosuppressive drugs	5 (7%)
Hemodialysis	3 (4%)
Unknown	28 (41%)

Diagnostics



Intracardiac Echo Is More Sensitive....

162 pts – lead extraction
152 IE, 10 lead malf

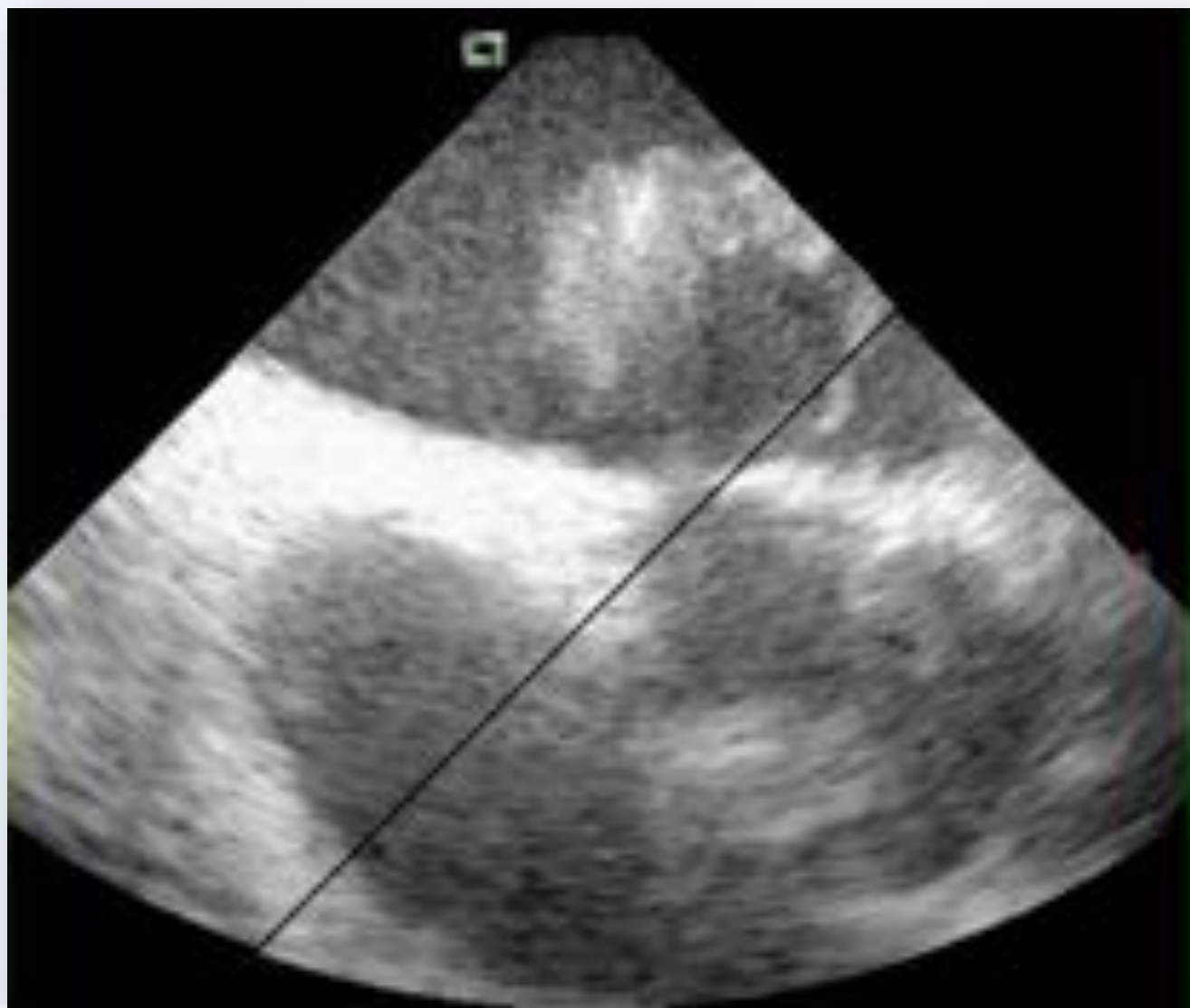
Table 3

**Echocardiographic Data
Related to the Duke and Sohail Criteria**

Criteria	TEE		ICE	
	Negative	Positive	Negative	Positive
Duke definite	12 (27)	32 (73)	0	44 (100)
Duke possible	46 (88)	6 (12)	38 (73)	14 (27)
Duke rejected	54 (96)	2 (4)	53 (95)	3 (5)
Duke definite and Sohail	20 (35)	38 (65)	0	58 (100)

Values are n (%).

TEE = transesophageal echocardiography; ICE = intracardiac echocardiography.



Microbiology

Pacer / ICD Infections (138 PPM, 51 ICDs)

