
Le Best of des endocardites infectieuses

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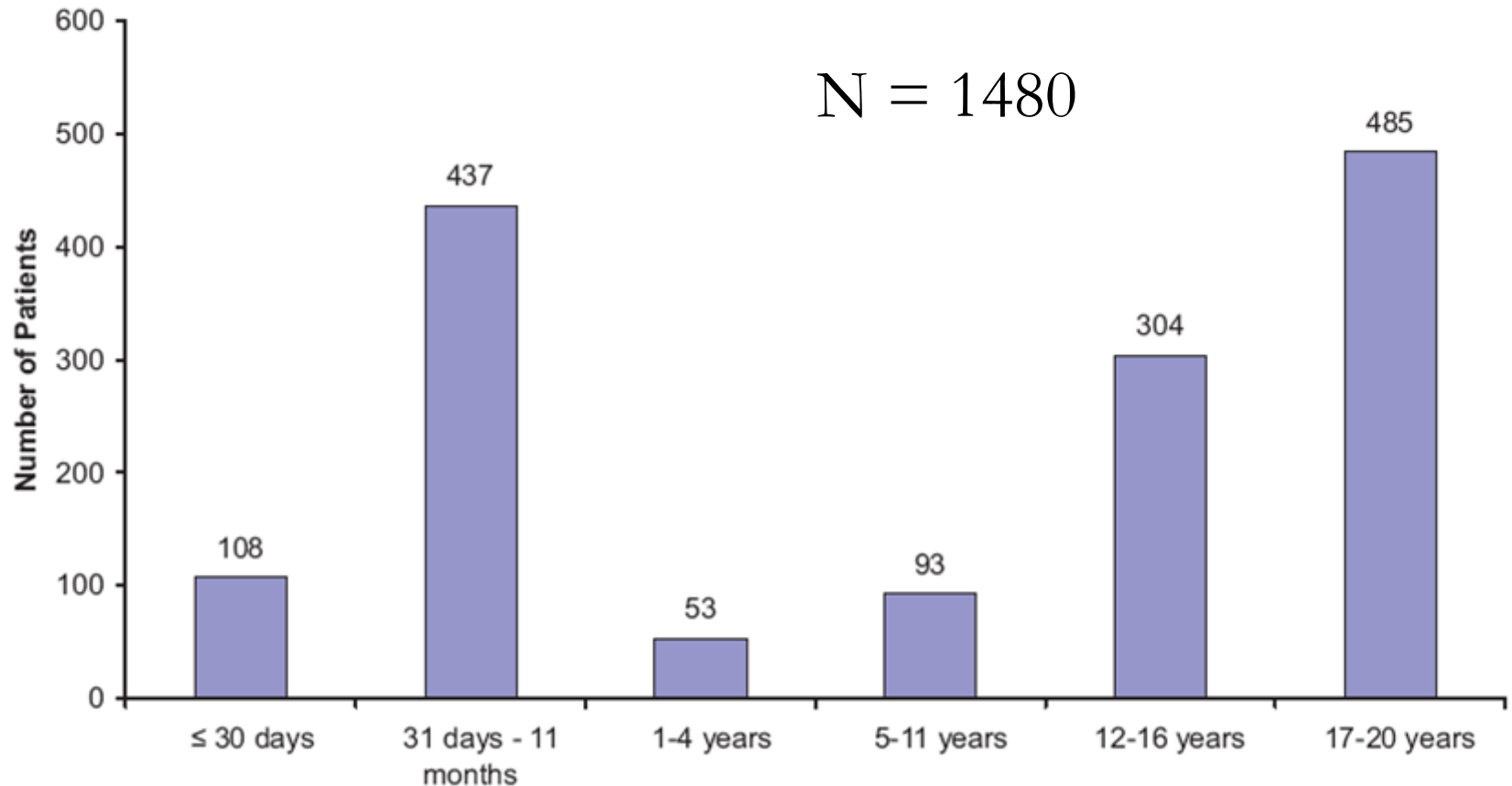
Parcours en 5 étapes

- Epidémiologie
 - Antibiothérapie
 - Chirurgie
 - Antibioprophylaxie
 - Aspirine
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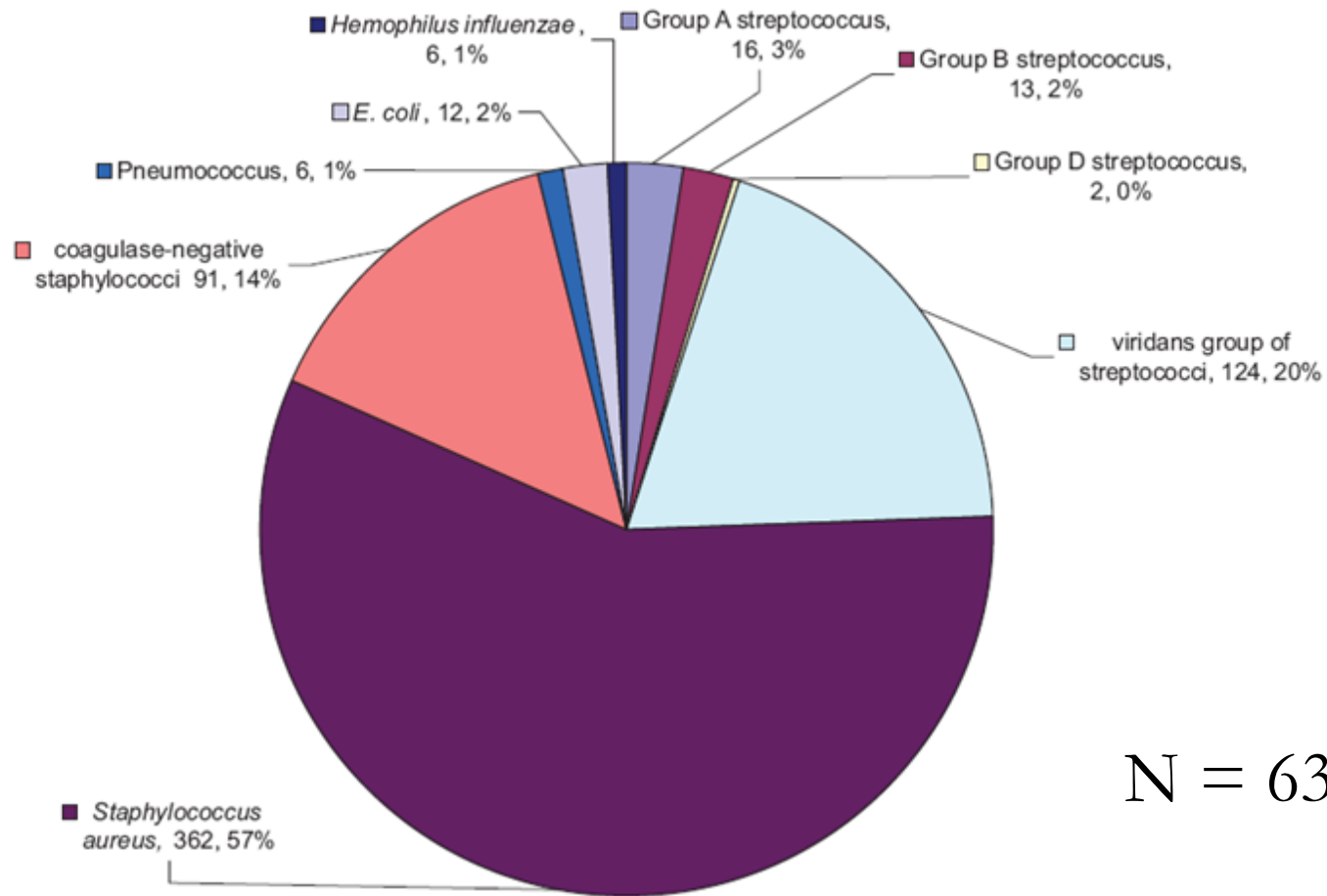
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Characteristics of Children Hospitalized With Infective Endocarditis

