Infective Endocarditis

MO ACP Hospitalist day, Osage Beach, MO. September 9, 2021

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EDUCATION/TRAINING :

MBBS 1999-2004 from Madurai Medical College , Madurai, India
MD (Gen Med) 2006-2009 from KMC, Manipal, India
ABIM residency (2010-13)/ABID fellowship(2013-15)/ABCC fellowship (2015-16) – University of Missouri – Columbia, MO

INTERESTS :

COVID-19, ARDS, Nosocomial Infections, Infective Endocarditis, Clinical Microbiology, CMV, Travel medicine.

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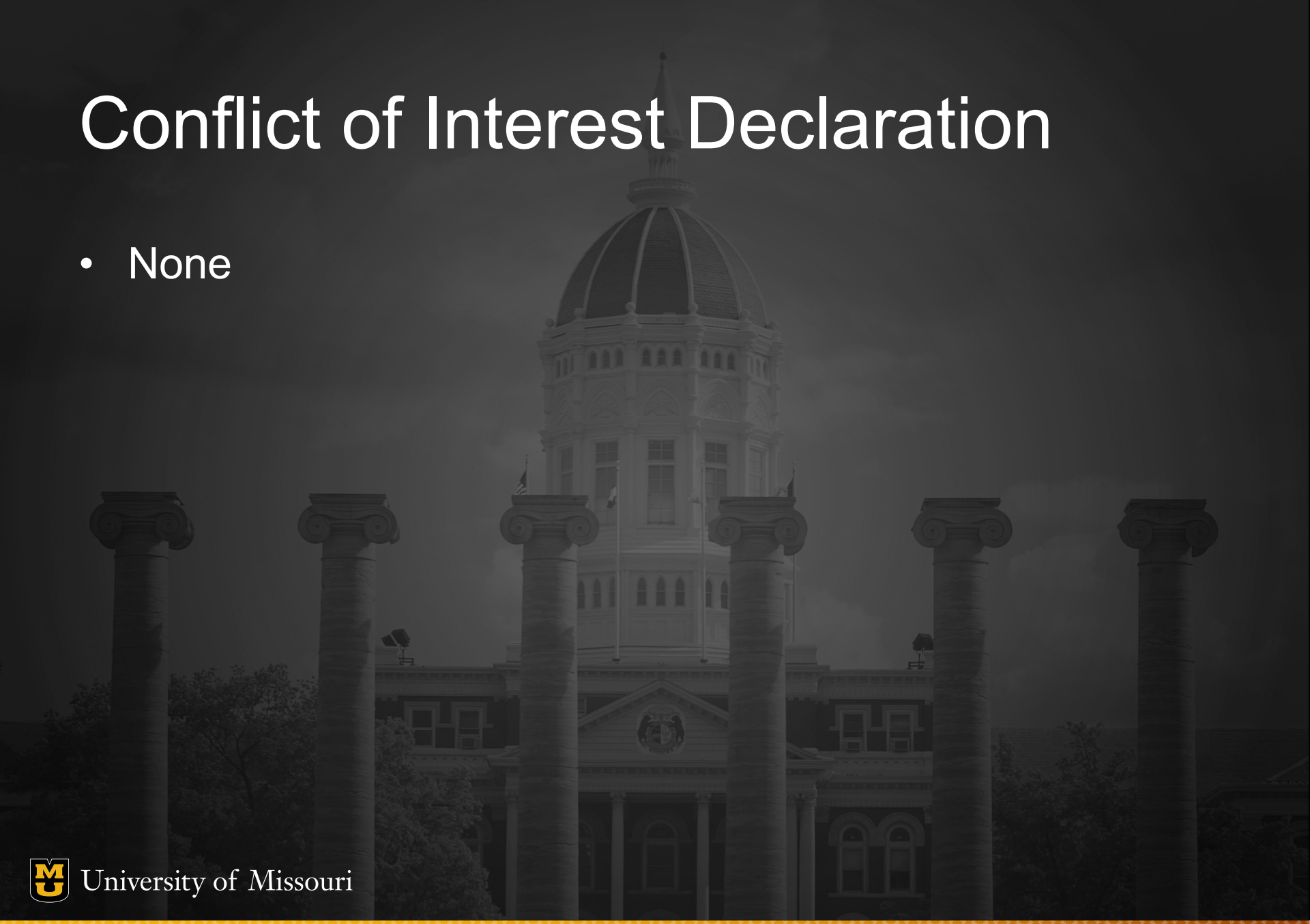
Conflict of Interest Declaration

- None



Synopsis

- Epidemiology
- Duke Criteria
- Clinical Management
  - Diagnosis
  - Treatment
  - Early surgical intervention and Barriers
- Multi-disciplinary team development
- IVDU
- *Will not be a regurgitation of guidelines!*

Epidemiology

- Annual incidence: 3-7/100,000 person years worldwide
- As a syndrome, 4th common cause of life-threatening infection
- 1.58 million DALYs
- > 50% are > 50 years of age (M>F)
  - If < 35 years of age F>M
- Complex disease
  - Require management by a TEAM of physicians
  - Recommendations be used to support and not supplant decisions in individual patient management

Lancet. 2012 Dec 15;380(9859):2197-223; Circulation 132.15 (2015): 1435-1486: JAMA. 2005 Jun 22;293(24):3012-21

Classification

- Duration of onset:
  - Acute: <2 weeks
  - Sub-acute: 2-6 weeks
- Disease types:
  - Native valve endocarditis
  - Prosthetic valve endocarditis
  - Cardiac device associated endocarditis
  - Drug-abuse related endocarditis
- Mode of acquisition:
  - Community acquired or Non health care associated
  - Health care associated
    - History of receiving intravenous therapy (including chemotherapy)
    - Transfer from a specialized nursing care facility
    - Hemodialysis
    - Hospitalization for 2 days or longer in the 90 days before the index admission

JAMA. 2017 Apr 25; 317(16): 1652–1660

Risk

Highest risk

- Valve prosthesis (valve itself or material used for repair)
  - Higher mortality
  - Higher rate of complications
- Prior H/o IE
- Untreated cyanotic congenital heart diseases (CHD) w/wo palliative shunts/ conduits/ prosthesis

At risk

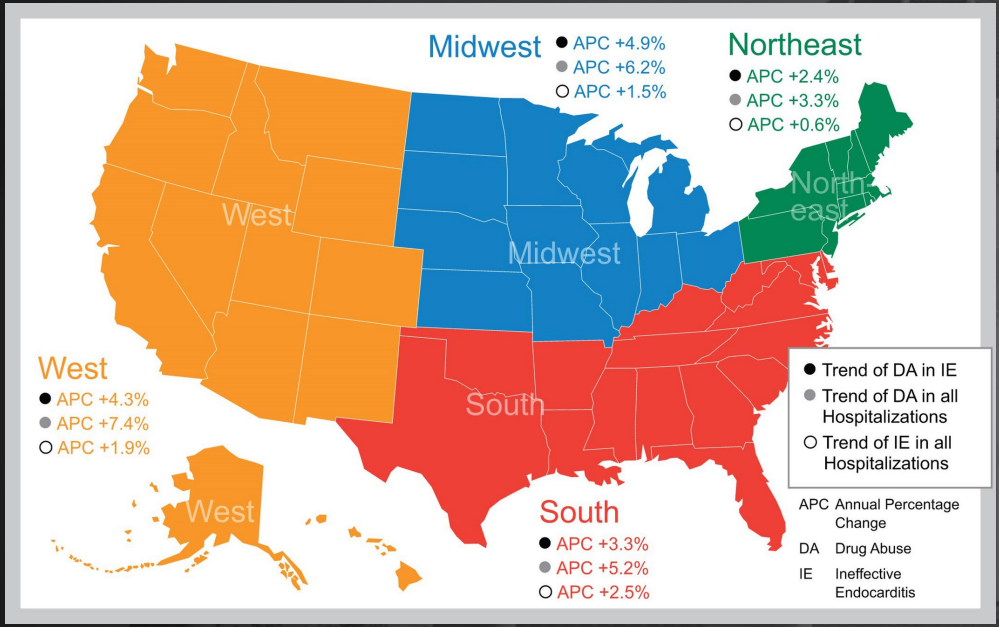
- Degenerative valve disease
- Diabetes Mellitus
- Intra-venous drug user
- Intra-vascular devices – Catheters, CIED

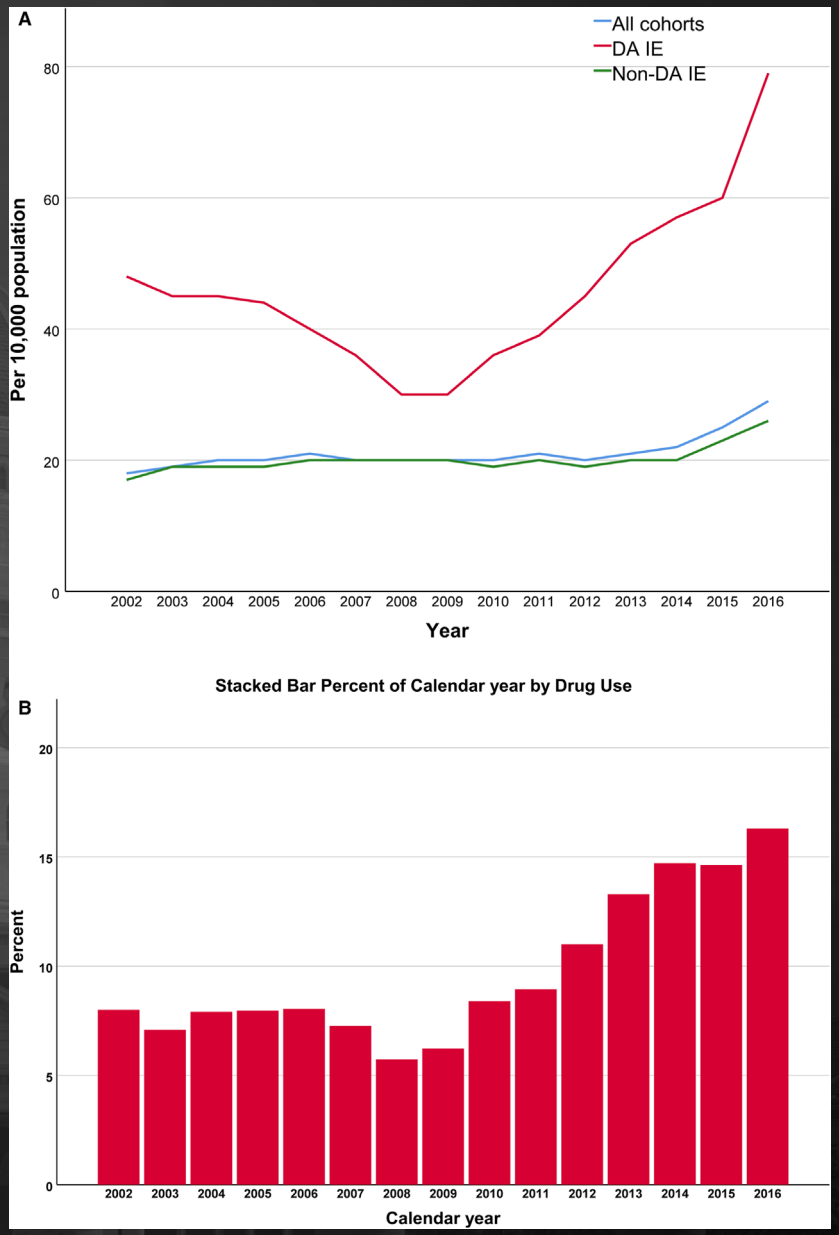
Lancet. 2016 Feb 27;387(10021):882-93

JAMA internal medicine. 2013 Sep 9;173(16):1495-504.

European heart journal. 2015 Nov 21;36(44):3075-128.

Drug Abuse - IE





Kadri, Amer N., et al. "Geographic trends, patient characteristics, and outcomes of infective endocarditis associated with drug abuse in the United States from 2002 to 2016." *Journal of the American Heart Association* 8.19 (2019): e012969.

Drug Dependance - IE

FIGURE 1. Incidence* of hospital discharge diagnoses of drug dependence–associated endocarditis,† by age group — North Carolina, 2010–2015

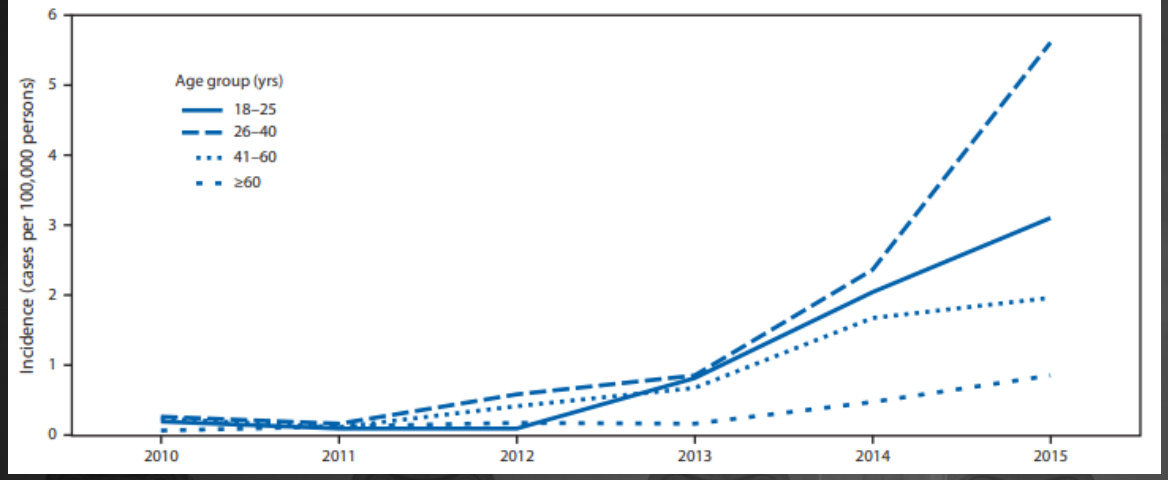
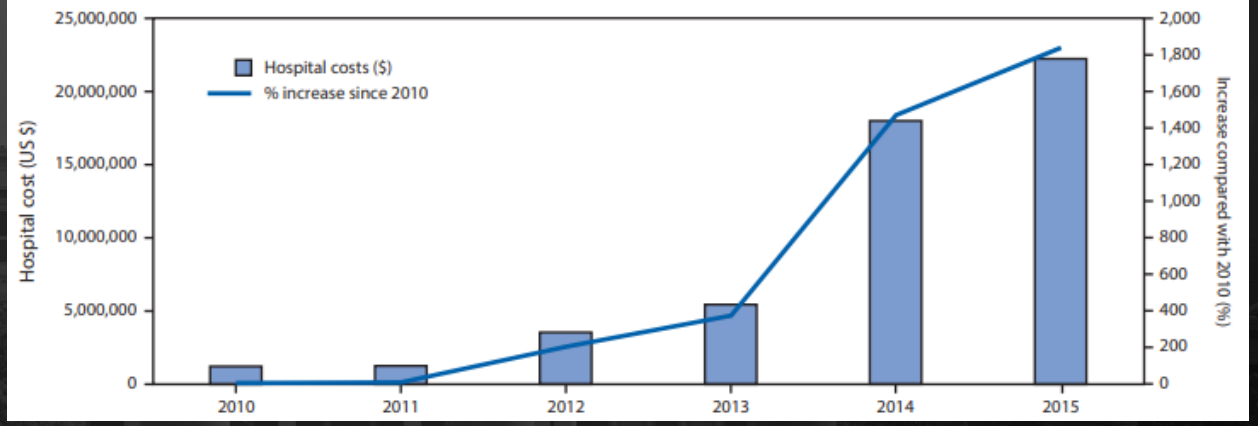


FIGURE 2. Hospital costs for persons with drug dependence–associated endocarditis and percentage increase since 2010 — North Carolina, 2010–2015



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Fleischauer AT, et al. E. Hospitalizations for Endocarditis and Associated Health Care Costs Among Persons with Diagnosed Drug Dependence — North Carolina, 2010–2015. MMWR Morb Mortal Wkly Rep 2017;66:569–573

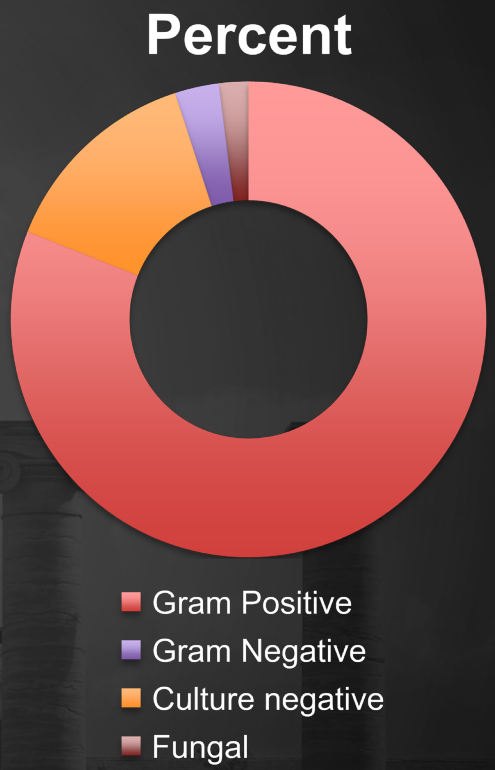
Microbiology

Microbiologic etiology by region in 2781 patients with definite endocarditis.

	Total Cohort n = 2781 n (%)	Patients admitted directly to study sites only[a] n= 1558 n (%)	Region				P value for the difference between regions
			North America n = 597 n (%)	South America n = 254 n (%)	Europe n = 1213 n (%)	Other n = 717 n (%)	
S. aureus	869 (31)	487 (31)	256 (43)	43 (17)	339 (28)	231 (32)	<0.001
Coag Neg staph.	304 (11)	161 (10)	69 (12)	18 (7)	156 (13)	61 (9)	0.005
Viridans group strep	483 (17)	288 (19)	54 (9)	66 (26)	198 (16)	165 (23)	<0.001
S. bovis	165 (6)	101 (7)	9 (2)	17 (7)	116 (10)	23 (3)	<0.001
Other strep	162 (6)	101 (7)	38 (6)	16 (6)	66 (5)	42 (6)	0.86
Enterococci	283 (10)	158 (10)	78 (13)	21 (8)	111 (9)	73 (10)	0.05
HACEK	44 (2)	26 (2)	2 (0.3)	6 (2)	19 (2)	17 (2)	0.02
Fungi / yeast	45 (2)	25 (2)	20 (3)	3 (1)	13 (1)	9 (1)	0.002
Polymicrobial	28 (1)	23 (2)	8 (1)	1 (0.4)	13 (1)	6 (1)	0.60
Culture negative	277 (10)	122 (8)	41 (7)	51 (20)	123 (10)	62 (9)	<0.001
Other	121 (4)	66 (4)	22 (4)	12 (5)	59 (5)	28 (4)	0.61

Abbreviations : strep = streptococci; HACEK = *Haemophilus spp., Aggregatibacter* (formerly *Actinobacillus) actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens,* and *Kingella* species; PVIE = prosthetic valve infective endocarditis.