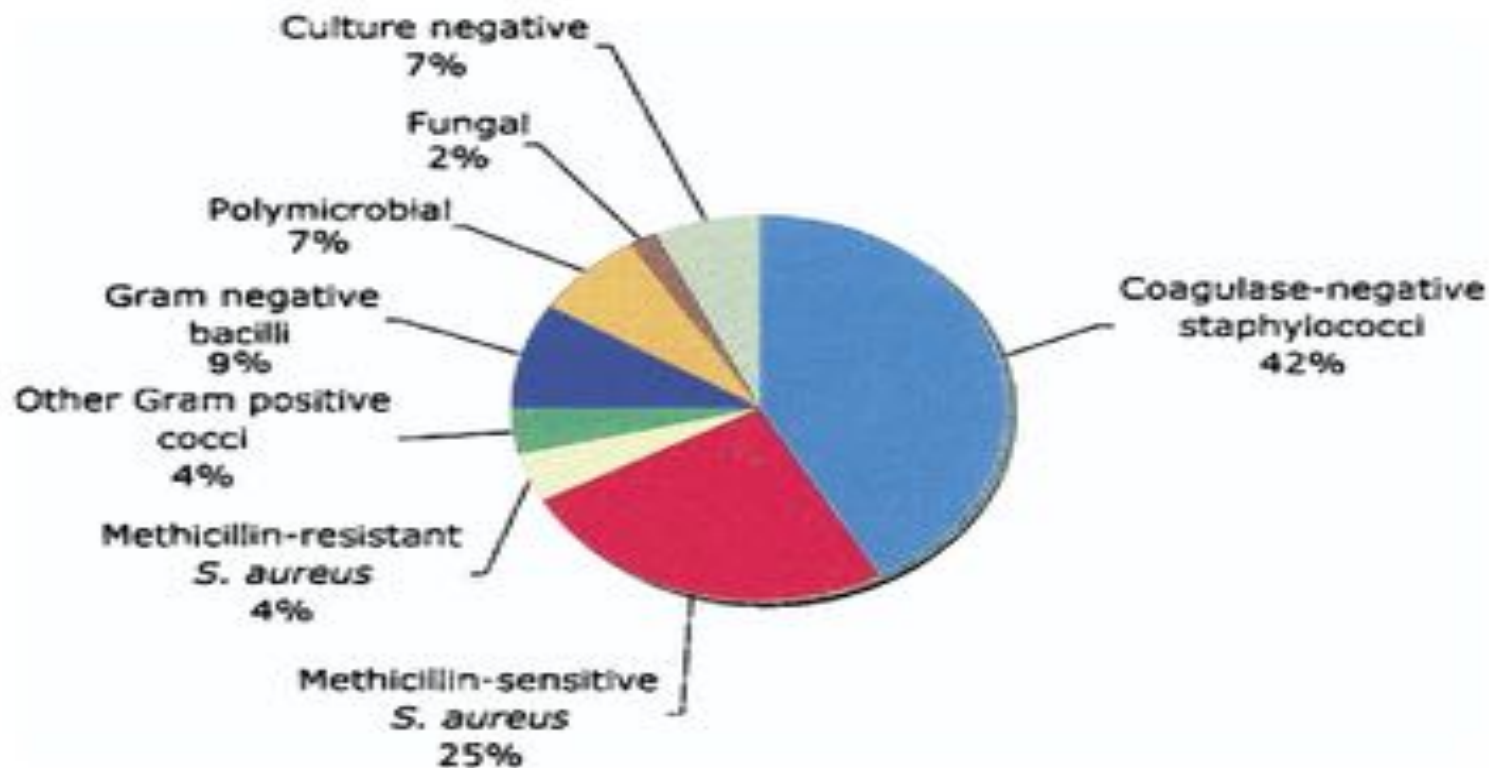


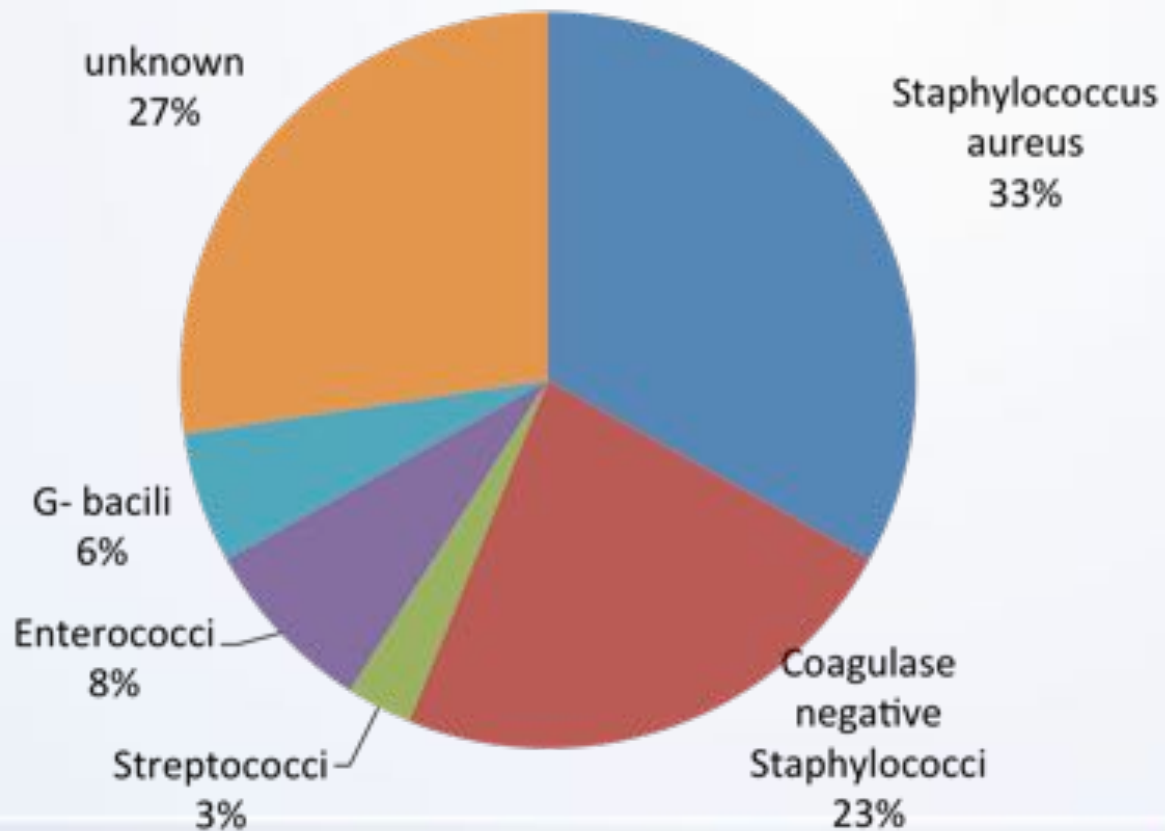
Figure 1 Microbiology of PPM/ICD Infections (n = 189)

ICD = implantable cardioverter-defibrillator; PPM = permanent pacemaker.

CIED Infections (IE) - IKEM

Agens

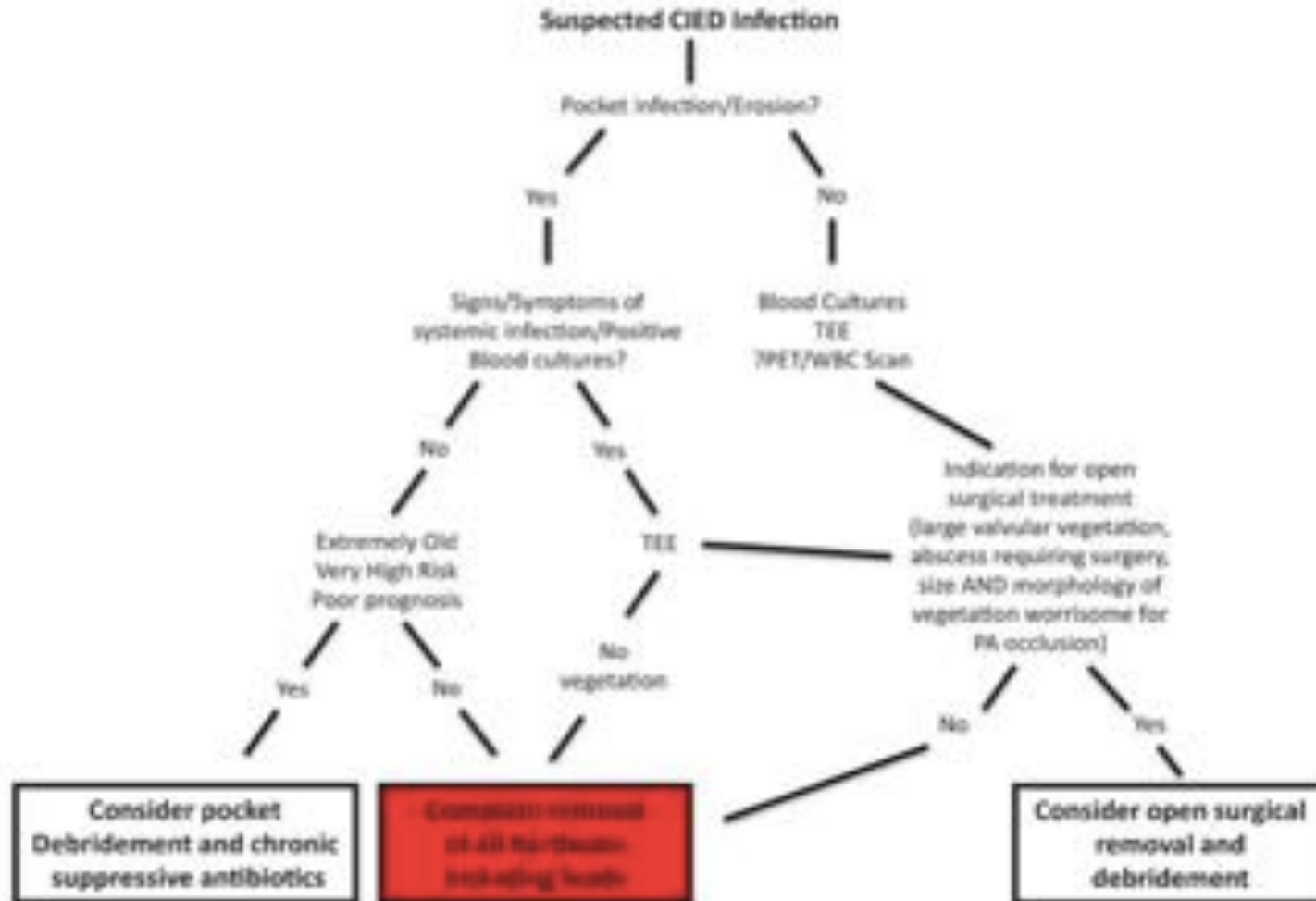
2005-2014 (n=69pts with IE)