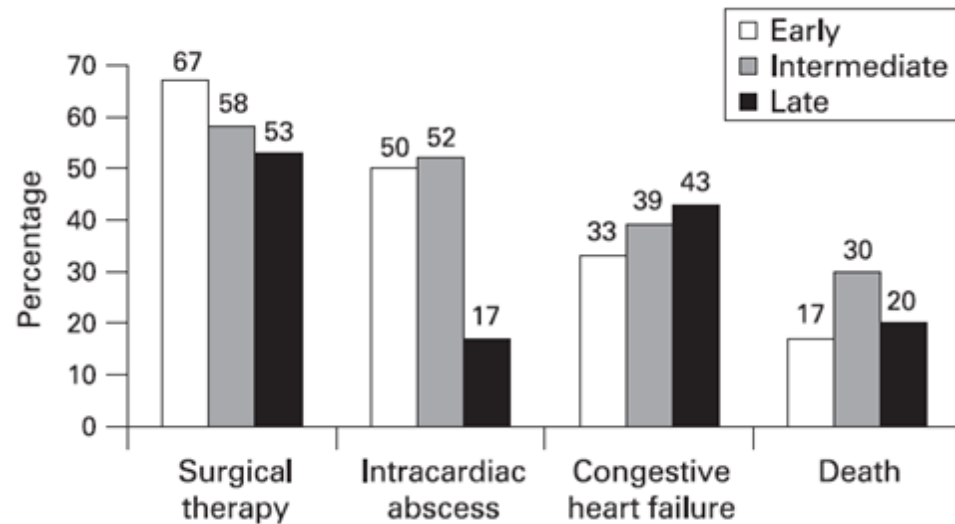
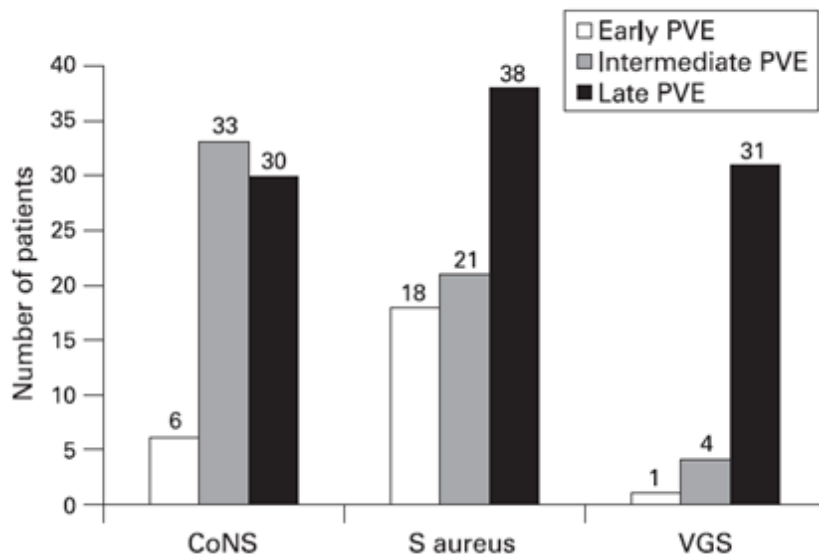


Characteristics of Children Hospitalized With Infective Endocarditis



Coagulase-negative staphylococcal PV IE: a contemporary update based on ICE-PCS

- 86 of 537 PVE IE were caused by CoNS



- Meti-resistance in 68% of CoNS strains

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Rifampin for Treatment of NV SA IE

- Etude cas-témoins (EI à SA sur VN – SAMS/R – CG/D)
 - 42 cas d'EI ayant reçu au moins une dose de RIF (méd 20 j)
 - 42 témoins appariés sur la date du diagnostic (2004-2005)

	cas	témoins	p
Sélection d'isolats RIF-R	9 (21%)	0	<0,001
Temps médian à RIF-R (n=9, jours, moy (range))	16 (11-26)	--	--
ALT > 5 x baseline	9 (21%)	1 (2%)	0,01
Interactions médicamenteuses	22 (52%)	0	<0,001

- Résultats complémentaires
 - Les résistances sont observées lorsque RIF a été introduite chez des patients encore bactériémiques
 - Mortalité plus élevée chez les cas (mais gravité possiblement plus élevée : plus de localisations SNC, plus d'AG)

Continuous versus Intermittent Infusion of Oxacillin for Rx of IE Caused by MSSA

■ Single-center retrospective study

- Continuous: 12 g daily over 24 h (n = 78)
- Intermittent: 2 g 6 times daily (n = 29)

	CI oxa N = 78	II oxa N = 29	P
30-day microbiological cure	73 (94)	23 (79)	0.03
30-day mortality	6 (8)	3 (10)	0.7
Time to apyrexia (days)	3	3	0.8
Duration of Ab Rx (days)	42	39	0.6
Co-administration of gentamicin	40 (51)	23 (79)	0.009

