

# PLACE

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

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## EPIDEMIOLOGIA DELLE INFEZIONI DEI DISPOSITIVI ELETTRONICI CARDIACI IMPIANTABILI (CIED)

**Alessandro Proclemer**

**Chairman Registro Italiano Pacemaker e Defibrillatori (RIP&RID AIAC)  
Fondazione IRCAB-Udine**



# Background-1

## ***Definition of CIED infection:***

CIED related systemic infection/endocarditis or local pocket infection/skin erosion.

## ***Patient selection and inclusion criteria:***

- 1) *Principal or Secondary Diagnosis* indicating CIED infection (ICD-9-CM code 966.6 or 966.61) or infective endocarditis (421.0-.1-.9).
- 2) *Procedural code* for pacemaker or ICD/CRT removal (3789, 3794-98,051-2) or lead removal (3777), as well as codes for sepsis (038, 785.82) or bacteriemia (790.7).
- 3) *Data* from National or local Pacemaker and ICD Registries



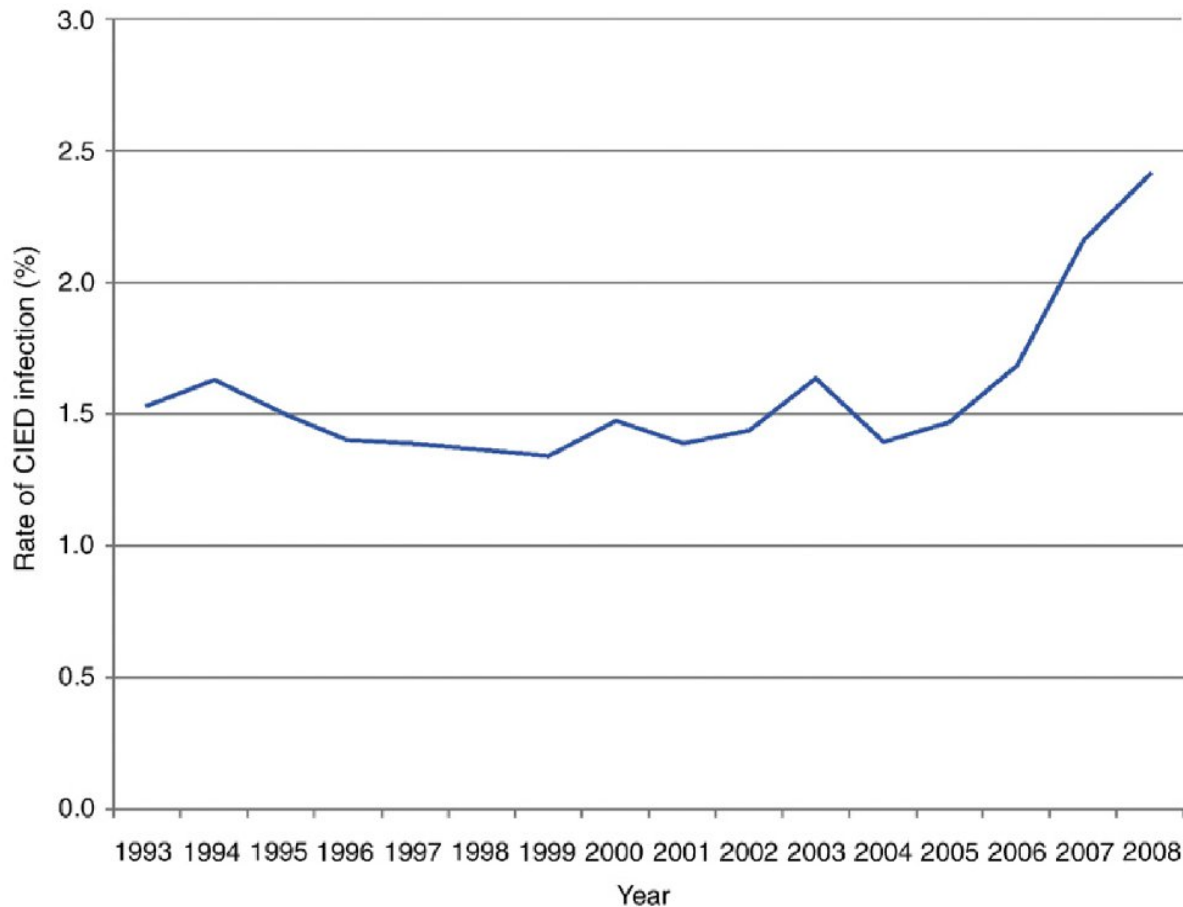
## Background-2

### ***Risk of underreporting PM/ICD infection rate :***

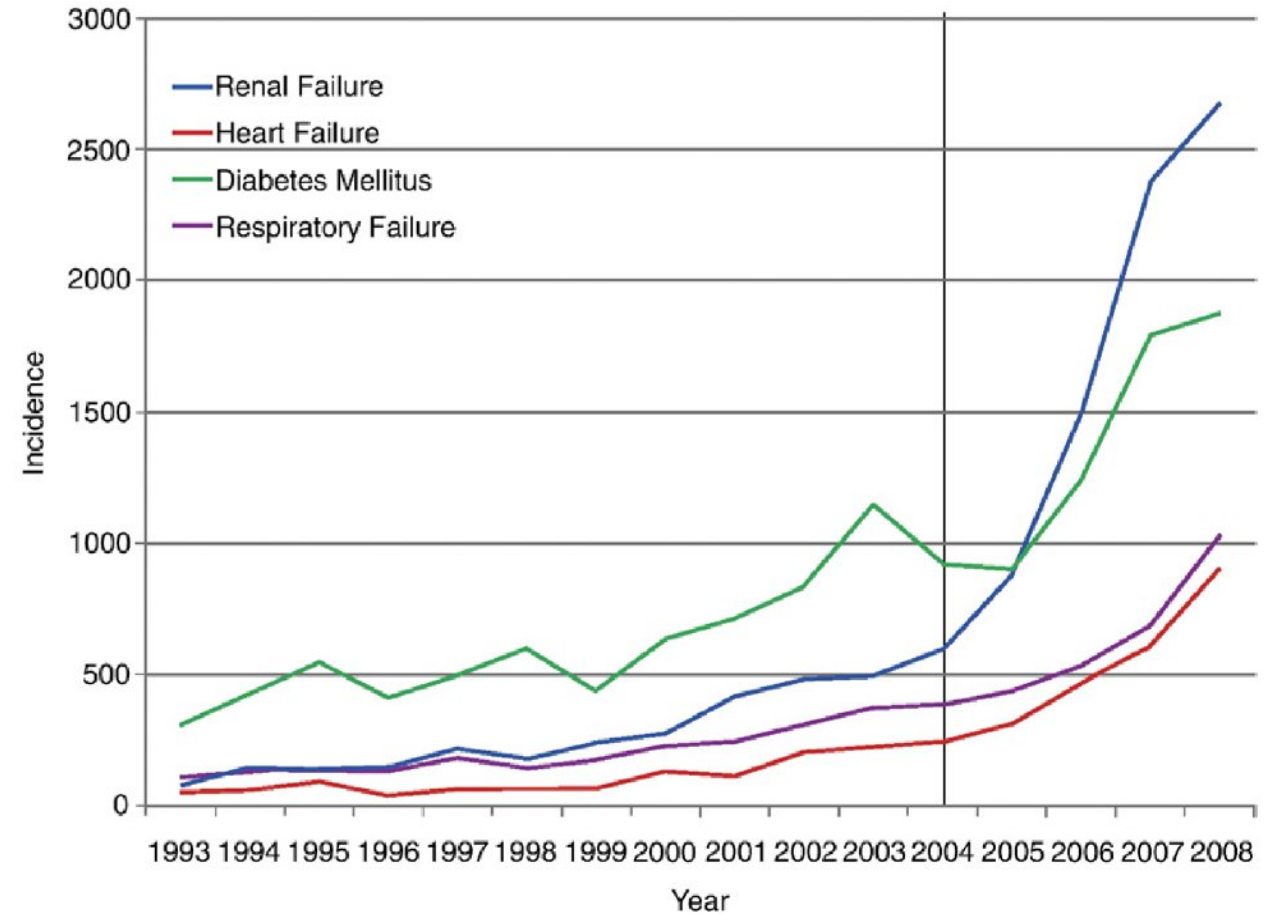
- 1) Device-related infections are usually counted only for patients who had their PM/ICDs removed and eventually replaced due to infection.
- 2) Large scale device registries include the possibility of undercoding the principal or secondary diagnosis indicating CIED infection.
- 3) Missing data