Management

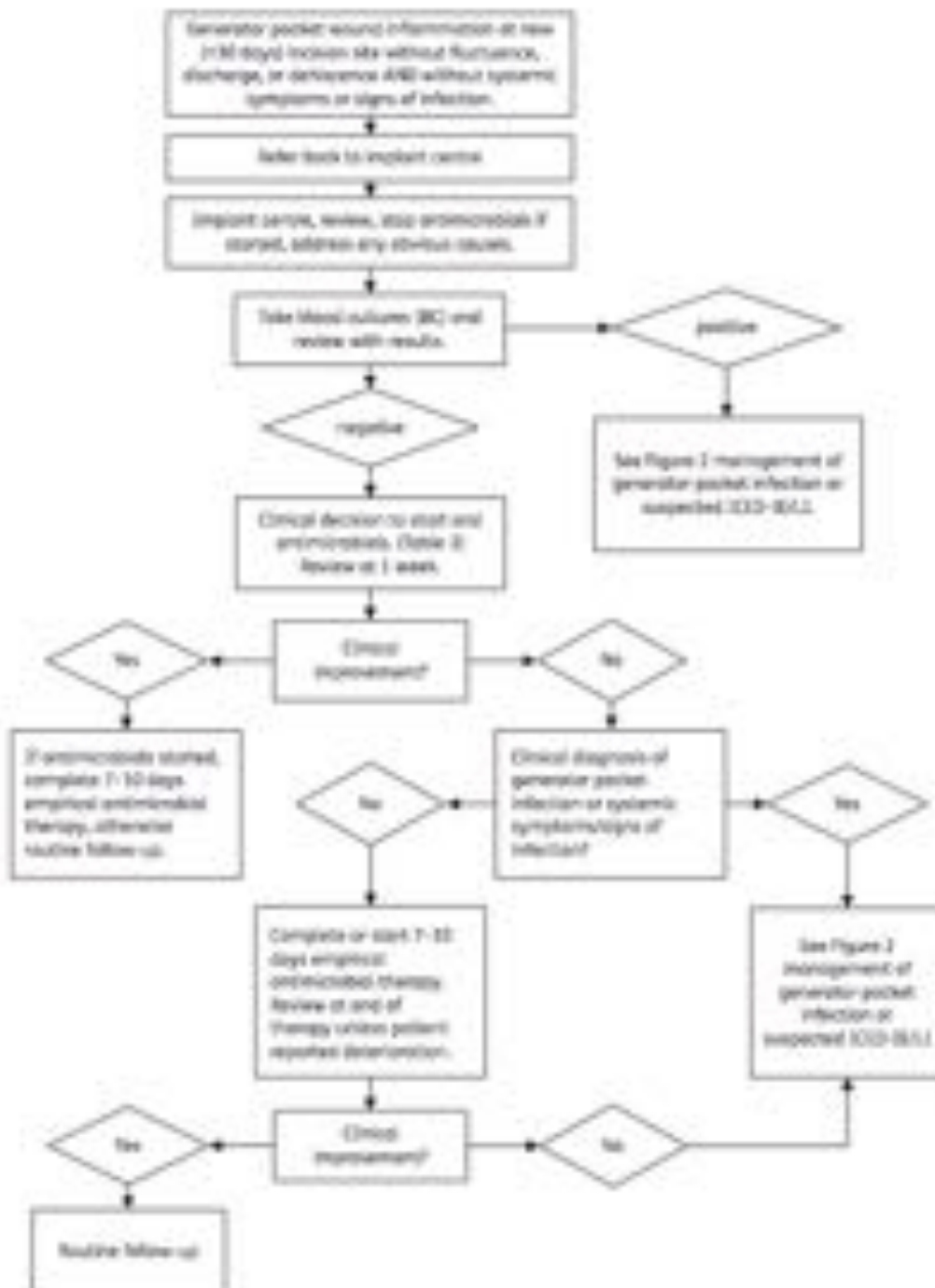


Management of CIED Infection



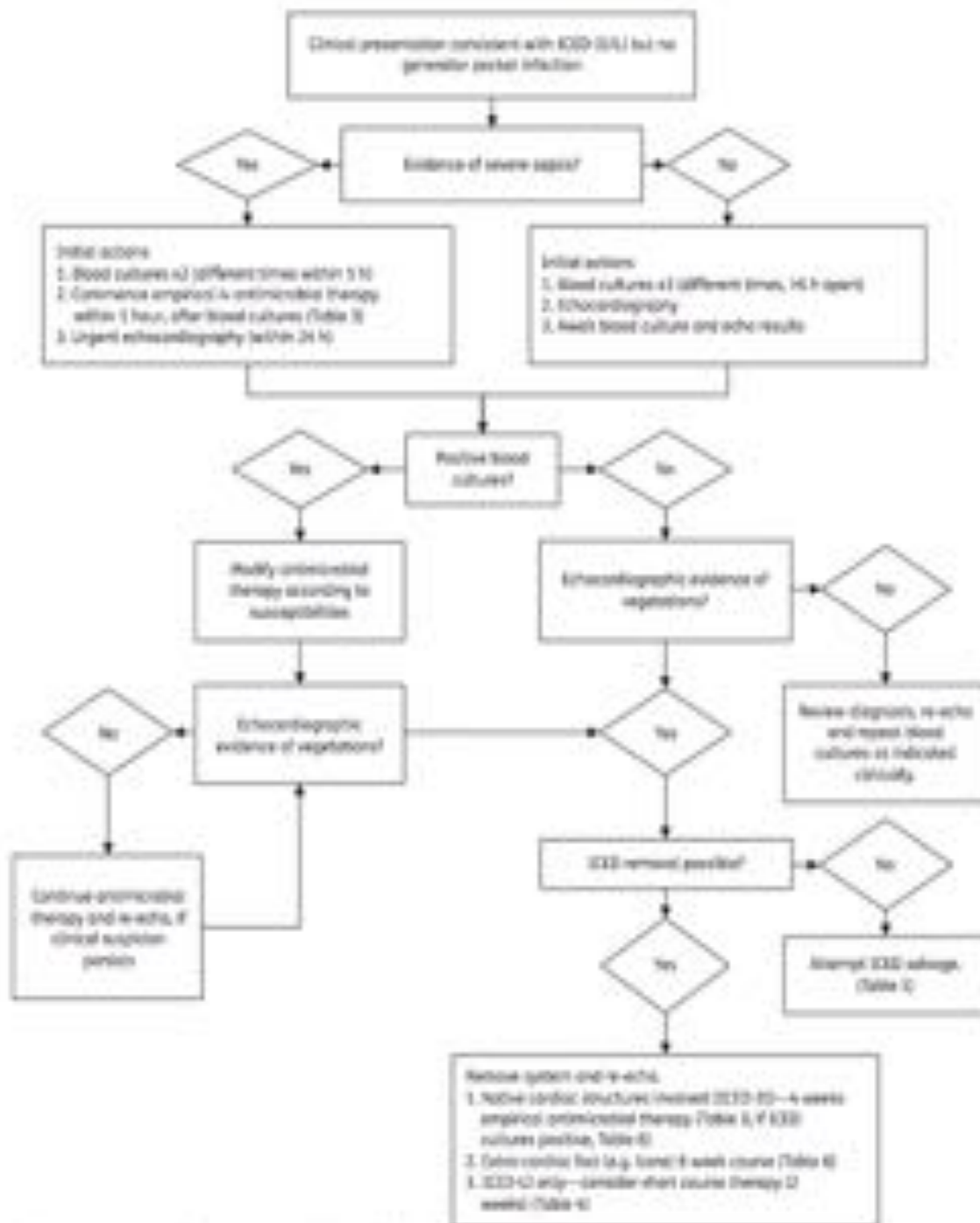
Management of early postimplantation inflammation (UK Guidelines)