[a]Excludes patients transferred to study hospitals from other health care facilities



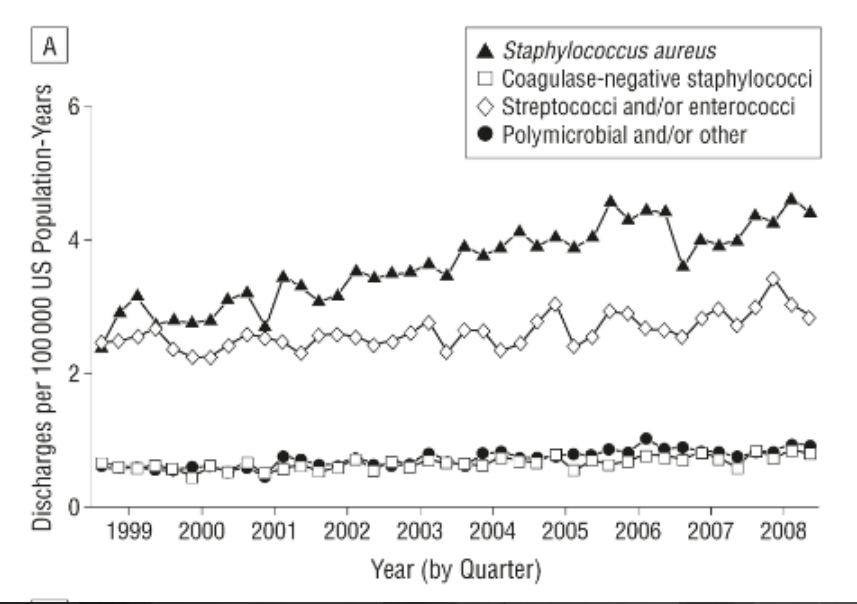
Arch Intern Med. 2009 Mar 9; 169(5): 463–473; JAMA. 2005 Jun 22;293(24):3012-21

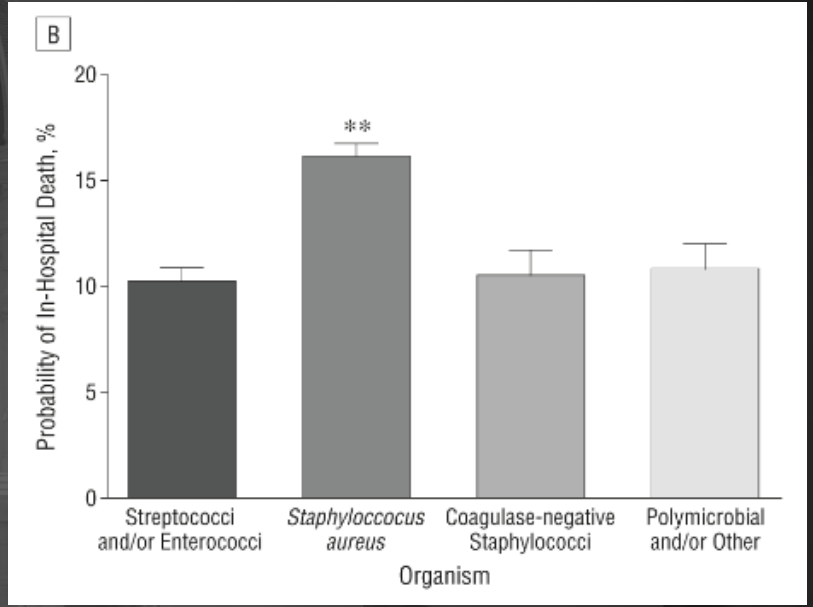
Microbiology

Organism	Native Valve Endocarditis		Prosthetic Valve Endocarditis at Indicated Time of Onset (Months) after Valve Surgery			Endocarditis in Injection Drug Users		
	Community-Acquired (n = 1718)	Health Care–Associated (n = 1110)	<2 (n = 144)	2–12 (n = 31)	>12 (n = 194)	Right-Sided (n = 346)	Left-Sided (n = 204)	Total (n = 675)[a]
Streptococci[b]	40	13	1	9	31	5	15	12
Pneumococci	2	—	—	—	—	—	—	—
Enterococci[c]	9	16	8	12	11	2	24	9
Staphylococcus aureus	28	52[d]	22	12	18	77	23	57
Coagulase-negative staphylococci	5	11	33	32	11	—	—	—
Fastidious gram-negative coccobacilli (HACEK group)[e]	3	—	—	—	6	—	—	—
Gram-negative bacilli	1	1	13	3	6	5	13	7
Candida spp.	<1	1	8	12	1	—	12	4
Polymicrobial/miscellaneous	3	3	3	6	5	8	10	7
Diphtheroids	—	<1	6	—	3	—	—	0.1
Culture-negative	9	3	5	6	8	3	3	3

Karchmer AW. Infective Endocarditis. In: *Harrison's Principles of Internal Medicine, 19e* NY: McGraw-Hill; 2014. Accessed January 01, 2018.

Microbiologic Trends





- Health care associated NVE: CVC/PICC, Pacemakers, Hemodialysis access, etc.
  - Higher mortality, Higher costs, Recurrent hospitalizations, etc
- ***S. aureus*** - commonest cause in 21st century, especially if health-care associated

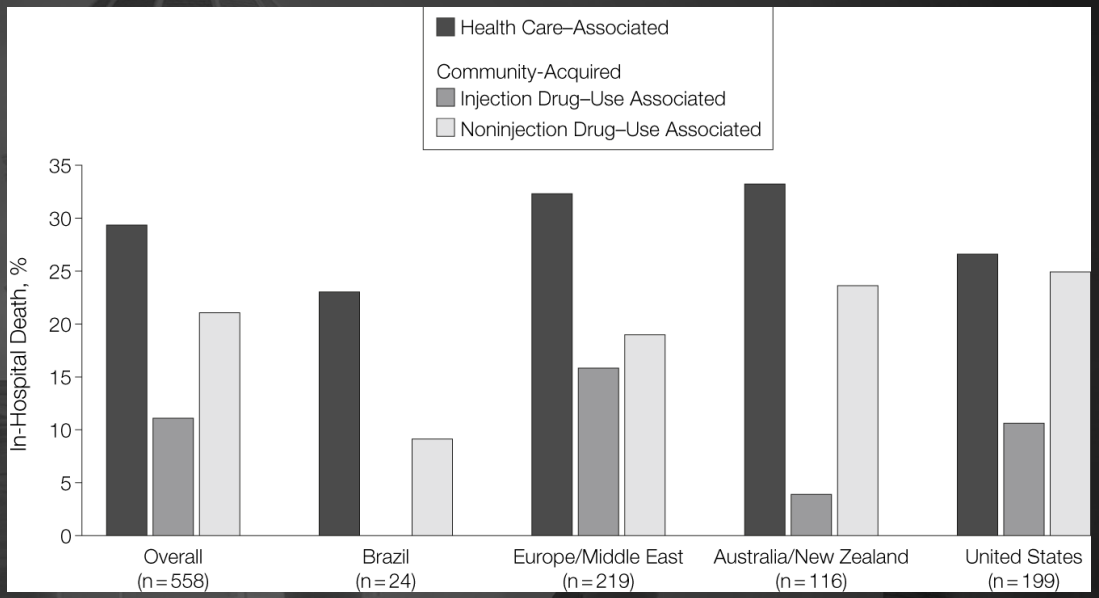
Arch Intern Med. 2012 Feb 27; 172(4): 363–365.; Arch Intern Med. 2009 Mar 9; 169(5): 463–473

Table 1. Microbiologic Etiology in 1779 Patients With Definite Endocarditis

	No. (%)
Staphylococcus	
S aureus	558 (31.6)
Coagulase-negative staphylococci	186 (10.5)
Streptococcus	
Viridans group streptococci	319 (18.0)
Streptococcus bovis	114 (6.5)
Other streptococci	91 (5.1)
Enterococci	188 (10.6)
HACEK	30 (1.7)
Non-HACEK gram-negative bacteria	38 (2.1)
Fungi	32 (1.8)
Polymicrobial	23 (1.3)
Other*	56 (3.1)
Culture negative	144 (8.1)

Abbreviation: HACEK, *Haemophilus* species (except *H influenzae*), *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species.

*Other organisms include: *Corynebacterium* species 10 (12.5%); *Gemella* species 7 (12.50%); *Lactobacillus* species 4 (7.14%); *Peptostreptococcus* 3 (5.36%); *Erysipelothrix rhusiopathiae* 2; *Lactococcus* species 2; *Actinomyces* species 2; *Bacillus* species 2; *Listeria monocytogenes* 1; *Rhodococcus* species 1; *Nocardia* species 1; *Mycobacterium fortuitum* 1; and *Micromonas micros* 1. For 2 patients, the microbiologic organism was not speciated.

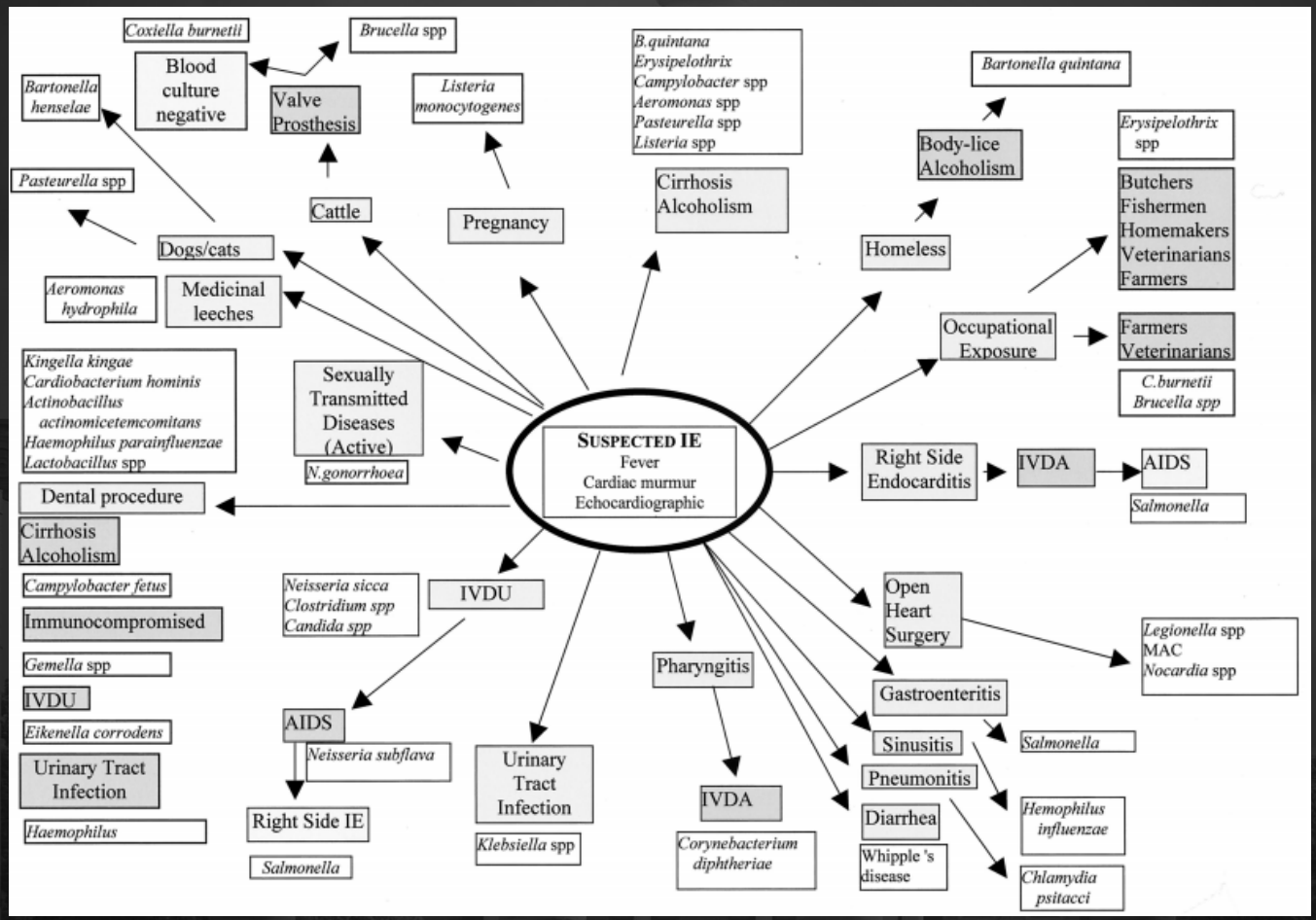


Fowler VG Jr, Miro JM, Hoen B, Cabell CH, Abrutyn E, Rubinstein E, Corey GR, Spelman D, Bradley SF, Barsic B, Pappas PA, Anstrom KJ, Wray D, Fortes CQ, Anguera I, Athan E, Jones P, van der Meer JT, Elliott TS, Levine DP, Bayer AS; ICE Investigators. Staphylococcus aureus endocarditis: a consequence of medical progress.

Take home message

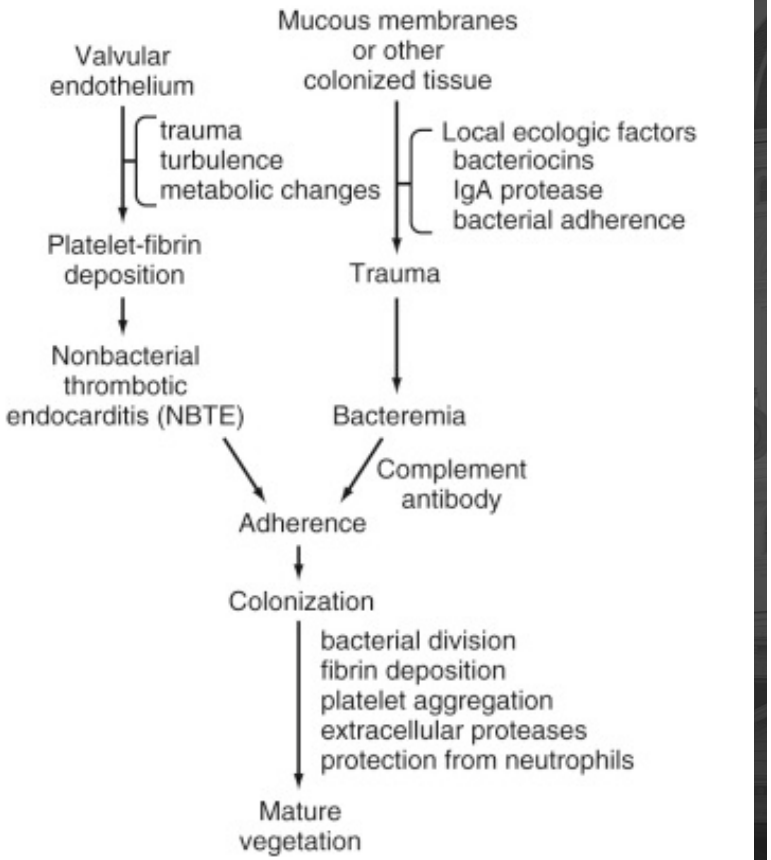
- Always think about IE in *S. aureus* bacteremia (SAB)
  - *Consider IE in differential for community acquired Enterococcus and Viridans Strep bacteremia.*
- Remember the "All or None" rules for (SAB)
  1. Fever and other s/s sepsis resolve in 48-72 hours
  2. Blood culture negative with appropriate therapy in 48-72h
  3. TEE negative or TTE with very good window for left heart valves
  4. Definite source control (remove CVC, drain abscess, etc)
  5. Non-immunocompromised host

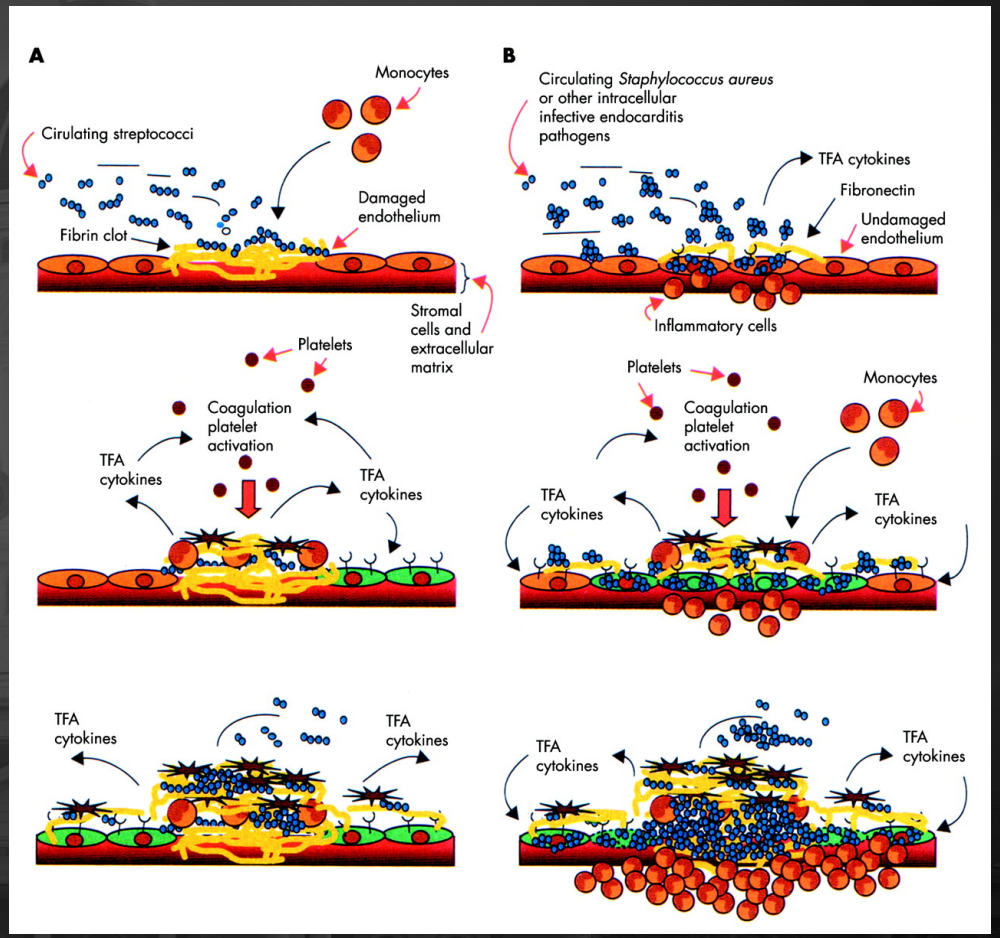
Rare / Fastidious Pathogens



Brouqui, P et al. "Endocarditis due to rare and fastidious bacteria." *CMR* - 14.1 (2001): 177-207.