Continuous versus Intermittent Infusion of Oxacillin for Rx of IE Caused by MSSA

Outcome	No. (%) of patients or days ^a		<i>P</i> value	OR (95% CI) ^b
	With gentamicin (<i>n</i> = 63)	Without gentamicin (<i>n</i> = 44)		
30-Day mortality	7 (11)	2 (5)	0.2	2.63 (0.5–13.3)
Hospital LOS ^c	20	21	0.8	
30-Day microbiological cure	57 (91)	39 (89)	0.8	1.22 (0.4–4.3)
Clearance of bacteremia	7	9	0.9	
Time to defervescence	4	2	0.02	

In multivariate analysis, CI single predictor of 30-day microbiological cure

Initial Low-Dose Gentamicin for *S. aureus* Bacteremia and Endocarditis Is Nephrotoxic

Renal toxic effects, by randomized treatment arms

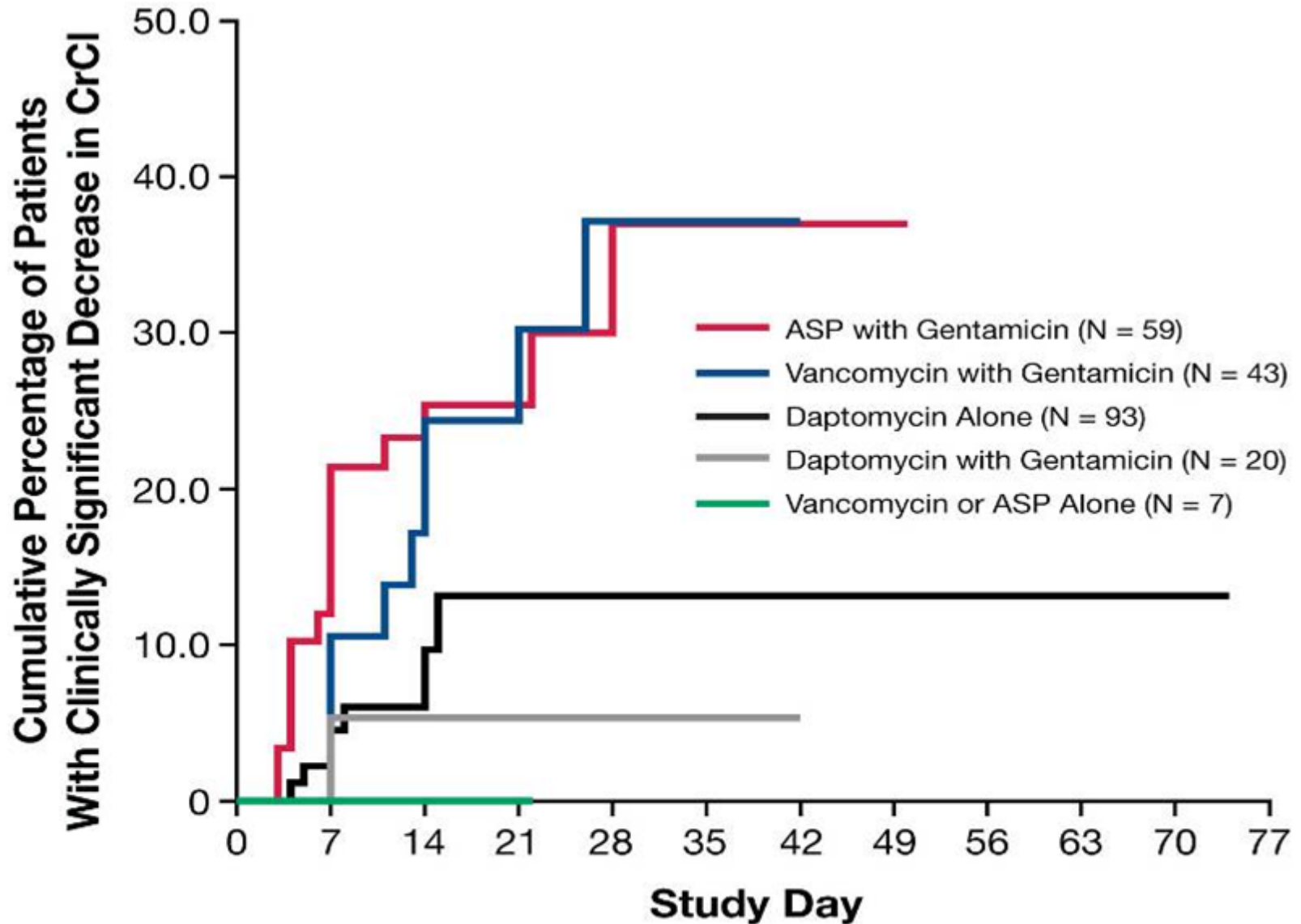
Toxic effect	Daptomycin arm	Standard therapy arm			
		Overall	<i>P</i> ^a	Vancomycin	ASP
Renal impairment adverse events					
Overall population	8/120 (7)	21/116 (18)	.01	10/53 (19)	11/63 (17)
Patients aged ≥65 years	2/30 (7)	12/38 (32)	.02	6/16 (38)	6/22 (27)
Patients with diabetes	3/44 (7)	12/42 (29)	.01	5/21 (24)	7/21 (33)
Clinically significant decrease in CrCl					
Overall population	9/113 (8)	26/109 (24)	.002	10/46 (22)	16/63 (25)
Patients aged ≥65 years	3/27 (11)	15/35 (43)	.01	5/13 (39)	10/22 (45)
Patients with diabetes	3/44 (7)	12/40 (30)	.01	5/19 (26)	7/21 (33)

Initial Low-Dose Gentamicin for *S. aureus* Bacteremia and Endocarditis Is Nephrotoxic

Incidence of decrease in creatinine clearance (CrCl)
by receipt of any initial low-dose gentamicin

	Received gentamicin, no. (%) of patients		<i>P</i> ^b
	Yes ^a (<i>n</i> = 122)	No ^a (<i>n</i> = 100)	
Decrease			
Clinically significant decrease in CrCl	27 (22)	8 (8)	.005
Sustained 50% decrease in CrCl	7 (6)	0 (0)	.02
Sustained 25% decrease in CrCl	26 (21)	9 (9)	.02
Discontinuation of use of study medication because of renal events	4 (3)	1 (1)	.38

Time to Clinically Significant Decrease in CrCl



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The impact of valve surgery on short- and long-term mortality in left-sided IE: do differences in methodological approaches explain previous conflicting results?