Sandoe JAT, et al.
J Antimicrob Chemother 2015; 70: 325–359

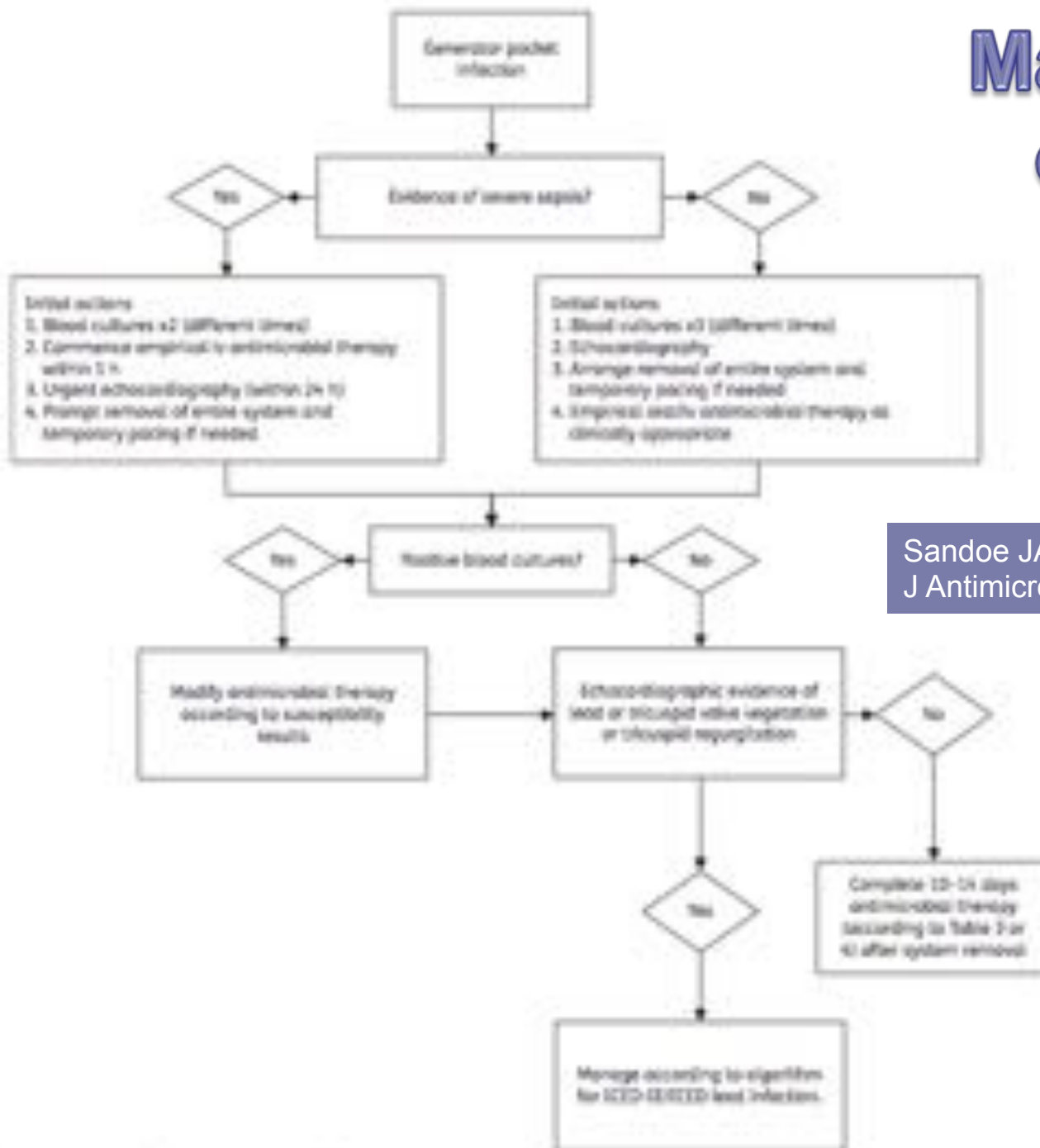


Management of suspected CIED IE/lead infection

Sandoe JAT, et al.
 J Antimicrob Chemother 2015; 70: 325–359



Management of pocket infection



Sandoe JAT, et al.
J Antimicrob Chemother 2015; 70: 325–359

Indications for System Extraction

Definite CIED infection with

Lead endocarditis

Valvular endocarditis

Pocket infection with abscess formation

Superficial erosion

Chronic draining sinus

Occult Gram-positive bacteremia

Persistent occult Gram-negative bacteremia

Valvular endocarditis without evidence of device infection

CIED indicates cardiac implantable electronic device.

