Diagnostic Criteria for Infective Endocarditis

2023 Duke ISCVID Criteria

Vance Fowler, MD,
on Behalf of the Working Group of the International Society of Cardiovascular Infectious Diseases (ISCVID)

April 16, 2023

Disclosures

Nature of Relevant Financial Relationship	Commercial Interest
Grant or research support	Allergan, Basilea; Contrafect; Genentech; Janssen; Karius; MedImmune, Merck; Pfizer, Regeneron
Paid consultant	Achaogen, Affinergy; Affinium; Affinivax, Amphliphi; Armata, Akagera, Aridis; Basilea; Bayer; Brii; C3J; Contrafect; Debiopharm; Destiny; Genentech/Roche; Integrated Biotherapeutics; Janssen; MedImmune; Medicines Co.; Regeneron; Novartis, Pfizer; Valanbio
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Endocarditis: The Only Constant is Change

Infect Dis Ther
https://doi.org/10.1007/s40121-023-00763-8

Check for updates

ORIGINAL RESEARCH

Epidemiological Changes and Improvement in Outcomes of Infective Endocarditis in Europe in the Twenty-First Century: An International Collaboration on Endocarditis (ICE) Prospective Cohort Study (2000–2012)

Juan Ambrosioni · Marta Hernández-Meneses · Emanuele Durante-Mangoni · Pierre Tattevin · Lars Olaison · Tomas Freiberger · John Hurley · Margaret M. Hannan · Vivian Chu · Bruno Hoen · Asunción Moreno · Guillermo Cuervo · Jaume Llopis · José M. Miró

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Endocarditis & Change

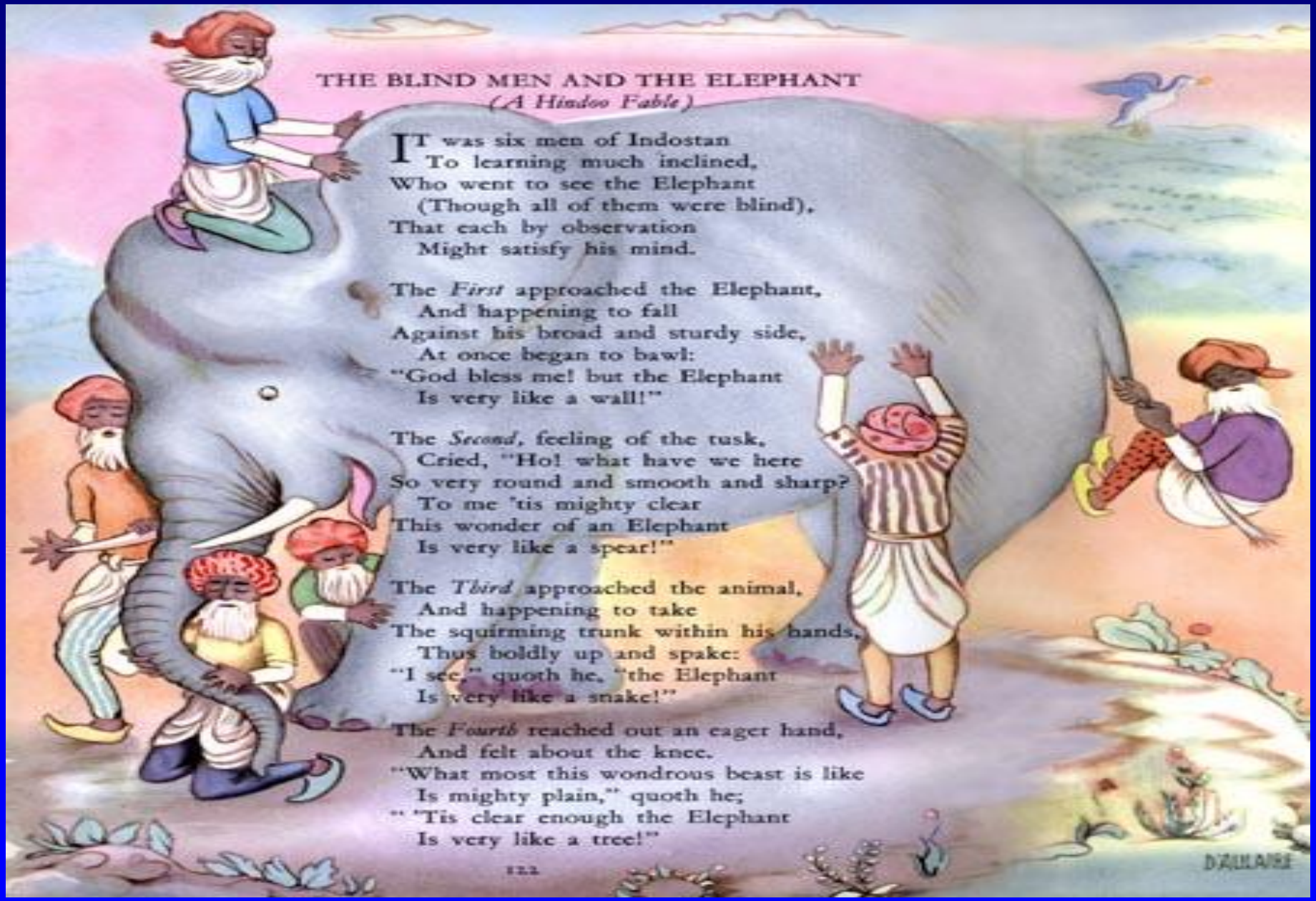
- **IE Criteria have not kept up**
- **The field needs a way to regularly update IE Criteria**

Why Do We Need Diagnostic Criteria for IE?

