

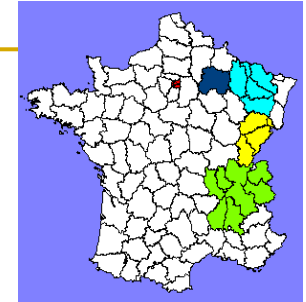


Infective endocarditis in chronic haemodialysis patients

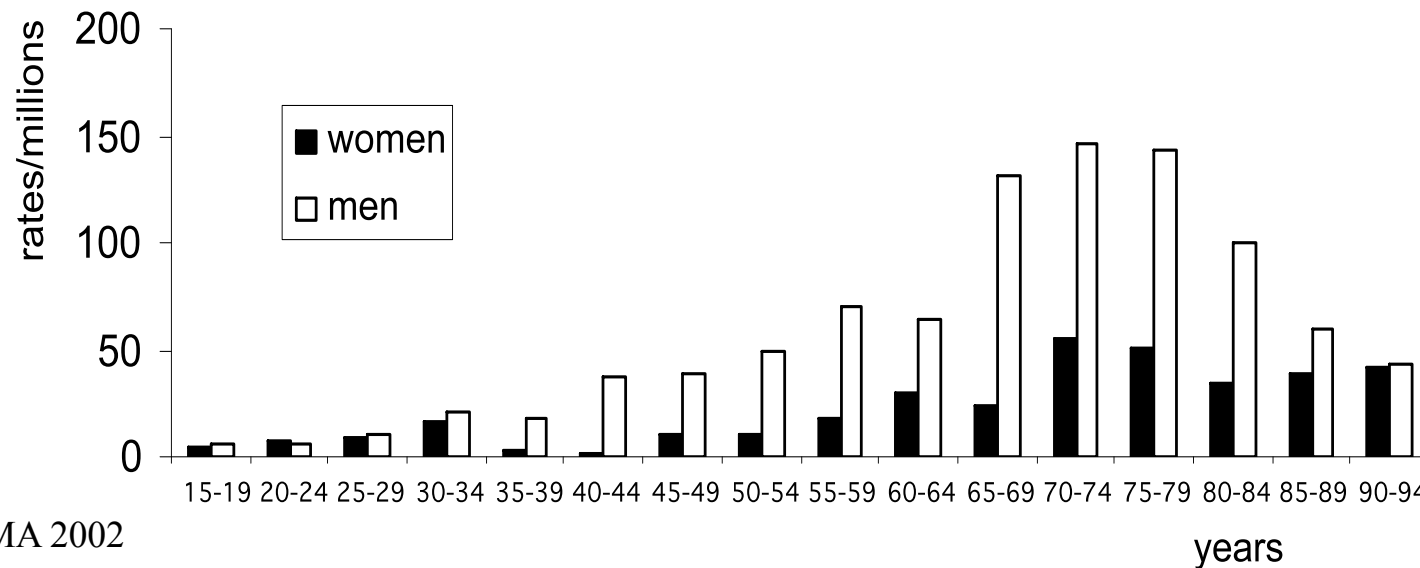