# 16-Year Trends (1993 to 2008) in the Infection Burden for Pacemakers and ICDs in the US

## Rate of CIED Infection

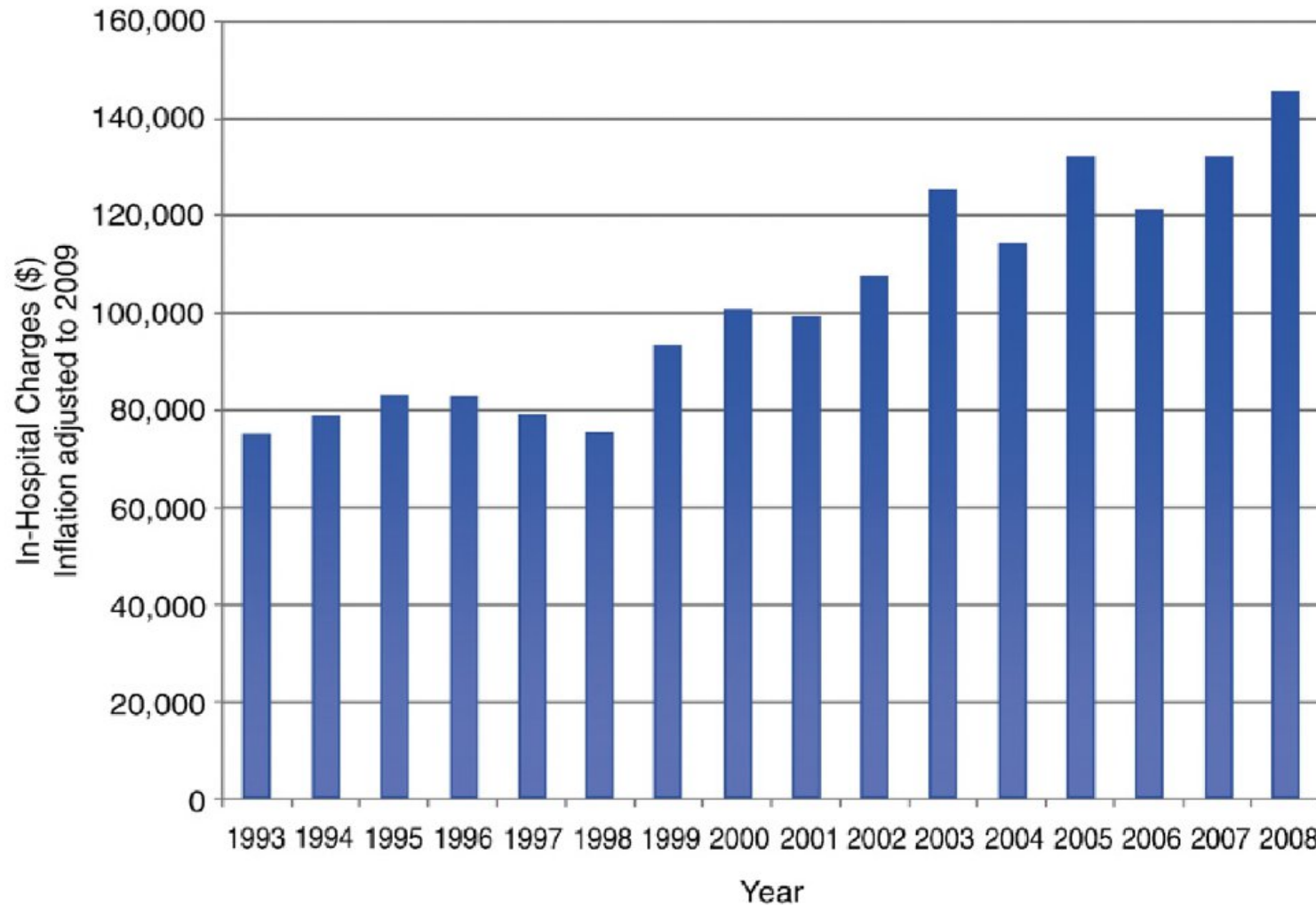


## Incidence of Comorbidities in Pts With CIED Infection



# 16-Year Trends (1993 to 2008) in the Infection Burden for Pacemakers and ICDs in the US

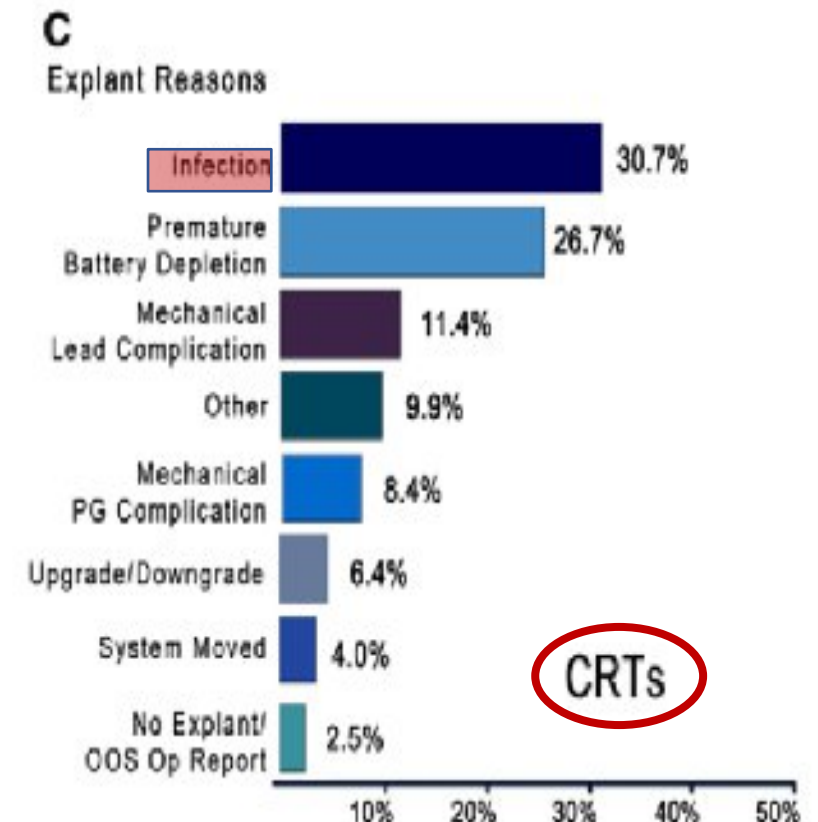
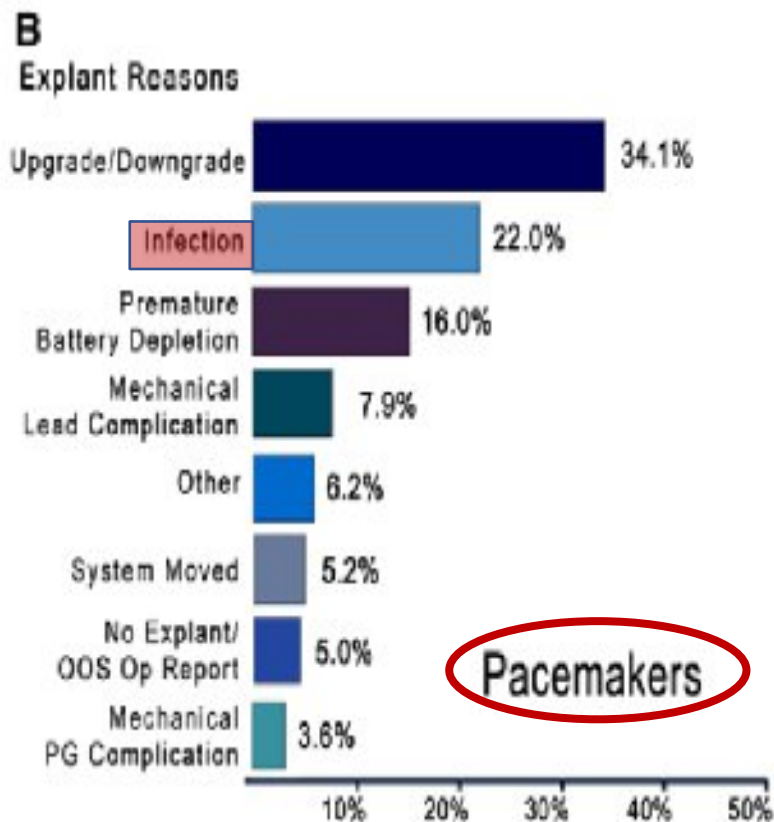
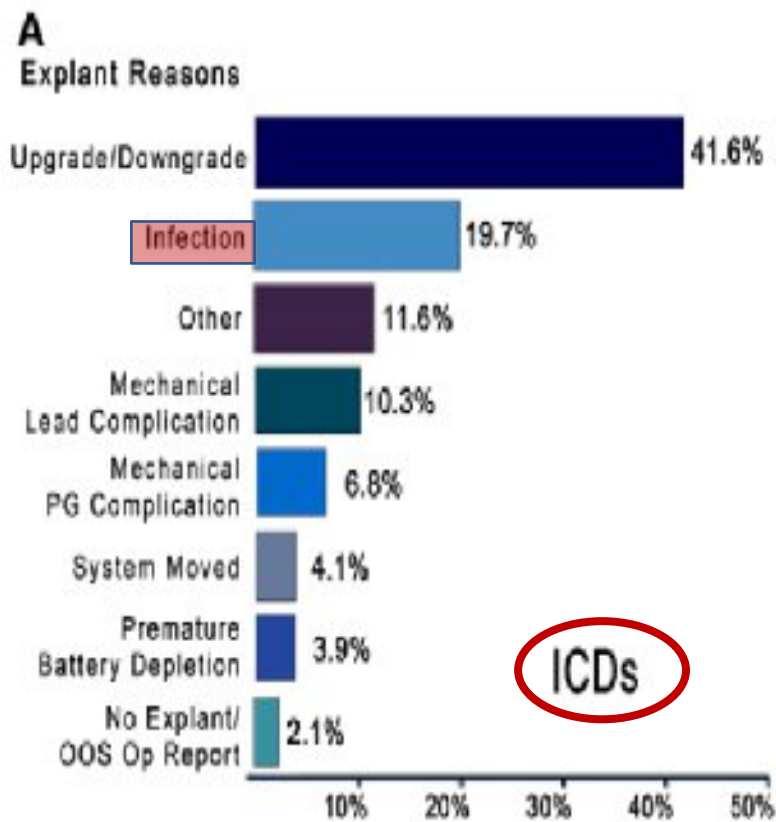
## In-Hospital Charges Associated With CIED Infection



# Multi-Center, Community-Based Cardiac Implantable Electronic Devices Registry: Population, Device Utilization, and Outcomes

. Kaiser US system survey (2007-13) : 11 924 ICDs, 33 519 PMs, 4472 CRTs

***Reasons for early device revision, explantation, or replacement (2007-2013):***

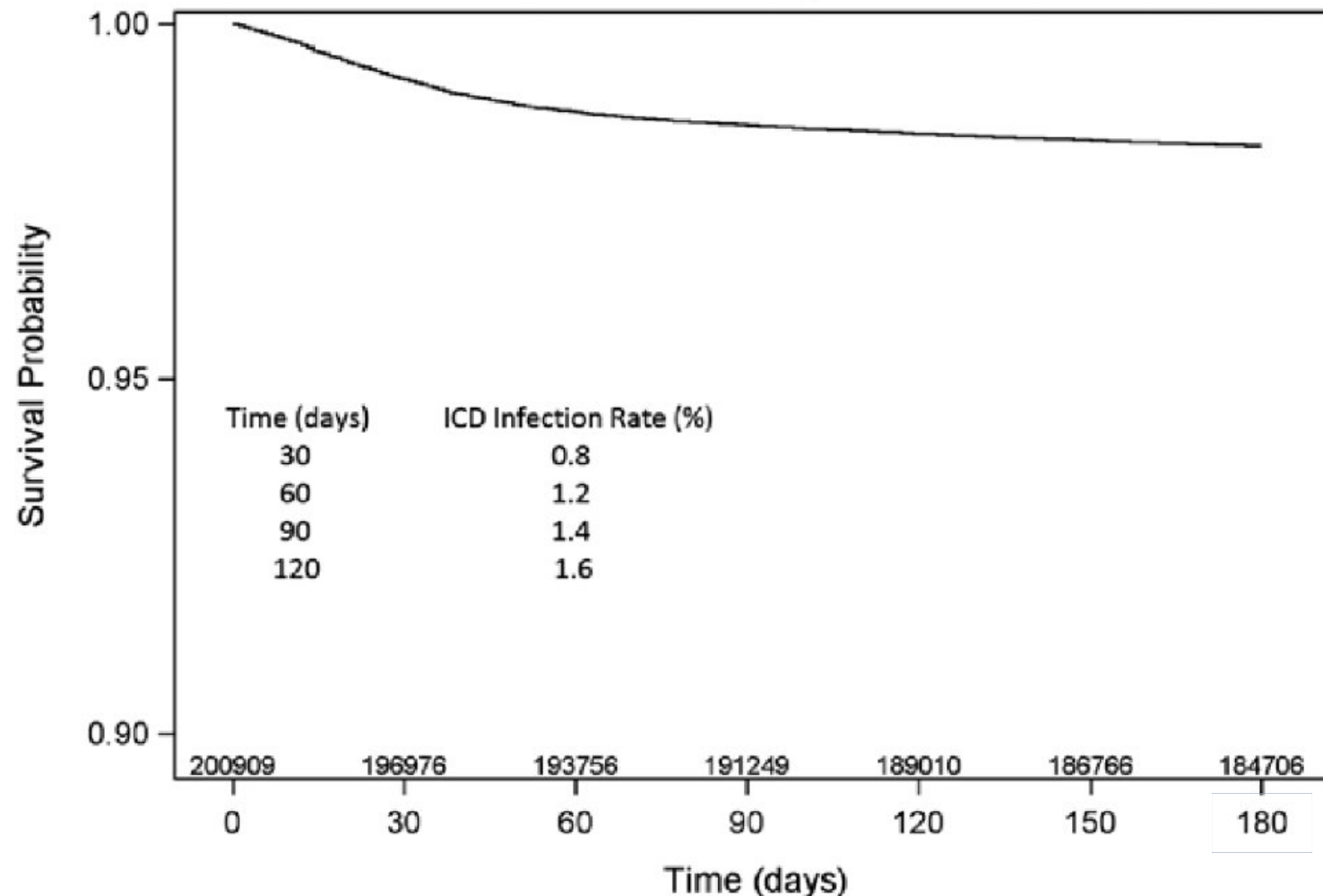




# Rates of and Factors Associated With Infection in 2009 Medicare Implantable Cardioverter-Defibrillator Implants

Results From the National Cardiovascular Data Registry

Kaplan-Meier Curve of ICD Infection  
with Number of Subjects at Risk



- The **6 month infection rate** was 1.4%, 1.5%, and 2.0% for single, dual, and biventricular ICDs, respectively ( $P < 0.001$ ).
- **ICD replacement** had a higher infection rate compared with initial implant (1.9% versus 1.6%,  $P < 0.001$ ).