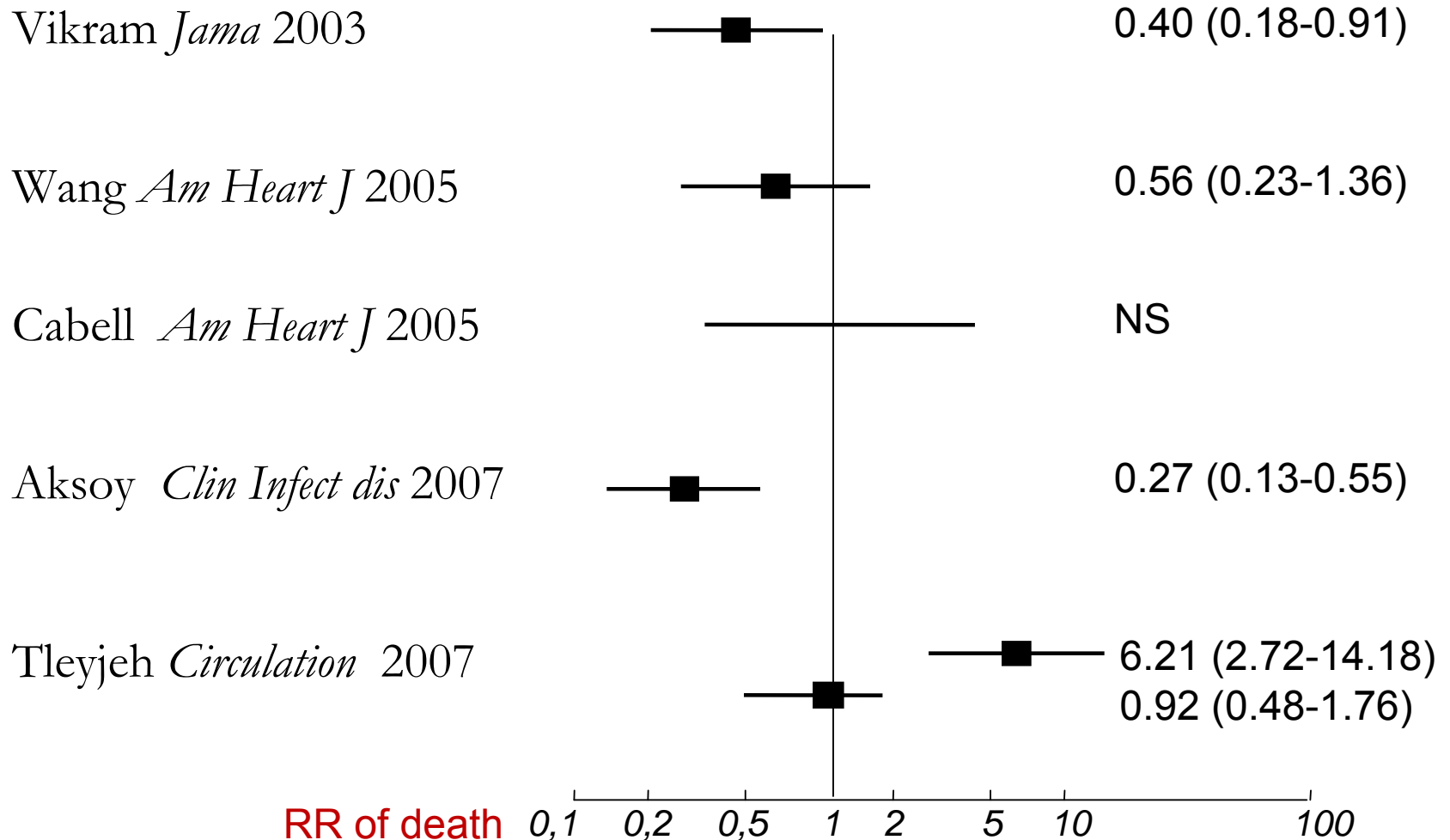
Overview of the 5 propensity analyses of the relation between early valve surgery and outcome of IE

	Vikram 2003	Wang 2005	Cabell 2005	Aksoy 2007	Tleyjeh 2007
N	513	367	1516	426	546
Valve Format Surg.	N–L Binary	P–L/R Binary	N–L/R Binary	N/P–L/R Binary	N/P–L time dep
Lead time	6 mo	Hospit	Hospit	5 years	6 mo
Mortality	⑧	⑨	⑨	↓	⑥

