

Infective Endocarditis

Changing epidemiology and outcome

Lessons from the Euro-Endo registry

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EuroValve

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Endocarditis: a changing disease

- **new high-risk subgroups**

- ✦ *IVDA*
- ✦ *elderly*
- ✦ *intracardiac devices*
- ✦ *nosocomial diseases*
- ✦ *hemodialysis*
- ✦ *congenital heart disease*
- ✦ *TAVI*

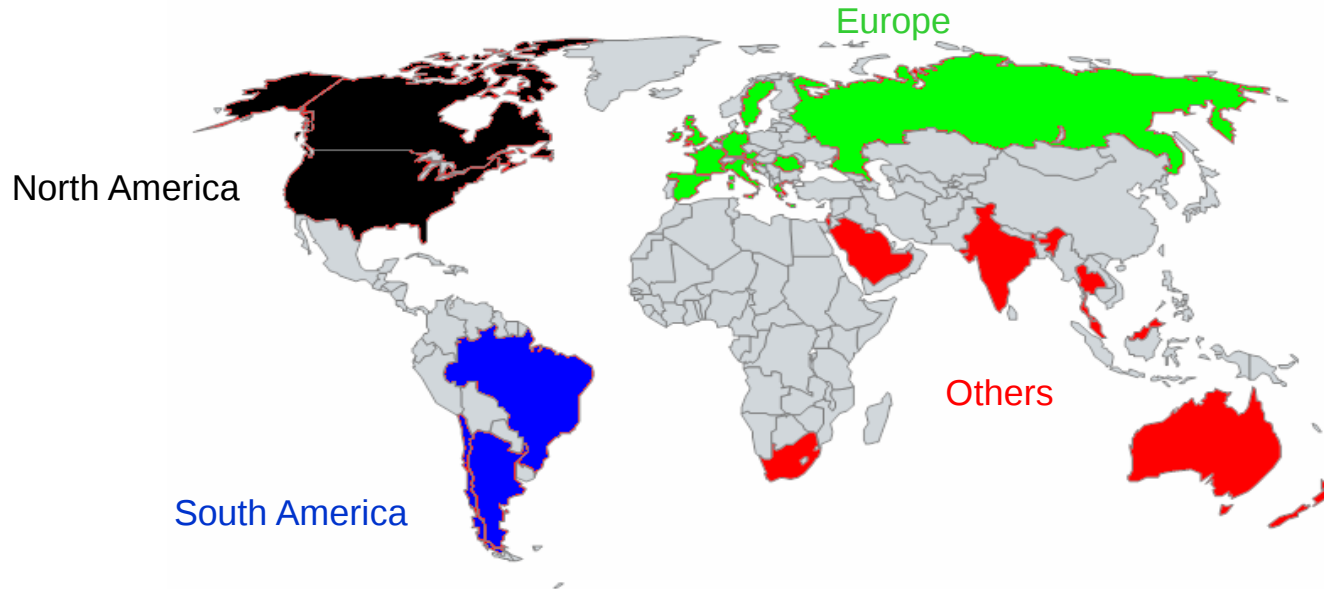
- **new imaging techniques**

- **new therapeutic strategies**



Clinical Presentation, Etiology, and Outcome of Infective Endocarditis in the 21st Century

The International Collaboration on Endocarditis–Prospective Cohort Study

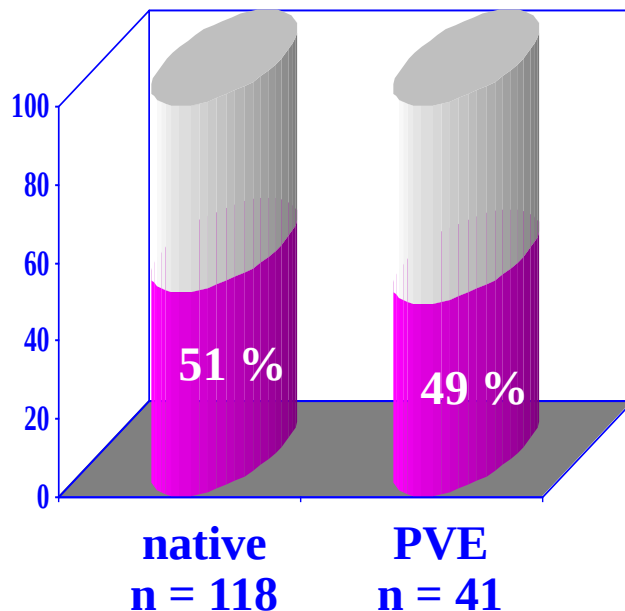


Arch Intern Med. 2009;169(5):463-473

Euro Heart Survey 2005

Tornos P – Heart 2005 ; 91 : 571-5

2-month inclusion in 2001



Surgery performed

Medical therapy only

Reasons for surgery

- ✦ CHF: 65%
- ✦ persistent sepsis: 45%
- ✦ embolism: 20%

European Infective Endocarditis (EURO ENDO) Registry

Main results

✓ *Gilbert Habib, chairman of the registry*

✓ *Patrizio Lancellotti, co-chairman*

✓ **Executive committee:**

Erwan Donal, Bernard Cosyns,

Bernard lung, Bernard Prendergast,

Pilar Tornos, Paola Erba, Bogdan Popescu

✓ **The EORP Team**

✓ **The EURO-ENDO investigators**

Clinical presentation, aetiology and outcome of infective endocarditis. Results of the ESC-EORP EURO-ENDO (European infective endocarditis) registry: a prospective cohort study