CIED Infections - IKEM

Management of IE

■ Conservative ■ surgical extr ■ percutaneous extr



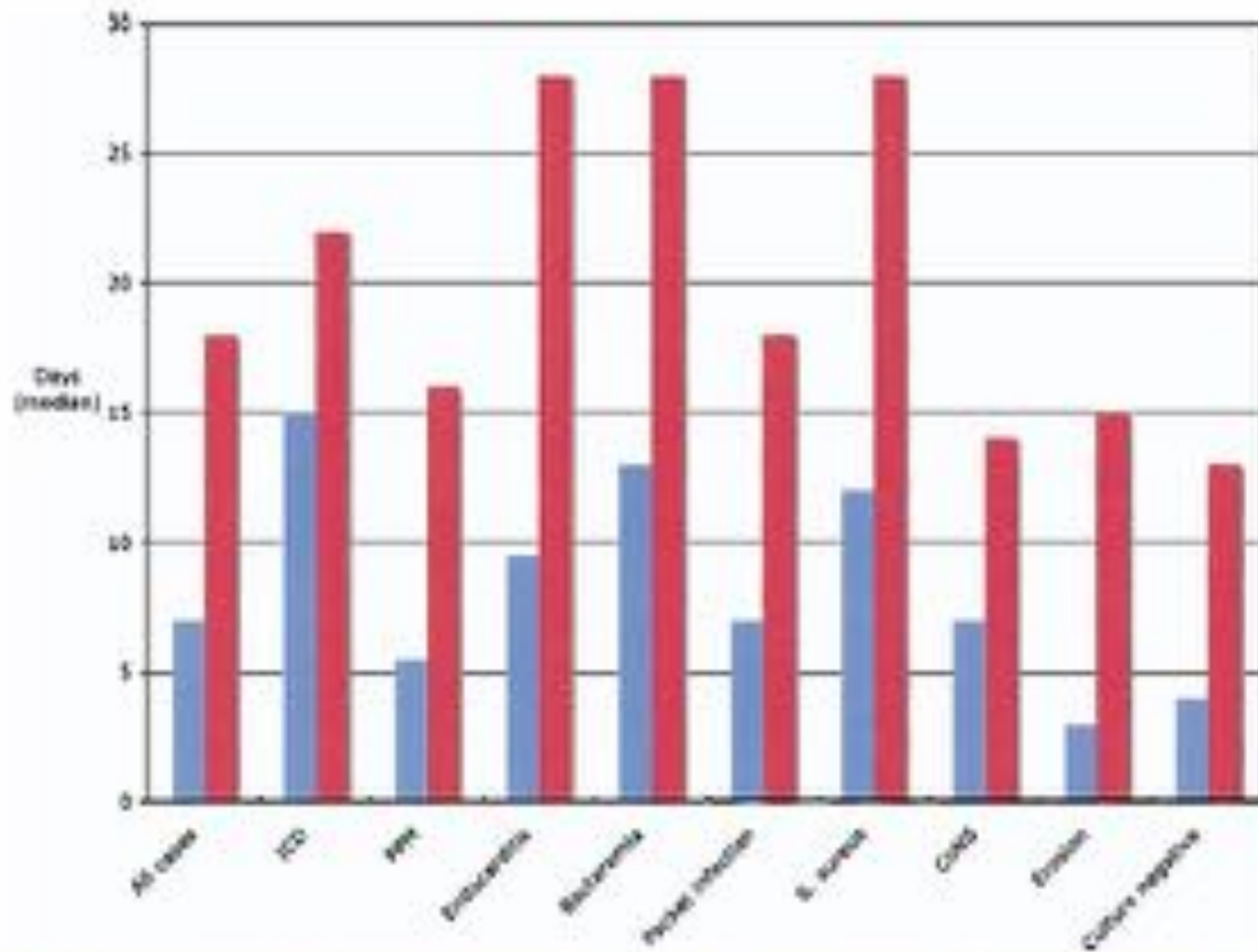


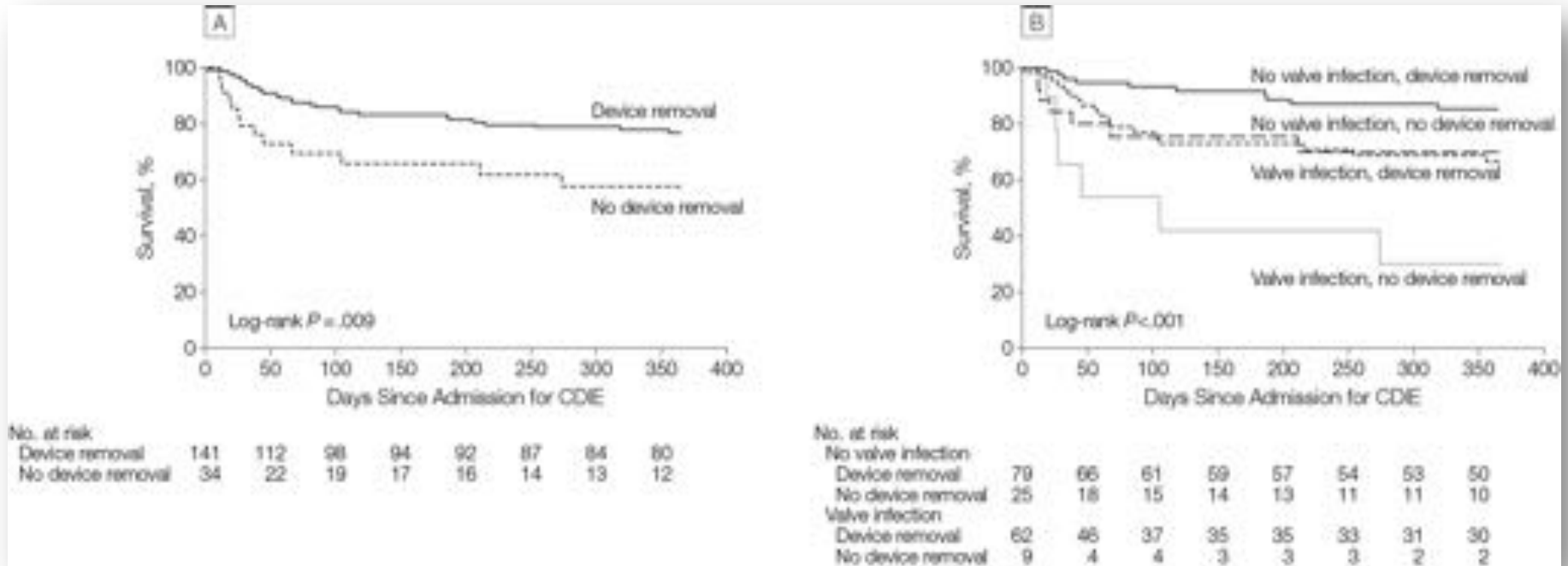
Figure 2 Timing of Reimplantation of New Cardiac Device and Duration of Postexplantation Antibiotic Treatment

Blue bars – time from explant to reimplant; red bars – post-explant antibiotic duration. CoNS – coagulase-negative staphylococci; other abbreviations as in Figure 1.

Prognosis

One-year survival related to device removal vs no removal during index hospitalization,

177 CIED IE out of 2760 IE cases



Prognosis of CIED Infection

- Infection endocarditis has poor prognosis (24.5-29 %) with FU up to one year
- Pocket infection is associated with much less mortality (5-6 %)
- Abnormal renal function is the most consistently identified risk factor for mortality
- Failure to remove an infected device is associated with relapse and mortality