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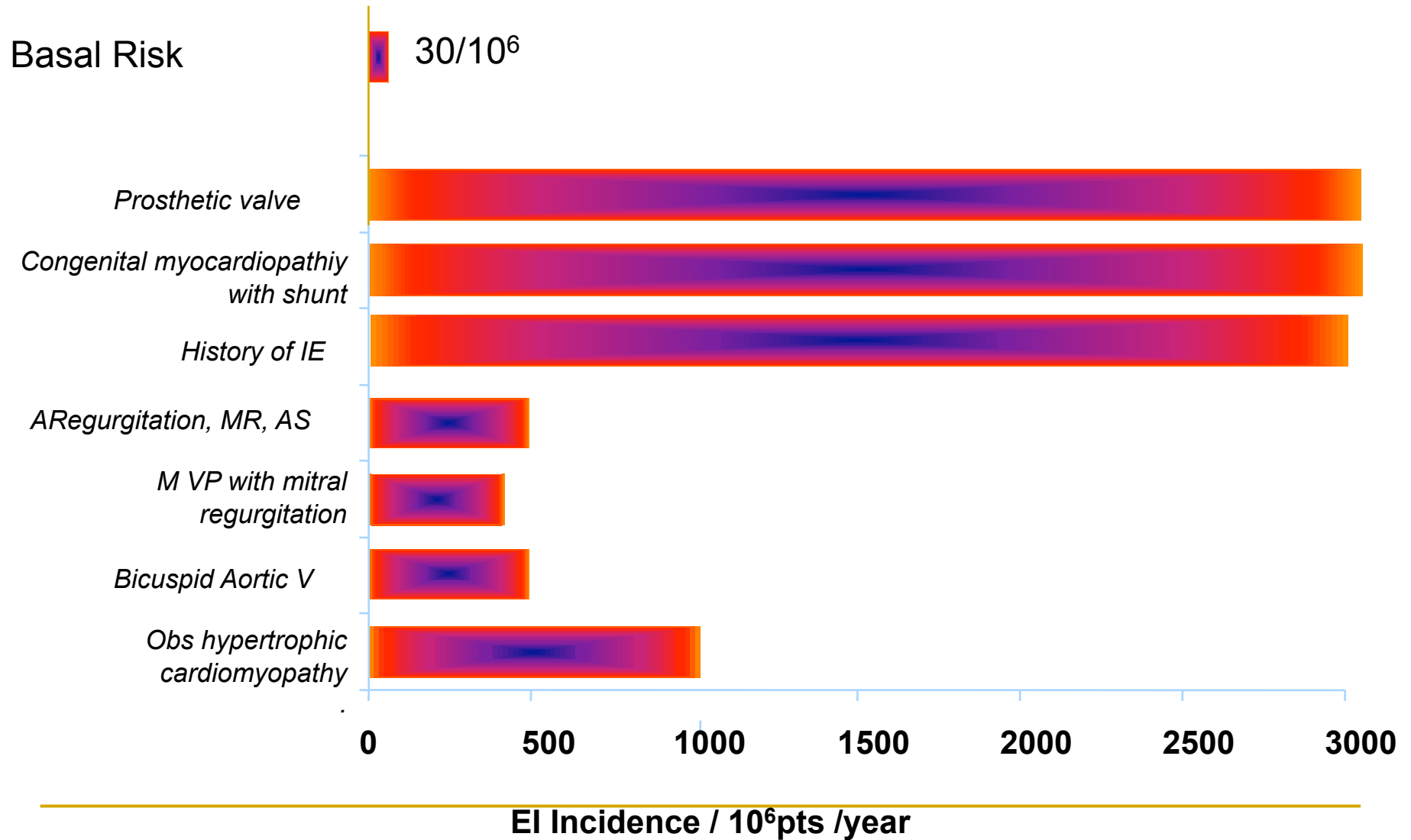
French study on IE, 1999