# Rates of and Factors Associated With Infection in 200 909 Medicare Implantable Cardioverter-Defibrillator Implants

## Results From the National Cardiovascular Data Registry

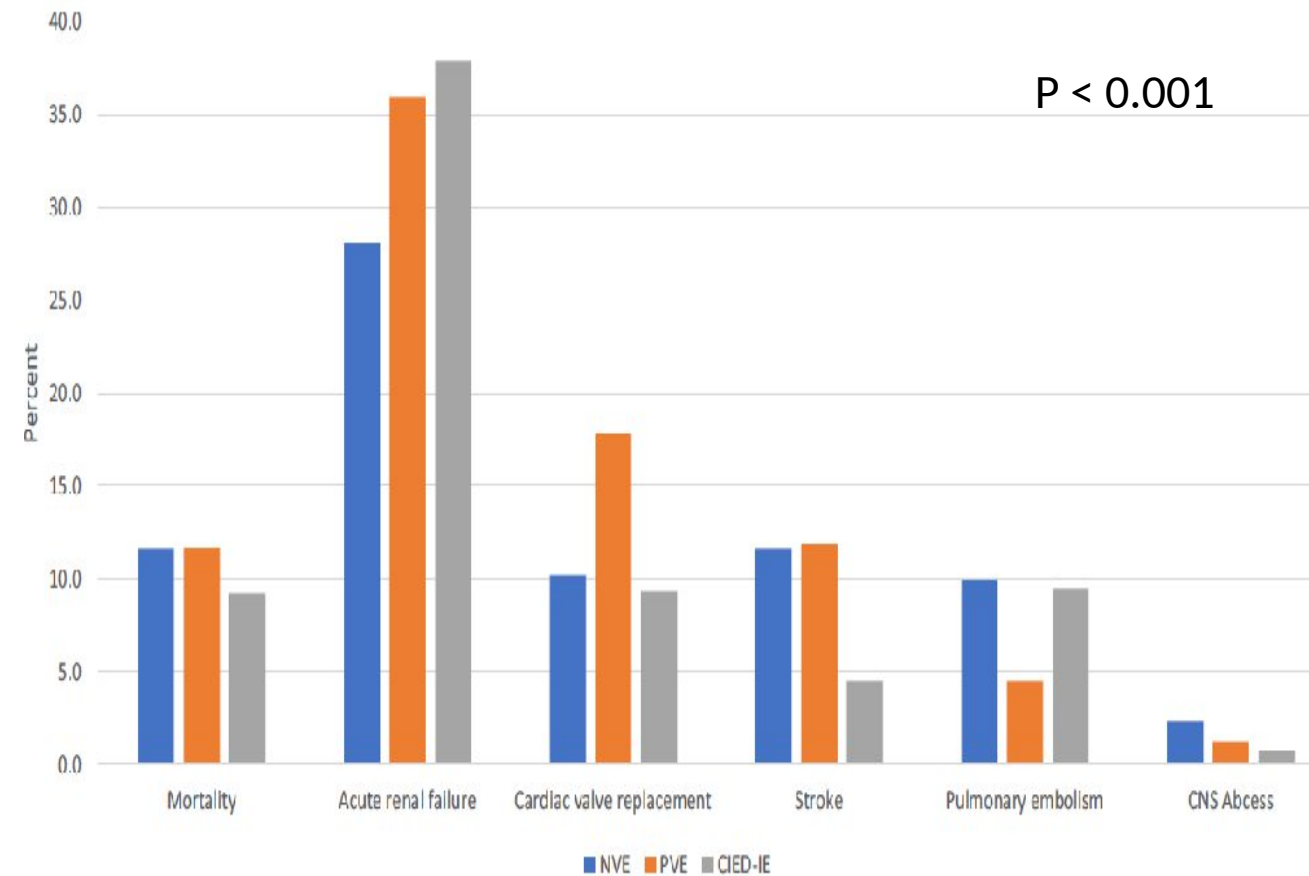
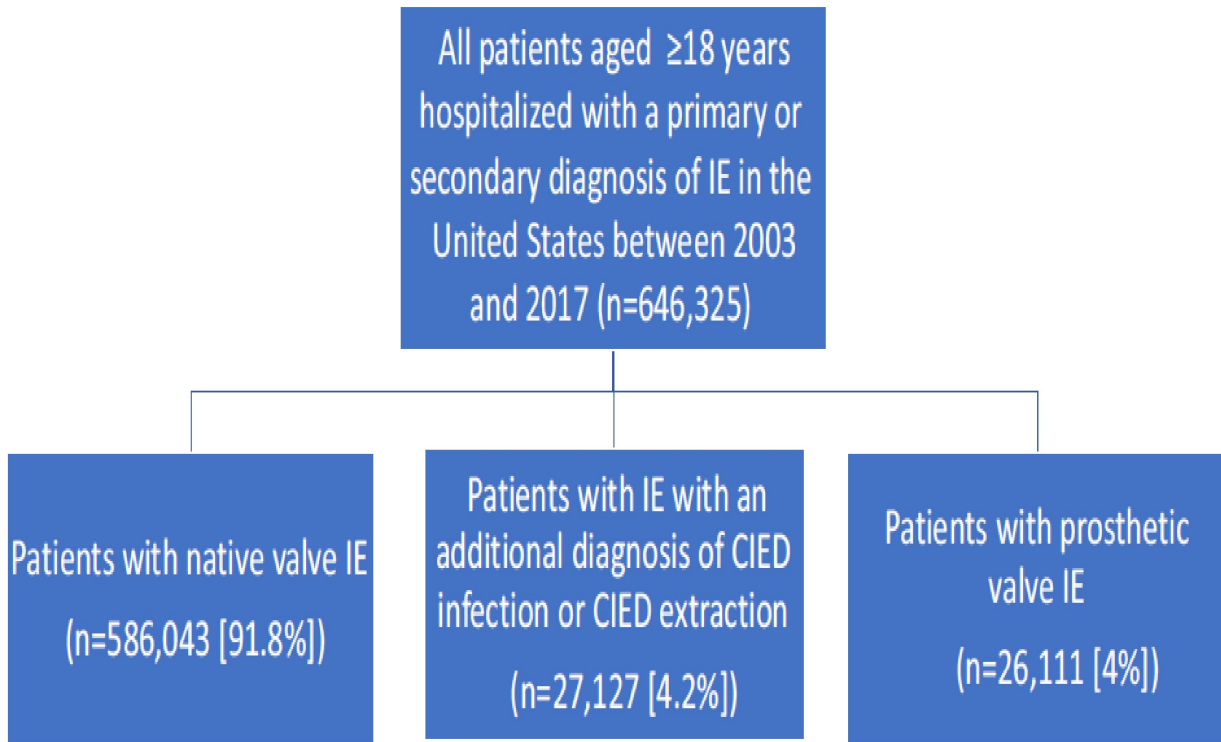
**Table 3. Multivariable Predictors of ICD Infection**

Effect	OR (95% CI)	P Value
<b>Clinical characteristics</b>		
Previous valvular surgery	1.525 (1.375–1.692)	<0.0001
Cerebrovascular disease	1.172 (1.076–1.276)	.0003
Chronic lung disease	1.215 (1.125–1.312)	<0.0001
Renal failure-dialysis	1.342 (1.123–1.604)	.0012
<b>Procedure factors</b>		
Reimplantation		
No	Reference	
Yes-device upgrade, malfunction, manufacturer advisory	1.354 (1.196–1.533)	<0.0001
Yes-battery change	1.090 (0.992–1.198)	
Adverse events	2.692 (2.304–3.145)	<0.0001
<b>Medications</b>		
Warfarin	1.155 (1.060–1.257)	0.001



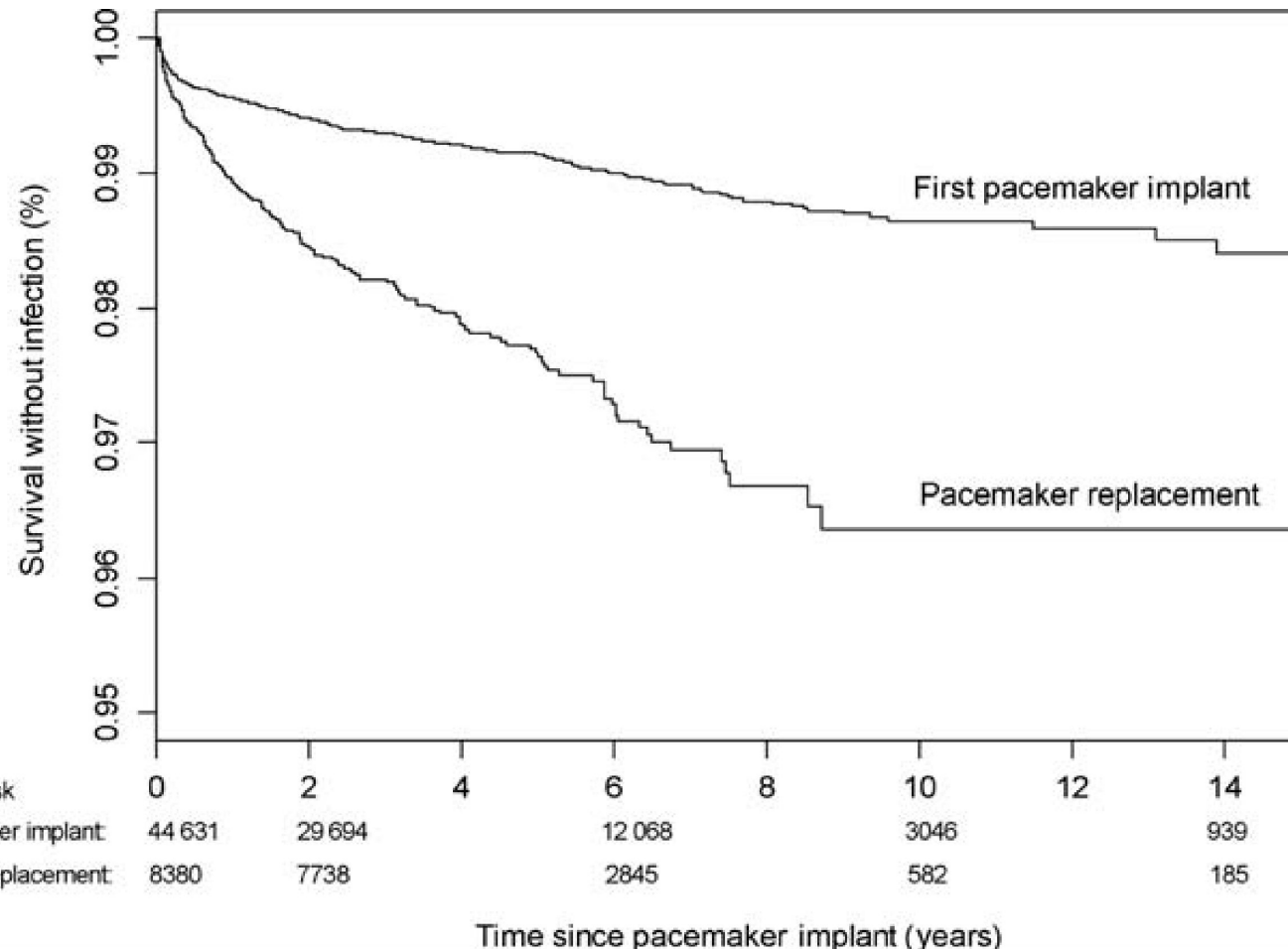
# 16-Year Outcomes of pts Hospitalized With CIED–Related Infective Endocarditis, Prosthetic Valve Endocarditis (PVE), and Native Valve Endocarditis (NVE): A Nationwide Study, 2003 to 2017