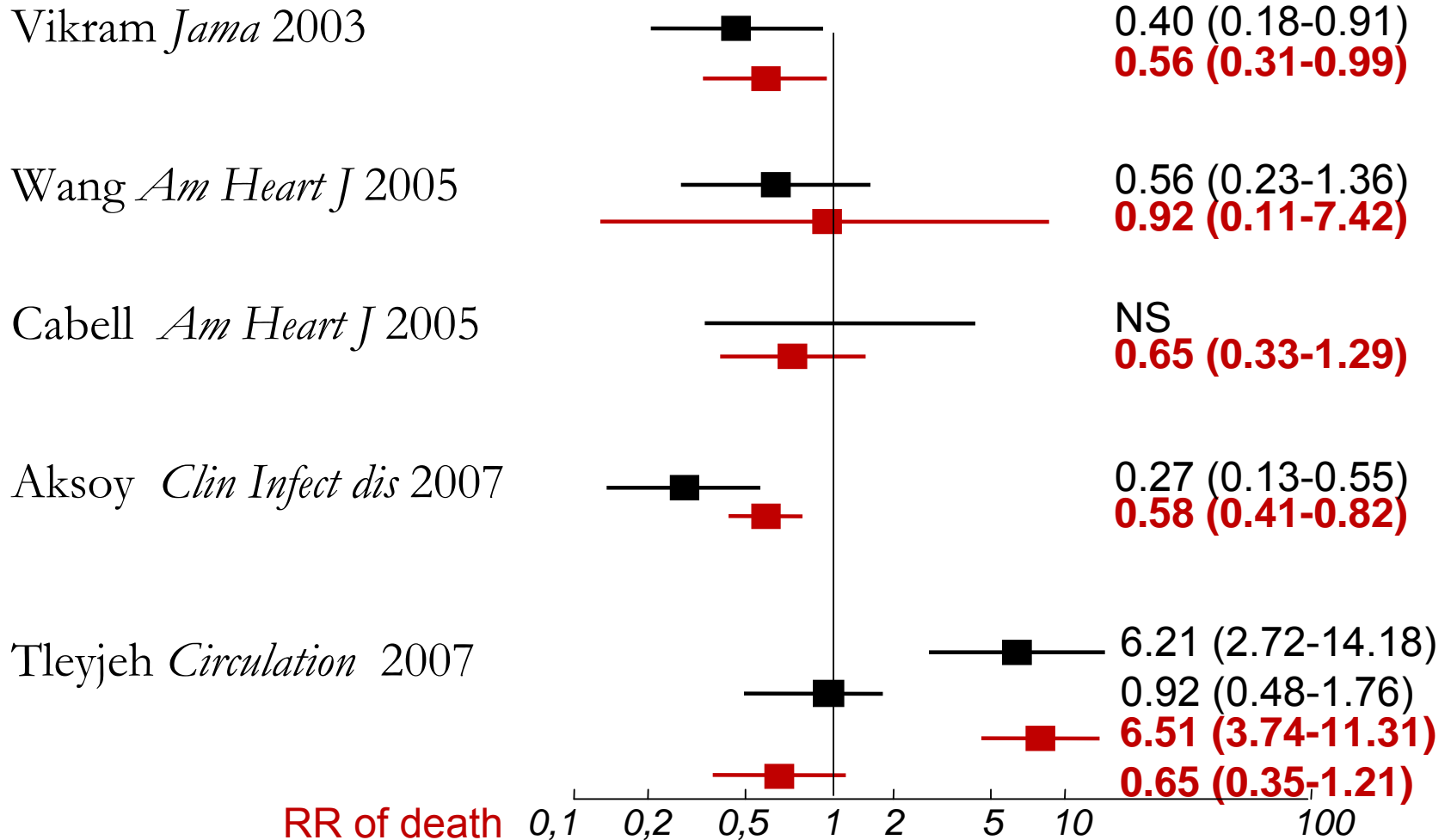
Objective and methods

- **Objective:** to evaluate whether conflicting results reported by previous studies could be explained by differences in their methodological approaches.
- **Methods**
 - Population: 559 IE patients from the French nationwide 1999 study, followed up for 5 years
 - Statistical analysis: we re-analyzed the relationship between valve surgery and mortality in our database, using each of the methods used in the five previous studies (i.e. inclusion criteria, follow-up duration, statistical model, surgery coding)

Results



Results



Relationship between early valve surgery and mortality (left-sided valve IE)

	Adjusted RR	
Post-operative surgery risk (0-14 days)	3.69 (2.17-6.25)	} Equity point = 188 Days
Long-term surgery risk (15 days-5 years)	0.55 (0.35-0.87)	

Conclusion

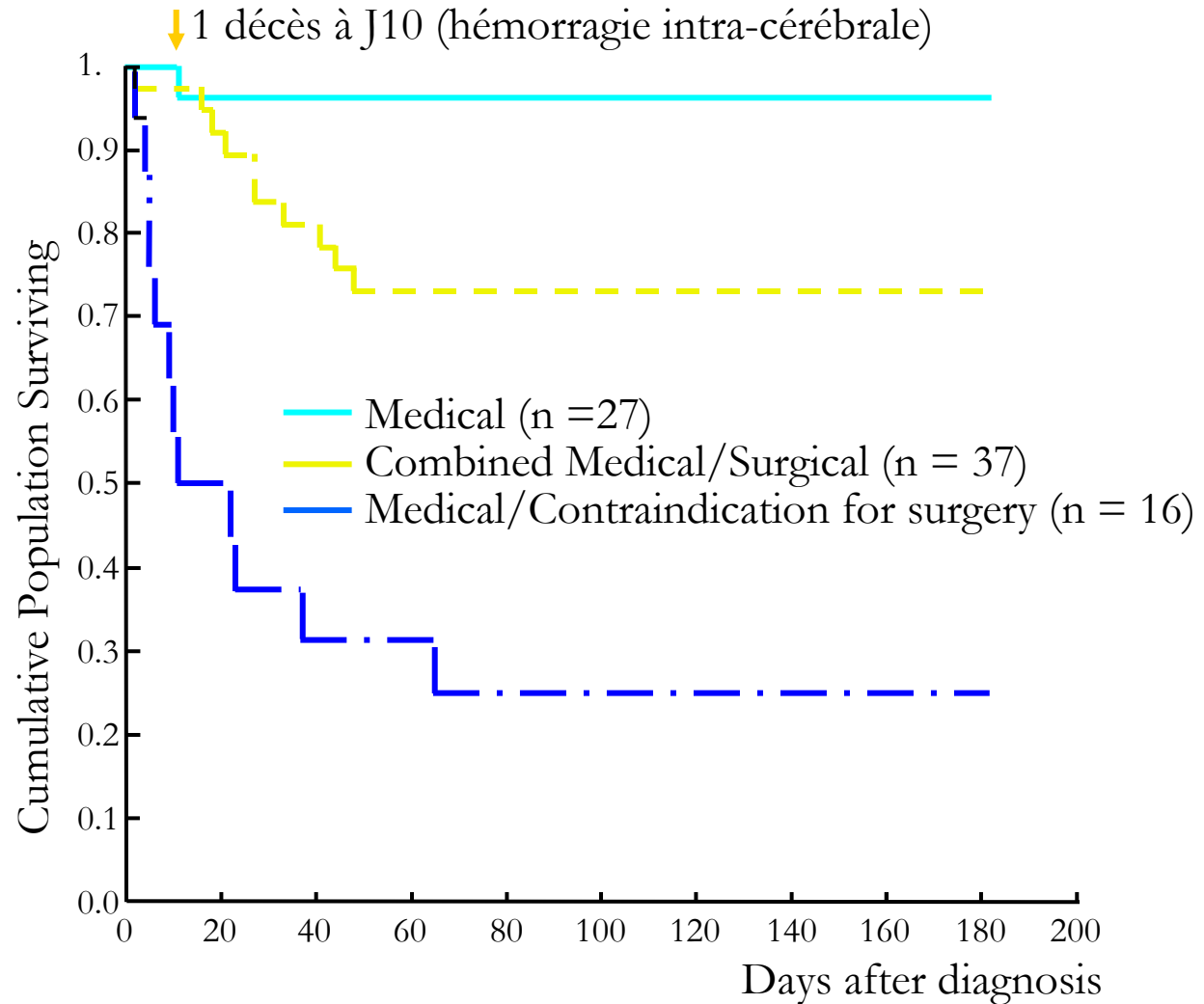
- ▶ Valve surgery is significantly associated with reduced long-term mortality in left-sided valve IE patients
- ▶ Conflicting results between previous reports could be due to differences in methods used ... and propensity analysis may not be the magic bullet some thought it could be
- ▶ Further well-designed studies are needed to:
 - ▶ better estimate the influence of VS on prognosis
 - ▶ define which patients would benefit the most from VS
 - ▶ define the best timing for VS during the acute phase