- 6 French regions (16 millions inhabitants)
- 390 patients (277 M / 113 F, mean age : 59 ± 17 yrs)
- **30 cases / year / million inhabitants**
 - Men: 44 / million
 - Women: 17 / million
 - Peak incidence: 145 /million in men 70 to 80 years of age



IE at risk valvulopathy



Infective endocarditis in chronic haemodialysis patients

- Epidemiology
 - Causative microorganisms
 - Diagnosis
 - Therapy
-

French study on IE, 1999

- 13/390 patients were on chronic HD
 - Extrapolation to the whole French population:
50 cases/year
 - Incidence in HD population (25,000 – 30,000 HD)
 - **1700 – 2000 IE/10⁶ HD patients**
 - **50-60 times higher than in overall population**
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Hospitalizations for bacterial endocarditis after initiation of chronic dialysis in the USA

Incidence ratio for primary hospitalizations for endocarditis in 1996

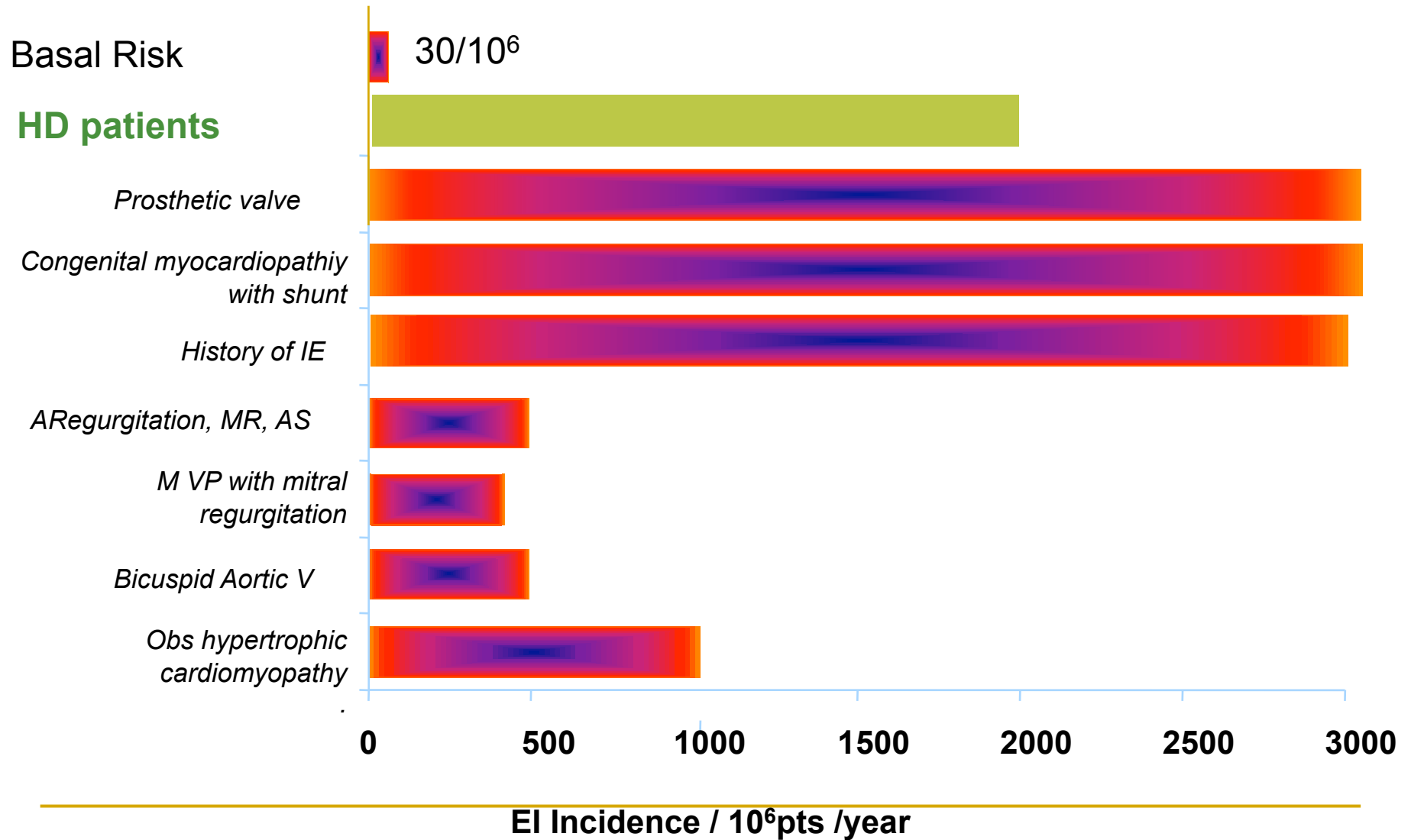
	Incidence per 100,000 person-years	Observed cases	Expected cases	Age-adjusted incidence ratio (compared with the general population)
Incidence in the general population ¹ (n = 263,998,000)	6.5	17,000	NA	NA
Incidence in hemodialysis patients, 1996 (n = 60,004)	483	290	3.9	17.86 (6.62–48.90)
Incidence in peritoneal dialysis patients, 1996 (n = 18,640)	248	20	0.5	10.54 (0.71–158.13)

Multiple hospitalizations for bacterial endocarditis in dialysis patients were used in this comparison.