Gilbert Habib ^{1,2*}, Paola Anna Erba ^{3,4}, Bernard lung ⁵, Erwan Donal⁶, Bernard Cosyns ⁷, Cécile Laroche⁸, Bogdan A. Popescu⁹, Bernard Prendergast¹⁰, Pilar Tornos¹¹, Anita Sadeghpour¹², Leopold Oliver¹³, Jolanta-Justina Vaskelyte¹⁴, Rouguiatou Sow ¹⁵, Olivier Axler¹⁶, Aldo P. Maggioni¹⁷, and Patrizio Lancellotti^{18,19,20}; on behalf of the EURO-ENDO Investigators[†]

2015



2019



European Heart Journal (2015) **36**, 3075–3123
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

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



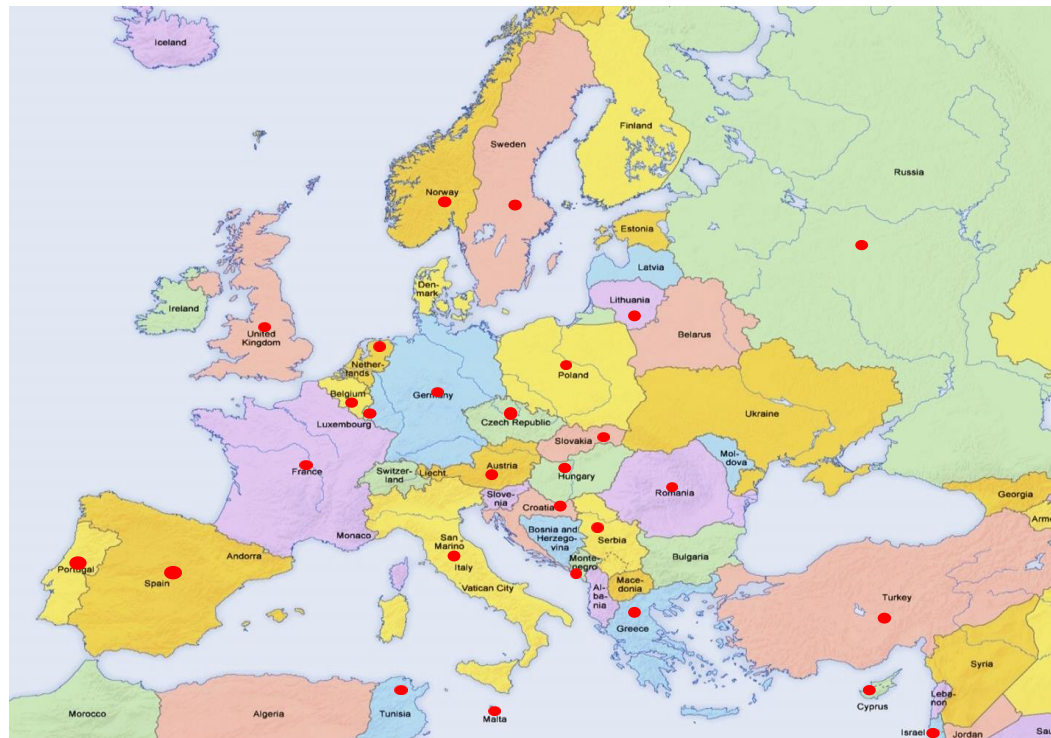
European Heart Journal - Quality of Care and Clinical Outcomes (2019) **5**, 202–207
doi:10.1093/ehjqcc/qcz018

COHORT PROFILE

The ESC-EORP EURO-ENDO (European Infective Endocarditis) registry

Gilbert Habib^{1,2*}, Patrizio Lancellotti^{3,4}, Paola-Anna Erba^{5,6}, Anita Sadeghpour⁷, Marwa Meshaal⁸, Antonia Sambola⁹, Shumaila Furnaz¹⁰, Rodolfo Citro¹¹, Julien Ternacle¹², Erwan Donal¹³, Bernard Cosyns¹⁴, Bogdan Popescu¹⁵, Bernard Jung¹⁶, Bernard Prendergast¹⁷, Cécile Laroche¹⁸, Pilar Tornos^{19,20}, Michal Pazdernik²¹, Aldo Maggioni²², and Chris P. Gale²³, on behalf of the EURO-ENDO Investigators[†]





The EURO-ENDO Registry



31 March 2018 - 3116 patients



EURO-ENDO:

Enrolment per Country

ESC / Affiliated countries

Affiliated Countries	Active Centres	CRF Locked
Iran	1	152
Brazil	7	129
Japan	9	63
Canada	4	60
Argentina	5	55
Pakistan	1	55
Korea, Republic of	2	31
Singapore	1	29
Saudi Arabia	1	27
India	2	24
United States	1	10
United Arab Emirates	1	6
Ecuador	1	5
13 Non-ESC countries	36	646

Total
40
Countries
156 Centres
3116
Patients

Number of patients included in the main analyses (database extracted on 19 July 2018)