Management of prosthetic valve infective endocarditis

- Décrire et comparer les caractéristiques cliniques et la mortalité à 6 mois des EI/PV opérées *vs.* EI/PV non opérées (cohorte observationnelle – 2000 à 2006)
- 80 EI sur prothèse valvulaire (mécanique ou biologique)
 - traitement médico-chirurgical, n = 37
 - traitement médical choisi, n = 27
 - traitement médical "forcé", n = 16
- Délai médian entre le diagnostic et la chirurgie :
 - tous germes confondus : 9 jours
 - *S. aureus* : 3,5 jours

Management of prosthetic valve infective endocarditis

Taux de mortalité à 6 mois :
23/80 (29%)



Survie à 6 mois (courbe de Kaplan-Meier)

Management of prosthetic valve infective endocarditis

Mortality by pathogen and treatment

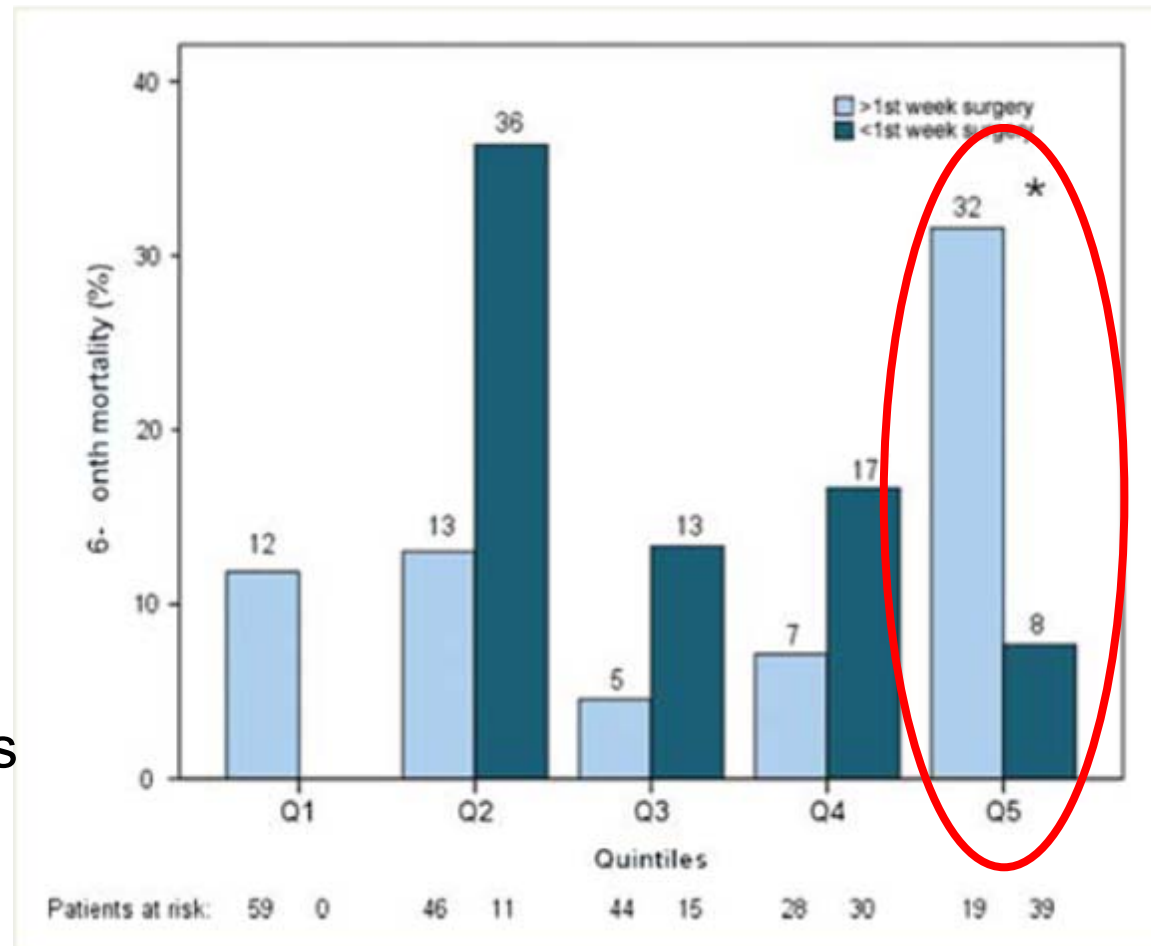
Mortality	Surgery (n = 37)	Deliberately conservative (n = 27)	Perforce conservative (n = 16)
Staphylococci	8 (22%)	0	8 (50%)
<i>S. aureus</i> (n = 23)	5 /12	0 /5	6 /6
Streptococci	0	0	0 0
Enterococci	1 (3%)	0	3 (19%)
Other micro-organisms	1 (3%)	1 (4%)	1 (6%)
Total mortality	10 (27%)	1 (4%)	12 (75%)

The timing of surgery influences mortality and morbidity in adults with severe complicated IE: a propensity analysis

	≤1st week surgery group (n = 95)	>1st week surgery group (n = 196)	P-value
6-month mortality	14 (15)	23 (12)	0.47
Relapses and postoperative valvular dysfunction	15 (16)	7 (4)	0.0005
Relapses	8 (8)	4 (2)	0.02
Postoperative valvular dysfunction	7 (7)	3 (2)	0.02

The timing of surgery influences mortality and morbidity in adults with severe complicated IE: a propensity analysis

- Patients of the 5th quintile
 - were younger
 - were more likely to have
 - Sa IE
 - CHF
 - larger vegetations