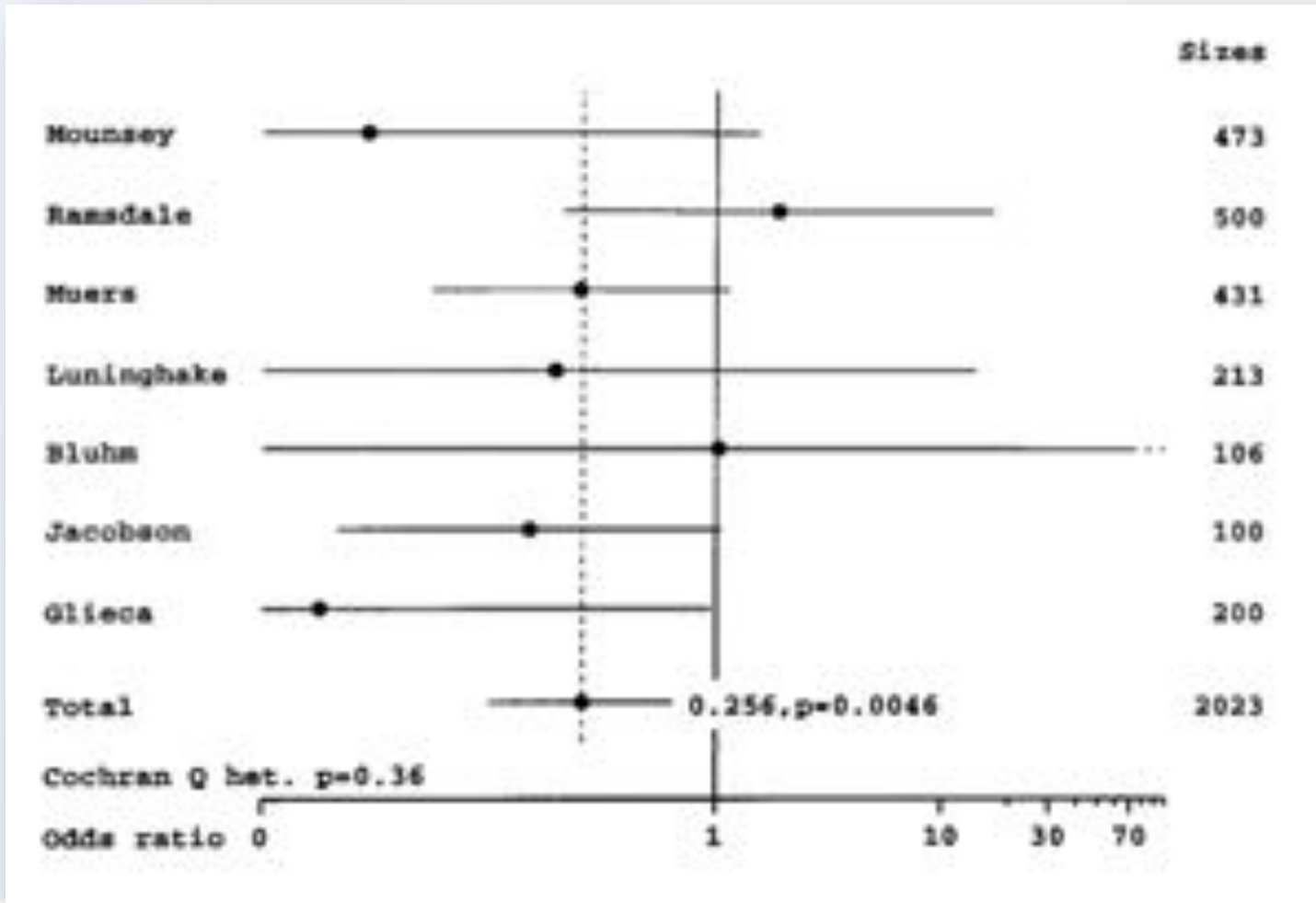
Prevention



Preventing Infections of CIEDs

- Meticulous attention to sterile technique
- Antibiotic Prophylaxis
- Procedure room
 - Positive pressure ventilation
 - Control Room
- Skin Preparation
- Wound Irrigation
- Skin Closure

Antibiotic Prophylaxis



Prevention of infection

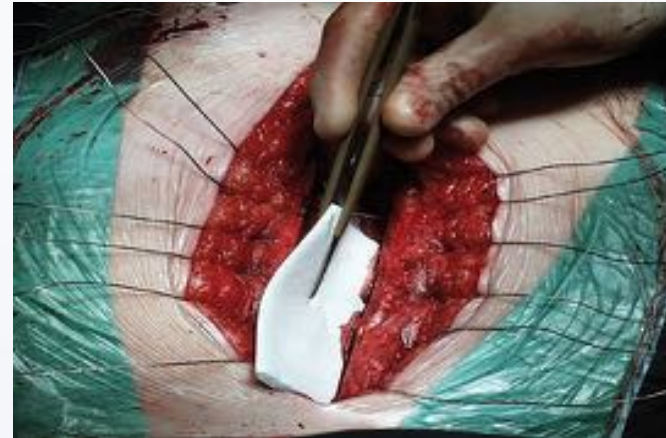
Tyrx (Absorbable Antibacterial Envelope)

- Rifampin and Minocycline



Collatamp 5x5x0.5cm

- gentamicinum, collagen



Antibacterial Envelope

AIGISRx® minocycline and rifampin-eluting antibacterial envelope (TyRX Inc., Monmouth Junction, NJ, USA)

A total of 260 antibacterial envelopes implanted (November 1, 2009 to April 30, 2012)
Control group (n=639) matched by age, sex and risk factors (2.8 ± 1.2)

Cardiac Implantable Electronic Device Infections among Cases and Controls

	Infections (n, %)	Unadjusted OR	P Value	Adjusted OR	P Value
Entire Cohort					
AIGISRx® Cases (n = 260)	1 (0.4%)	0.13 [0.02–0.95]	0.044	0.09 [0.01–0.73]	0.024
Controls (n = 639)	19 (3%)				
Propensity Score-Matched Cohort					
AIGISRx® Cases (n = 209)	1 (0.5%)	0.11 [0.01–0.85]	0.035	–	–
Controls (n = 209)	9 (4.3%)				

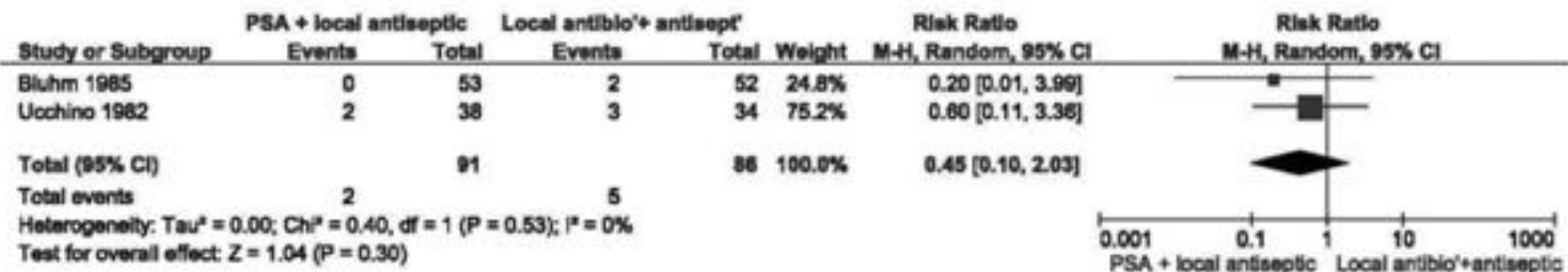
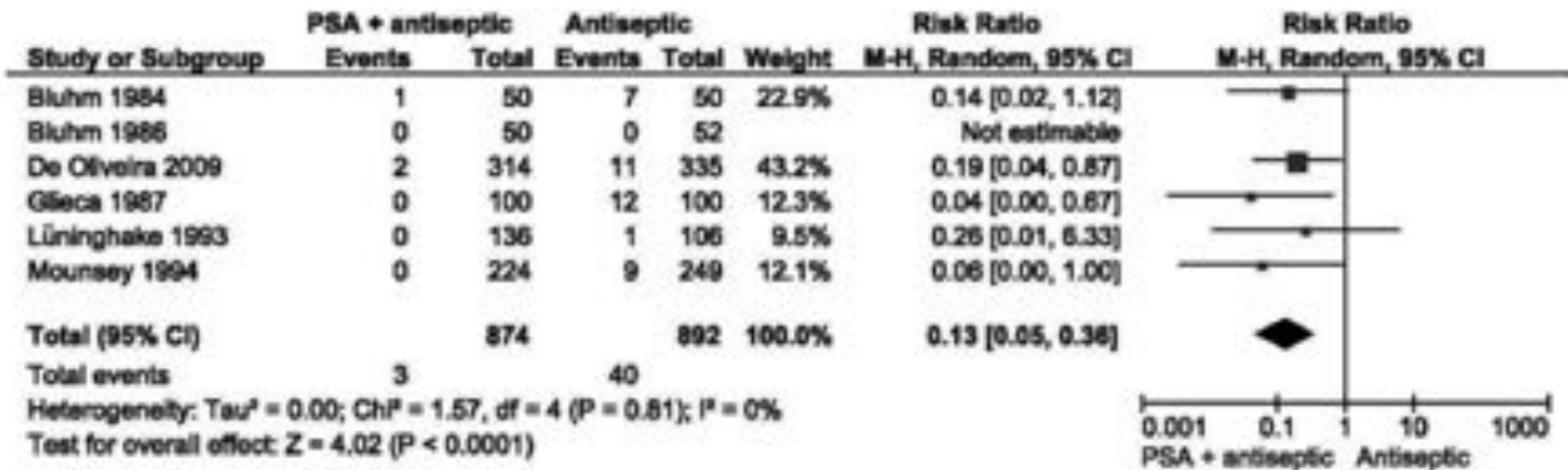
CIED = cardiac implantable electronic device; OR = odds ratio, followed by 95% confidence interval.