ESC Countries	Active Centres	Patients
France (including AEPEI & New Caledonia)	18	459
Spain	1	77
Italy	12	292
Egypt	11	262
Czech Republic	4	189
Netherlands	11	173
Germany	7	137
Belgium	6	132
United Kingdom	6	130
Serbia	4	73
Greece	3	68
Turkey	7	63
Portugal	5	63
Croatia	5	59
Lithuania	2	49
Poland	1	40
Russian Federation	3	39
Luxembourg	1	38
Austria	1	36
Israel	2	21
Moldova, Republic of	1	21
Montenegro	1	12
Romania	1	12
Norway	3	11
Malta	1	8
Tunisia	1	3
Uzbekistan	1	2
27 ESC countries	120	2470

Together with

EURO-ENDO: End-points

- **Primary end-point:** In-hospital and 1-year mortality

- **Secondary end-points:**
 1. One-year morbidity (hospitalizations, need for surgery, relapses)
 2. Clinical, epidemiological, microbiological, and therapeutic characteristics
 3. Non invasive imaging techniques performed
 4. Implementation of the ESC guidelines, concerning
 - The practical use of echocardiography and other imaging techniques
 - The type and duration of antibiotic therapy
 - The indications of surgical therapy

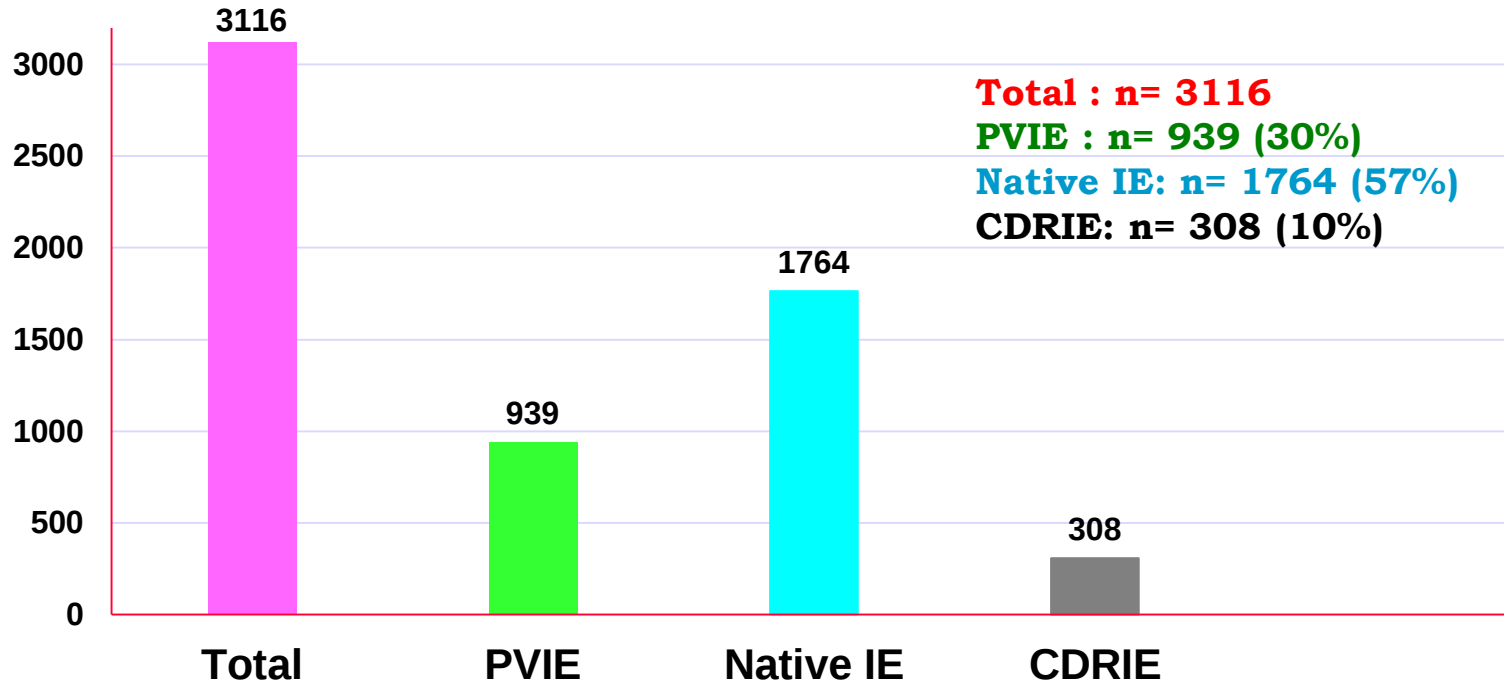
EURO-ENDO REGISTRY

1. Demographics and characteristics
2. Portal of entry, bacteriology
3. Prognosis, complications

EURO-ENDO REGISTRY

1. ***Demographics and characteristics***
2. Portal of entry, bacteriology
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Types of endocarditis in EURO-ENDO



Main demographics and characteristics

1. Increasing age of the population with IE and the frequency of PVIE
2. Majority of male patients

	Total (n =3116)	Prosthesis+Repair (n = 939)	Native (n =1764)	PM/ICD (n = 308)	P-value
Demography					
Age (years)					
N	3116	939	1764	308	
Mean $\pm$ SD	59.25 $\pm$ 18.03	63.36 $\pm$ 16.81	55.61 $\pm$ 18.45	66.77 $\pm$ 14.11	<0.0001
Age $\geq$ 65 years	1443 / 3116 (46.3%)	538 / 939 (57.3%)	662 / 1764 (37.5%)	194 / 308 (63.0%)	<0.0001
Age $\geq$ 80 years	375 / 3116 (12.0%)	141 / 939 (15.0%)	163 / 1764 (9.2%)	56 / 308 (18.2%)	<0.0001
Females (%)	969 / 3116 (31.1%)	292 / 939 (31.1%)	553 / 1764 (31.3%)	86 / 308 (27.9%)	0.4901