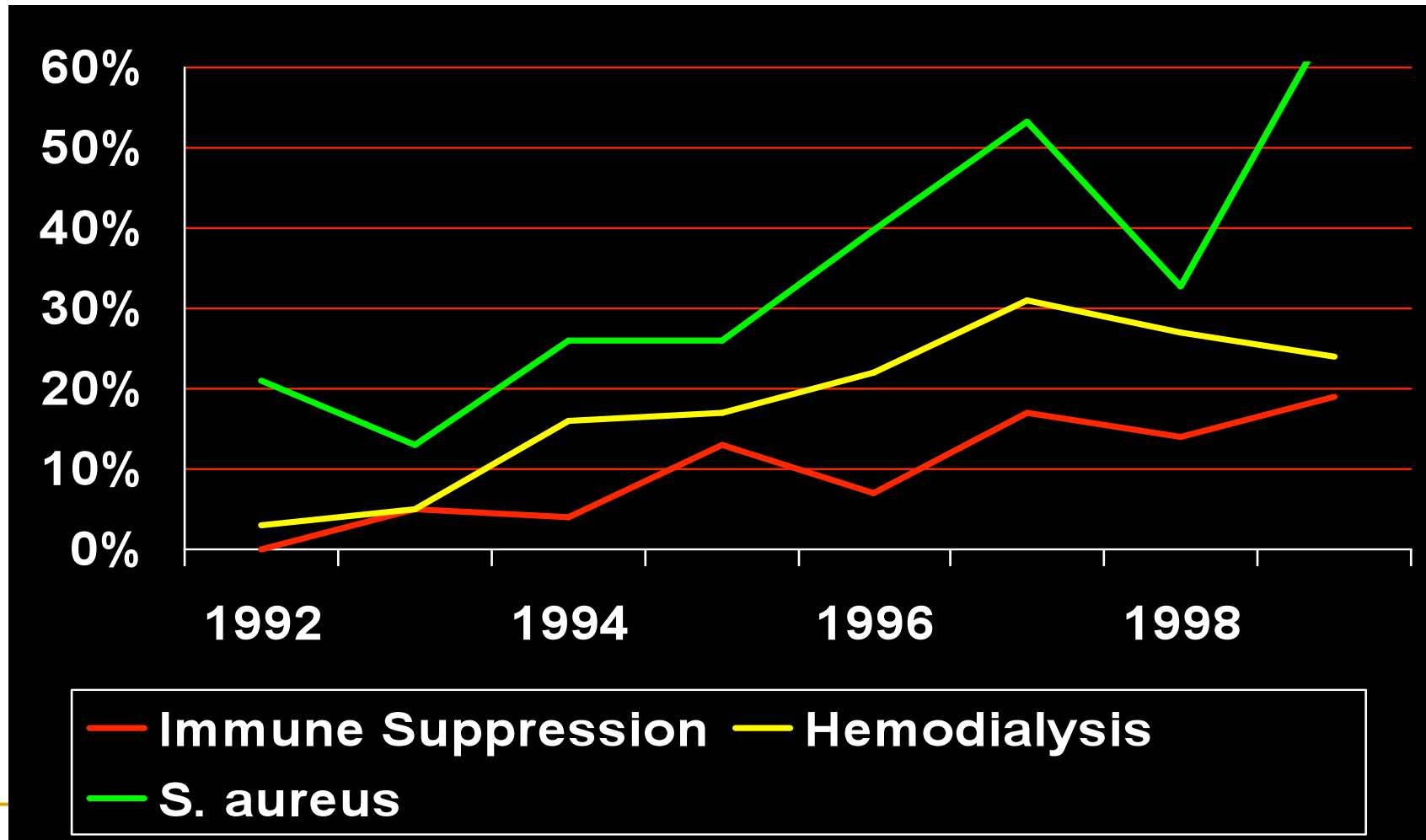
95% CI = 95% confidence interval. NA = Not available.