Cost Analysis of Antibacterial Envelope

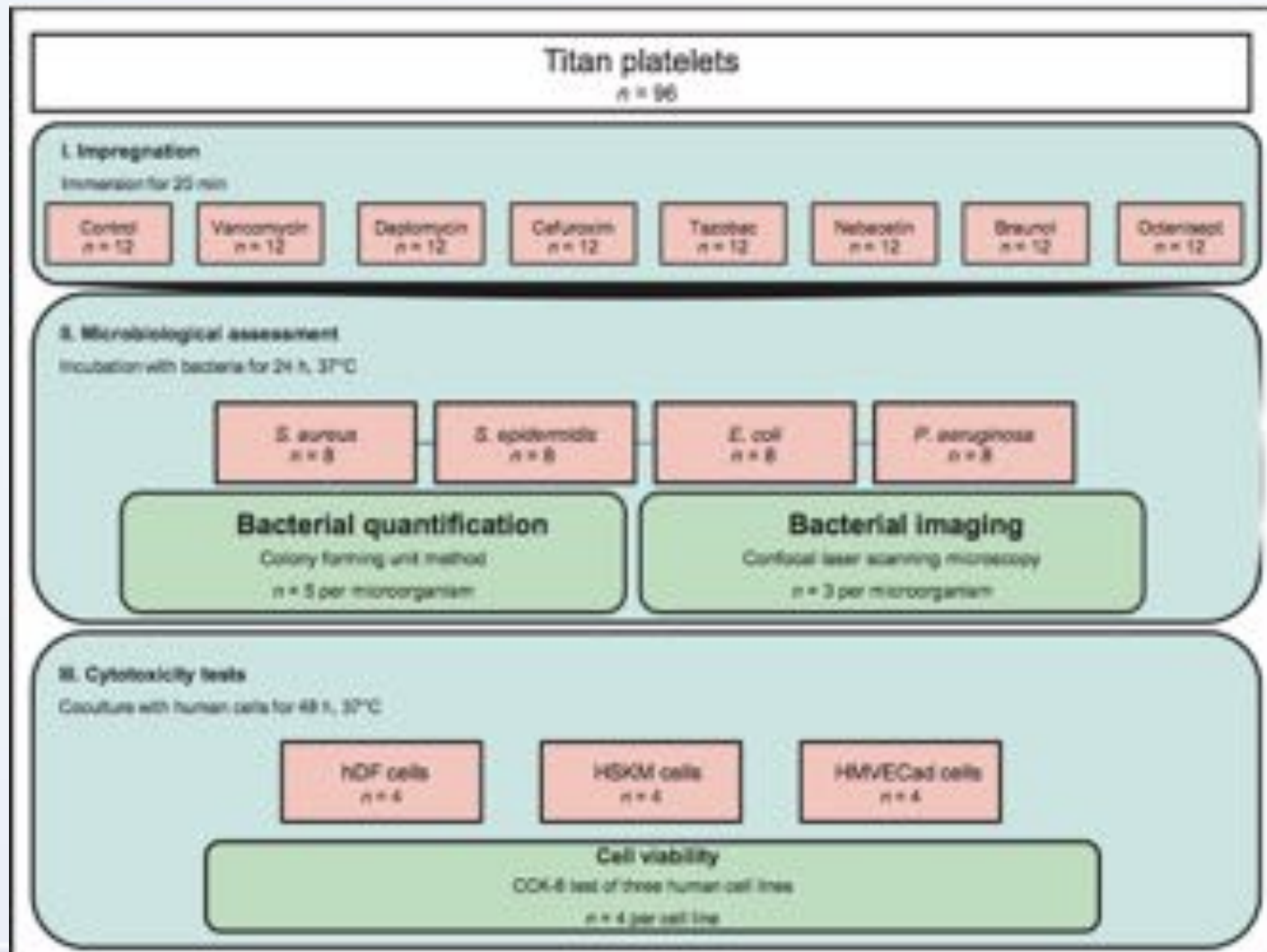
	N	Infection Rate (N)	Infection care cost	Differential cost*
All Patients	365	1.71% (6.20)	\$342,854	\$23,863
Preoperative risk score <3	179	1.03% (1.85)	\$101,708	- \$54,729
Preoperative risk score ≥3	186	2.45% (4.55)	\$250,115	\$87,560
Early Reintervention	12	6.67% (0.80)	\$43,941	\$33,453

Infection Rate	Infections	Infection care cost	Differential cost*
0.56%	2.03	\$111,346	- \$205,023
1.59%	5.76	\$316,371	\$2
1.93%	7.00	\$384,481	\$68,112
4.3%	15.57	\$854,976	\$538,607