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Main risk factors

Main risk factors: IVDA, cancer, hemodialysis and chronic renal failure

	Total (n =3116)	Prosthesis+Repair (n = 939)	Native (n =1764)	PM/ICD (n = 308)	P-value
Risk factors					
Previous stroke/TIA	340 / 2860 (11.9%)	132 / 867 (15.2%)	160 / 1626 (9.8%)	34 / 273 (12.5%)	0.0003
Arterial Hypertension	1502 / 3111 (48.3%)	531 / 938 (56.6%)	726 / 1762 (41.2%)	194 / 306 (63.4%)	<0.0001
Chronic renal failure	553 / 3113 (17.8%)	191 / 938 (20.4%)	255 / 1762 (14.5%)	83 / 308 (26.9%)	<0.0001
Dialysis	163 / 3113 (5.2%)	28 / 938 (3.0%)	107 / 1762 (6.1%)	18 / 308 (5.8%)	<0.0001
HIV	31 / 3038 (1.0%)	3 / 916 (0.3%)	24 / 1726 (1.4%)	2 / 294 (0.7%)	0.0212
Cancer	361 / 3088 (11.7%)	107 / 930 (11.5%)	210 / 1746 (12.0%)	31 / 308 (10.1%)	0.6230
Intravenous drug dependency	212 / 3067 (6.9%)	20 / 930 (2.2%)	184 / 1729 (10.6%)	3 / 305 (1.0%)	<0.0001
Alcohol abuse	228 / 3003 (7.6%)	44 / 910 (4.8%)	166 / 1691 (9.8%)	12 / 301 (4.0%)	<0.0001
Immunosuppressive treatment	104 / 2840 (3.7%)	21 / 856 (2.5%)	71 / 1620 (4.4%)	8 / 270 (3.0%)	0.0450
Long corticothrapy	127 / 2840 (4.5%)	28 / 856 (3.3%)	84 / 1620 (5.2%)	13 / 270 (4.8%)	0.0871
Intravenous catheter	250 / 3104 (8.1%)	63 / 934 (6.7%)	150 / 1760 (8.5%)	24 / 306 (7.8%)	0.2672

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EURO-ENDO REGISTRY

1. Demographics and characteristics
2. ***Portal of entry, bacteriology***
3. Prognosis, complications

Guidelines changes and incidence of IE

French surveys on IE 2008

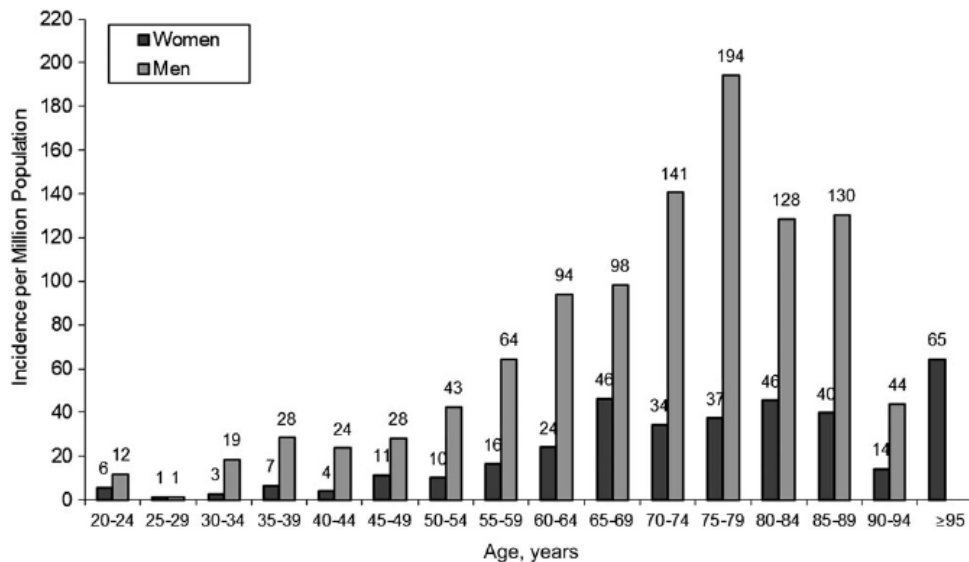


Figure 1. Incidence of infective endocarditis in the study population, by age and sex.