Pathogenesis





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Heart 2006;**92:**879-885;

Fowler et al. Endocarditis and Intravascular infections. In Mandell, Douglas and Bennett's Principles and Practice of infectious Diseases. 8th Edition, 2015. Elsevier inc

Modified Duke Criteria

Major Criteria

- Blood Culture +ve
  - Typical organism from 2 separate cultures drawn 12h apart:
    - S.aureus, Viridans Streptococci, S.bovis, HACEK, CA-Enterococcus (no primary focus)

  (Or)

  - Other organisms: Persistent +ve blood culture of all 3 or ≥ 4 separate cultures with first and last sample drawn >1 hour apart
  - Single +ve blood culture for *C.burnetii* or anti-phase 1 IgG >1:800
- Echo +ve for IE

Minor Criteria

- Predisposing heart condition or IVDU
- T > 38 C
- Vascular (emboli) – arterial, septic pulmonary, mycotic, conjunctival petechiae, Janeway's
- Immunologic – glomerulonephritis, Osler nodes, Roth spots, RF
- Incomplete microbiological evidence (does not meet major criteria)

Modified Duke Criteria

- Definite
  - Pathological or Microbiological: Microorganisms demonstrated by culture or histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis
  - Clinical: 2 Major criteria, 1 major criterion and 3 minor criteria, or 5 minor criteria
- Possible
  - 1 Major and 1 minor criterion or 3 minor criteria
- Rejected
  - Firm alternative diagnosis explaining evidence of IE; or resolution of IE syndrome with antibiotic therapy for ≤4 d; or no pathological evidence of IE at surgery or autopsy with antibiotic therapy for ≤4 d; or does not meet criteria for possible IE as above

Limitations

- Modified Duke Criteria designed for research purposes
  - LOWER SENSITIVITY for PVE and Cardiac Device associated endocarditis
  - ~ 30% of cases are “possible” due to equivocal or negative Echocardiography or blood cultures
- Other imaging modalities have evolved for PVE
  - Cardiac CT +/- angiography (younger)
  - ^{18}FDG-PET or SPECT – show regions of inflammation

J Am Coll Cardiol. 2017 Jan 24;69(3):325-344 Millar BC, et al. Heart 2016;102:796–807

Echocardiography – AHA 2015

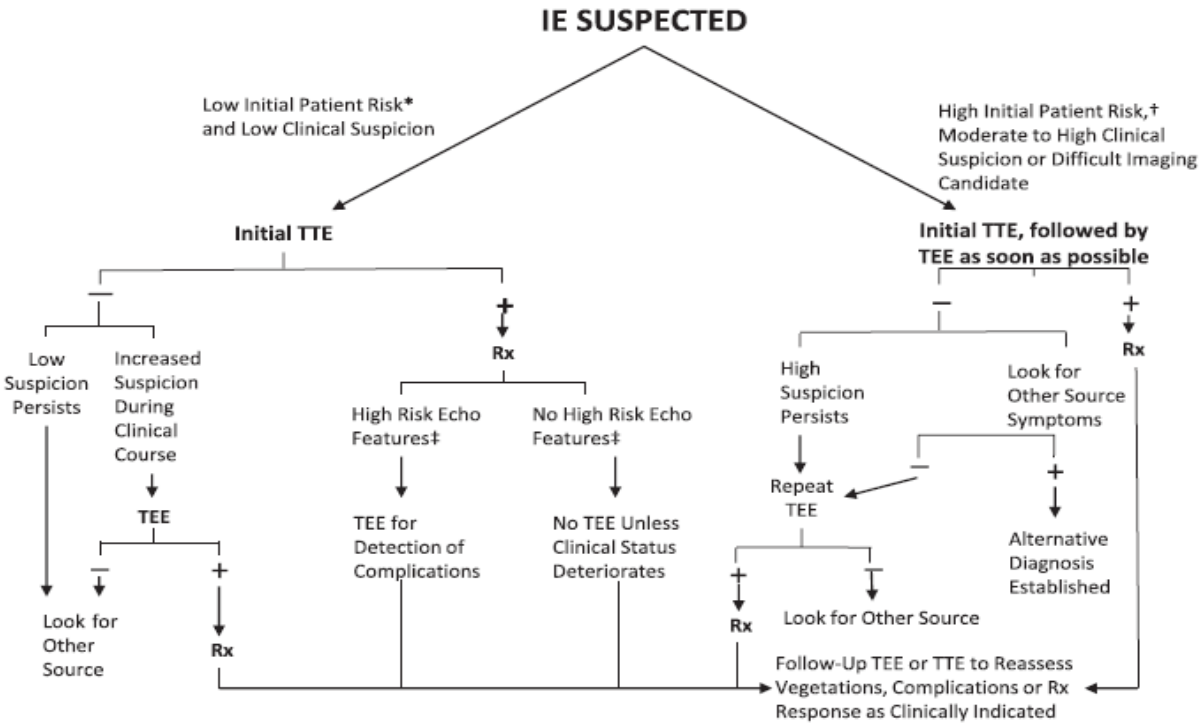


Figure. An approach to the diagnostic use of echocardiography (echo). Rx indicates prescription; TEE, transesophageal echocardiography; and TTE, transthoracic echocardiography. *For example, a patient with fever and a previously known heart murmur and no other stigmata of infective endocarditis (IE). †High initial patient risks include prosthetic heart valves, many congenital heart diseases, previous endocarditis, new murmur, heart failure, or other stigmata of endocarditis. ‡High-risk echocardiographic features include large or mobile vegetations, valvular insufficiency, suggestion of perivalvular extension, or secondary ventricular dysfunction (see text). Modified from Baddour et al.[12] Copyright © 2005, American Heart Association, Inc.

Echocardiography – AHA 2015

Table 4. Use of Echocardiography During Diagnosis and Treatment of Endocarditis

Early
Echocardiography as soon as possible (<12 h after initial evaluation)
TEE preferred; obtain TTE views of any abnormal findings for later comparison
TTE if TEE is not immediately available
TTE may be sufficient in small children
Repeat echocardiography
TEE after positive TTE as soon as possible in patients at high risk for complications
TEE 3–5 d after initial TEE if suspicion exists without diagnosis of IE or with worrisome clinical course during early treatment of IE

Pitfalls with Echo

- < 3mm or embolized - may not be detected
- Pre-existing severe lesions:
  - MVP, degenerative lesions, prosthetic valves
- Shielding or blooming artefact
- Reduced echogenicity from PV or peri-valve calcifications
- Prolapsed cusps, ruptured chordae, cardiac tumors, myxoma, Marantic endocarditis

Millar BC, et al. Heart 2016;102:796–807

Early surgical intervention

Table 5. Clinical and Echocardiographic Features That Suggest Potential Need for Surgical Intervention

Vegetation
Persistent vegetation after systemic embolization
Anterior mitral leaflet vegetation, particularly with size >10 mm*
≥1 Embolic events during first 2 wk of antimicrobial therapy*
Increase in vegetation size despite appropriate antimicrobial therapy*†
Valvular dysfunction
Acute aortic or mitral insufficiency with signs of ventricular failure†
Heart failure unresponsive to medical therapy†
Valve perforation or rupture†
Perivalvular extension
Valvular dehiscence, rupture, or fistula†
New heart block†‡
Large abscess or extension of abscess despite appropriate antimicrobial therapy†

See text for a more complete discussion of indications for surgery based on vegetation characterizations.

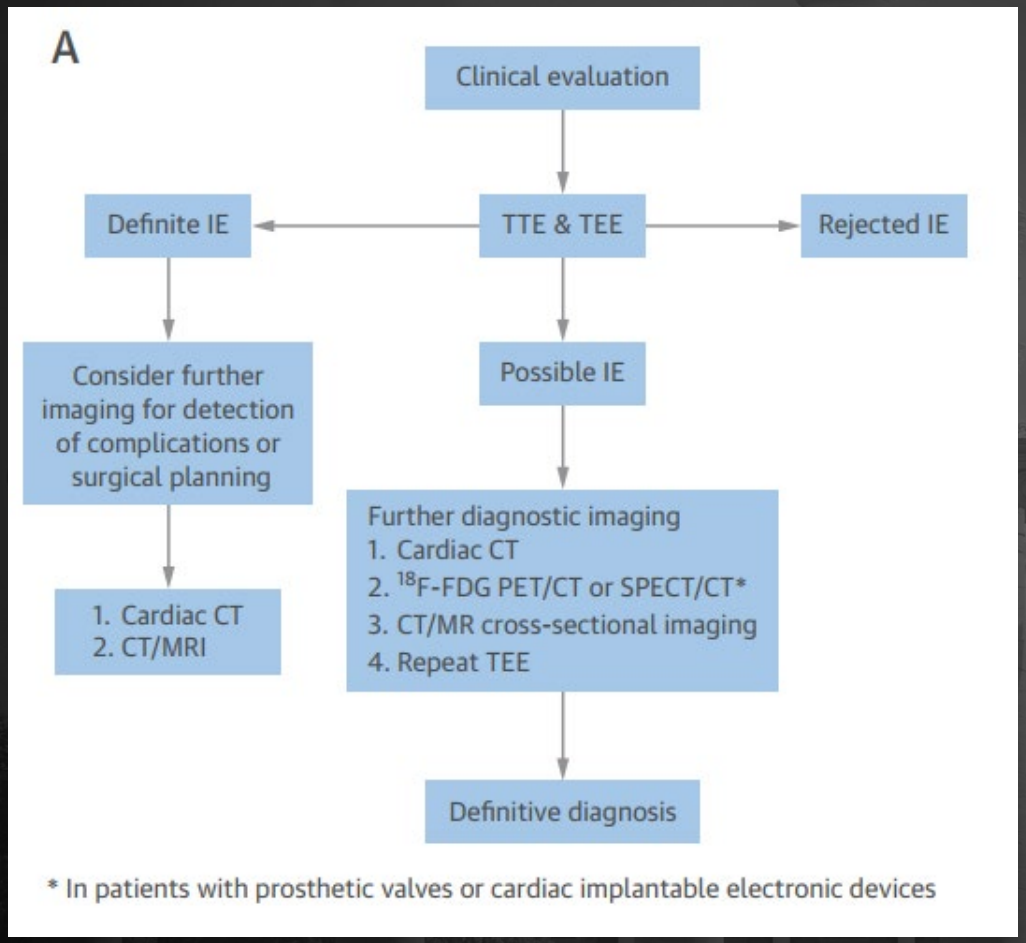
*Surgery may be required because of risk of embolization.

†Surgery may be required because of heart failure or failure of medical therapy.

‡Echocardiography should not be the primary modality used to detect or monitor heart block.

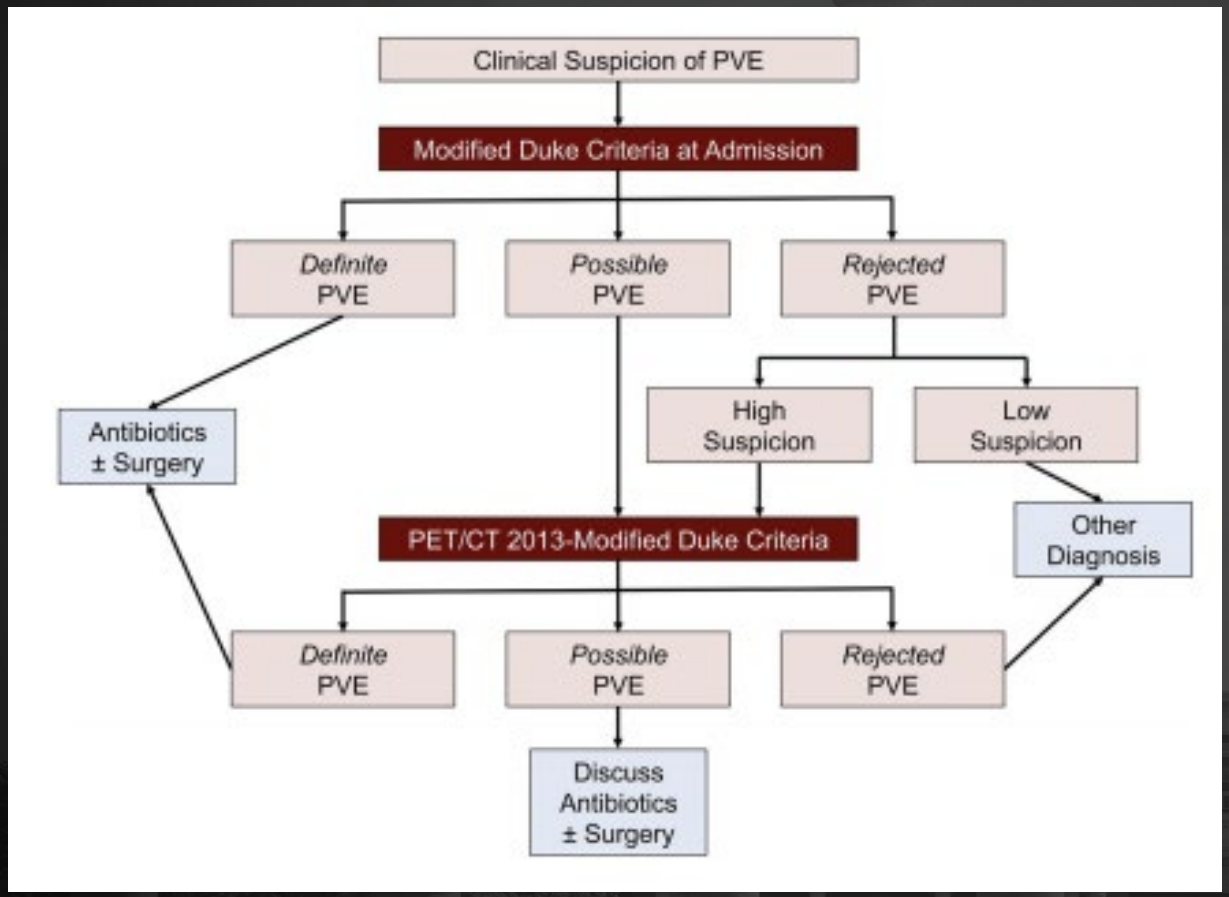
- Greatest risk for embolization with ≥ 10mm vegetations
- Mobility characteristics alone is not a surgical indication

Integrated approach – CT/MRI/PET



- Cardiac CT helpful for complications
  - Para-valvular anatomy, mycotic aneurysms
  - Less prosthetic artefacts
  - Angiogram for coronaries
- CT/MRI/PET (non-cardiac)
  - Identify Embolic complications

FDG-PET for PVE



- FDG - PET
  - PVE
    - Limited studies
    - Improved diagnosis
  - Not for NVE
  - Not helpful for early post-op (inflammation)

J Am Coll Cardiol. 2017 Jan 24;69(3):325-344

Millar BC, et al. Heart 2016;102:796–807

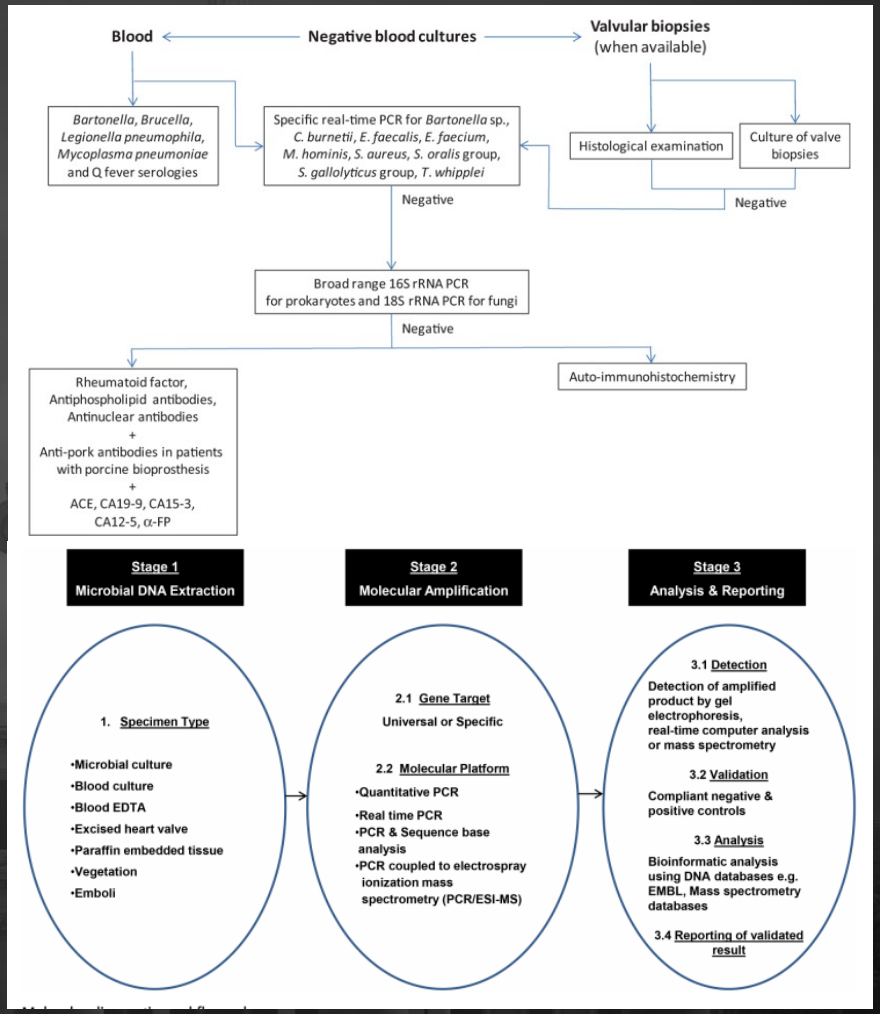
Diagnostic goal

- To initiate appropriate empirical antibiotic therapy as early as possible
- To identify patients at high risk for complications who may be best managed by early surgery
- Note:
  - Case definitions should not replace clinical judgement
  - If suggestive features are absent, then a negative Echo should prompt search for alternate source of fever and sepsis

Circulation 132.15 (2015): 1435-1486

Fastidious pathogens

- Coxiella (cell culture)
- Chlamydia (cell culture)
- Bartonella
- Legionella
- Brucella
- Mycoplasma
- T. Whipplei



Medicine (Baltimore). 2017 Nov; 96(47): e8392.

Millar BC, et al. Heart 2016;102:796–807

Culture negative IE

Comparison of microorganisms identified in patients with positive (n=635) or negative (n=283) blood cultures.