**Study population** **Outcomes of patients hospitalized**



# Infection after pacemaker implantation: infection rates and risk factors in a cohort study of 46299 consecutive patients

## Time to infection after first PM implantation



**Time to infection more than 365 days:**

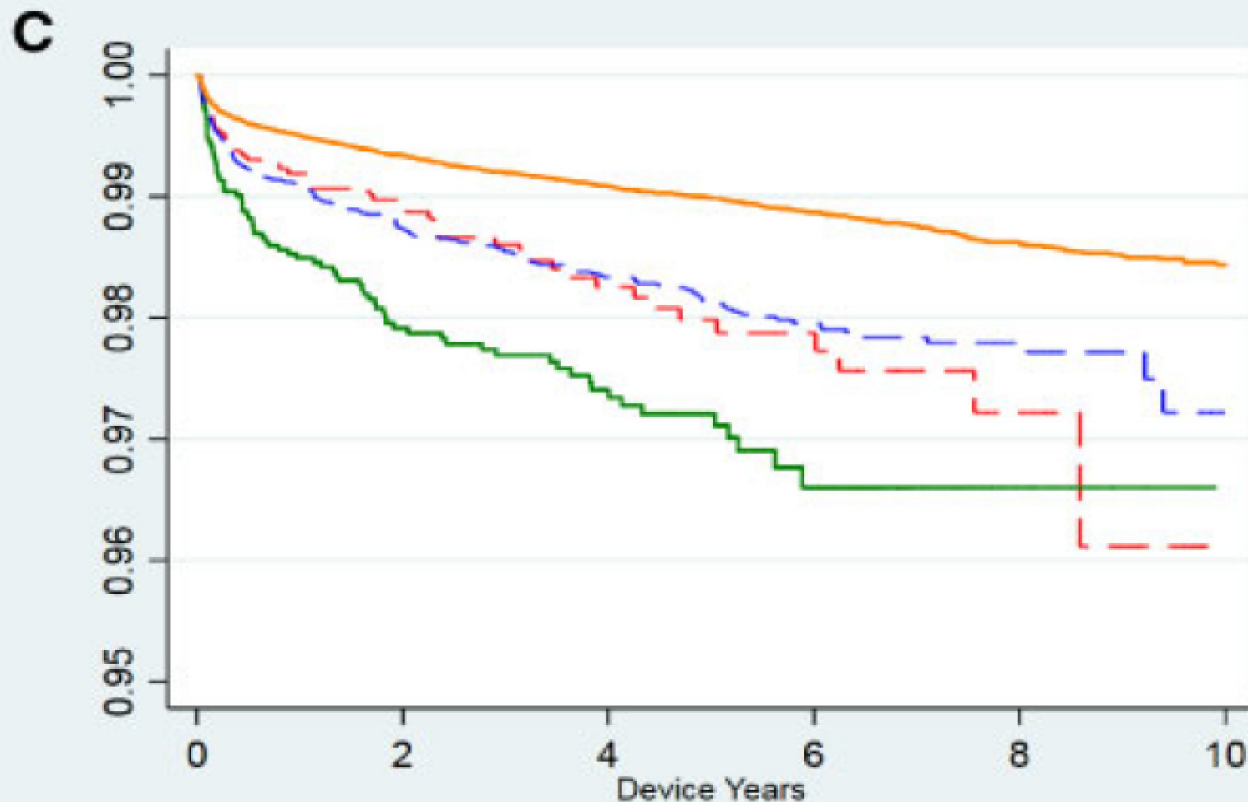
- 1.02/1000 PM-years after the first implantation
- 3.26/1000 PM-years after replacement

**Increased risk of PM infection:**

- a greater number of PM operations (including replacements),
- male sex, younger age,
- implantation during the earliest part of the study and absence of antibiotics

# Incidence of device-related infection in 97 750 patients: clinical data from the complete Danish device-cohort (1982–2018)