Selton Suty et al. Clin Infect Dis 2012;54:1230-9

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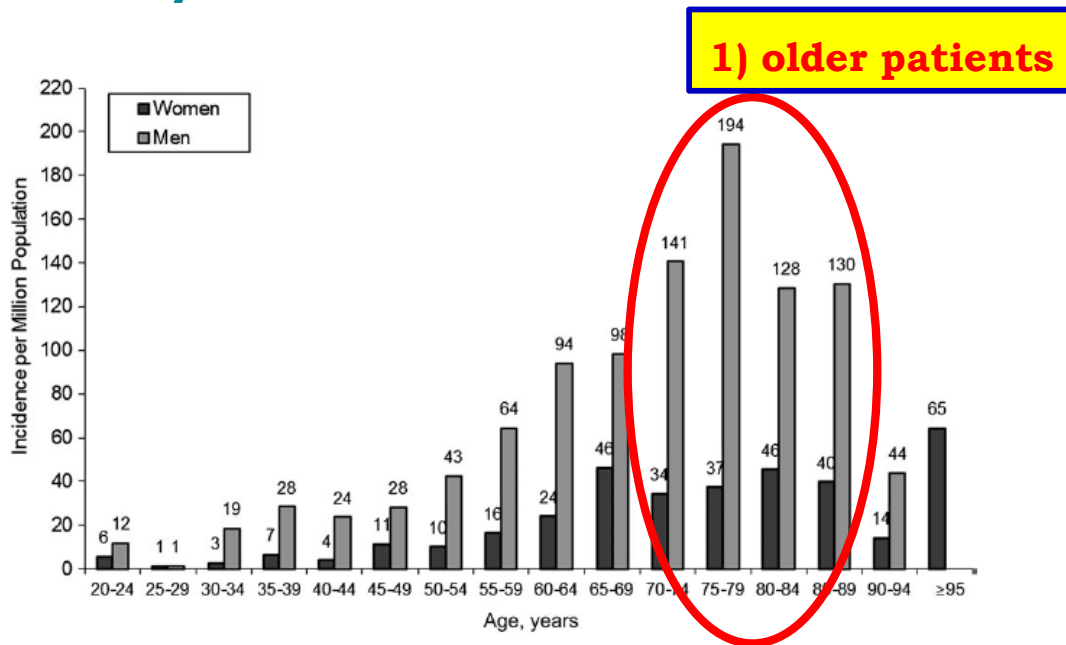


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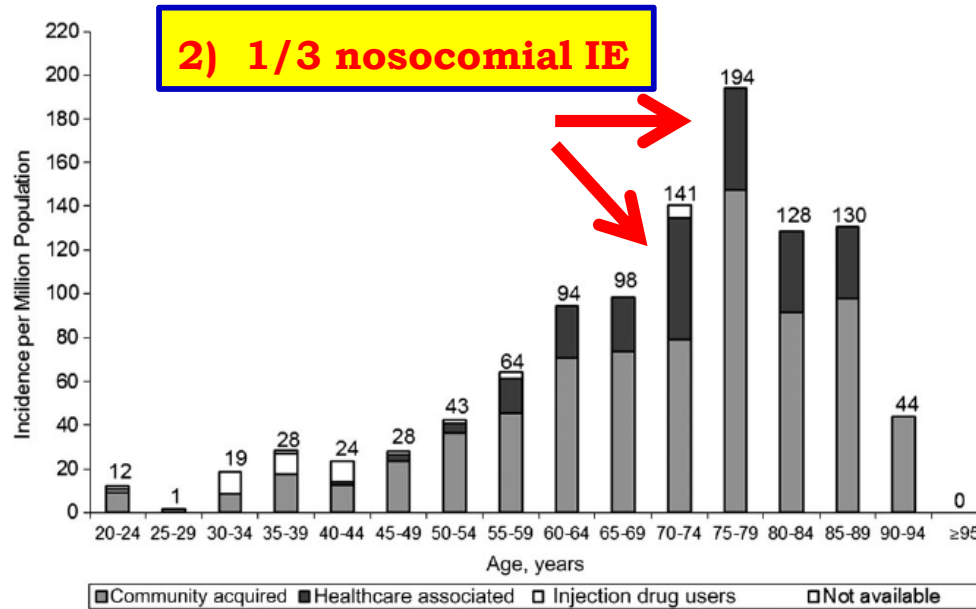
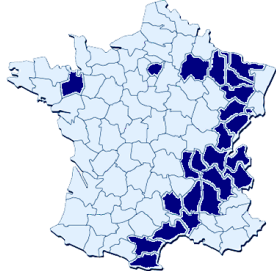


Figure 2. Incidence of infective endocarditis in the male population, by age and by mode of acquisition.