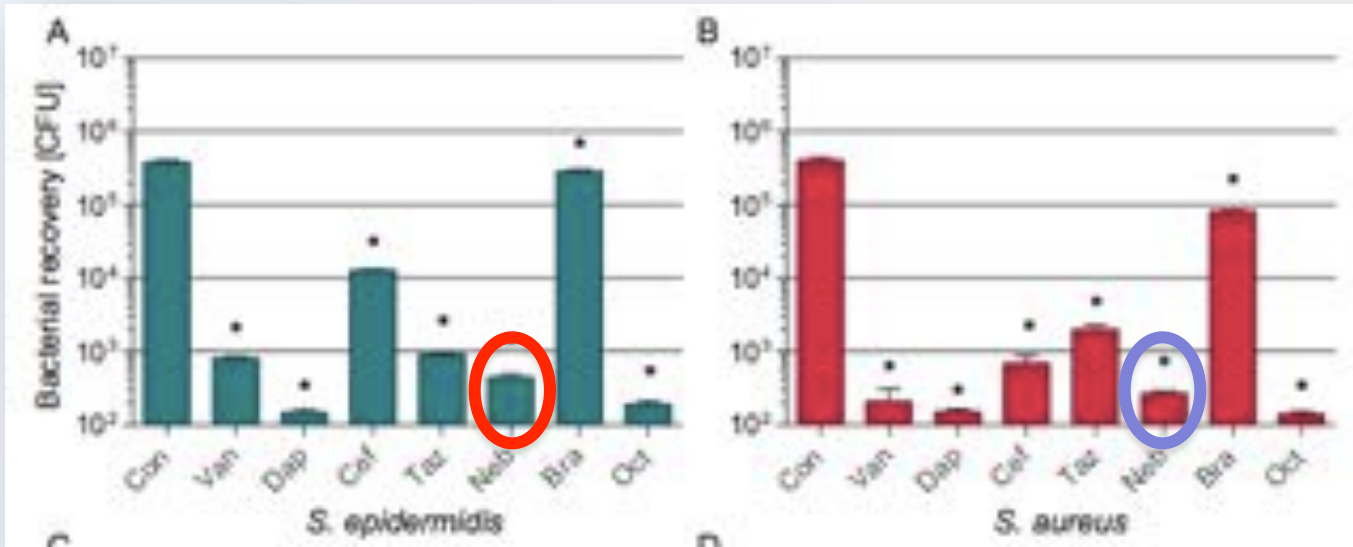
ATB – Antiseptics – Local ATB



Antimicrobial Pretreatment of CIEDs

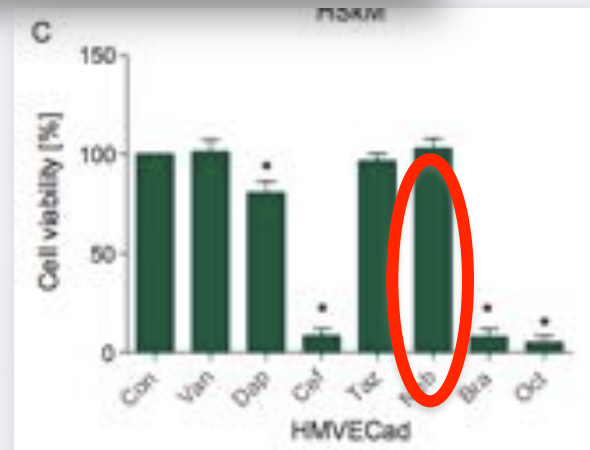


Antimicrobial Pretreatment of CIED



Impact of bacterial pretreatment of pacemaker castings on bacterial adherence.

Proliferation of microvascular endothelial cells in the presence of antimicrobially treated castings



Nebacetin appears to be safe and effective candidate for CIED impregnation

Marsch G, et al. Europace (2014) 16, 604–611

Conclusions

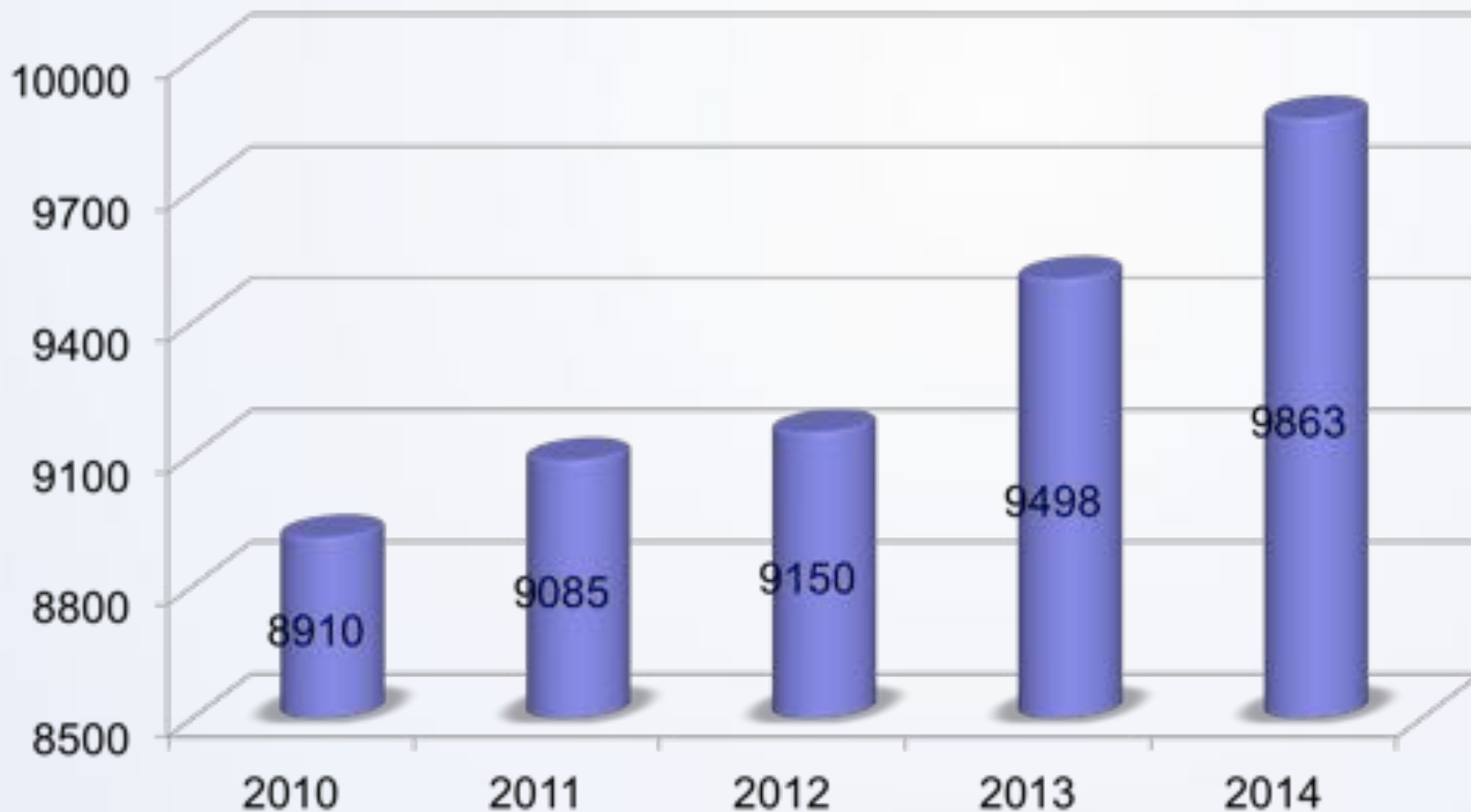
- Number of CIEDs are increasing
- CIED infections complicate patient care
- Cure of infection may be difficult to achieve without device removal
- Prevention focuses on implant technique, sterile environment, ATB prophylaxis and adequate volume

- Future developments should be directed toward:
 - devices more resistant to infection
 - antimicrobial envelopes
 - antimicrobial agents with enhanced activity
 - staphylococcal vaccines

Thank you very much for your attention...



Czech Pacemaker Registry – (2010- 2014)



Czech ICD Registry – (1984 – 2014)