¹ From the National Hospital Discharge Survey.

IE at risk situations



Hemodialysis: a major cause of IE



HD: Predisposing factor for IE

- Increased Incidence of degenerative heart valve diseases:
 - Calcific aortic stenosis
 - Mitral annular calcifications
 - Mitral regurgitation/stenosis
 - Increased risk of bacteraemia:
1/100 pts months
-

Complications and outcome of SA BSI in HD patients

- Retrospective 3-center German study
 - 109 HD patients with SA BSI
 - Source of bacteremia = vascular access in 55 pts
 - 30 patients (29%) had tunneled, cuffed catheters

Complications/outcome	Nosocomial (n=49)	Community-acquired (n=60)	Total (n=109)
Any complication	14.3%	18.3%	16.5%
Infective endocarditis	0	1.7%	0.9%
Osteomyelitis/arthritis	4.1%	6.7%	5.5%
Abscess	0	5.0%	2.8%
Septic emboli	2.0%	0	0.9%
Mortality at 12 weeks	36.7%	26.7%	30.6%

Infective endocarditis in chronic haemodialysis patients

- Epidemiology
 - **Causative microorganisms and prognosis**
 - Diagnosis
 - Therapy
-

Causative Microorganisms in HD Pts with Infective Endocarditis

	Nori <i>et al.</i>	Spies <i>et al.</i>	Doulton <i>et al.</i>	Maraj <i>et al.</i>	McCarthy
Episodes of IE in series	<i>n</i> = 54	<i>n</i> = 40	<i>n</i> = 30	<i>n</i> = 30	<i>n</i> = 17
<i>Staphylococcus aureus</i>	40%	50%	63%	80%	40%
MRSA	20%	15%	7%	23%	
Coagulase-negative <i>Staphylococcus</i>	22%	12%	13%	3%	10%
<i>Enterococcus</i> species	33%	23%	10%	7%	20%
<i>Streptococcus</i> species			10%	3%	25%
Gram-negative species	13%	10%			
<i>Candida</i> species		3%		3%	
<i>Aspergillus</i> species					5%
Negative blood culture	2%	10%			
Calendar year		90-01	80-02	90-00	83-97

S. aureus: 40-80%

In-hospital and 1-year Mortality Rate of HD Pts with Infective Endocarditis

	Nori <i>et al.</i>	Spies <i>et al.</i>	Doulton <i>et al.</i>	Maraj <i>et al.</i>	McCarthy and Steckelberg
Episodes of IE in series	<i>n</i> = 54	<i>n</i> = 40	<i>n</i> = 30	<i>n</i> = 30	<i>n</i> = 17
Mortality rate					
Inhospital	37%	52%	30%	25%	45%
1-year			46%	56%	75%

Poor Prognosis

Determinants of In-hospital Mortality (Chu US)

- 267 definite or possible IE
- In-hospital death 19% (20% definite, 16% possible)

TABLE 2. Independent Variables Associated With In-Hospital Death

Variable	OR	95% CI	P
Male gender	0.58	0.28–1.13	0.110
Diabetes mellitus	2.48	1.24–4.96	0.010
<i>S aureus</i> organism	2.06	1.01–4.20	0.046
APACHE II score at admission	1.07	1.01–1.12	0.021
Embolic event	2.79	1.15–6.80	0.024

- Echographic data, NYHA , non associated with prognosis

- **S. aureus** associated with mortality

Determinants of embolic events (Thuny 2005)