Selton Suty et al. Clin Infect Dis 2012;54:1230-9

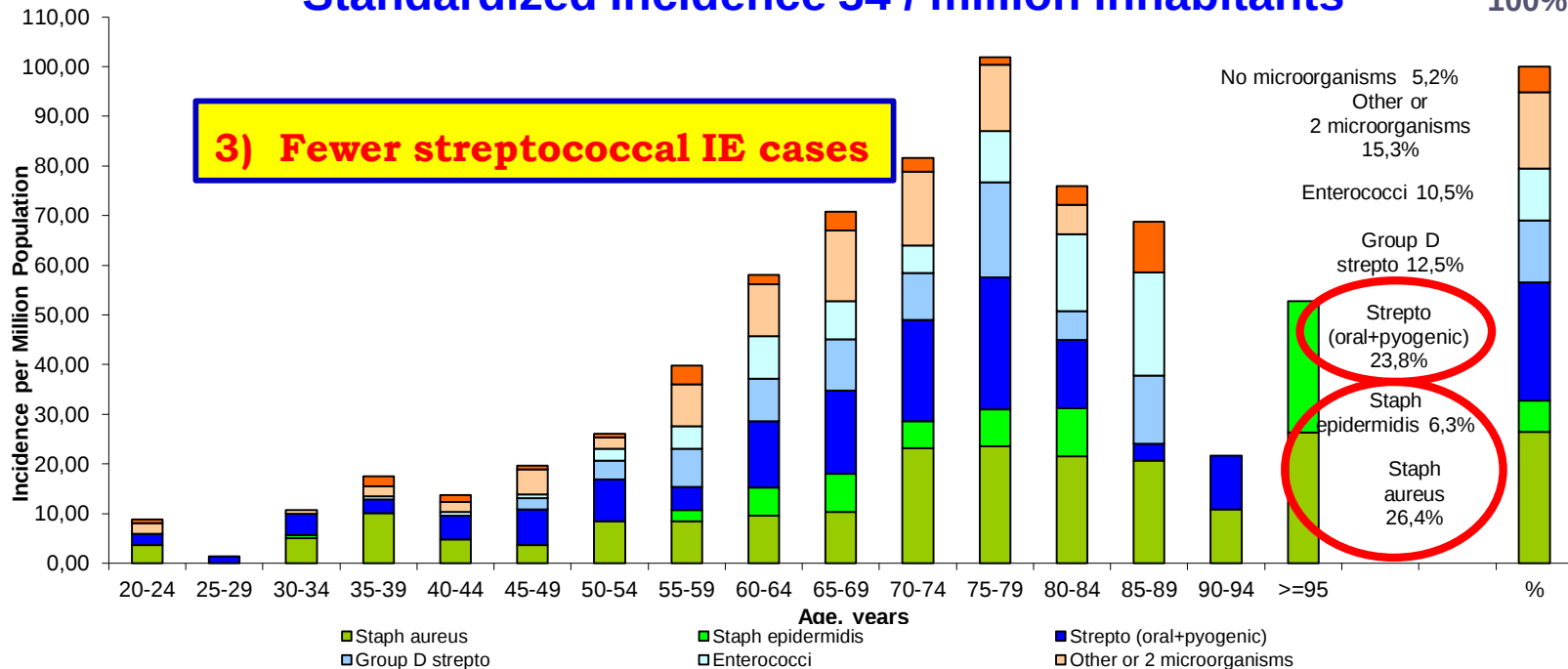


Incidence of IE by age and microorganism

Selton Suty et al. Clin Infect Dis 2012;54:1230-9 - Duval et al. J Am Coll Cardiol 2012;59:1968-76