## Time to infection after de novo implant



PM: 1.19%

ICD: 1.91%

CRT-PM: 2.04%

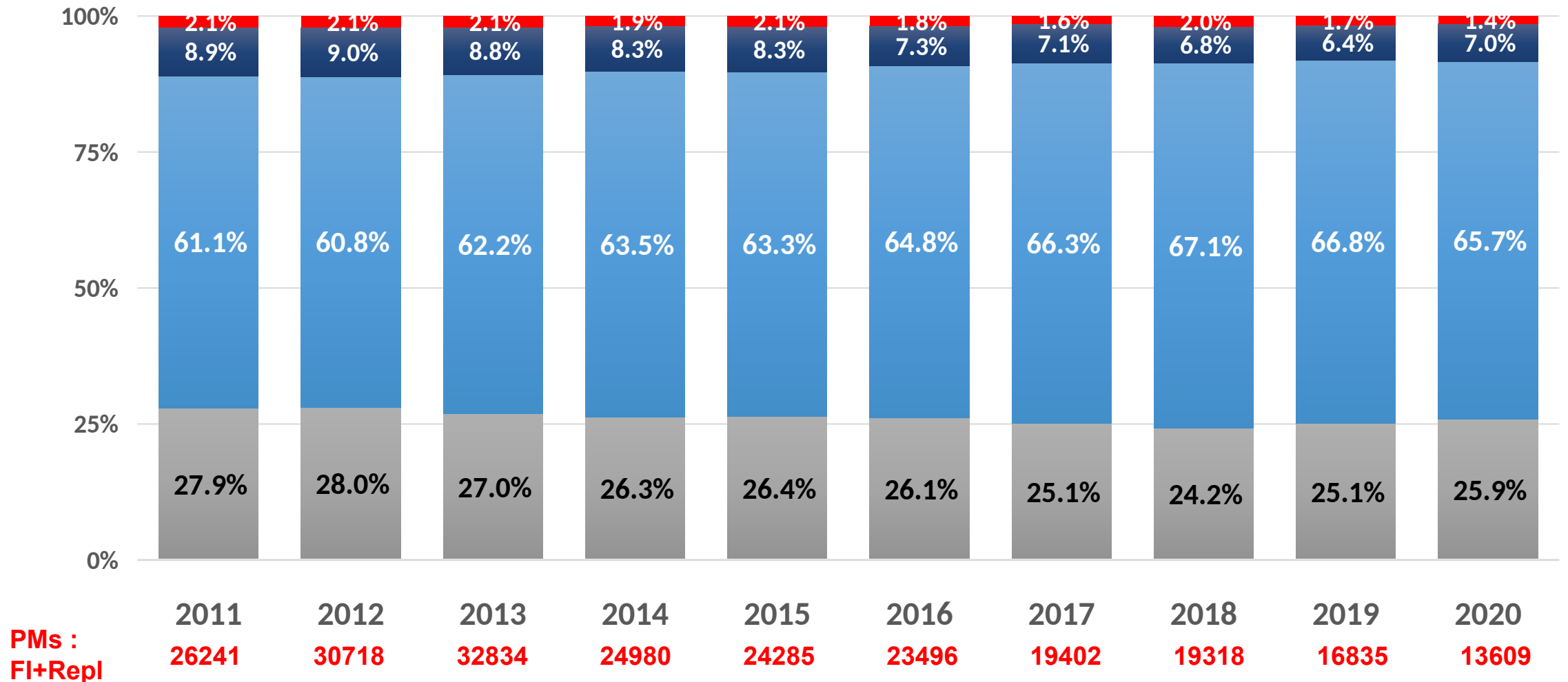
CRT-ICD: 4.38%

### DEVICE RELATED INFECTION RISK:

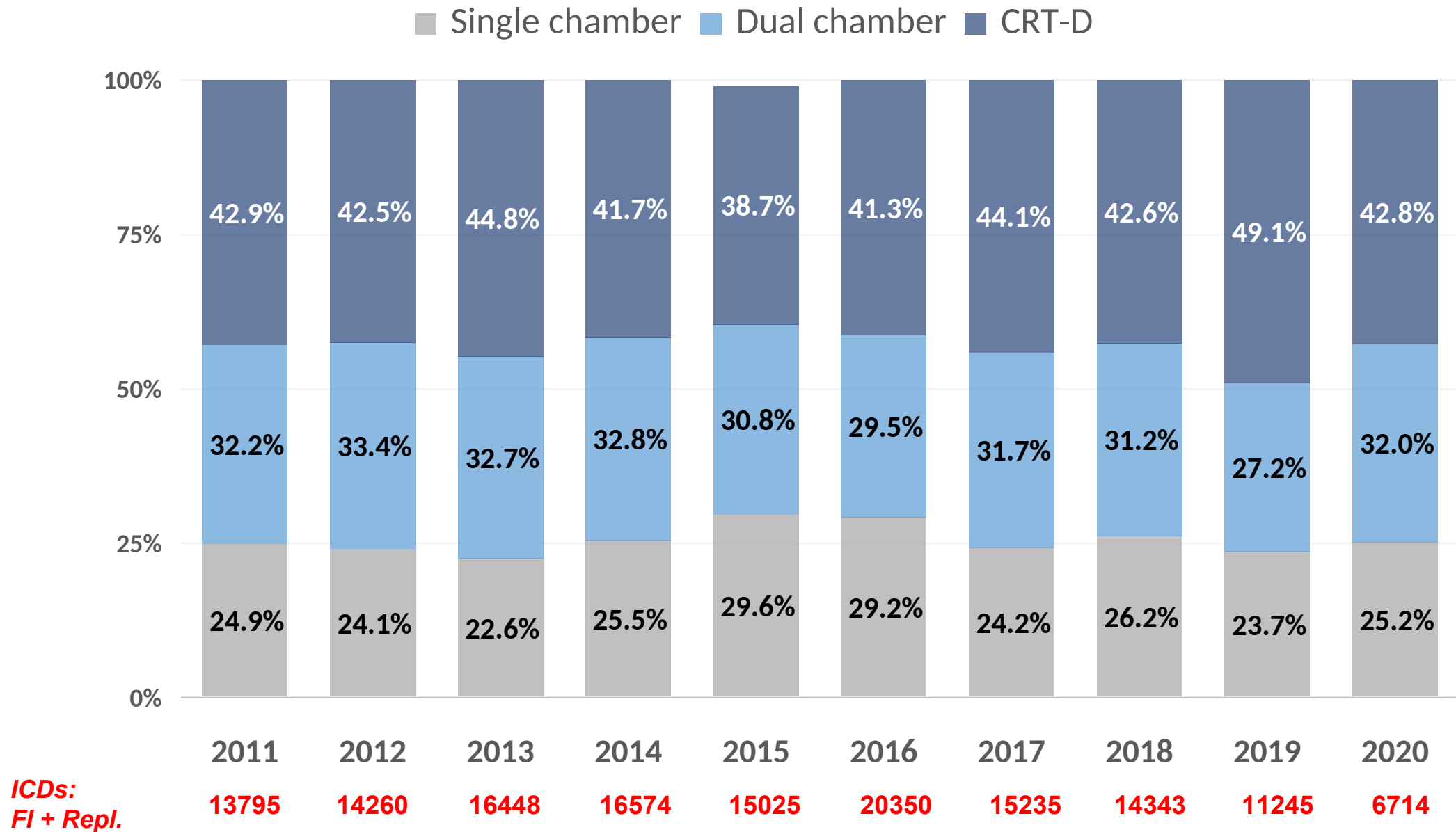
- . Implantation of complex devices (CRT-D)
- . Reoperations, prior DRI
- . Male sex, and younger age

# Pacemaker types in Italy (2011-2020)

■ AAI/VVI-R ■ DDD-R ■ VDD-R ■ CRT-P

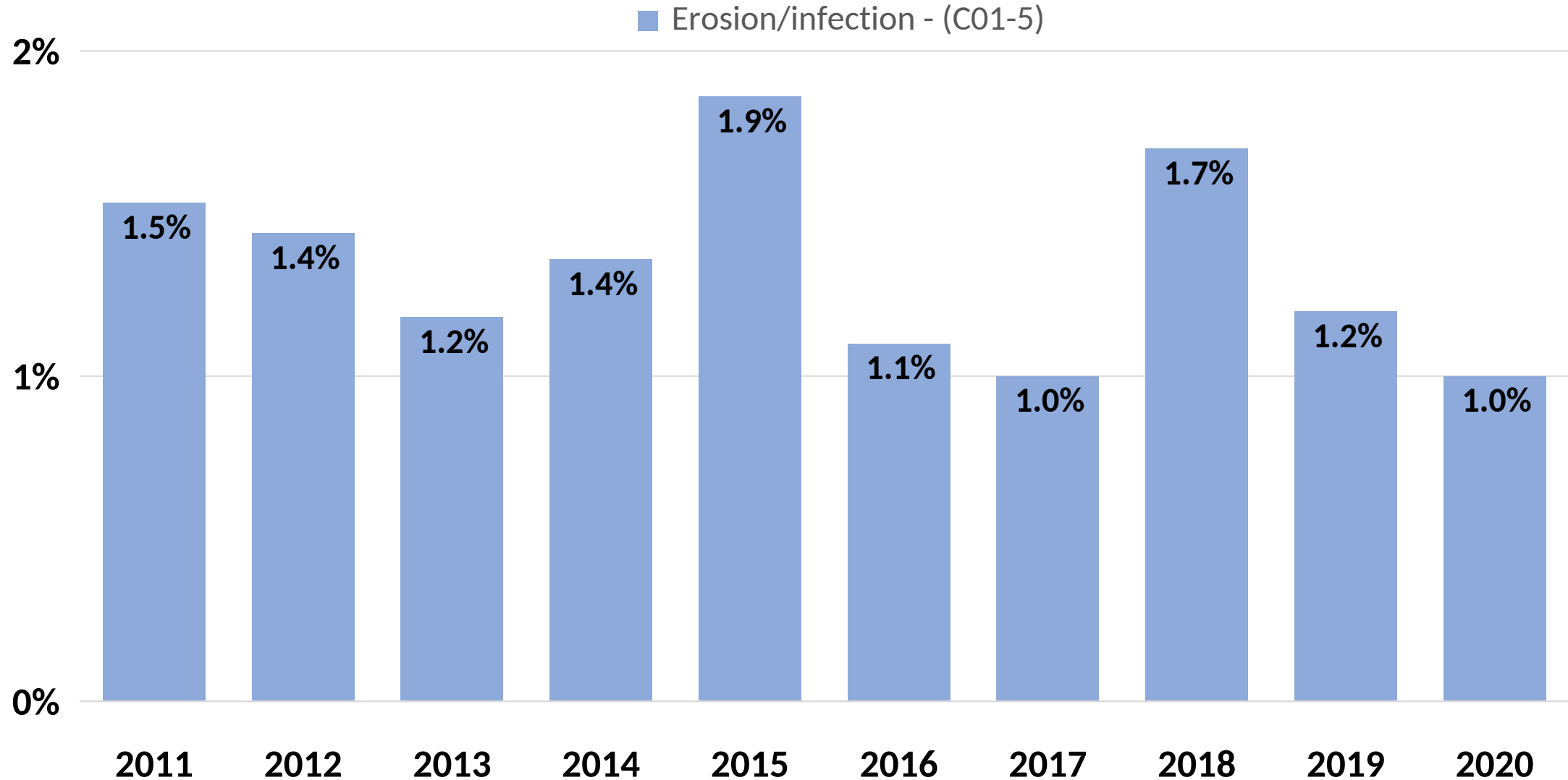


# ICD types in Italy (2011-2020)



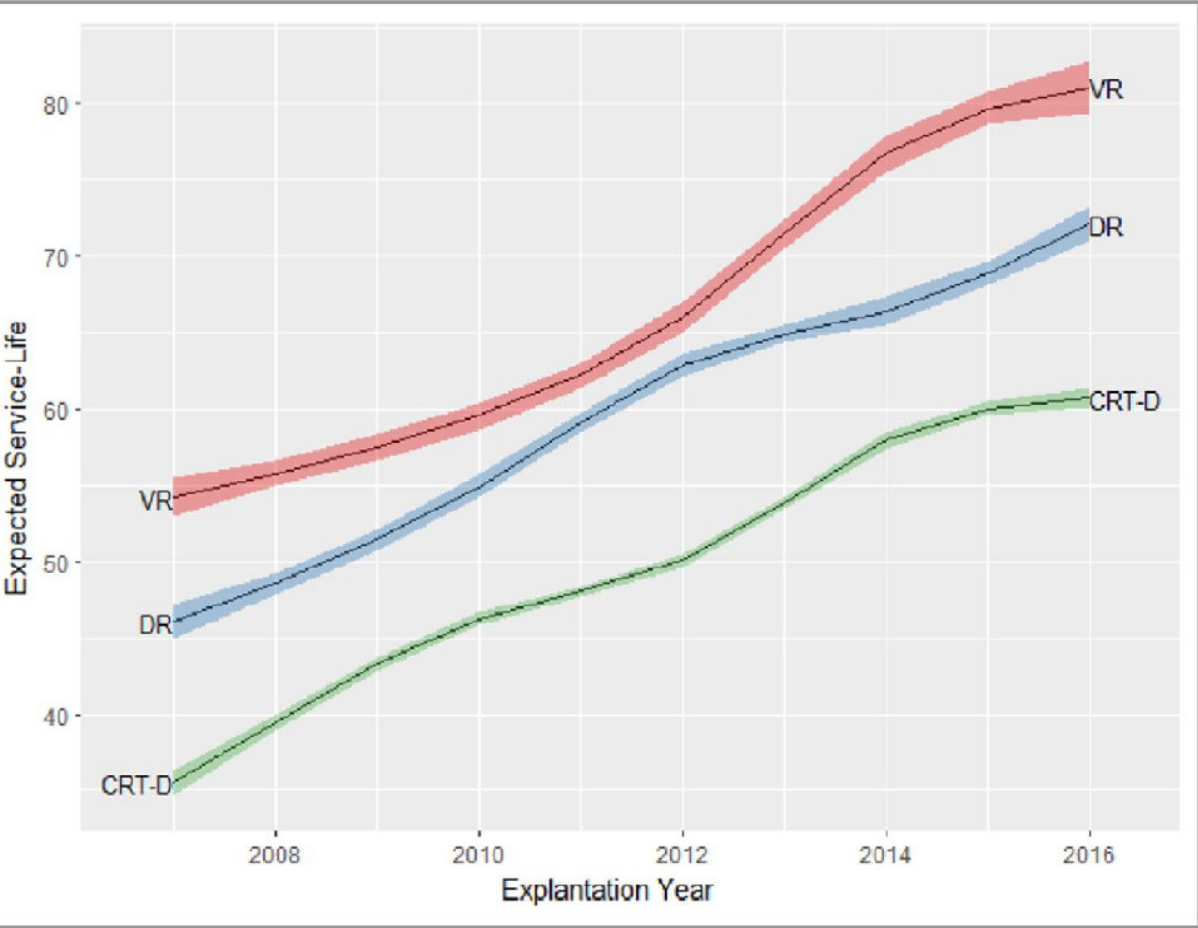


# PM replacement rate for infection (2011-2020)



# Favorable Trend of Implantable Cardioverter-Defibrillator Service Life in a Large Single-Nation Population: Insights From 10-Year Analysis of the Italian Implantable Cardioverter-Defibrillator Registry

Stefano Poli, MD; Giuseppe Boriani, MD; Massimo Zecchin, MD; Domenico Facchin, MD; Maurizio Gasparini, MD; Maurizio Landolina, MD; Renato Pietro Ricci, MD; Corrado Lanera, PhD; Dario Gregori, PhD; Alessandro Proclemer, MD



	Primary Prevention	Secondary Prevention	Combined
ICD-VR	3797 (20.2)	3278 (31.7)	7075 (24.3)
ICD-DR	4733 (25.1)	3478 (33.6)	8211 (28.2)
CRT-D	10 284 (54.7)	3588 (34.7)	13 872 (47.5)
Combined	18 814 (100)	10 344 (100)	29 158 (100)

Figure 3. Model fitted by implantable cardioverter-defibrillator (ICD) type: trend of the expected service

# Favorable Trend of Implantable Cardioverter-Defibrillator Service Life in a Large Single-Nation Population: Insights From 10-Year Analysis of the Italian Implantable Cardioverter-Defibrillator Registry