- **S. aureus** associated with embolic events

TABLE 3. Predictors of Embolic Events in Multivariate Analysis

	<i>P</i>	Adjusted Odds Ratio	95% CI
Total-EE			
<i>S bovis</i>	<0.001	3.9	1.86–8.21
<i>S aureus</i>	0.002	2.4	1.15–4.83
New-EE			
Vegetation length >10 mm	0.004	9	1.98–40.8
Severe vegetation mobility	0.04	2.4	1.02–5.42
<i>S bovis</i>	0.19	1.9	0.73–4.74
<i>S aureus</i>	0.12	2	0.84–4.76

Clinical and Echocardiography prognostic factors for early and late **mortality** among chronic HD pts with IE

Early mortality	Late mortality
Septic embolism Mitral valve involvement Vegetation size >2 cm ³ at TEE	Age >65 years Diabetes as cause of ESRD Cerebrovascular accident/transient ischaemic attack Mitral valve involvement (especially if mitral annular calcification or severe mitral valvular regurgitation) IE related to MRSA and VRE

Infective endocarditis in chronic haemodialysis patients

- Epidemiology
 - Causative microorganisms and prognosis
 - Diagnosis
 - Therapy
-

Diagnosis

Clinical presentation

- Distinguish IE from uncomplicated access infection
 - Fever less commonly present:
 - 45-70% vs 80-90%
 - Increased inflammatory markers: non specific
 - Left > right heart
-

Risk of endocarditis among pts with prosthetic valves and *S. aureus* bacteremia

- 12-week prospective evaluation of all patients with a PV or ring who were treated for *S. aureus* bacteremia at Duke University Medical Center.
- Overall rate of definite PV IE : **26/51 (51%)**.
- All patients with a prosthetic valve who develop *S. aureus* bacteremia should be aggressively screened for the diagnosis of endocarditis.

High suspicion features of infective endocarditis mandating TEE after TTE in chronic haemodialysis patients

Presence of new-onset congestive heart failure

Presence of stigmata of endocarditis

Development of HD-related hypotension, particularly in a previously hypertensive patient

Prior or repeated past episodes of IE

Prior valvular surgery

Typical organisms for IE (i.e. *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, *Enterococcus* species, and *Streptococcus* species) as causative pathogens

Relapsing bacteraemia after antibiotic discontinuation, regardless of the causative pathogen

Patients with HD catheters

Infective endocarditis in chronic haemodialysis patients

- Epidemiology
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-

Therapy

- Vancomycin should not be used for MSSA:
 - Lower bactericidal activity
 - Selection of VRE
 - MRSA:
 - Vancomycin trough plasma level 15-20 mg/L
 - Linezolid, Daptomycin ?
 - Inhibitory quotient:
 - C_{min} / MIC : 10-30 ?
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Vancomycin vs. Cefazolin for Rx of HD-dependent pts with MSSA bacteremia