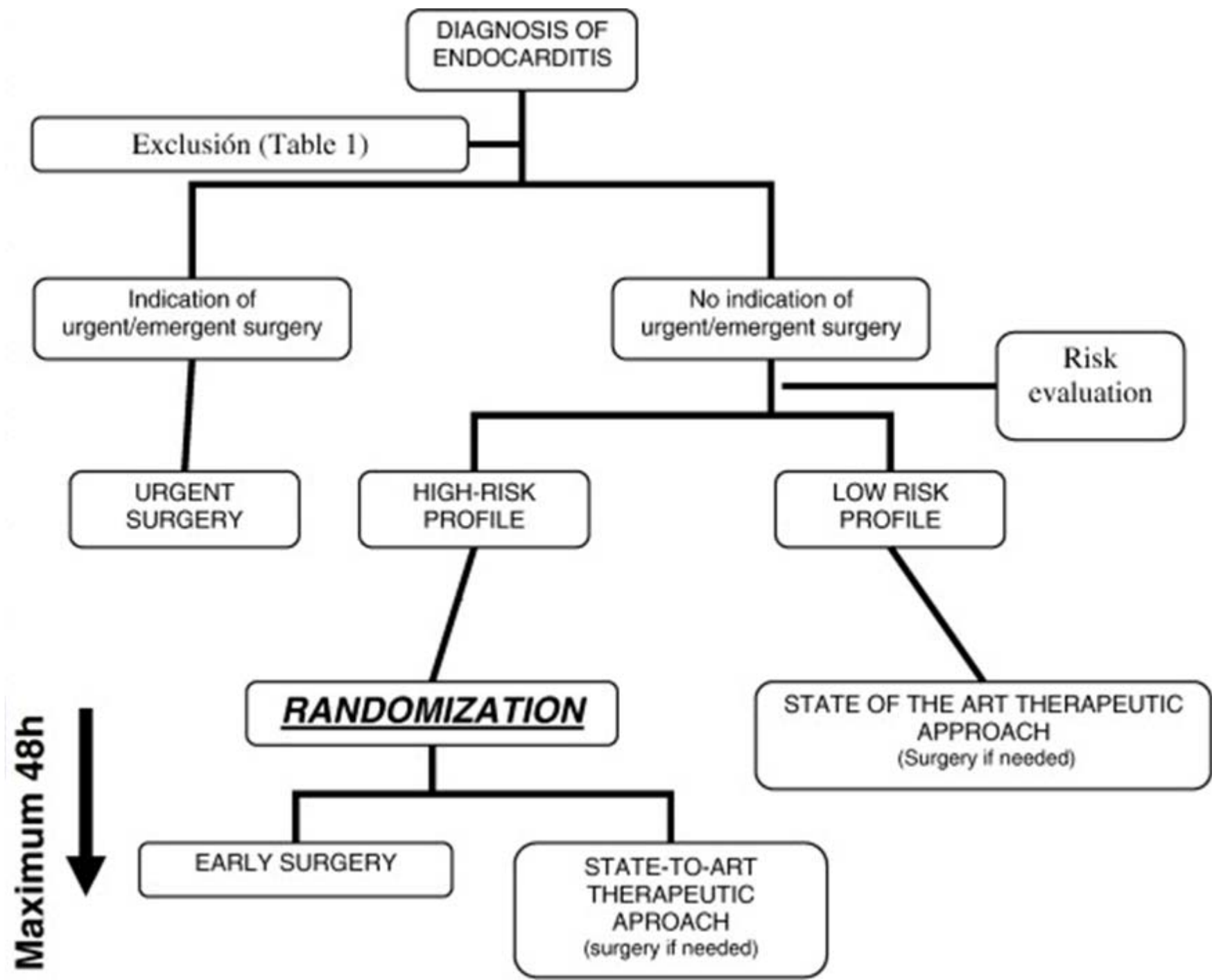
A clinical trial to move forward?

Rationale, design, and methods for the early surgery in infective endocarditis study (ENDOVAL 1): A multicenter, prospective, randomized trial comparing the state-of-the-art therapeutic strategy versus early surgery strategy in infective endocarditis

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Study objectives and inclusion criteria

- to compare the 30-day mortality rate in high-risk patients with active infective endocarditis between
 - an early surgical approach (surgery within the first 48 hours after inclusion or 5 days after initial diagnosis)
 - and the state-of-the-art treatment in this disease (medical treatment followed by elective surgery)
- Inclusion criteria
 - Patients >18 years old.
 - Duke definite IE
 - At least one of the following risk factors:
 - Periannular complications
 - New onset auriculo-ventricular block
 - New onset severe valvular insufficiency
 - Early-onset prosthetic valve endocarditis
 - *Staphylococcus aureus* endocarditis
- Exclusion criteria
 - Urgent indication for surgery
 - Patients referred for surgery



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 - **Antibioprophylaxie**
 - Aspirine
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National Institute for Health and Clinical Excellence : prophylaxis against infective endocarditis

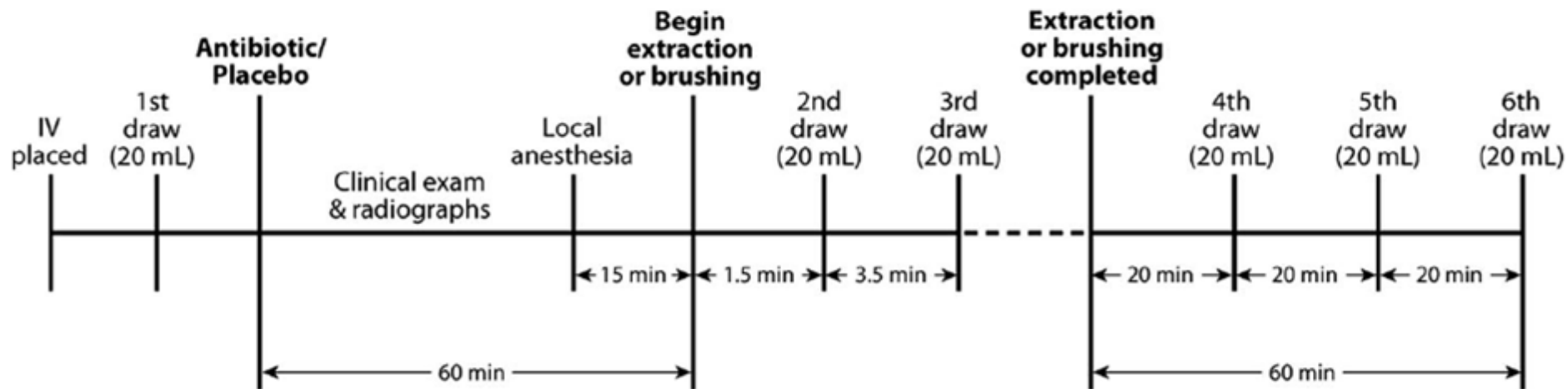
- Antibiotic prophylaxis against infective endocarditis is not recommended :
 - for people undergoing dental procedures
 - for people undergoing the following non-dental procedures:
 - upper and lower gastrointestinal tract
 - genitourinary tract ; this includes urological, gynaecological and obstetric procedures, and childbirth
 - upper and lower respiratory tract ; this includes ear, nose and throat procedures and bronchoscopy
- Chlorhexidine mouthwash should not be offered as prophylaxis against infective endocarditis undergoing dental procedures