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**Table 3.** Causes of Replacement According to Device Characteristics and Indication to Implantation

	Primary Prevention			Secondary Prevention			Combined
	ICD-VR	ICD-DR	CRT-D	ICD-VR	ICD-DR	CRT-D	
Battery end of life	2650 (69.8)	3502 (74.0)	9470 (92.1)	2297 (70.1)	2602 (74.8)	3302 (92.0)	23 823 (81.7)
Recall/system malfunction	35 (0.9)	59 (1.2)	120 (1.2)	53 (1.6)	51 (1.5)	36 (1.0)	354 (1.2)
CRT upgrading	781 (20.6)	824 (17.4)	0 (0.0)	702 (21.4)	565 (16.2)	0 (0.0)	2872 (9.8)
Infection/erosion	46 (1.2)	80 (1.7)	182 (1.8)	38 (1.2)	66 (1.9)	73 (2.0)	485 (1.6)
Not available	285 (7.5)	268 (5.7)	512 (5.0)	188 (5.7)	194 (5.6)	177 (4.9)	1624 (5.6)



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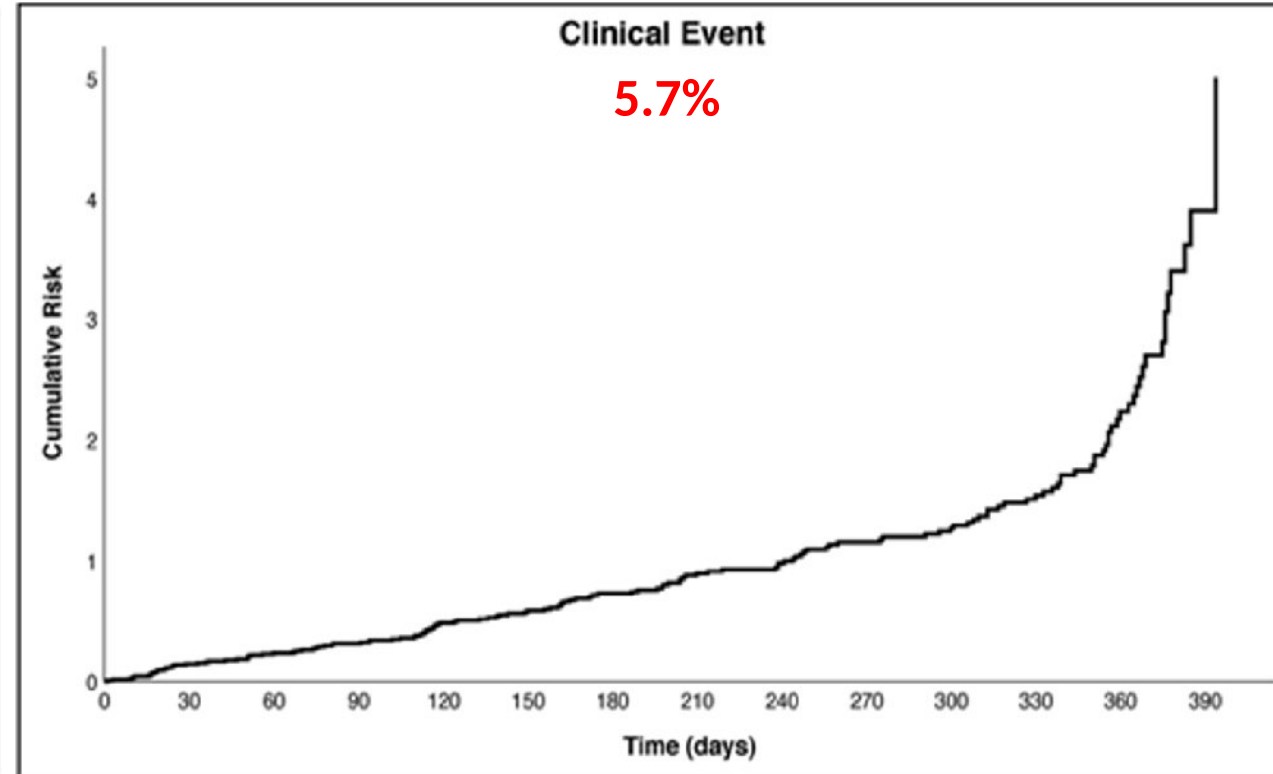
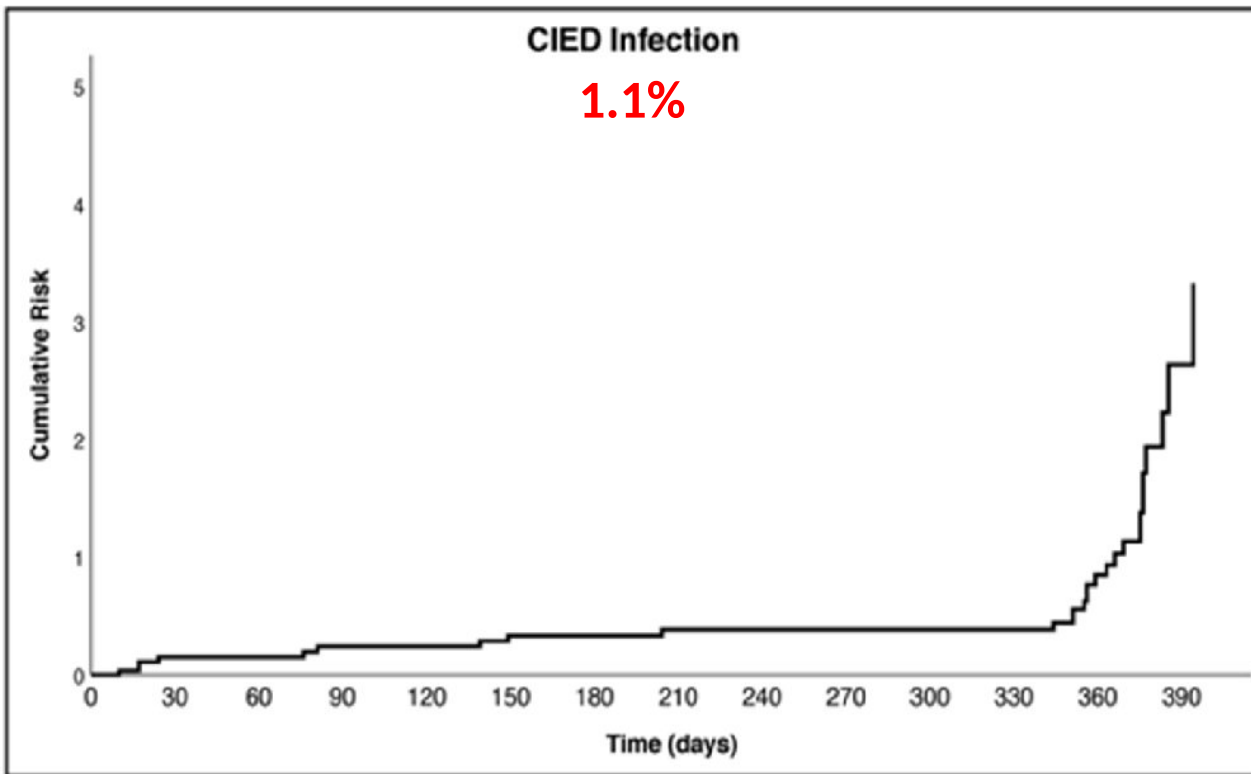
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**Table 4.** Causes of Replacement Before and From Calendar Year 2012

	Explantation Before Calendar Year 2012	Explantation From Calendar Year 2012
Battery end of life	9424 (72.4)	13 602 (84.2)
CRT upgrading	2141 (16.5)	1528 (9.5)
Infection/erosion	288 (2.2)	197 (1.2)
Recall/system malfunction	163 (1.3)	191 (1.2)
Not available	997 (7.7)	627 (3.9)

# Incidence and Predictors of Infections and All-Cause Death in Patients with CIED: The Italian Nationwide RI-AIAC Registry

- 18 centres enrolled 2675 consecutive patients undergoing a CIED procedure and entered a 12-months FU
- 1785 (66.7%) patients received a PM, 450 (16.8%) an ICD, 106 (4.0%) a CRT-P and 329 (12.3) a CRT-D.



**Multivariate analysis:** 1) the type of procedure (revision/upgrading/reimplantation) (OR: 4.08, 95% CI: 1.38–12.08) and 2) diabetes (OR: 2.22, 95% CI: 1.02–4.84) were the main factors associated to CIED infection



Comparison of outcomes in infected CIED between complete, partial, and failed lead removal:  
an ESC-EHRA-EORP ELECTRa (European Lead Extraction ConTrolled) registry

**Table 3** Infection characteristics

Variables	Class	Statistic	Total (N = 1863)	Complete lead removal (N = 1743)
Time from first symptoms of infection to removal (days)		Median (IQR)	42.00 (18.00–105.00)	41.00 (18.00–103.00)
Local CIED infections		n/N (%)	1169/1863 (62.75%)	1095/1743 (62.82%)
Systemic CIED infections		n/N (%)	679/1863 (36.45%)	635/1743 (36.43%)

**Table 6** Predictors for failed lead removal: multivariate analysis on lead level

Covariables	Reference level	Class level	Odds ratio (95% CI)	P-value
Gender	Male	Female	1.14 (0.49–2.62)	0.7649
Age (class)	≥65 years	<65 years	2.68 (1.22 5.91)	0.0146
Diabetes mellitus	No	Yes	1.38 (0.57–3.31)	0.8961
Chronic kidney disease	No	Yes	1.37 (0.54–3.48)	0.054
Systemic infections	No	Yes	1.43 (0.68–3.01)	0.349