Standardized Incidence 34 / million inhabitants

100%

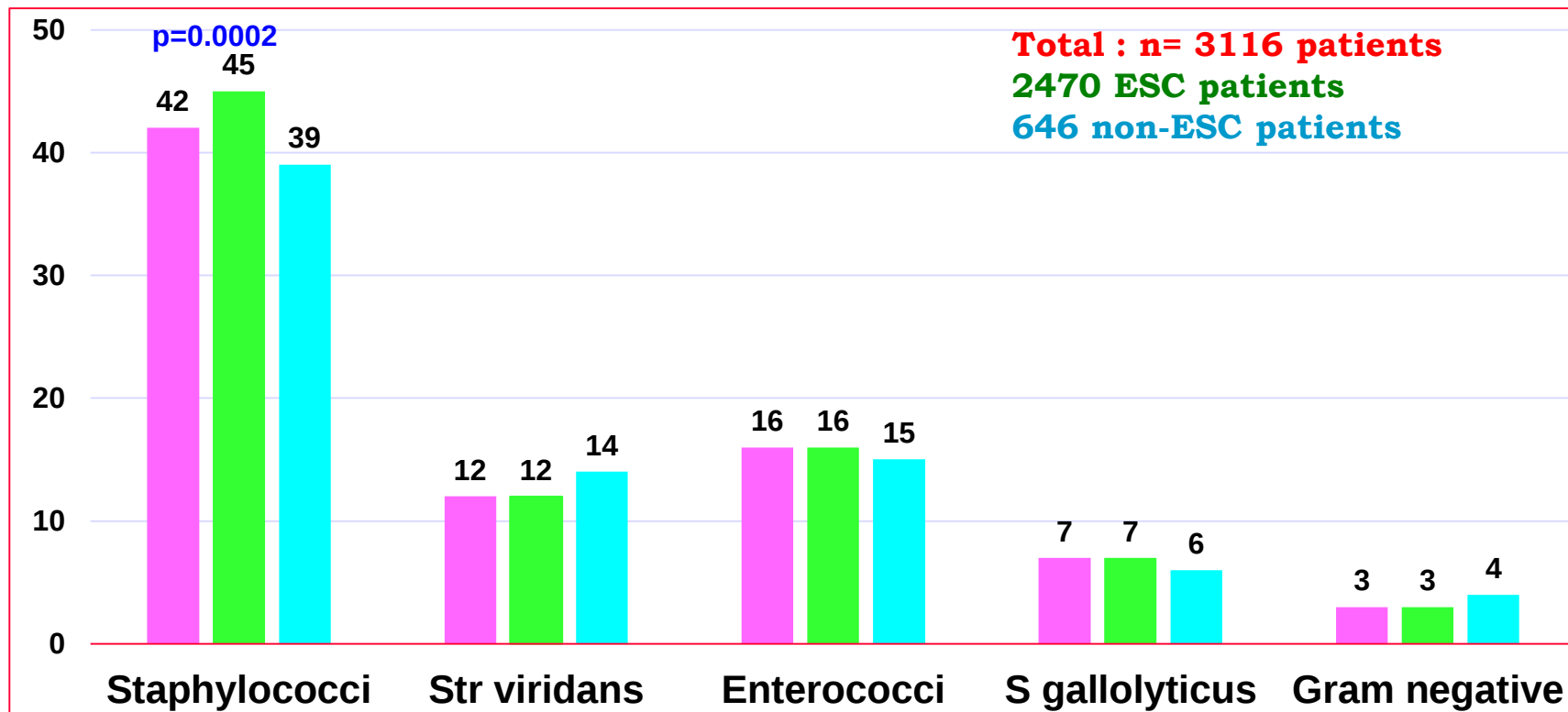


3 repeat population-based one-year surveys

Duval X – JACC 2012

		1991 N = 323	1999 N = 331	2008 N = 339
No known valvular disease	↗	34%	49%	47%
Oral streptococci	→	24%	18%	21%
Group D streptococci	↗↘	17 %	25%	12%
Staphylococci	↗	21%	27%	36%
Surgical Rx	↗	30%	49%	52%
In-hospital lethality	↘↗	21%	16%	21%

Blood cultures results



Portal of entry and bacteriology

1. The most frequent preceding non-cardiac interventions performed within the last 6 months were dental procedure (7.9%), gastrointestinal intervention (3.4%), colonoscopy (3.3%) and urogenital intervention (2.8%).
2. The portal of entry was dental in 9.8%, digestive in 6.3%, and genitourinary in 4.5%.
3. The low frequency of dental portal of entry in EURO-ENDO, combined with the low frequency of oral streptococci is reassuring in the wake of the 2009 and 2015 ESC guidelines, which recommended restricting the use of antibiotic prophylaxis to high risk populations undergoing at-risk dental procedures
4. The high frequency of enterococci (15.8%) observed in EURO-ENDO represents a significant change compared with the 8% and 10% frequency observed in the 2002 French survey and 2009 ICE Cohort Study, respectively

EURO-ENDO REGISTRY

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Complications under therapy

1. Embolic events were the most frequent complication, observed in 20.6% of patients, followed by acute renal failure (17.7%) and heart failure (14.1%)
2. Similar frequency between European and non-European countries (21.1% vs 18.4%).

	Total (n =3116)	ESC (n =2470)	Non-ESC (n = 646)	P-value
Embolic events	641 / 3116 (20.6%)	522 / 2470 (21.1%)	119 / 646 (18.4%)	0.1289
Hemorrhagic Stroke	79 / 3116 (2.5%)	62 / 2470 (2.5%)	17 / 646 (2.6%)	0.8612
Spondylitis	145 / 3116 (4.7%)	125 / 2470 (5.1%)	20 / 646 (3.1%)	0.0348
CHF	439 / 3116 (14.1%)	376 / 2470 (15.2%)	63 / 646 (9.8%)	0.0004
Mycotic aneurysm	58 / 3116 (1.9%)	33 / 2470 (1.3%)	25 / 646 (3.9%)	<0.0001
Acute renal failure	550 / 3116 (17.7%)	429 / 2470 (17.4%)	121 / 646 (18.7%)	0.4188
Persistent fever (>7 days)	351 / 2840 (12.4%)	276 / 2194 (12.6%)	75 / 646 (11.6%)	0.5103
Increasing vegetation size	201 / 3116 (6.5%)	154 / 2470 (6.2%)	47 / 646 (7.3%)	0.3377
New abscess	193 / 3116 (6.2%)	151 / 2470 (6.1%)	42 / 646 (6.5%)	0.7155
AV block	128 / 2840 (4.5%)	112 / 2194 (5.1%)	16 / 646 (2.5%)	0.0047

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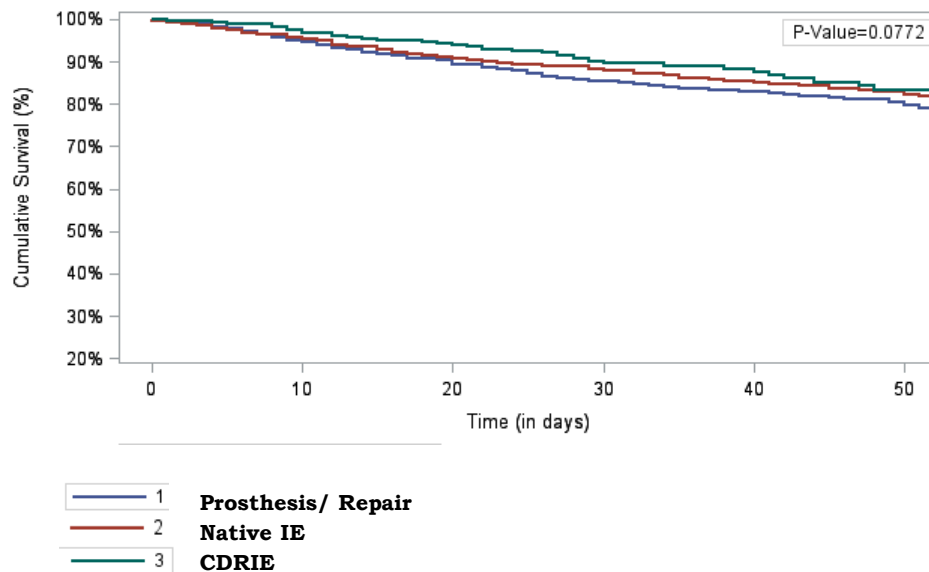
Surgical therapy

1. Surgery was performed during hospitalization in 1596 (51.2%) patients.
2. Following ESC guidelines, theoretical indication for cardiac surgery was present in 2160 (69.3%) patients.