Microorganism	Positive blood culture, %	Negative blood culture, %	P*	Odds ratio (95% CI)
Intracellular bacteria				
Bartonella sp	0	19 (6.7)	<.01	Undefined
Coxiella burnetii	0	23 (8.1)	<.01	Undefined
T whipplei	0	3 (1.1)	.03	Undefined
Gram-positive bacteria				
Enterococcus sp	90 (14.2)	15 (5.3)	<.01	0.34 (0.18–0.42)
Streptococcus sp	206 (32.4)	24 (8.5)	<.01	0.19 (0.12–0.31)
Staphylococcus sp	266 (41.9)	31 (10.9)	<.01	0.17 (0.11–0.26)
Other gram-positive bacilli	9 (1.4)	15 (5.3)	<.01	5.05 (1.9–13.85)
Gram-negative bacteria				
HACEK bacteria	6 (0.9)	1 (0.3)	.67	0.38 (0.02–3.36)
Other gram-negative bacteria	47 (7.4)	1 (0.3)	<.01	0.04 (0.00–0.30)
Other microorganisms				
Other bacteria	4 (0.6)	2 (0.7)	1.0	1.28 (0.15–9.45)
Fungi	7 (1.1)	1 (0.3)	.43	0.32 (0.01–2.66)
Total	635	135†		

Fournier, Pierre-Edouard, et al. "Blood culture-negative endocarditis: improving the diagnostic yield using new diagnostic tools." *Medicine* 96.47 (2017).

Other causes of Culture negativity

- Prior antibiotic administration
- Insufficient quantity of blood drawn
- Poor microbiological methods
- NBTE
  - Neoplasia: Atrial myxoma, marantic, carcinoid
  - Autoimmune: Rheumatic carditis, SLE, PAN and Behçet's
  - Post-valvular surgery : Thrombus, stitch, postsurgery changes
  - Other: eosinophilic heart disease, ruptured mitral chordae, and myxomatous degeneration).

Karius Testing – Adults – Limited Data in IE

156. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Infective Endocarditis (IE) Using the Karius Plasma Next Generation Sequencing (NGS) Test

Session: Oral Abstract Session: Cool Findings in Bacteremia and Endocarditis
Thursday, October 4, 2018: 11:00 AM
Room: W 2002

Background: The variable clinical presentation of IE requires a diagnostic tool that accurately detects a wide range of organisms, including in culture-negative (CN) scenarios. A sensitive molecular diagnostic assay that quantitates pathogen DNA could be a useful tool to diagnose IE and evaluate response to antimicrobial therapy.

Methods: We prospectively enrolled 30 hospitalized adult patients evaluated for acute IE classified using the Duke Criteria. Residual plasma samples within 24 hours and/or fresh whole blood within 48–72 hours of enrollment blood culture were collected. Additional samples were collected every 2-3 days for up to 7 time points until discharge. Samples were shipped to the Karius laboratory (Redwood City, CA) for testing. Cell-free DNA was extracted and NGS was performed. Human sequences were removed and remaining sequences were aligned to a curated pathogen database of over 1000 organisms. Organisms present above a predefined statistical threshold were reported. Quantity of DNA for each reported pathogen was expressed as molecules/µL.

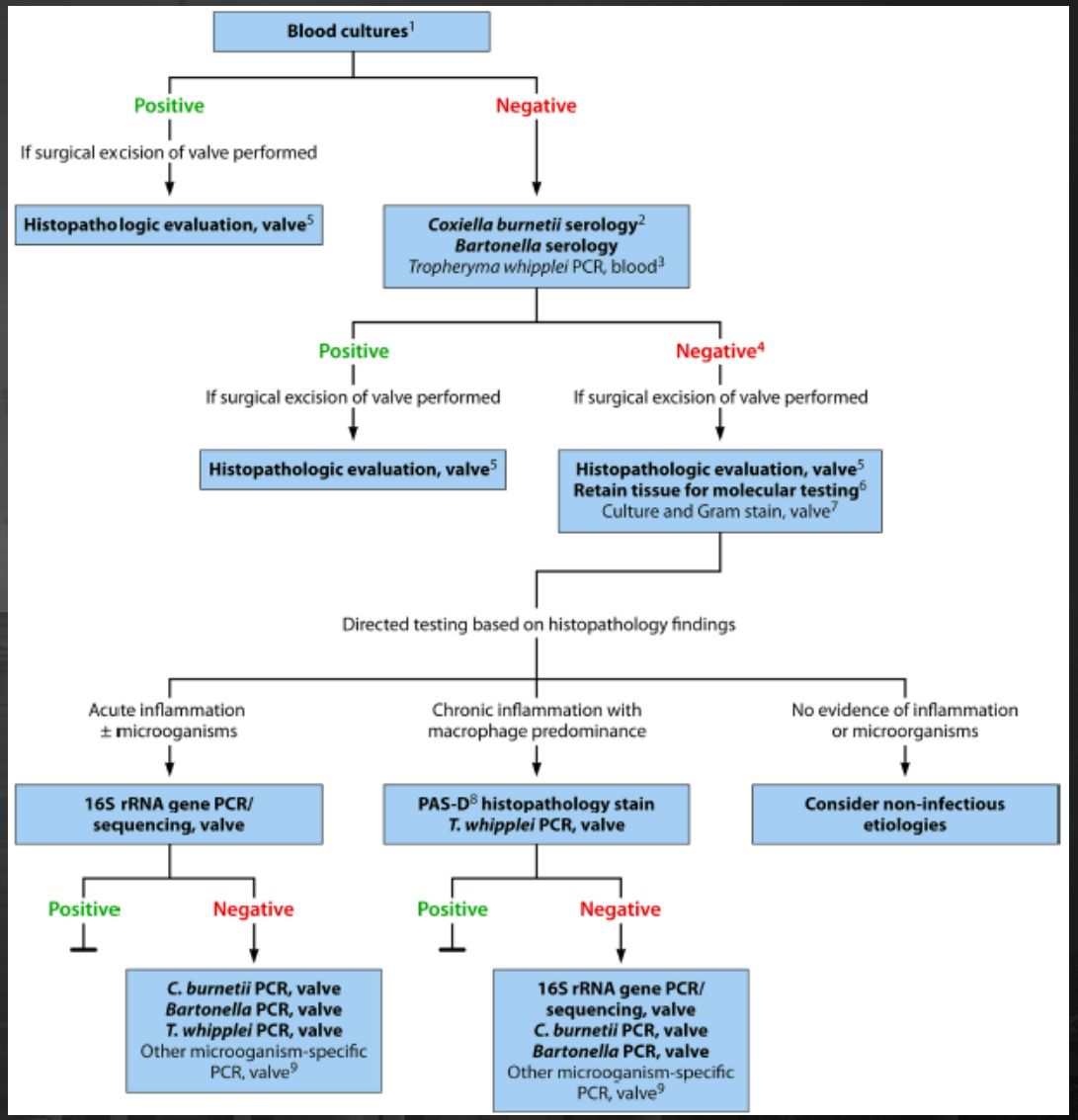
Results: Of 29 patients eligible for analysis, 18 had prosthetic valves and 7 had implanted cardiac devices. 24 patients had Definite IE. 20 patients had positive blood cultures (including *S. aureus, S. epidermidis, E. faecalis, S. agalactiae, Pantoea ananatis, S. sanguinis, C. albicans*); NGS identified the same organism isolated in all 20 patients as well as *E. cloacae* complex, and *E. faecalis* in 2 of 4 CN Definite IE patients. For 1 CN patient with Possible IE, NGS identified *E. coli*. NGS and BC were negative for 4 patients with Rejected IE. NGS identified the IE etiology in patients pre-treated with antibiotics up to 20 days prior to sample collection. Pathogen DNA signal was often observed in both initial and repeat plasma samples, while repeat blood cultures remained negative.

Conclusion: This novel, cell-free pathogen quantitative NGS plasma assay accurately identified causative organisms in patients with IE, even when blood cultures were negative due to pre-treatment with antibiotics. Pathogen DNA, detected in plasma longer than blood culture is a promising biomarker to aid in the diagnosis and monitoring of IE, particularly culture-negative IE.

Pratik Shah, MS[1], Felicia Ruffin, MSN, RN[2], Hon Seng, BS[3], Desiree Hollemon, MSN, MPH[3], Laura Winn, BA[4], Caitlin Drennan, BS[4], Ka Lok Chan, MS[5], Huy Quach, MS[6], Timothy Blauwkamp, PhD[3], Galit Meshulam-Simon, PhD[6], David Hong, MD[3] and Vance G. Fowler Jr., MD[7], (1)Infectious Diseases, Duke University Health System, Durham, NC, (2)Division of Infectious Diseases, Duke University Medical Center, Durham, NC, (3)Karius, Inc., Redwood City, CA, (4)Duke University Health System, Durham, NC, (5)Karius inc., Redwood City, CA, (6)Karius Inc., Redwood City, CA, (7)Duke University, Durham, NC

Algorithm for Culture Negative Infective Endocarditis

- Applied in the context of clinical evaluation of the patient and other findings (e.g., echocardiography)
- Blood cultures done first, collect before antibiotic therapy
- Cardiac valve tissue with organism-specific PCR assays is more sensitive than blood or serum
  - Abundance of organisms



Liesman, RM., et al. "Laboratory diagnosis of infective endocarditis." *J Clin Micro* 55.9 (2017): 2599-2608.

Antimicrobial therapy

- Considerations:
  - Prolonged, Parenteral, Bactericidal therapy
  - Inoculum effect
    - Less actively multiplying – PBPs are less often present.
    - Quantitatively more beta lactamase.

Treatment - Streptococci

Pathogen	Susceptibility	NVE		PVE	
		Drug	Duration	Drug	Duration
VGS/ S.bovis	Pen Highly S (MIC ≤0.12 µg/mL)	Ceftriaxone 2g or Pen G (II a, B)	4 weeks	(Ceftriaxone or Pen G) **+/-** Gentamicin (II a, B)	6 weeks (Pen G/Cef) 2 weeks (Gent)
		(Ceftriaxone or Pen G) + Gentamicin	2 weeks		
	Pen R (MIC >0.12 µg/mL to <0.5 µg/mL and ≥0.5 µg/mL)	Pen G or ceftriaxone + Gent (II a, B)	4 weeks (Pen G/Cef), 2 weeks (Gent)	Pen G or ceftriaxone + Gent (II a, B)	6 weeks (both)
		Vancomycin (Class II a, C)	4 weeks	Vancomycin (Class II a, B)	6 weeks

Treatment - Staphylococci

Pathogen	Susceptibility	NVE		PVE	
		Drug	Duration	Drug	Duration
Staph (CONS or S.aureus)	Oxacillin S (MSSA)	Nafcillin (Class I, C)	6 w (L sided) *2 w (Uncomplicated right sided)*	Nafcillin + Rifampin + Gent	≥6 weeks (Pen and Rif) 2 weeks (Gent)
		Cefazoliin (Class I, B)	6 w (Left sided)		
	Oxacillin R (MRSA)	Vanc (Class I, C)	6 weeks	Vancomycin + Rifampin + Gent	≥6 weeks (Vanc and Rif) 2 weeks (Gent)
		Daptomycin (Class I, B)	6 weeks		

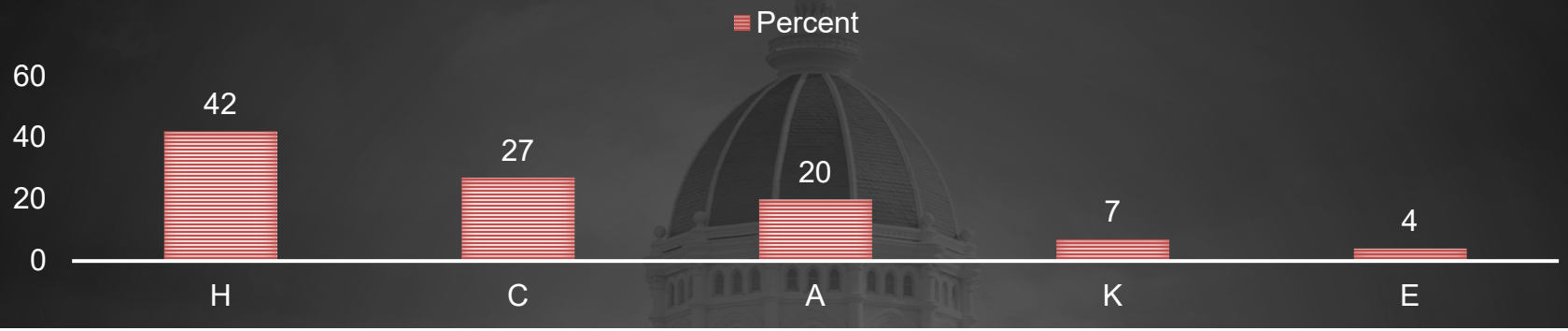
Treatment - Enterococci

Pathogen	Susceptibility	NVE		PVE	
		Drug	Duration	Drug	Duration
Entero - coccus	Pen S Gent S	Ampicillin or Pen G (II a, B) + Gentamicin	4 weeks (S/S <30 days) 6 weeks (S/S >30 days)	Ampicillin or Pen G (II a, B) + Gentamicin	6 weeks
		Ampicillin + Ceftriaxone	6 weeks	Ampicillin + Ceftriaxone	6 weeks
	Pen S Gent R	Ampicillin + Ceftriaxone	6 weeks	Ampicillin + Ceftriaxone	6 weeks
		Ampicillin or Pen G + Streptomycin	4-6 weeks		

Treatment - Enterococci

Pathogen	Susceptibility	NVE		PVE	
		Drug	Duration	Drug	Duration
Entero – coccus	(Unable to tolerate B-lactam)	Vancomycin (II a, B) + Gentamicin	6 weeks	Same	6 weeks
	Pen R	Vancomycin (II b, C) + Gentamicin	6 weeks	Same	6 weeks

HCAKE (re-abbreviated - most to least common)



Regimen	Dose and Route	Duration, wk	Strength of Recommendation	Comments
Ceftriaxone sodium*	2 g/24 h IV or IM in 1 dose	4, NVE; 6, PVE	*Class IIa; Level of Evidence B*	Preferred therapy: cefotaxime or another third- or fourth-generation cephalosporin may be substituted.
Or				
Ampicillin sodium	2 g IV every 4 h		*Class IIa; Level of Evidence B*	Ampicillin sodium may be an option if the growth of the isolate is sufficient to permit in vitro susceptibility results.
Or				
Ciprofloxacin†	1000 mg/24 h orally or 800 mg/24 h IV in 2 equally divided doses		*Class IIb; Level of Evidence C*	Fluoroquinolone therapy‡ may be considered for patients unable to tolerate cephalosporin and ampicillin therapy; levofloxacin or moxifloxacin may be substituted; fluoroquinolones generally is not recommended for patients <18 y old. Treatment for 6 wk is reasonable in patients with PVE (*Class IIa; Level of Evidence C*).

Gram Negative Endocarditis (Non-HACEK)

Organism	Patients Infected, *n*	Antibiotic Treatment, *n/n* (%)	Surgical Treatment, *n/n* (%)	Complications, *n/n* (%)†	In-Hospital Mortality, *n/n* (%)
Escherichia coli	14	Monotherapy with β-lactam: 5/14 (36) Combination therapy: 9/14 (64)‡	4/14 (29)	11/14 (79)	3/14 (21)
Pseudomonas aeruginosa	11	Monotherapy with aminoglycoside: 3/11 (27) Combination therapy: 8/11 (73)§	6/11 (55)	8/11 (73)	4/11 (36)
Klebsiella species	5	Monotherapy: 4/5 (80)‖ Combination therapy: 1/5 (20)¶	2/5 (40)	2/5 (40)	2/5 (40)
Serratia species	4	Monotherapy: 0/4 (0) Combination therapy: 4/4 (100)**	4/4 (100)	3/4 (75)	0/4 (0)
Other	15	Monotherapy with β-lactam: 6/15 (40) Combination therapy: 8/15 (53)†† Missing: 1/15 (7)	9/15 (60)	10/15 (67)	3/15 (20)

* HACEK = *Haemophilus* species, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, or *Kingella* species.
† Defined as paravalvular complications, intracardiac abscess, conduction abnormality, persistently positive blood cultures, stroke, other systemic embolization, or congestive heart failure.
‡ β-Lactam + aminoglycoside (6 of 14); β-lactam + aminoglycoside + quinolone (2 of 14); β-lactam + quinolone (1 of 14).
§ β-Lactam + aminoglycoside (5 of 11); β-lactam + quinolone (2 of 11); aminoglycoside + quinolone (1 of 11).
‖ β-Lactam (3 of 5); quinolone (1 of 5).
¶ β-lactam + quinolone (1 of 5).
** β-Lactam + quinolone (2 of 4); β-lactam + aminoglycoside (2 of 4).
†† β-Lactam + aminoglycoside (4 of 15); β-lactam + quinolone (2 of 15); β-lactam + quinolone + trimethoprim–sulfamethoxazole (1 of 15); β-lactam + trimethoprim–sulfamethoxazole (1 of 15).

Annals of internal medicine. 2007 Dec 18;147(12):829-35

Fungal Endocarditis

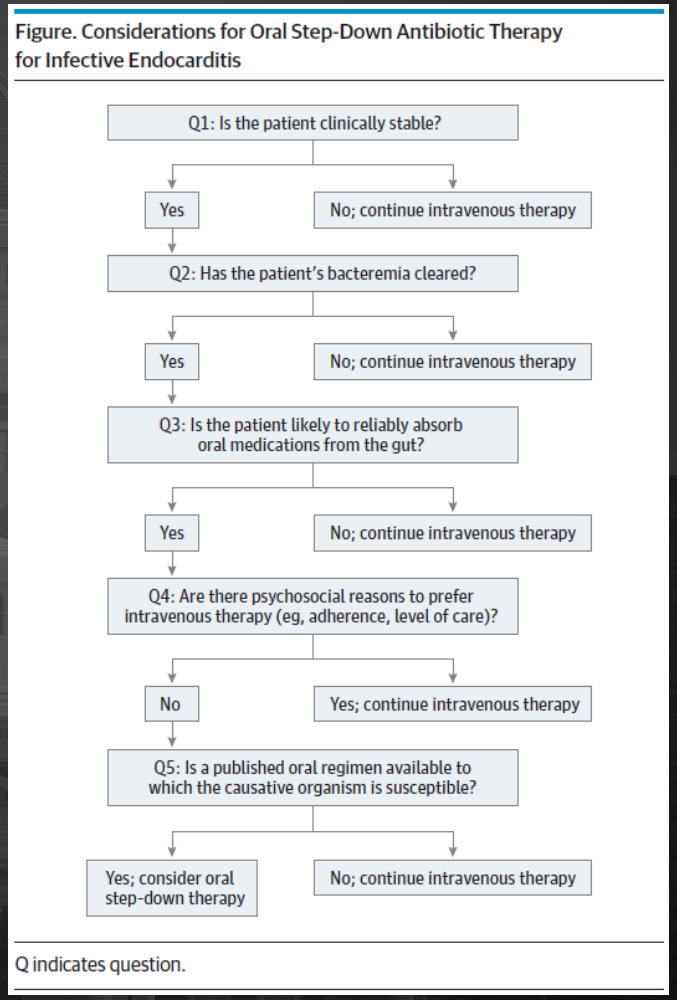
- **2-4% of all cases**
- **Recommendations**
  - **Valve surgery should be done in most cases of fungal IE (*Class I; Level of Evidence B*).**
  - **After completion of initial parenteral therapy, life longsuppressive therapy with an oral azole is reasonable(*Class IIa; Level of Evidence B*).**
- Ampho, Flucytosine, Azoles, Echinocandins
- ID consult, IDSA guidelines for specific fungi

Variables	Fungus	Data
Yeast (n = 101)	Candida species	95/101 (94.1)
	C albicans	46
	C parapsilosis	17†
	Candida tropicalis	8†
	Candida glabrata	2
	Candida krusei	3
	Candida lusitaniae	1
	Candida chaetamion	1
	Candida zeylanoides	1
	Not specified	18
	Trichosporon inkin	1
	Histoplasma capsulatum	2
	Saccharomyces cervisiae	1
	Cryptococcus neoformans	1
	Hansenula anomala	1
Mold (n = 39)	Aspergillus species	28/39 (71.8)
	A fumigatus	15
	Aspergillus nidulans	1
	Aspergillus flavus	2
	Aspergillus terreus	5
	Aspergillus niger	2
	Not specified	3
	Scedosporium apiospermum	1
	Scedosporium prolificans	1
	Phaeocremonium parasiticum	1
	Acremonium species	1
	Fusarium dimerum	1
	Phialemonium curvatum	1
	Microascus cinereus	1
	Bipolaris spicifera	1
	Scopulariopsis brevicaulis	3
Yeast plus mold	*F solani* and *C parapsilosis*	1
Not mentioned		10
Negative culture		1

Chest 2002, **122**:302–310.