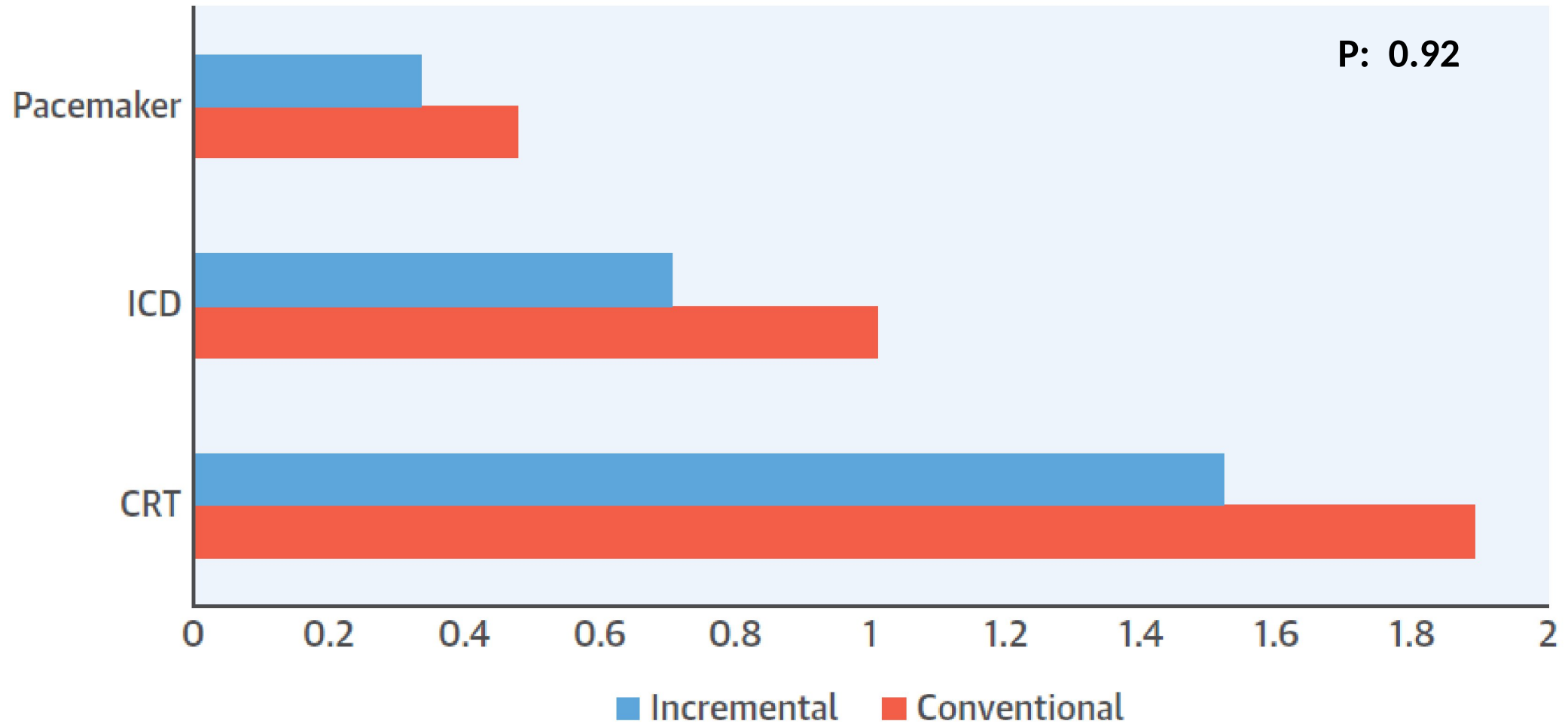


# Final comments

- 1) The CIED infection rates reported in the recent prospective studies appear low and related to more complex procedures and devices.
- 2) The clinical risk and the costs of CIED infection are still high especially in some subgroups of patients.
- 3) Large scale and national prospective CIED registries are mandatory in order to have benchmark data and to monitor the local and regional activity.
- 4) Standardized prophylaxis and procedures are essential to limit the risk of

# Prevention of Arrhythmia Device Infection Trial: *The PADIT Trial*

Risk of Hospital Admission for CIED Infection at 1 Year (%)



# Incidence and Predictors of Infections and All-Cause Death in Patients with CIED: The Italian Nationwide RI-AIAC Registry

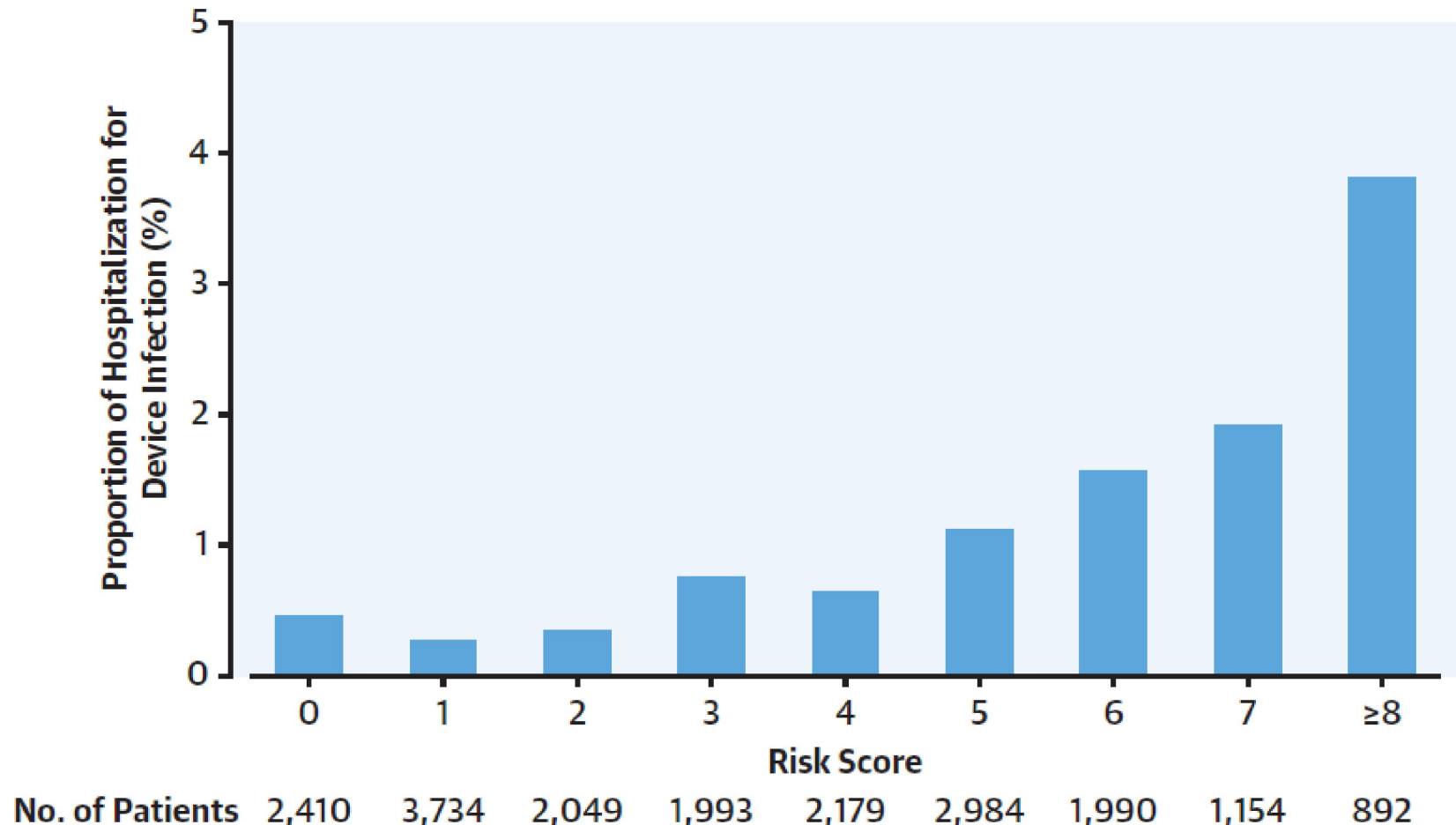
## Logistic regression analysis for clinical events occurrence

	Univariate Analysis		Multivariate Analysis		Score Points
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	
Age Classes					
<65 years (ref.)	-	-	-	-	0
65-74 years	2.32 (1.05–5.17)	0.039	2.07 (0.92–4.65)	0.079	1
≥75 years	4.04 (1.96–8.34)	<0.001	3.10 (1.45–6.64)	0.006	2
CIED					
Pacemaker (ref)	-	-	-	-	
Any Other CIED	0.7 (0.49–1.02)	0.062	0.95 (0.64–1.41)	0.798	
Prolonged Temporary Pacing	3.06 (1.58–5.94)	0.001	2.9 (1.45–5.77)	0.002	1
eGFR <60 mL/min	2.55 (1.83–3.57)	<0.001	2.03 (1.43–2.88)	<0.001	1
Pre-Dialysis/Dialysis	1.62 (1.25–2.11)	<0.001			
Diabetes Mellitus	1.58 (1.09–2.28)	0.015	1.43 (0.98–2.08)	0.063	1
Use of Oral Corticosteroids	2.47 (1.2–5.08)	0.014	2.60 (1.25–5.40)	0.010	1
Hospital-Acquired Infection	3.21 (1.41–7.32)	0.006	3.29 (1.29–8.35)	0.012	1

Score 2: clinical events in 37.3 %

# Risk Factors for Infections Involving Cardiac Implanted Electronic Devices

**CENTRAL ILLUSTRATION** Rate of Device Infection Stratified by PADIT Infection Risk Score

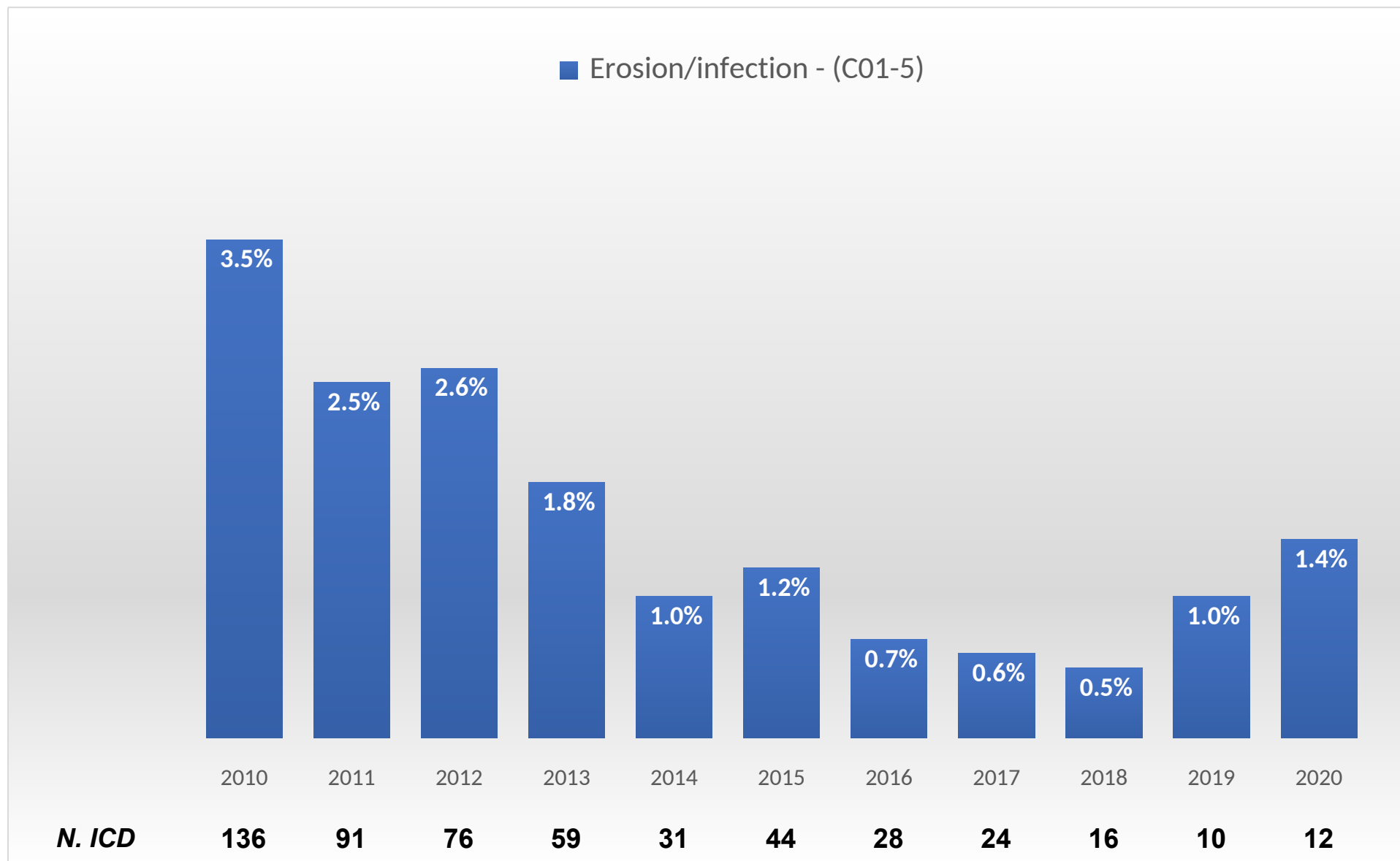


## PADIT Score:

- Age
- Procedure type
- Renal insufficiency
- Immunocompromission
- No. previous procedures