ACC/AHA 2008 guidelines update on valvular heart disease : focused update on infective endocarditis

- Recommandations de classe IIa (classe II : "benefit >> risk, it is reasonable to perform/administer treatment")
- L'antibioprophylaxie est recommandée pour :
 - les gestes concernant la sphère bucco-dentaire : actes invasifs touchant soit la gencive, soit la région périapicale des dents ou actes entraînant une plaie de la muqueuse buccale
 - les gestes concernant la sphère ORL \Leftrightarrow patients à haut risque+atteinte muqueuse (ex. : adénoïdectomie et amygdalectomie)
- L'antibioprophylaxie n'est plus recommandée pour
 - les gestes concernant la sphère ORL (sauf exceptions ci-dessus)
 - les gestes touchant la sphère digestive et la sphère urologique

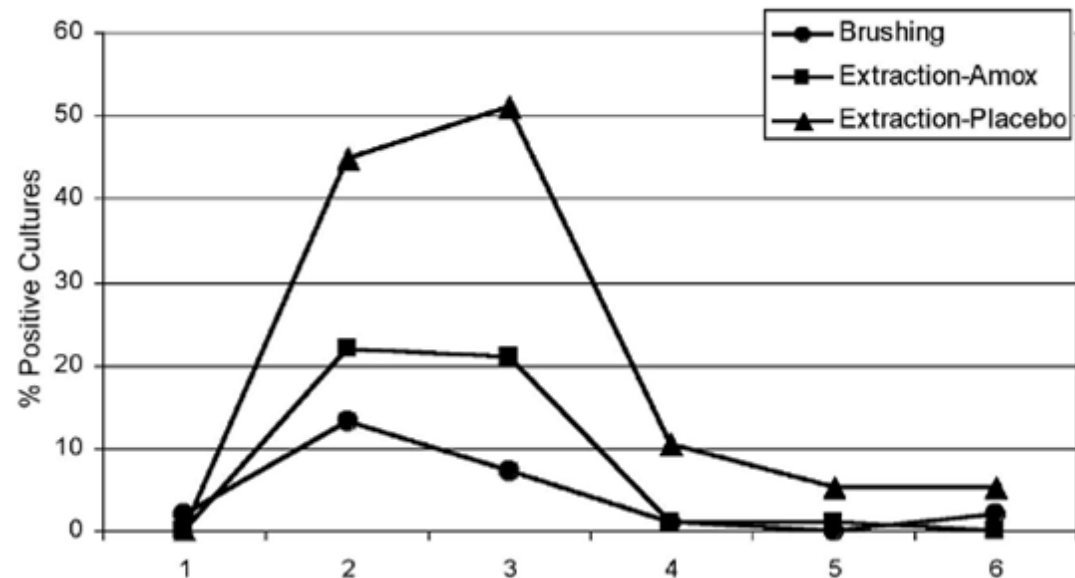
Bacteremia Associated With Toothbrushing and Dental Extraction

- Patients presented to urgent care service with the need for extraction of at least 1 erupted tooth
- Exclusion criteria
 - fewer than 10 teeth; use of systemic antibiotics within the previous 2 weeks
 - need for antibiotic prophylaxis based on current guidelines
 - systemic disease; history of penicillin allergy;
 - temperature 100.5°F; facial cellulitis
 - manipulation of the gingival tissues (eg, chewing, toothbrushing) within 1 hour



Bacteremia Associated With Toothbrushing and Dental Extraction

- 600 patients screened, 290 randomized
 - 98 toothbrushing
 - 96 extraction+amox
 - 96 extraction+Pcb
- 98 bacteremia
 - 32 IE-causing bacteria
 - Similar magnitudes ($4 \log_{10}$ CFU/ml) in all groups



Is antibiotic prophylaxis for dental extraction relevant?

Parcours en 5 étapes

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 - Antibioprophylaxie
 - **Aspirine**
-

Effect of long-term aspirin use on embolic events in infective endocarditis

- Post-hoc analysis of patients screened for enrolment in the MATIE trial
 - Patients excluded because of long-term aspirin treatment (n = 84)
 - Patients randomized to placebo arm (n = 55)

Effect of long-term aspirin use on bleeding and embolism

Outcome	Unadjusted Model		Adjusted Model *	
	OR (95% CI)	p	OR (95% CI)	p
Bleeding	2.35 (0.97 – 5.70)	.059	2.08 (0.83 – 5.23)	.118
Embolism	0.80 (0.36 – 1.78)	.582	0.91 (0.40 – 2.07)	.825

* Adjusted for age and clinical characteristics

Chronic antiplatelet therapy and mortality among patients with infective endocarditis

- Retrospective study in Canada, 1991-2006
 - Modified Duke criteria for definite/possible IE
 - Chronic antiplatelet therapy (CAPT): ASA or clopidogrel for > 6 months prior to admission
 - 241 patients, of whom 75 patients had CAPT
 - Predictors of embolism
 - Decreased risk: older age
 - Increased risk: vegetation size, CHF, heart block
 - No effect: CAPT
-

Chronic antiplatelet therapy and mortality among patients with infective endocarditis

■ Predictors of increased mortality

- ❑ Higher age,
- ❑ High Charlson comorbidity score
- ❑ Aortic valve involvement,
- ❑ perivalvular abscess

■ Predictors of decreased mortality

- ❑ Valve replacement: aOR 0.28, 95% CI 0.09-0.84
- ❑ **CAPT:** aOR 0.27, 95% CI 0.11-0.64
no dose effect (ASA 325 mg or 80 mg)