Step-Down Oral Therapy for IE

- 21 observational studies
- Most had an initial course of IV therapy
- None found oral step-down therapy to be inferior
- Multiple studies had improved clinical cure rate and mortality rate among patients treated with oral step-down
- 3 RCTs - oral step-down antibiotic therapy is at least as effective as IV-only therapy in right-sided, left-sided, or prosthetic valve IE.
    - In the largest trial (POET), at 3.5 years of follow-up, oral step-down antibiotic therapy had a significantly improved cure rate and mortality rate in comparison to intravenous-only therapy.



Spellberg B et al. Evaluation of a Paradigm Shift From Intravenous Antibiotics to Oral Step-Down Therapy for the Treatment of Infective Endocarditis: A Narrative Review. *JAMA Intern Med.* 2020;180(5):769–777.

Table 1. Peak Blood Levels vs MICs Achieved by Antibiotics Used to Treat Infective Endocarditis in Published Studies

Oral drug	Peak blood level, μg/mL[a]	MIC_{90}, μg/mL[b]	Peak blood level to MIC_{90} ratio
Antibiotics with peak blood level to MIC_{90} ratio ≤1			
Tetracycline, 250 mg	1	≥4	0.125
Erythromycin, 500 mg	0.5	≥4	0.125
Sulfanilamide, 4000 mg[5-9]	50	50-70	0.8
Antibiotics with peak blood level to MIC_{90} ratio >1			
Penicillin V, 500 mg, for *Streptococcus* spp	5	1	5
Amoxicillin, 1000 mg, for *Streptococcus* spp	10	1	10
Levofloxacin, 750 mg, for *Staphylococcus* spp	9	4	2.25
Moxifloxacin, 400 mg, for *Staphylococcus* or *Streptococcus* spp			
Staphylococcus aureus	4	4	1
Streptococcus spp	4	0.25	16
Rifampin, 600 mg, for gram-positive cocci	7	1	7
TMP-SMX, 320 mg/1600 mg, for *Staphylococcus* spp	100	4.75	22
Linezolid, 600 mg, for gram-positive cocci	15	2	7.5
Clindamycin, 600 mg, for *Staphylococcus* spp	10	2	5

Abbreviations: MIC, minimum inhibitory concentration; MIC_{90}, minimum inhibitory concentration of the antibiotic needed to kill 90% of clinical isolates encountered; spp, species; TMP-SMX, trimethoprim-sulfamethoxazole.

[a] Data on peak blood levels are from Table 9A in *The Sanford Guide to Antimicrobial Therapy 2019*[10]; data on TMP-SMX are from the sulfamethoxazole component.

[b] Data from the JMI Laboratories SENTRY program and other studies of both staphylococci and streptococci.[11-15] Data on MIC_{90} of penicillin and amoxicillin are shown only for susceptible or intermediate streptococci, not including resistant strains or staphylococci. These results are shown for comparative purposes only. Pharmacodynamic considerations for antibiotic effectiveness are based on more than just peak levels (eg, time above MIC is associated with the effectiveness of β-lactams, and total exposure over a 24-hour period divided by MIC is associated with the effectiveness of most of the other agents). However, if the peak level never exceeds the MIC, then the drug cannot achieve any time above the MIC.

Spellberg B et al. Evaluation of a Paradigm Shift From Intravenous Antibiotics to Oral Step-Down Therapy for the Treatment of Infective Endocarditis: A Narrative Review. *JAMA Intern Med.* 2020;180(5):769–777.

Table 4. Summary of Oral Step-Down Antibiotic Dosing Used in Published Clinical Studies[a]

Drug	Organism	Dose
Amoxicillin	Sensitive streptococci or enterococci (for streptococci, with or without combination; and for enterococci, only in combination with rifampin, moxifloxacin, linezolid, or clindamycin)	1 g 4 times daily
Dicloxacillin	Sensitive staphylococci (only in combination with rifampin or fusidic acid)	1 g 4 times daily
Levofloxacin[b]	Sensitive staphylococci (only in combination with rifampin or fusidic acid)	750 mg once daily
Moxifloxacin	Sensitive streptococci, enterococci, or staphylococci (only in combination with amoxicillin, rifampin, clindamycin, or linezolid)	400 mg once daily
TMP-SMX	Sensitive staphylococci	960 mg/ 4 800 mg daily
Linezolid	For sensitive gram-positive cocci (for most patients in published studies, linezolid was used alone; in some studies,[52,57,58] linezolid was given as a combination regimen with rifampin, fusidic acid, moxifloxacin, clindamycin, or amoxicillin)	600 mg twice daily
Rifampin	Only as adjunctive agent (see above for other antibiotics rifampin has been combined with) and never as a single agent	600 mg once or twice daily
Clindamycin	Only as adjunctive agent (see above for other antibiotics clindamycin been combined with) and never as a single agent	600 mg 3 times daily
Fusidic acid	Only as adjunctive agent (see above for other antibiotics fusidic acid has been combined with) and never as a single agent	750 mg twice daily

Spellberg B et al. Evaluation of a Paradigm Shift From Intravenous Antibiotics to Oral Step-Down Therapy for the Treatment of Infective Endocarditis: A Narrative Review. *JAMA Intern Med.* 2020;180(5):769–777.

Early Valve Surgery – AHA 2015

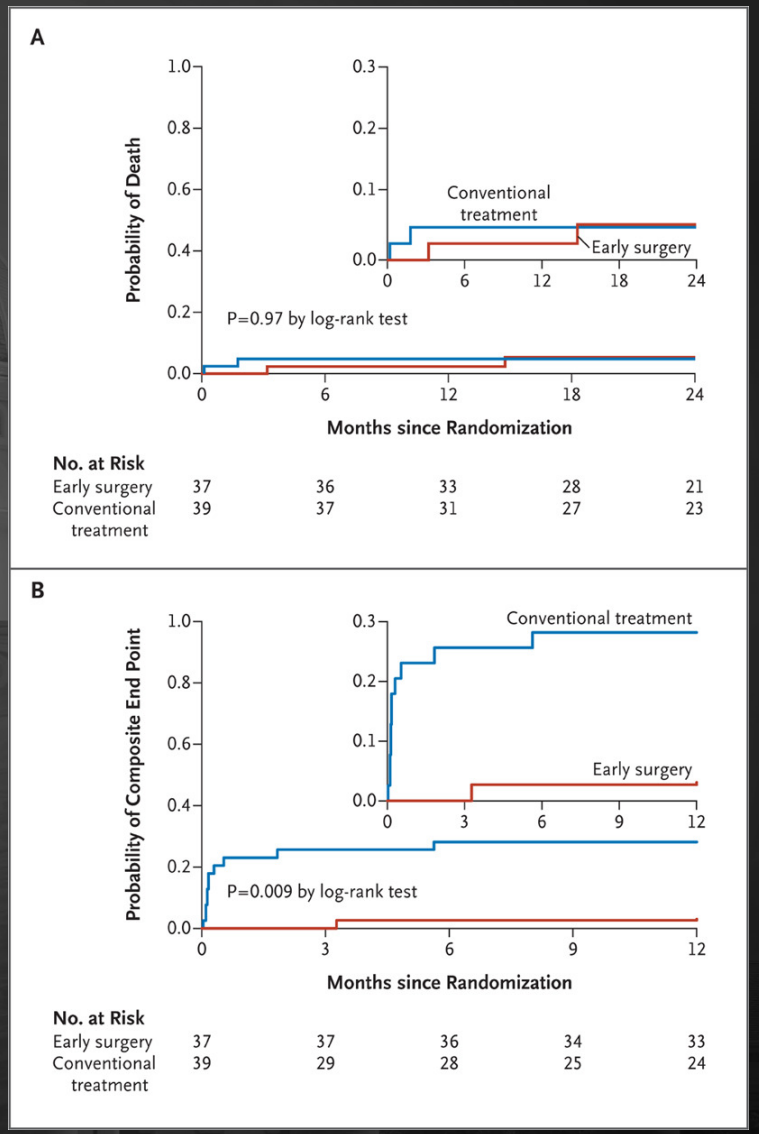
Class I a, B	Class II b (Level of evidence)
Valve dysfunction leading to s/s HF	Recurrent embolic (B)
Heart block, annular or aortic abscess, destructive penetrating lesions	Increase in size of vegetation despite Abx (B)
Persistent bacteremia >5-7 days of Abx (no mets)	Severe valve regurgitation and mobile vegetations >10 mm (B)
Fungi, VRE, MDR G-ve	mobile vegetations >10 mm involving the anterior leaflet of the mitral valve + other relative indications for surgery ©

	AHA Guidelines 2015 (89)	Class, Level of Evidence	ESC Guidelines 2015 (68)	Class, Level of Evidence	Timing†
Heart failure	Early surgery* is indicated in patients with IE who present with valve dysfunction resulting in symptoms or signs of HF	I, B	Aortic or mitral NVE, or PVE with severe acute regurgitation, obstruction, or fistula causing refractory pulmonary edema or cardiogenic shock	I, B	Emergency
	Early surgery* is indicated in patients with PVE with symptoms or signs of HF resulting from valve dehiscence, intracardiac fistula, or severe prosthetic valve dysfunction	I, B	Aortic or mitral NVE, or PVE with severe regurgitation or obstruction causing symptoms of HF, or echocardiographic signs of poor hemodynamic tolerance	I, B	Urgent
Uncontrolled infection	Early surgery* is indicated in patients when IE is complicated by heart block, annular or aortic abscess, or destructive penetrating lesions	I, B	Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)	I, B	Urgent
	Early surgery* is reasonable for patients with relapsing PVE	IIa, C			
	Early surgery* should be considered, particularly in patients with IE caused by fungi or highly resistant organisms (e.g., VRE, multidrug-resistant gram-negative bacilli)	I, B	Infection caused by fungi or multiresistant organisms	I, C	Urgent/elective
	Early surgery* is indicated for evidence of persistent infection (manifested by persistent bacteremia or fever lasting >5–7 d, and provided that other sites of infection and fever have been excluded) after the start of appropriate antimicrobial therapy	I, B	Persisting positive blood cultures despite appropriate antibiotic therapy and adequate control of septic metastatic foci	IIa, B	Urgent
			PVE caused by staphylococci or non-HACEK gram-negative bacteria	IIa, C	Urgent/elective
Prevention of embolism	Early surgery* is reasonable in patients who present with recurrent emboli and persistent or enlarging vegetations despite appropriate antibiotic therapy	IIa, B	Aortic or mitral NVE, or PVE with persistent vegetations >10 mm after ≥1 embolic episode despite appropriate antibiotic therapy	I, B	Urgent
	Early surgery* is reasonable in patients with severe valve regurgitation and mobile vegetations >10 mm	IIa, B	Aortic or mitral NVE with vegetations >10 mm, associated with severe valve stenosis or regurgitation, and low operative risk	IIa, B	Urgent
	Early surgery* may be considered in patients with mobile vegetations >10 mm, particularly when involving the anterior leaflet of the mitral valve and associated with other relative indications for surgery	IIb, C	Aortic or mitral NVE, or PVE with isolated very large vegetations (>30 mm)	IIa, B	Urgent
			Aortic or mitral NVE, or PVE with isolated large vegetations (>15 mm) and no other indication for surgery	IIb, C	Urgent

J Am Coll Cardiol. 2017 Jan 24;69(3):325-344

EASE Trial - 2012

- 76 patients, RCT, ITT
- L – NVE (severe valve disease and large vegetations)
- Early surgery <48 hours reduced composite end-point (in-hospital death, embolic events)
- Limitations: >2/3 of conventional underwent Sx eventually; excluded valve abscess/ heart failure/ fungal; predominant streptococcal etc



Kang, DH, et al. "Early surgery versus conventional treatment for infective endocarditis." *NEJM* 366.26 (2012): 2466-2473.

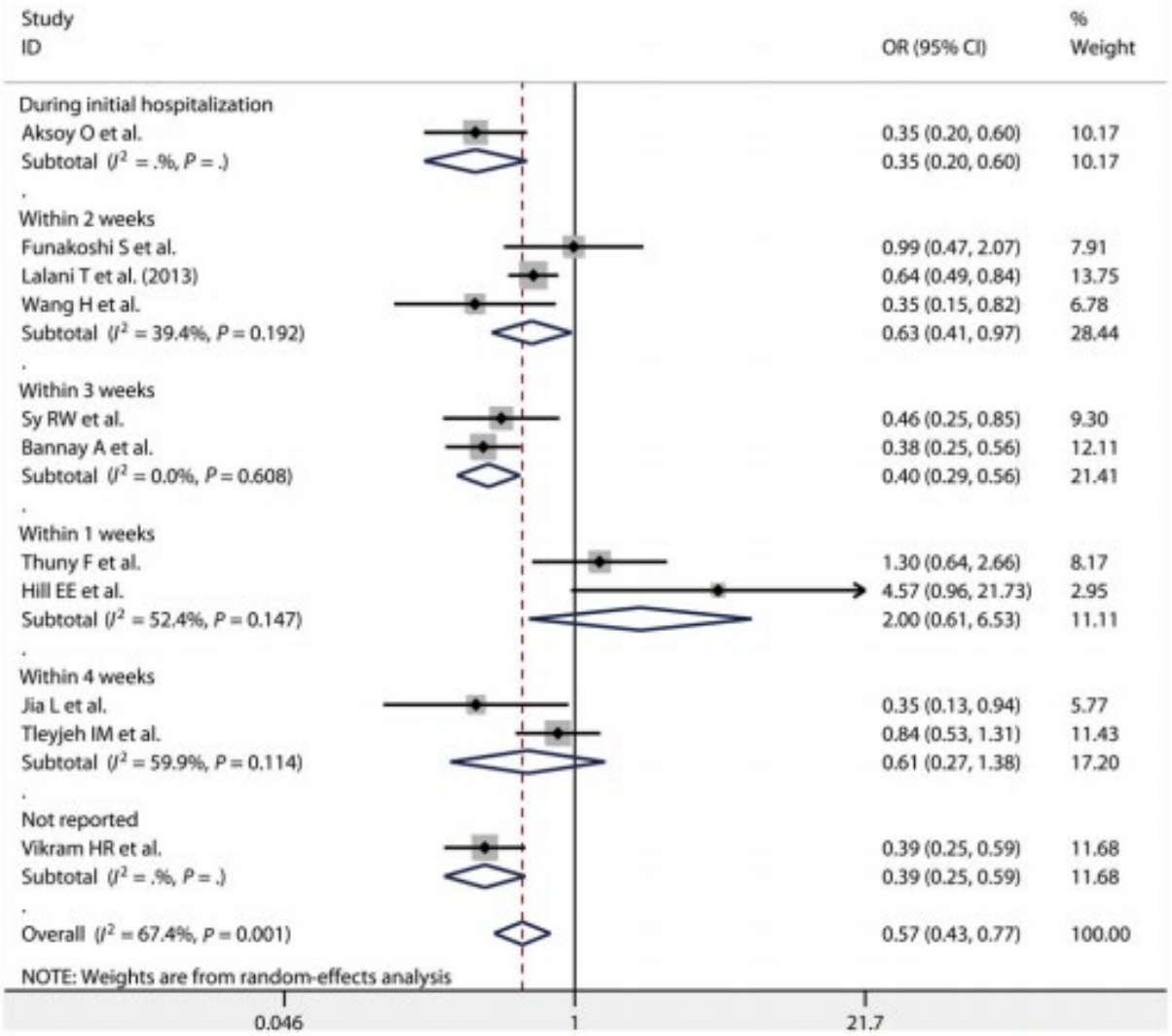


Figure 3: Long-term mortality in patients with IE, comparing early surgery versus non-early surgery, including subgroup analysis for different operation time periods. IE: infective endocarditis; OR: odds ratio; CI: confidence interval.

University of Missouri

Liang F, Song B, Liu R, Yang L, Tang H, Li Y. Optimal timing for early surgery in infective endocarditis: a meta-analysis. Interact Cardiovasc Thorac Surg. 2016 Mar;22(3):336-45.