# 10 y ICD replacement indication - 3



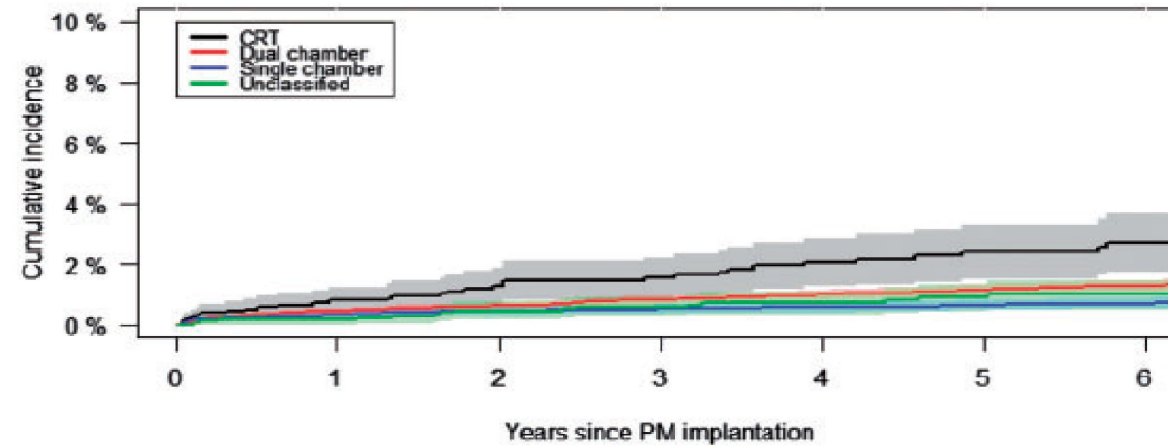
# Multi-Center, Community-Based Cardiac Implantable Electronic Devices Registry: Population, Device Utilization, and Outcomes

**Kaiser US system survey (2007-13) : 11 924 ICDs, 33 519 PMs, 4472 CRTs**

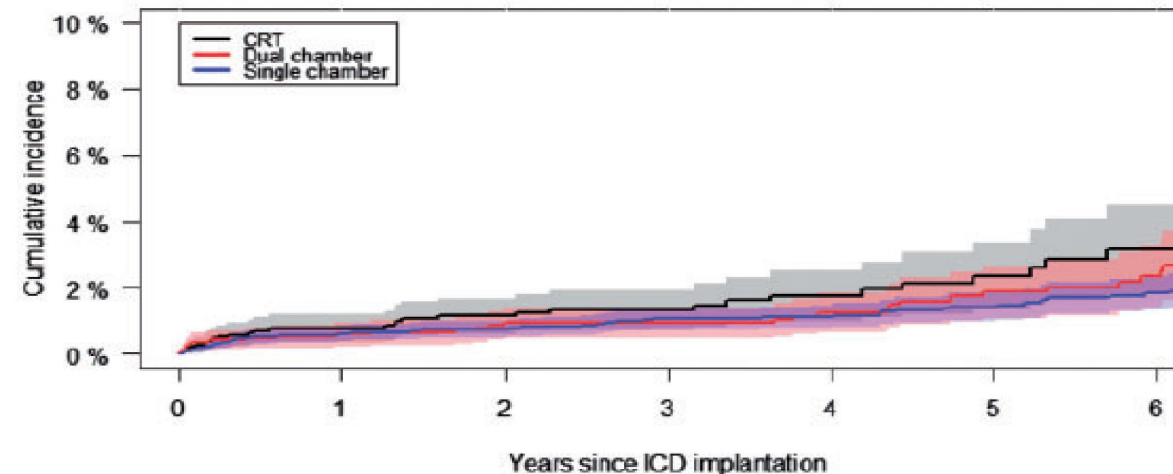
## ***Complications Following ICD or PM Implant, 2007–2013 :***

Complication	ICD	PM	CRT
	N (%)	N (%)	N (%)
Total N (initial and replacement)	11 924	33 519	4472
Tamponade	18 (0.15)	89 (0.27)	11 (0.25)
Pneumothorax	25 (0.21)	172 (0.51)	6 (0.13)
Hematoma	32 (0.27)	64 (0.19)	17 (0.38)
Infection			
Deep	71 (0.60)	170 (0.51)	44 (0.98)
Organ space	5 (0.04)	12 (0.04)	4 (0.09)
Superficial	2 (0.02)	9 (0.03)	1 (0.02)

# Infective endocarditis and risk of death after CIED implantation: a nationwide cohort study (Danish Reg.)



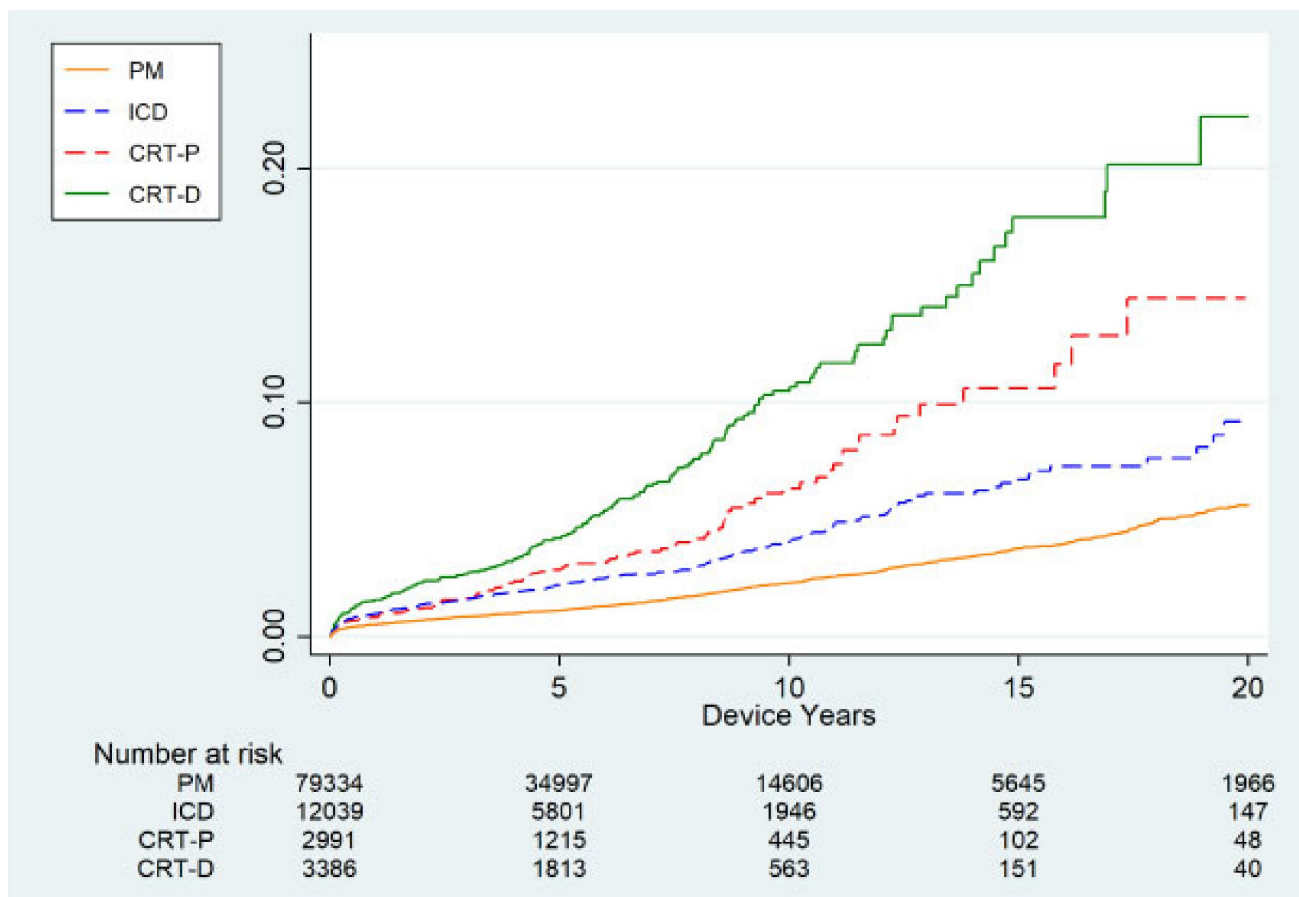
CRT	1567	1223	937	760	584	466	356
Dual chamber	20597	16801	13800	11077	8889	7054	5571
Single chamber	10097	7646	6243	5073	4080	3227	2524
Unclassified	2540	1843	1441	1192	853	610	438



CRT	1750	1310	938	640	423	288	187
Dual chamber	1907	1582	1255	956	724	542	419
Single chamber	4570	3758	3116	2514	1989	1494	1092

# Incidence of device-related infection in 97 750 patients: clinical data from the complete Danish device-cohort (1982–2018)

**Lifetime risk of device-related infection (DY: device years)**



**PM: 2.04/1000 DY**

**ICD: 3.84/1000 DY**

**CRT-PM: 4.38/1000 DY**

**CRT-ICD: 6.76/1000 DY**

## **DEVICE RELATED INFECTION RISK:**

- . Implantation of complex devices (ICD- CRT)
- . Reoperations, prior DRI
- . Male sex, and younger age

# Real-life outcome of ICD and CRT-D replacement/upgrade in a contemporary population: observations from the multicentre DECODE registry

- Prospective multicentre cohort study aimed at estimating **medium- to long-term Adverse Effects** in a large population of patients undergoing ICD/CRT-D replacement/upgrade from 2013 to 2015

**Table 3** Analysis of secondary endpoints

Endpoint	Number of patients, <i>n</i> (%)	Event rate, events/100 years (95% CI)	Time to event (days), median (25th–75th)
CIED-related	26 (2.6)	3.3 (2.2–4.6)	73 (4–108)
Bleeding	25 (2.5)	3.4 (2.3–4.7)	7 (1–8.5)
Procedure-related infection	12 (1.2)	1.6 (0.9–2.6)	45.5 (24–81)
Wound-related	17 (1.7)	2 (1.2–3.1)	39 (8–85)