Variables associated with treatment failure

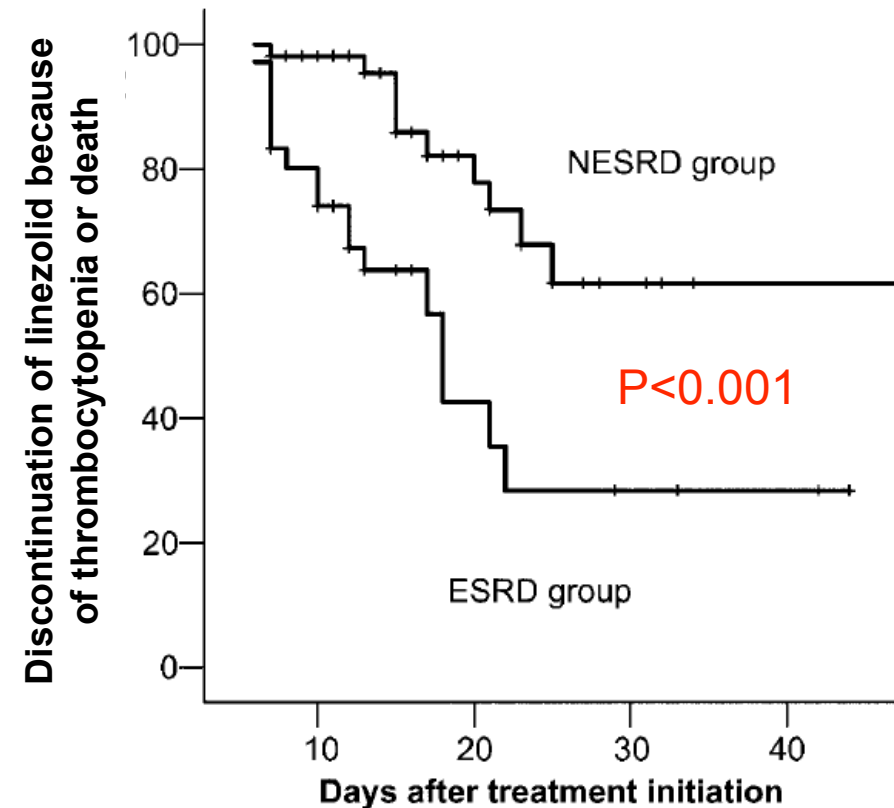
Variable	Bivariable analysis		Multivariable analysis	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Age >50 years	0.79 (0.35–1.81)	.58	...	
Male sex	1.98 (0.86–4.55)	.11	...	
APACHE II score >20	1.43 (0.59–3.50)	.42	...	
Vancomycin as principal therapy	3.02 (1.13–8.08)	.02	3.53 (1.15–13.45)	.04
Retention of hemodialysis access ^a	5.08 (1.95–13.24)	<.01	4.99 (1.89–13.76)	.001

^a Data were available for 112 patients, regardless of the source of infection status.

High frequency of Linezolid-associated thrombocytopenia and anemia among patients with end-stage renal disease

- Retrospective c/c study
 - G+ bacterial infections
 - 28 ESRD patients
 - 63 non ESRD patients

	ESRD	Non ESRD	p
PLT<100 G/L	79%	43%	0.003
Anemia	71%	37%	0.003



Antibiotic dosing and monitoring guidelines in HF-HD patients with SA BSI

Drug	Dosing	Monitoring
Cloxacillin	2 g IV q6h	Rash
Cefazolin	1-2 g IV after HD	Rash

Surgery

- Modify indications of the general population ?
 - Which type of prosthesis ?
 - Bioprosthesis valve rather than mechanical one
 - Limited life expectancy: bioprosthesis degeneration uncommon
 - ESRD: Risk factor for **bleeding** in pts with warfarin
-

Indications for surgery in IE

state-of-the-art

- Indications for surgery in IE are well defined
 - Congestive heart failure
 - Refractory infection
 - Severe anatomical/functional valve damages
 - Benefits of surgery in IE are supported by clinical experience, not evidence-based
 - Absence of randomized trials
 - Unavoidable biases of observational studies
 - Overall, sicker patients are selected for surgery
 - The sickest patients are not operated on.
-

Take home messages

- IE in chronic haemodialysis pts:
 - highly frequent
 - complex diagnosis
 - should be considered in all HD pts with bacteraemia:
TEE, TTE
 - mainly due to *S. aureus*: poorer prognosis
 - complex therapy:
 - Prolonged antibiotherapy: drug plasma level monitoring
 - Surgery indications:
Bioprosthesis valve rather than mechanical one
- Prophylaxis:
 - hygiene
 - prevention of valvulopathy ?
 - *S. aureus* vaccine ?