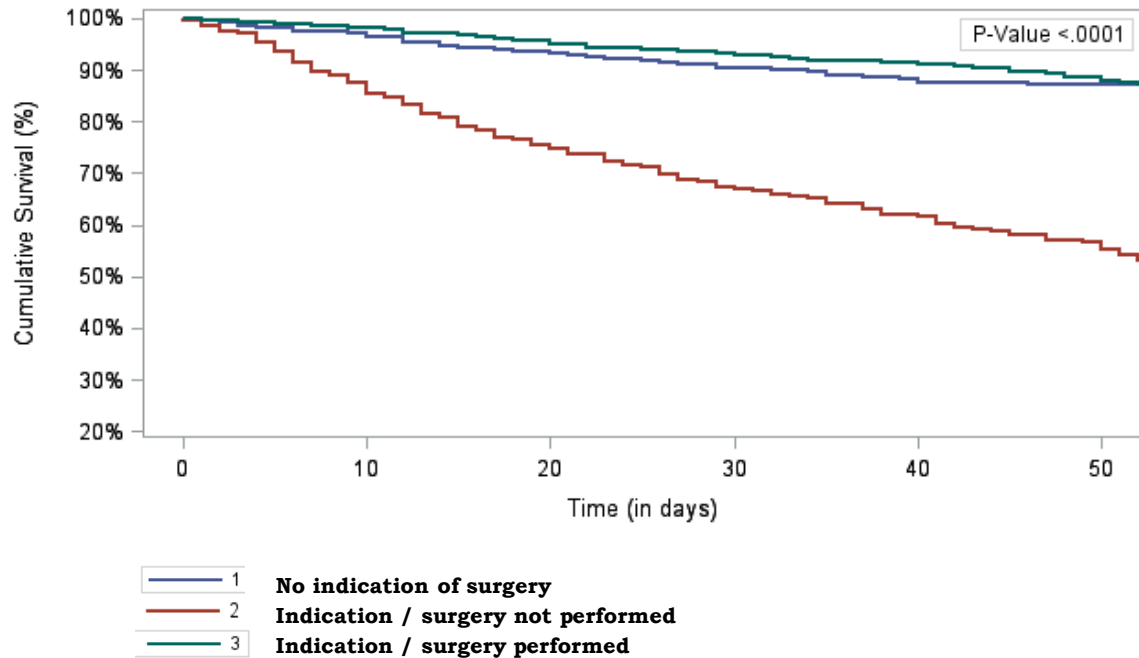
	Total (n =3116)	ESC (n =2470)	Non-ESC (n = 646)	P-value
Theoretical Indication of cardiac surgery	2160 / 3115 (69.3%)	1747 / 2470 (70.7%)	413 / 645 (64.0%)	0.0010
Indication				
Haemodynamic	999 / 2160 (46.3%)	788 / 1747 (45.1%)	211 / 413 (51.1%)	0.0283
Embolic	693 / 2160 (32.1%)	590 / 1747 (33.8%)	103 / 413 (24.9%)	0.0005
Infectious	1387 / 2160 (64.2%)	1077 / 1747 (61.6%)	310 / 413 (75.1%)	<0.0001
Other	207 / 2160 (9.6%)	159 / 1747 (9.1%)	48 / 413 (11.6%)	0.1175
Cardiac surgery performed	1596 / 2160 (73.9%)	1275 / 1747 (73.0%)	321 / 413 (77.7%)	0.0485

1-month mortality in EURO-ENDO

1. 532 In-hospital deaths = 17.1%
2. Similar in ESC vs non-ESC countries



1-month mortality in EURO-ENDO



Multivariate predictors of in-hospital death

	Hazard Ratio	95% CI	p value
Charlson index	1.07	[1.04-1.11]	<0.0001
Creatinine >2mg/dl	1.58	[1.19-2.11]	<0.0017
CHF	2.09	[1.58-2.77]	<0.0001
Vegetation length > 10mm	2.12	[1.64-2.73]	<0.0001
Cerebral complication	2.21	[1.61-3.04]	<0.0001
Abscess	1.50	[1.07-2.10]	0.0186
Indication - not performed	2.84	[2.00-4.03]	<0.001
Indication - performed	0.63	[0.43-0.92]	0.0169

Take-home messages: EURO-ENDO registry

1. IE more frequently affects men around 60 years of age
2. PVIE, CDRIE, nosocomial, staphylococcal and enterococcal endocarditis are more frequent
3. Oral streptococcal endocarditis is less frequent, and its frequency has not increased since implementation of the 2009 and 2015 recommendations restricting indications for antibiotic prophylaxis.
4. The prognosis of IE is still unacceptably poor and more aggressive management of this deadly disease remains necessary

EURO-ENDO ancillary studies

1. *Cancer and IE*
2. *Device related IE*
3. *Influence of age and gender in IE*
4. *Comparison of the patterns of IE between regions in Europe and in the world*
5. *Infective endocarditis in patients with congenital heart disease*
6. *Risk of embolic events and death in infective endocarditis*
7. *Culture positive vs culture negative endocarditis*
8. *How are imaging techniques used in Europe?*
9. *Characteristics and outcomes in patients with recurrent endocarditis*
10. *Heart failure in IE*

La Timone Hospital; Marseille, France