Model	Study name	Odds ratio	Lower limit	Upper limit	p-Value	Events / Total Group-A	Group-B
	Olaison et al 1996	0.37	0.12	1.16	0.088	4 / 26	33 / 100
	Bishara et al 2001	0.59	0.22	1.61	0.303	5 / 44	37 / 208
	Vikram et al 2003	0.39	0.25	0.59	**<0.001**	37 / 230	94 / 283
	Mournvillier et al 2004	0.43	0.25	0.74	0.002	35 / 104	67 / 124
	Cabell et al 2005	0.80	0.60	1.07	0.133	83 / 610	149 / 906
	Wang A et al 2005	1.05	0.64	1.73	0.838	36 / 148	47 / 201
	Aksoy et al 2007	0.35	0.20	0.60	**<0.001**	23 / 78	139 / 255
	Hill et al 2008	4.57	0.96	21.73	0.056	12 / 58	2 / 37
	Nadji et al 2008	0.55	0.31	0.98	0.044	19 / 106	58 / 204
	Sy et al 2009	0.46	0.25	0.85	0.013	20 / 62	82 / 161
	Cooper et al 2009	0.26	0.08	0.83	0.023	6 / 25	17 / 31
	kim et al 2010	0.79	0.17	3.66	0.760	3 / 64	4 / 68
	Lalani et al 2010	0.53	0.40	0.70	**<0.001**	87 / 720	172 / 832
	Bannay et al 2011	0.38	0.25	0.56	**<0.001**	61 / 240	99 / 209
	Thuny et al 2011	1.30	0.64	2.66	0.472	14 / 95	23 / 196
	Funakoshi et al 2011	0.99	0.47	2.07	0.974	13 / 73	25 / 139
	Kang et al 2012	0.51	0.04	5.92	0.593	1 / 37	2 / 39
	Lalani et al 2013	0.64	0.49	0.84	0.001	133 / 490	196 / 535
	Galvez-Acebal et al 2014	1.03	0.79	1.34	0.823	149 / 417	211 / 602
	Martinez-Selles et al 2014	0.72	0.54	0.96	0.024	106 / 437	173 / 563
	Chu et al 2015	0.46	0.36	0.60	**<0.001**	128 / 733	173 / 552
Fixed		0.62	0.57	0.69	**<0.001**		
Random		0.61	0.50	0.74	**<0.001**		

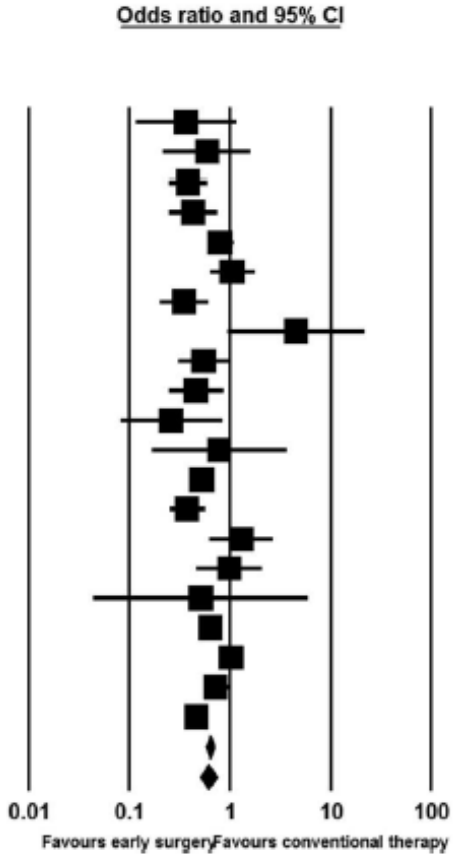
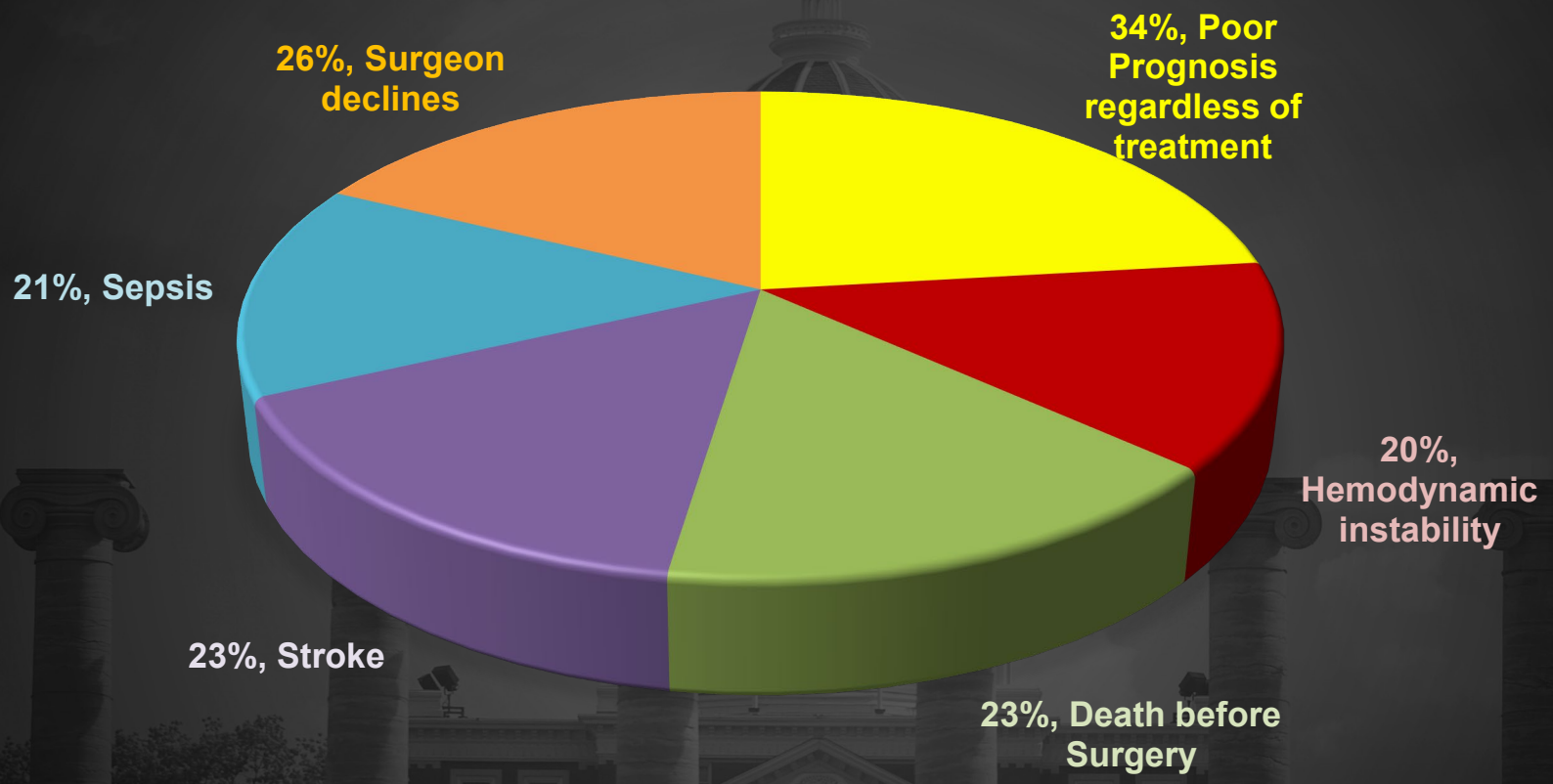


Figure 2 Comparison of all-cause mortality between early surgery (at 20 days or less) and conventional therapy (late surgery at >20 days or medical therapy).

Narayanan, Mahesh Anantha, et al. "Early versus late surgical intervention or medical management for infective endocarditis: a systematic review and meta-analysis." *Heart* 102.12 (2016): 950-957.

REASONS FOR DECLINING SURGERY



- 24% with a guideline indication still do not undergo surgery

Circulation. 2014 Jan 1;131(2):131-40.

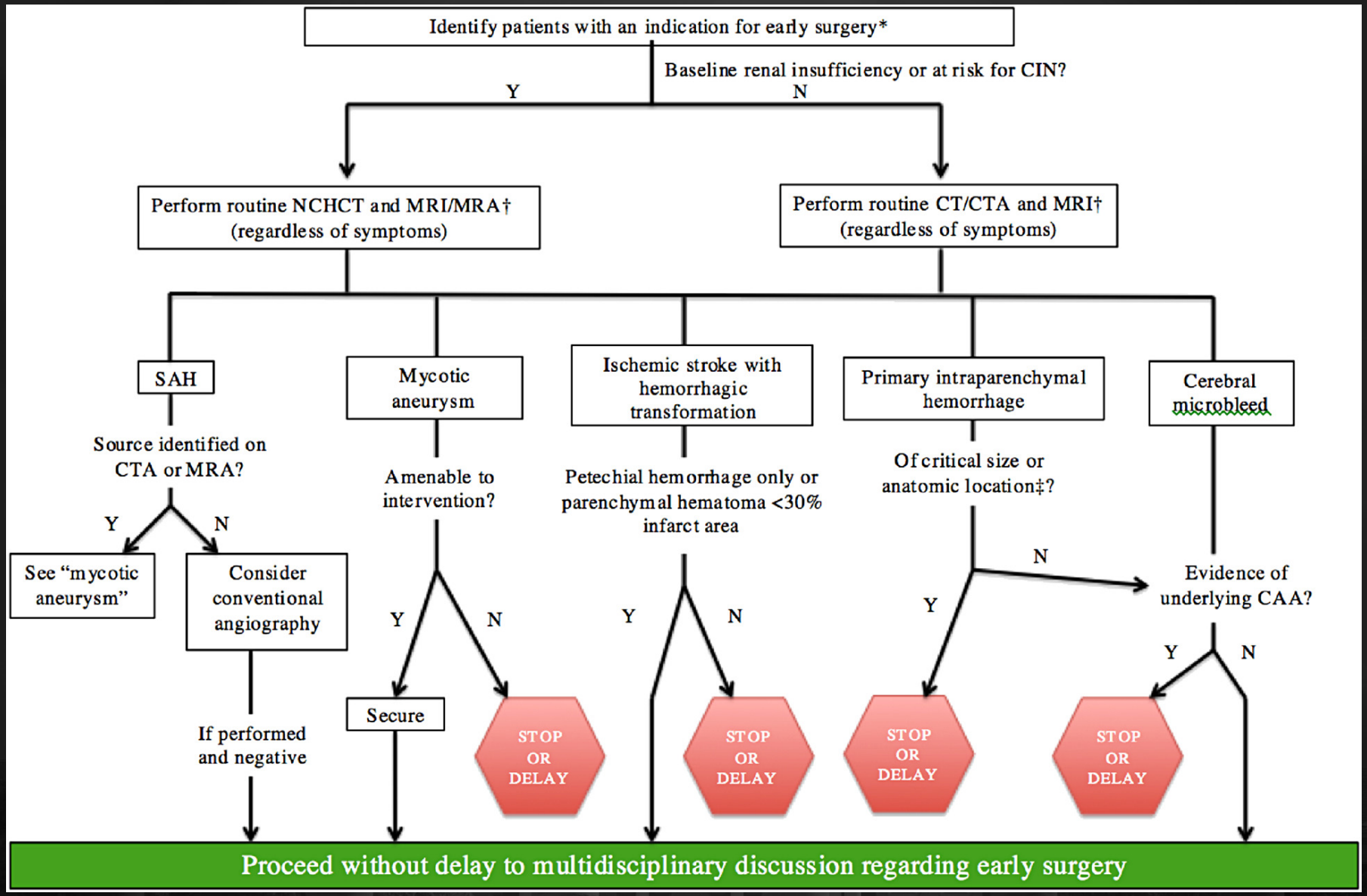
Table 5. Reasons for Lack of Surgery Among Patients With Surgical Indications

Reason for Lack of Surgery	Overall(n=181)*	Staphylococcus aureus(n=61)	Non–S aureus(n=120)	OR (95% CI)*P* Value
Stroke†	37 (22.7)	15 (30)	22 (19.5)	1.77 (0.76–4.04)
Intracranial hemorrhage	24 (15.2)	6 (13.3)	18 (15.9)	0.81 (0.25–2.35)
Heart failure	18 (11.7)	6 (13.3)	12 (11)	1.24 (0.36–3.89)
Sepsis	33 (21)	16 (32.7)	17 (15.7)	2.60 (1.08–6.14)
Hemodynamic instability	40 (19.8)	14 (21.5)	26 (19)	1.17 (0.52–2.56)
Prognosis poor regardless of treatment	55 (33.7)	21 (44.7)	34 (29.3)	1.95 (0.91–4.15)
Patient refused	23 (15)	13 (26.5)	17 (15.9)	0.79 (0.24–2.32)
Patient died before surgery	37 (23.3)	4 (9.5)	24 (21.8)	1.29 (0.54–2.99)
Resources not available	8 (5.5)	12 (26.1)	4 (3.8)	2.63 (0.46–14.78)
Surgeon declined to operate	40 (25.8)	10 (24.4)	28 (25.7)	1.02 (0.42–2.37)
Other	46 (32.6)	12 (25.5)	36 (36)	0.57 (0.22–1.38)
Future surgery anticipated or scheduled	39 (26)	12 (25.5)	27 (26.2)	0.97 (0.40–2.20)
STS-IE score, median (25th, 75th percentiles)	27 (15, 37)	32 (20, 39)	24 (15, 35)	*P*=0.01

Chu, Vivian H., et al. "Association between surgical indications, operative risk, and clinical outcome in infective endocarditis: a prospective study from the International Collaboration on Endocarditis." *Circulation* 131.2 (2015): 131-140.

Cardiac Surgical Risk for Mortality

- Non-Specific Scores
  - Society of Thoracic Surgeons – Score (STS-score)
  - European System for Cardiac Operative Risk Evaluation (Euro Score)
- IE – Specific (listed based on highest to lowest predictive capacity)
  - STS-IE
  - Risk – Endocarditis Score (RISK-E)
  - Prosthesis, Age >70, Large Intracardiac Destruction, Staphylococcus, Urgent Surgery, Female Sex (PALSUSE)
  - De Feo-Cotrufo Score
  - Costa Score



- Venn, R. A., et al. "Surgical timing in infective endocarditis complicated by intracranial hemorrhage." *American heart journal* 216 (2019): 102.

Multi-disciplinary Teams for Infective Endocarditis

University of Missouri

Authors	Methods, Valves	Development, structure and Function of MDT	Reported statistically significant outcomes
Bothelho-Nevers et al, France	Observational before[1991-2001, N = 173] - after [2002-2006, N = 160] study Type of Valve: Both NVE and PVE cases included Duke Criteria: Only Definite IE	Standardized diagnostic and therapeutic protocol: 1. 1994 – diagnosis kit was implemented(systematic serology testing, blood cultures, microbiological and histological analysis of removed valves) 2. 2002 - MDT was fully implemented with a protocol/ medical-surgical guide - Final decisions were taken in multi-disciplinary way	1. Mortality decreased from 18.5% (before) to 8.2% (after). 2. Improved compliance for antimicrobial therapy 3. Reduction in embolic events, renal failure, multiple organ failure syndromes
Chirillo et al, Italy	Observational before [1996-2002, N = 102] and after [2003 – 2009, N = 190] study. Type of valve: Only NVE Duke Criteria: Only Definite IE	Standardized diagnostic and therapeutic model: 1. 2003 – Mandated referral to MDT –cardiology, infectious disease, microbiology, cardiac surgery. 2. Particular attention to standardization of blood cultures and echocardiography	1. Overall Mortality decreased from 28% (before) to 13%(after) [surgical mortality 47% to 13%, 3 year mortality 34% to 16%] 2. Less culture negative IE 3. Less renal failure
Carrassco-Chinchilla F et al, Spain	Prospective cohort study (2008-2011, N = 72) compared to historical cohort (1996-2007, N = 155) Type of Valve: NVE and PVE but only left sided IE Duke Criteria: Definite or possible	Since 2008 – Alerta Multidisciplinaria en endocarditis infecciosa (AMULTEI) [Multidisciplinary Alert strategy in Infective Endocarditis] MDT structure: • Clinical – internal medicine, infectious diseases • Microbiological • Echocardiography • Cardiac surgery involved if Duke criteria satisfied	Early surgery was more frequently performed Incidence of shock was significantly lower during hospitalization Mortality was lower while in-hospital and during first month of follow-up.
Camou et al, France	Retrospective Observational – descriptive study on the results of 4.5 years of activity of their MDT (2013-2017) Type of Valve: NVE and PVE Duke Criteria: Definite or possible IE	Since 2010 – a weekly regional endocarditis multi-disciplinary meeting aimed at diagnostic confirmation, therapeutic strategy and prospective follow-up of patients MDT structure: • Cardiologist • Infectious diseases specialist • Cardiac Surgeon • Microbiologist • Imaging specialists • Intensivist	Did not evaluate pre-MDT period, hence no conclusions could be made. Non-significant difference in mortality between community acquired and hospital acquired IE (9% vs 14%)

Authors	Methods, Valves	Development, structure and Function of MDT	Reported statistically significant outcomes
Ruch et al, France	Observational pre-(retrospective, Jan 2012- Dec 2016) and post- MDT (Jan – Dec 2017) implementation. Type of valve: NVE and PVE Duke criteria: Only Definite IE	Since 2012 – Centralized database called "Registre des Endocardites Infectieuses" collected medical, paramedical, therapeutic decisions for all patients with diagnosis of IE. MDT structure: Infectious diseases specialist Cardiologist Cardiac surgeon Echocardiographer	Non-significant decrease in in-hospital mortality (pre-MDT 20.3% vs post-MDT 14.7%) Significant reduction between pre- vs post-MDT : 1. Time to surgery (16.4 days vs post-MDT 10.3 days) 2. Antibiotic days (55.2 vs 47.2 days) 3. Hospital days (40.6 vs 31.9 days) 4. Multi-variate analysis: post-MDT period was positively associated with survival.
Issa N et al, France	Prospective observational study (Jan 2013 – Mar 2016, N = 357 patients) Type of valve: NVE and PVE Duke criteria: Definite or possible	Since 2010- MDT weekly meetings	
Kaura et al, UK	Observational before (Aug 2009 – Jun 2012) and after (Jul 2012 – Apr 2015) study	Since 2012 – MDT was implemented. Initial evaluation by cardiologist for suspected cases, followed by TTE/TEE and later referred to MDT if clinical suspicion is high. MDT structure: • Two cardiologists • One microbiologist • One cardiac imaging specialist • One cardiac surgeon • Nurse coordinator	Reduction in time to IE specific antibiotic therapy (4±4 days to 2.5± 3.5 days) and time to surgery (7.8±7.3 days vs 5.3±4.2 days) Improved survival from 42.9% to 66.7%
Mestres et al, Spain	An editorial describing a 30-year perspective and experience on the structure of MDT (1985-2014)	Since 1979 – Working group on IE – database creation, cardiovascular tissue bank, collaboration with infectious diseases, cardiology and cardiac surgery 1. Since 1993 – Storage of pathogenic strains – experimental endocarditis laboratory 2. Since 1994 – Weekly meetings on IE MDT main structure: • Infectious diseases specialist • Microbiologist • Specialists in heart valve disease and cardiac imaging • Cardiac surgeon • Pathologist • Specialist in OPAT	No data on outcomes reported