Risk Factors for Infective Endocarditis

Oral Hygiene and Nondental Exposures

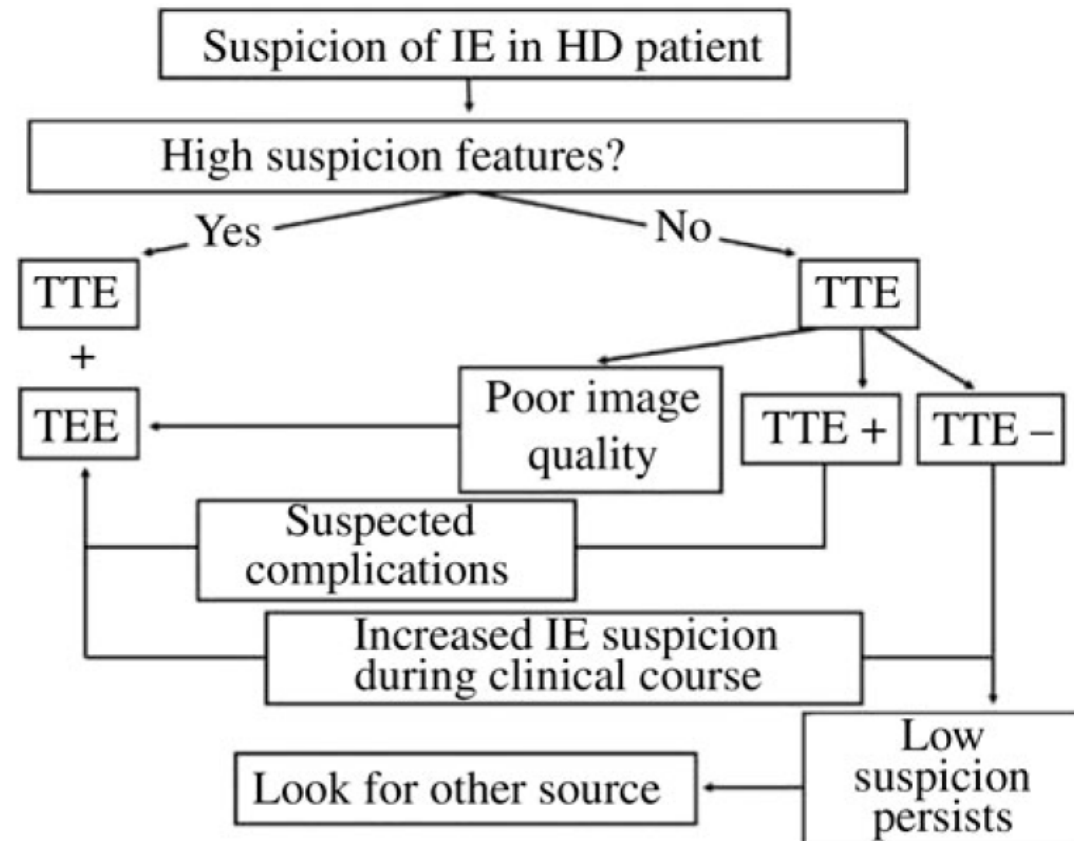
Brian L. Strom, MD, MPH; Elias Abrutyn, MD; Jesse A. Berlin, ScD; Judith L. Kinman, MA;
Roy S. Feldman, DDS, DMSc; Paul D. Stolley, MD, MPH; Matthew E. Levison, MD;
Oksana M. Korzeniowski, MD; Donald Kaye, MD

Background—The risks of infective endocarditis (IE) associated with various conditions and procedures are poorly defined.

Methods and Results—This was a population-based case-control study conducted in 54 Philadelphia, Pa–area hospitals from 1988 to 1990. Community-acquired IE cases unassociated with intravenous drug use were compared with matched community residents. Subjects were interviewed for risk factors. Diagnoses were confirmed by expert review of medical record abstracts with risk factor data removed. Cases were more likely than controls to suffer from prior severe kidney disease (adjusted OR [95% CI]=16.9 [1.5 to 193], $P=0.02$) and diabetes mellitus (adjusted OR [95% CI]=2.7 [1.4 to 5.2], $P=0.004$). Cases infected with skin flora had received intravenous fluids more often (adjusted OR [95% CI]=6.7 [1.1 to 41], $P=0.04$) and had more often had a previous skin infection (adjusted OR [95% CI]=3.5 [0.7 to 17], $P=0.11$).

- Prognosis of IE in the general population

Echocardiography Algorithm for Suspected Infective Endocarditis in chronic haemodialysis patients



Linezolid vs. vancomycin for *S. aureus* bacteremia: metaanalysis of 5 RCT