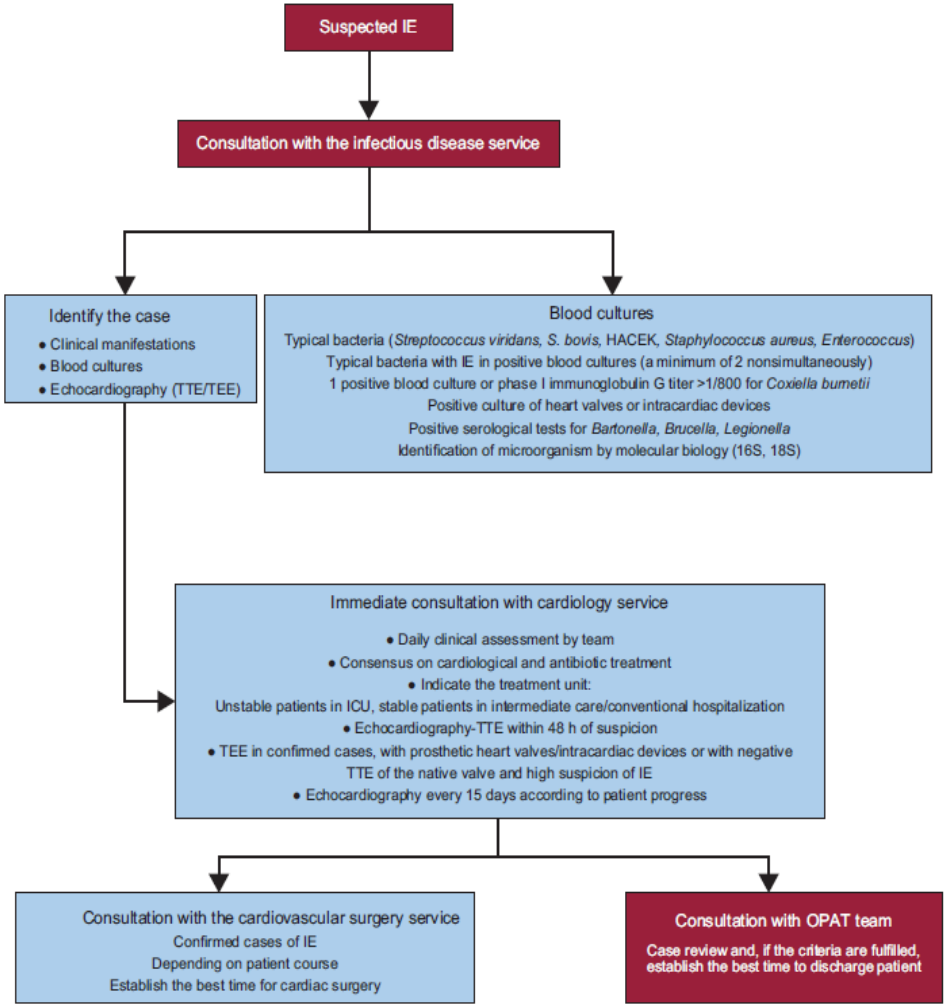


Figure 2. Care process of patients with infective endocarditis admitted to hospital with a cardiovascular surgery service. HACEK, *Haemophilus parainfluenzae*, *H. aphrophilus*, *H. paraphrophilus*, *H. influenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*, and *K. denitrificans*; ICU, intensive care unit; IE, infective endocarditis; OPAT, outpatient parenteral antibiotic therapy; TEE, transesophageal echocardiography, TTE, transthoracic echocardiography.

Mission Statement

- To standardize and improve the management of patients with infective endocarditis by developing a multi-disciplinary team in order to enable continued quality improvement.

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Retrospective Review of Infective Endocarditis 2007-2012

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University of Missouri-Columbia School of Medicine

1288

Background

- IE accounts for 0.1% of all admissions at our institution and comprises a significant portion of infectious diseases consultations
- Here, retrospective review of our experience with IE as defined by the modified Duke Criteria from 2007-2012

Clinical Features

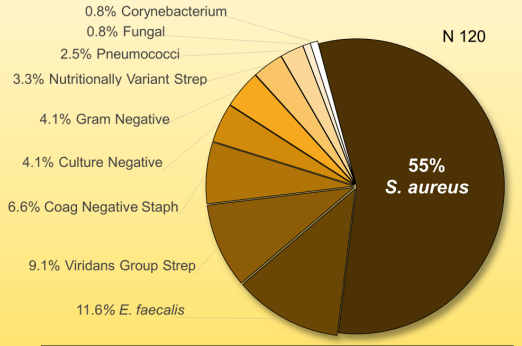
Fever	112 (93%)
New/Changed Murmur	67 (55%)
Osler's Nodes	3 (2%)
Janeway Lesions	0
Roth's Spots	5 (4%)
Conjunctival Hemorrhages	3 (2%)
Splenomegaly	13 (10%)
Splinter Hemorrhages	2 (1%)
Elevated ESR	65 (54%)
Elevated CRP	54 (45%)
Elevated RF	11 (9%)
Hematuria	7 (5%)

Baseline Characteristics/Predisposing Conditions

Number of Patients	120
Male: Female	69:51
Mean Age (Range) Y	48.6 (18-90)
Definite IE : Possible IE	98:22

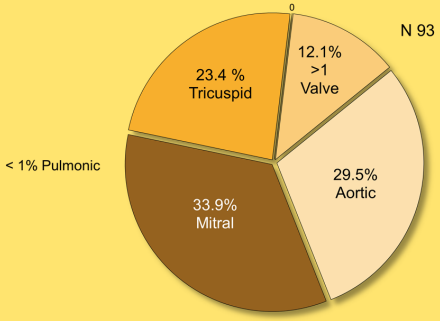
Hemodialysis	24 (20%)
Diabetes	26 (21%)
HIV	4 (3%)
Cancer	5 (4%)
Presentation <1 Month	102 (85%)
IV Drug use (IVDU)	26 (21%)
Previous IE	27 (22%)
Invasive Procedure < 60d	22 (18%)
Long-Term IV	16 (13%)
Congenital Heart Defect	2 (1%)
Native Valve Predisposition	32 (26%)
Intracardiac Device	5 (4%)
Prosthetic Valve	27 (22%)
Dental Procedure	23 (19%)

Distribution of Microorganisms All Cases

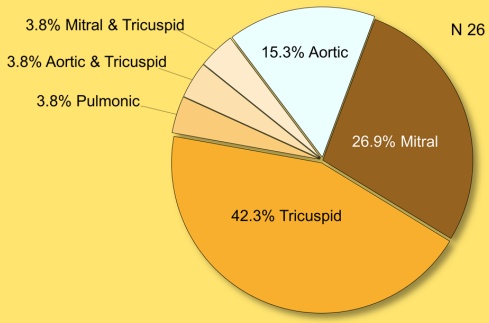


	Native Valve (n 67)	Native Valve IVDU (n 26)	Prosthetic Valve (n 27)
S. aureus	55.2%	69.2%	40.7%
Viridans Group Strep	5.9%	3.8%	22.2%
E. faecalis	11.9%	7.6%	14.8%
Nutritionally Variant Strep	Ø	11.5%	3.7%
Gram Negative	2.9%	7.6%	3.7%
Other	24.1%	Ø	Ø

Frequency of Native Valve Infected



Frequency of Infected Valve - IVDU



Complications/Mortality

CHF: 15%, CVA: 9.1%, Septic Emboli: 41.6%
Death: 9.1%, Persistent Bacteremia: 2.5%
Surgery: 30%, Time to surgery: 21d [1-120]

Conclusions

-Most presented early with few classical findings
-Nutritionally variant strep more common in IVDU
-Early surgery was rare in our series
-All 3 cases of Pneumococci were in alcoholics

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Team Development – Tuckman Model


ID


ID


ID


PIP

Forming	Storming	Norming	Performing
Performance Improvement Professional – Ms. Terhune Myself and Fellows – Drs. Vyas, Vasudevan and Chen. •Key role in direct care of IE patients (FRONTLINE experts)	Literature review Multi-Disciplinary team Review evidence for past year 2016-17 Focus on cases with early intervention that did not undergo surgery	Discuss with key service providers and formulate plan **Cardiothoracic Surgery Cardiology** **Internal Medicine** **Intensive Care Unit**	Develop a standardized approach for UMHC Integrate into EMR – Clinical Decision support Implement from small focus group (IM, CCM) and proceed to large group (Entire hospital) Measure variation and adapt - QI


ID/CC


Cardiology


CTS

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Methods

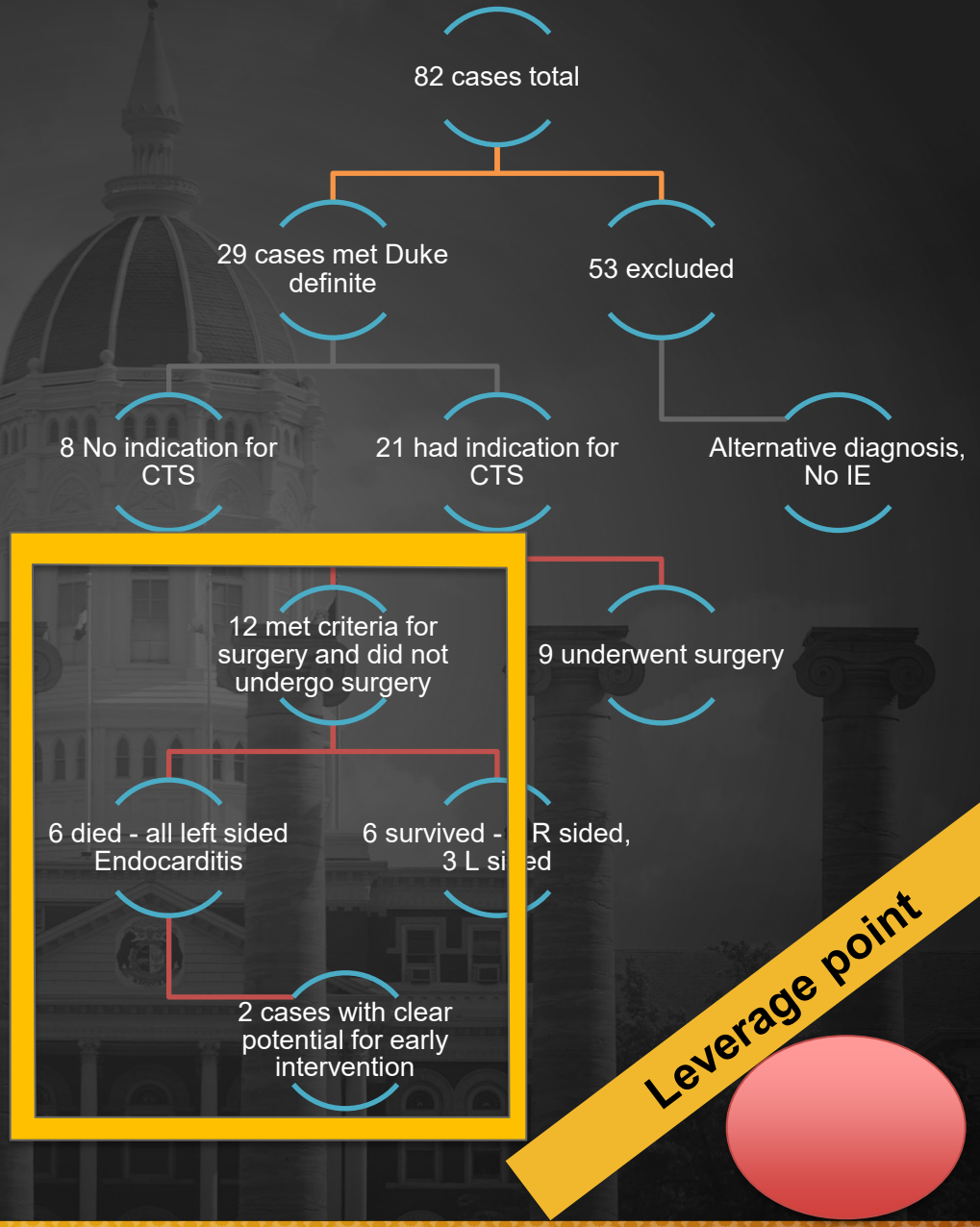
- https://www.vizientinc.com/
- Period: Jan – Dec 2016 (Quarters 1-4)
- For each case, confirmed Duke Criteria and noted down who was primary service (Internal Medicine, Family Medicine, Cardiology, CTS) and which consult teams were involved (ID, Cardiology, CT surgery). We explored charts for indications for surgery (ID consult, Cardiology notes) and noted how many qualifying cases actually underwent surgery and how many did not.
- For cases who did not undergo surgery, explored for the reason behind not doing surgery and outcomes. For cases who underwent surgery, outcomes and complications.

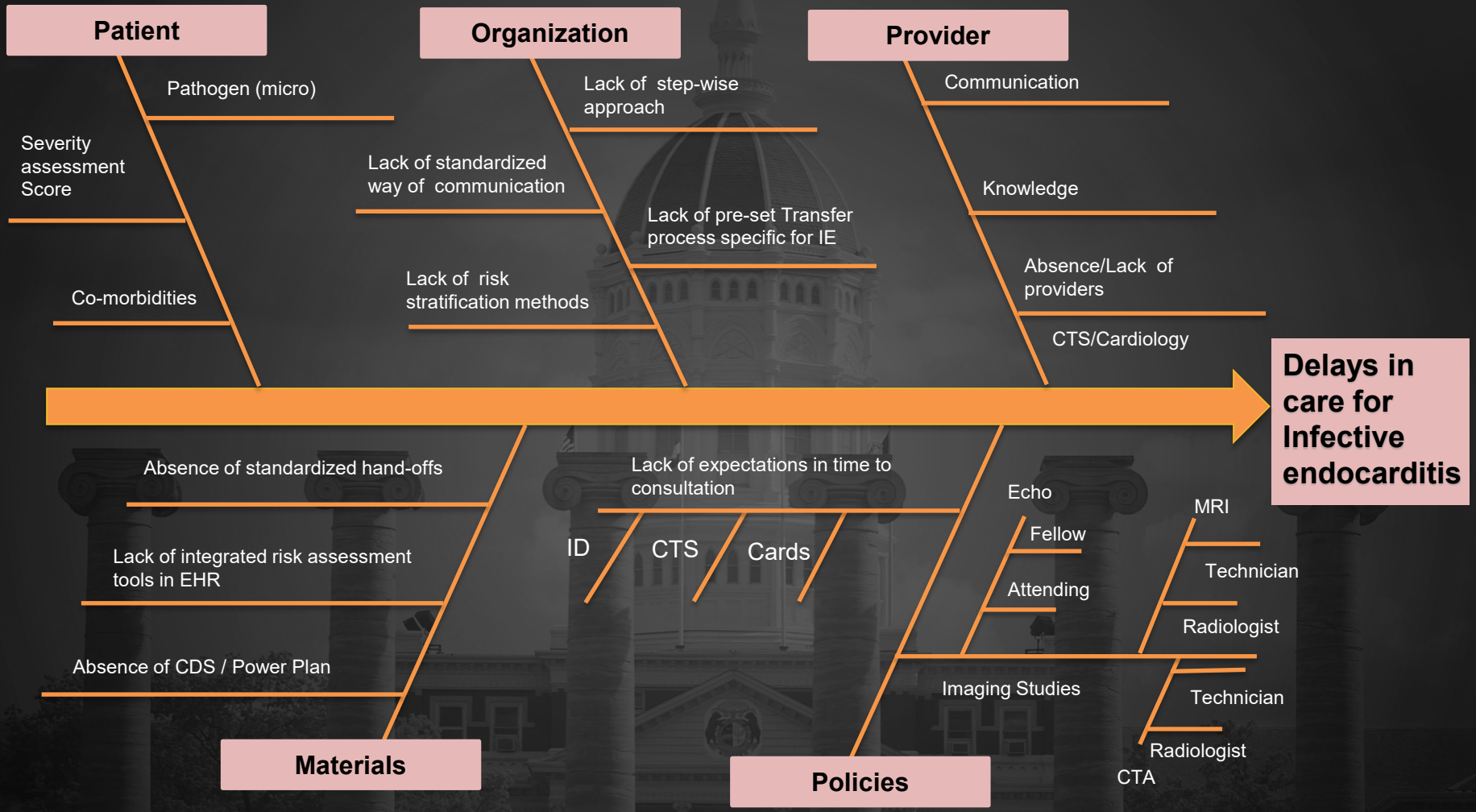
421 - AC/SUBAC ENDOCARDITIS	ACUTE AND SUBACUTE ENDOCARDITIS			
4210	4210 - AC/SUBAC BACT ENDOCARD	ACUTE AND SUBACUTE ENDOCARDITIS	ACUTE AND SUBACUTE BACTERIAL ENDOCARDITIS	
4211	4211 - AC INF ENDOCARD IN DCE	ACUTE AND SUBACUTE ENDOCARDITIS	ACUTE AND SUBACUTE INFECTIVE ENDOCARDITIS IN DISEASES CLASSIFIED ELSEWHERE	
4219	4219 - AC/SUBAC ENDOCARD NOS	ACUTE AND SUBACUTE ENDOCARDITIS	ACUTE ENDOCARDITIS, UNSPECIFIED	
4249	4249 - ENDOCARDITIS NOS	OTHER DISEASES OF ENDOCARDIUM	ENDOCARDITIS, VALVE UNSPECIFIED	
42490	42490 - ENDOCARDITIS UNSPECIFIED	OTHER DISEASES OF ENDOCARDIUM	ENDOCARDITIS, VALVE UNSPECIFIED	ENDOCARDITIS, VALVE UNSPECIFIED, UNSPECIFIED CAUSE
42491	42491 - ENDOCARDITIS IN OTH DIS	OTHER DISEASES OF ENDOCARDIUM	ENDOCARDITIS, VALVE UNSPECIFIED	ENDOCARDITIS IN DISEASES CLASSIFIED ELSEWHERE
42499	42499 - ENDOCARDITIS NEC	OTHER DISEASES OF ENDOCARDIUM	ENDOCARDITIS, VALVE UNSPECIFIED	OTHER ENDOCARDITIS, VALVE UNSPECIFIED

I33 - Acute and subacute endocarditis	
I330	I330 - Acute and subacute infective endocarditis
I339	I339 - Acute and subacute endocarditis, unspecified
I38	I38 - Endocarditis, valve unspecified
I39	I39 - Endocarditis and heart valve disord in dis classd elswhr
M3211	M3211 - Endocarditis in systemic lupus erythematosus

Results

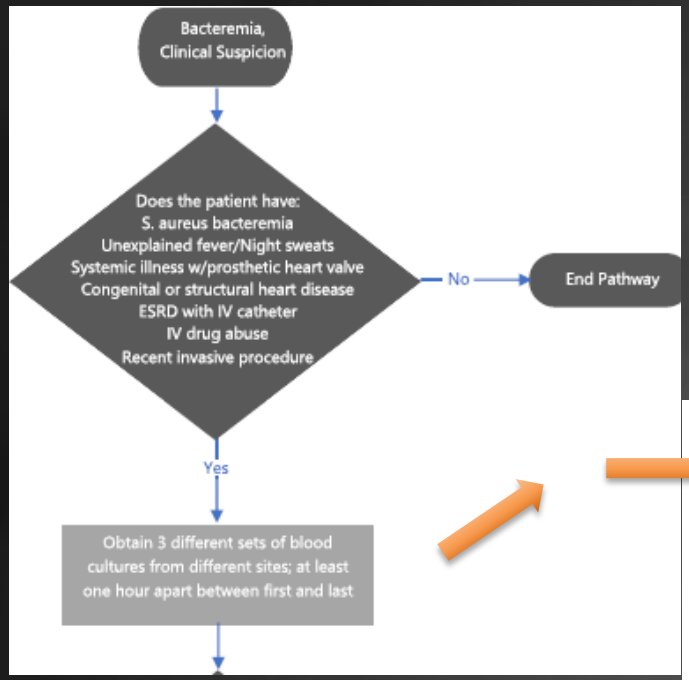
- 29 cases met Duke critteria
- 21 (72.4%) had indications for surgery per IDSA/ATS
  - 9/21 (42.9%) underwent surgery
- 12/21 (57.1%) did not undergo surgery, of which 6/12 (50%) died.
- Of all 9 cases with Left sided IE, 2/9 (22.2%) had potential for early intervention.

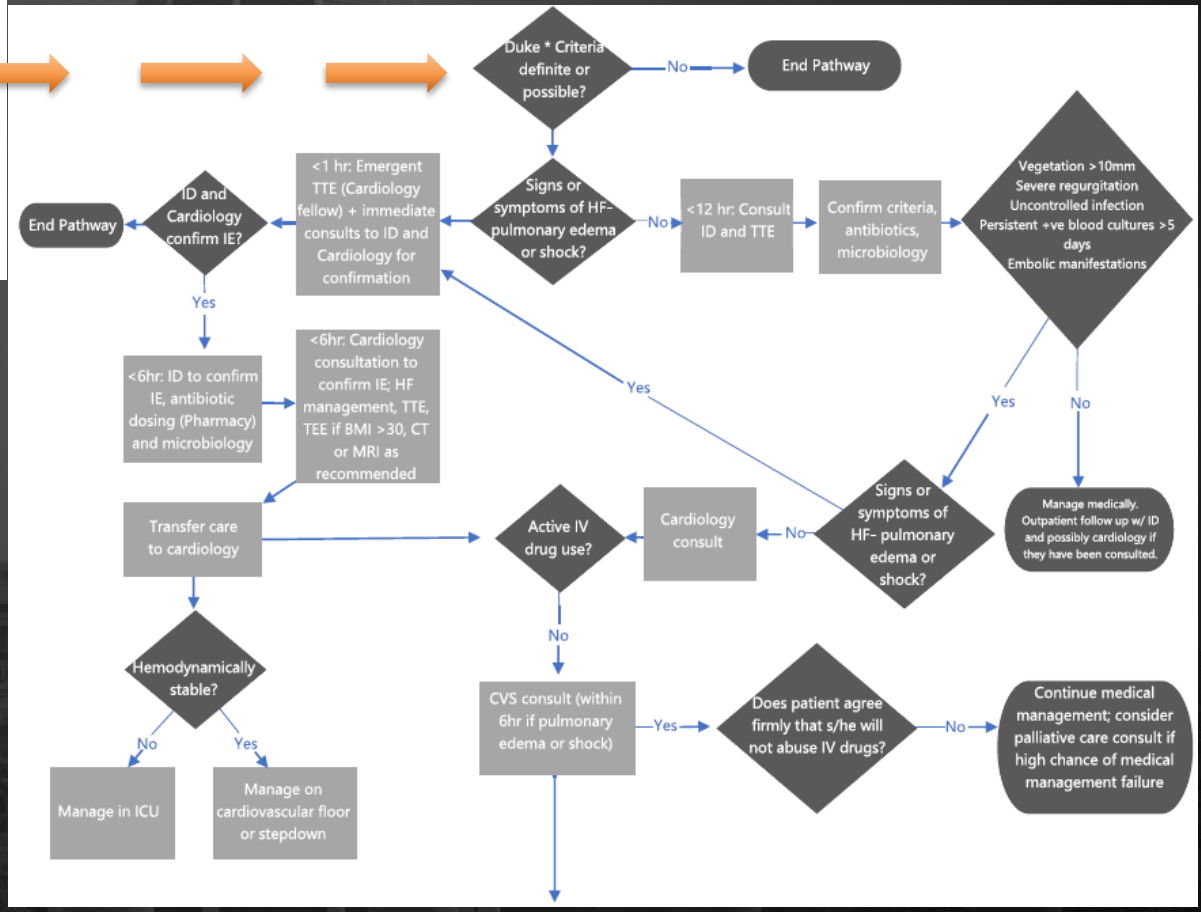



Patient
Pathogen (micro)
Severity assessment Score
Co-morbidities
Organization
Lack of step-wise approach
Lack of standardized way of communication
Lack of pre-set Transfer process specific for IE
Lack of risk stratification methods
Provider
Communication
Knowledge
Absence/Lack of providers
CTS/Cardiology
Delays in care for Infective endocarditis
Absence of standardized hand-offs
Lack of integrated risk assessment tools in EHR
Absence of CDS / Power Plan
Materials
Lack of expectations in time to consultation
ID
CTS
Cards
Policies
Echo
Fellow
Attending
Imaging Studies
MRI
Technician
Radiologist
Technician
Radiologist
CTA

Clinical Decision Support Algorithm for IE

University of Missouri, Columbia, MO





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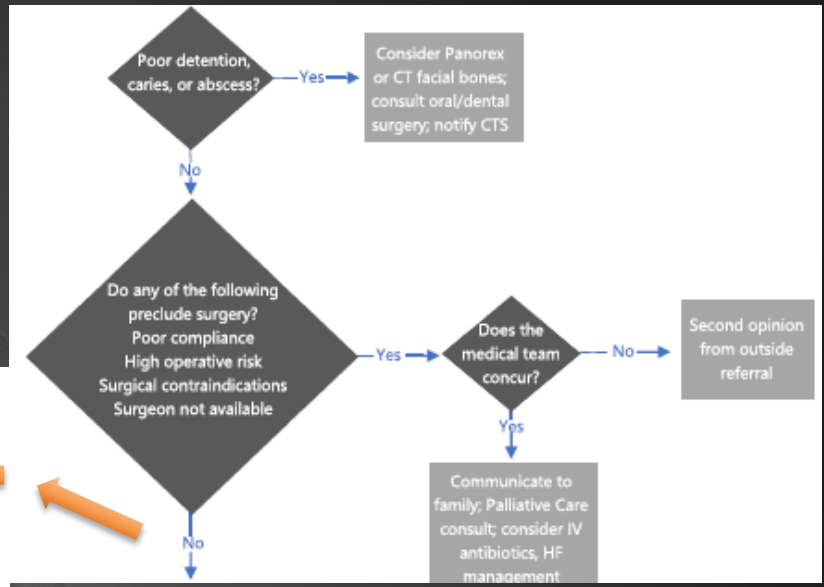
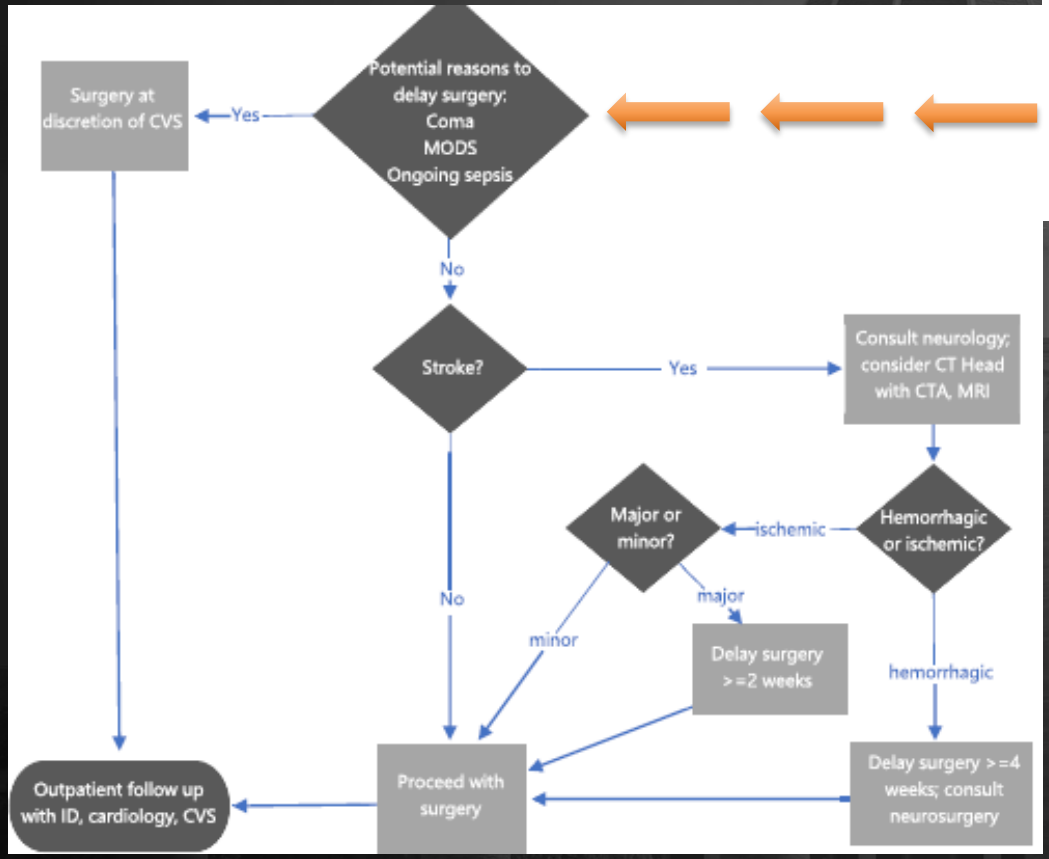
Clinical Decision Support Algorithm for IE

University of Missouri, Columbia, MO

Continued…….





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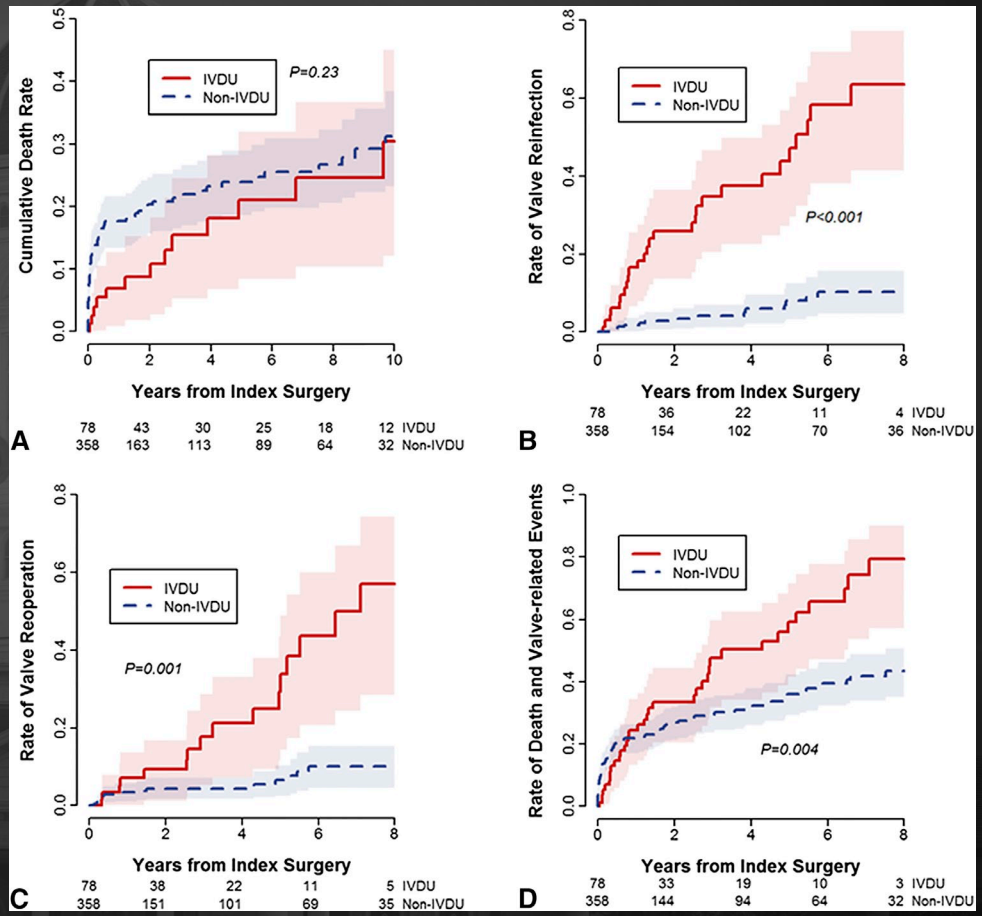
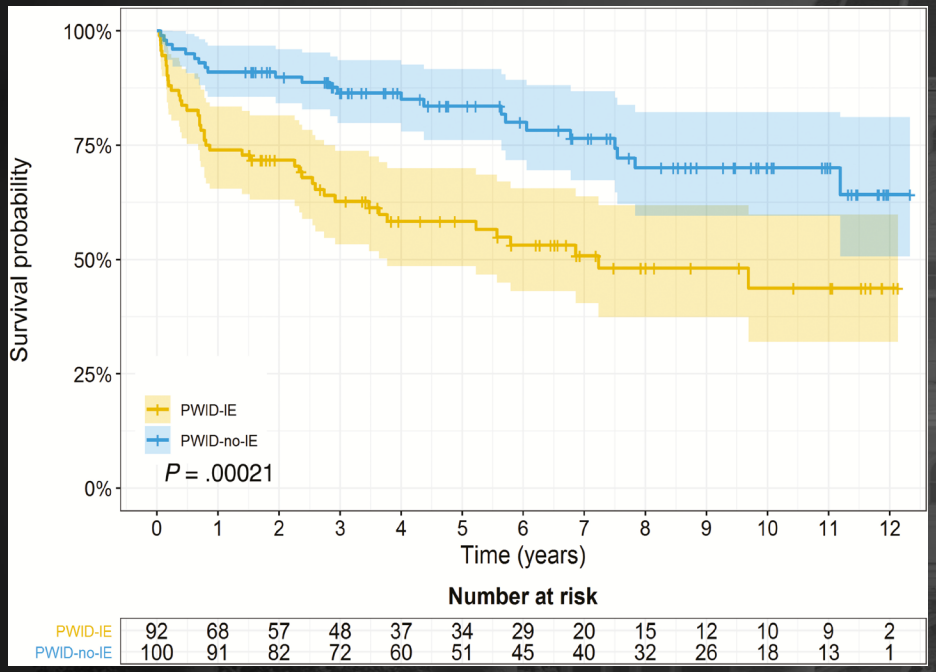
IVDU – Surgical Outcomes

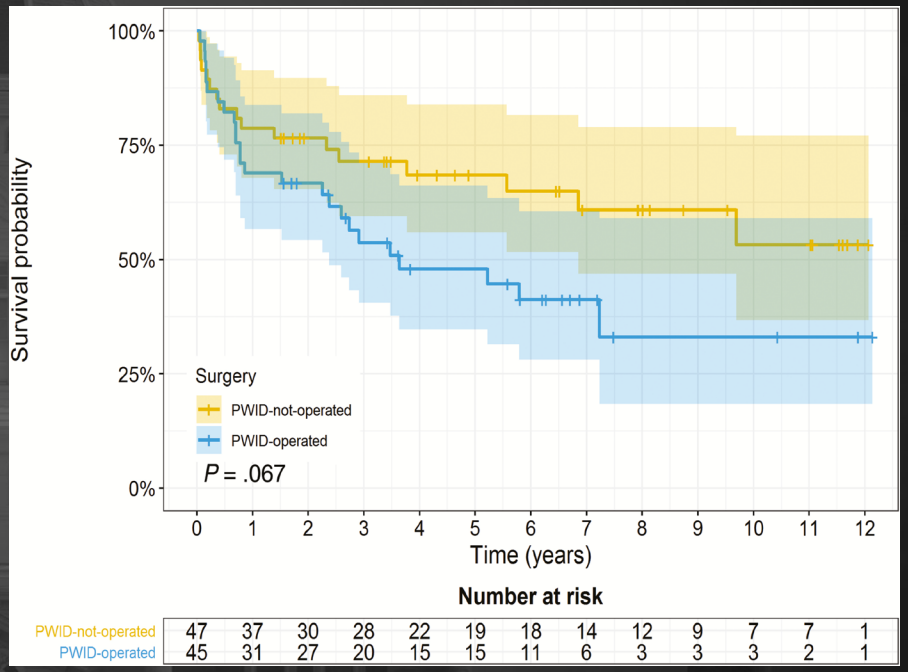
- Younger (35.9 ± 9.9 years) – fewer cardiovascular risk factors than non IVDU
- Median follow up 29.4 months (4.7 – 72.6 months)
- Operative mortality was lower (OR 0.25, CI 0.06 – 0.71)
- Overall mortality was not significantly different
- Higher risk of valve related complications (HR 3.82, CI 1.95-7.49)
  - Primarily re-infection (HR 6.2, CI 2.56 – 15.0)



Kim, Joon Bum, et al. "Surgical outcomes of infective endocarditis among intravenous drug users." *The Journal of thoracic and cardiovascular surgery* 152.3 (2016): 832-841.

IVDU – IE vs other infections (no-IE)





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Straw S, Baig MW, Gillott R, Wu J, Witte KK, O'Regan DJ, Sandoe JAT. Long-term outcomes are poor in intravenous drug users following infective endocarditis, even after surgery. Clin Infect Dis. 2019 Sep 3. pii: ciz869. doi: 10.1093/cid/ciz869. [Epub ahead of print] PubMed PMID: 31504326.

Should we offer surgery for relapsing IVDU ?

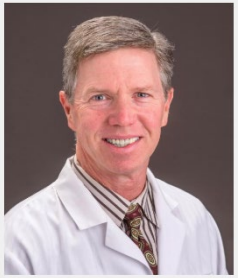
- Not Easy to Answer – Complicated scenarios
  - Stigma – Social, Financial, Long-Term impact – clouded medical judgement
  - We are ineffective in our measures beyond the hospital
  - Lack of interventional and behavioral studies on long term impact – More research is needed
- Our answer as an institution ?
  - Probably, YES!
    - Humanitarian and ethical - reasonable evidence for improving short-term outcomes which may give a few years with reasonable QOL
    - Beyond 2nd relapse – individualized approach – discussion between surgeon and patient

Acknowledgements

HOME / OUR STORIES / PHYSICIAN ENGAGES COLLEAGUES TO HELP PATIENTS WITH HEART VALVE INFECTION

Physician Engages Colleagues to Help Patients with Heart Valve Infection

ROBERT PIERCE, MD



SERVICE LINE
Family Medicine

SPECIALTIES
Family Medicine

INTERESTS
Community Medicine

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Accepting New Patients

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Hospitalist

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Internal Medicine

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STEVAN WHITT, MD

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Thank You for your attention!