- Clinical Management:
  Decision-making

- Research:
  Definitions

Why Definitions are Important for IE Research



Infective Endocarditis: An Analysis Based on Strict Case Definitions

C. FORDHAM VON REYN, M.D.; BARRY S. LEVY, M.D., M.P.H.; ROBERT D. ARBEIT, M.D.; GERALD FRIEDLAND, M.D.; and CLYDE S. CRUMPACKER, M.D.; Boston, Massachusetts

Definite

Direct evidence of infective endocarditis based on histology from surgery or autopsy, or on bacteriology (Gram stain or culture) of valvular vegetation or peripheral embolus.

Probable

A. Persistently positive blood cultures* plus one of the following:
   1. New regurgitant murmur, or
   2. Predisposing heart disease† and vascular phenomena‡

B. Negative or intermittently positive blood cultures§ plus all three of the following:
   1. Fever
   2. New regurgitant murmur, and
   3. Vascular phenomena

Possible

A. Persistently positive blood cultures plus one of the following:
   1. Predisposing heart disease, or
   2. Vascular phenomena

B. Negative or intermittently positive blood cultures with all three of the following:
   1. Fever
   2. Predisposing heart disease, and
   3. Vascular phenomena

C. For viridans streptococcal cases only: at least two positive blood cultures without an extra-cardiac source, and fever.

Rejected

A. Endocarditis unlikely, alternate diagnosis generally apparent
B. Endocarditis likely, empiric antibiotic therapy warranted
C. Culture negative endocarditis diagnosed clinically, but excluded by postmortem

Annals of Internal Medicine. 1981;94(Part 1):505-518.

1980s:
Changes in Imaging

Echocardiography in Infective Endocarditis: Reassessment of Prognostic Implications of Vegetation Size Determined by the Transthoracic and the Transesophageal Approach

ANDREAS MÜGGE, MD, WERNER G. DANIEL, MD, GÜNTER FRANK, MD,
PAUL R. LICHTLEN, MD, FACC
Hannover, West Germany

(J Am Coll Cardiol 1989;14:631–8)

IMPROVEMENT IN THE DIAGNOSIS OF ABSCESSES ASSOCIATED WITH ENDOCARDITIS BY TRANSESOPHAGEAL ECHOCARDIOGRAPHY

WERNER G. DANIEL, M.D., ANDREAS MÜGGE, M.D., RANDOLPH P. MARTIN, M.D., OLIVER LINDERT, M.D.,
DIRK HAUSMANN, M.D., BARBARA NONNAST-DANIEL, M.D., JOACHIM LAAS, M.D.,
AND PAUL R. LICHTLEN, M.D.

N Engl J Med 1991; 324:795-800.

Year	Diagnostic Criteria	Improvement
1981	Von Reyn	1. Definite, Probable, Possible, Rejected

New Criteria for Diagnosis of Infective Endocarditis: Utilization of Specific Echocardiographic Findings

DAVID T. DURACK, M.B., D.Phil., ANDREA S. LUKES, B.A. , DAVID K. BRIGHT, M.D., Pharm. D., and the DUKE ENDOCARDITIS SERVICE,* *Durham, North Carolina*

200 March 1994 The American Journal of Medicine Volume 96

Duke vs. von Reyn Criteria:

1) Major & Minor Criteria
2) Echocardiography

Major Criteria

Positive blood culture for infective endocarditis
- Typical microorganism for infective endocarditis from two separate blood cultures
  - Viridans streptococci,* *Streptococcus bovis,* HACEK group, *or*
  - Community-acquired *Staphyloccus aureus* or enterococci, in the absence of a primary focus, *or*
- Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from:
  - (i) Blood cultures drawn more than 12 hours apart, *or*
  - (ii) All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart

Evidence of endocardial involvement
- Positive echocardiogram for infective endocarditis
  - (i) Oscillating intracardiac mass, on valve or supporting structures, *or* in the path of regurgitant jets, *or* on implanted material, in the absence of an alternative anatomic explanation, *or*
  - (ii) Abscess, *or*
  - (iii) New partial dehiscence of prosthetic valve, *or*
- New valvular regurgitation (increase or change in pre-existing murmur not sufficient)

Minor Criteria

Predisposition: predisposing heart condition *or* intravenous drug use

Fever: ≥ 38.0°C (100.4°F)

Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions

Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor

Microbiologic evidence: positive blood culture but not meeting major criterion as noted previously† *or* serologic evidence of active infection with organism consistent with infective endocarditis

Echocardiogram: consistent with infective endocarditis but not meeting major criterion as noted previously

Duke vs. von Reyn Criteria:

3) Exclude "Probable" Criteria

Infective Endocarditis: An Analysis Based on Strict Case Definitions

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B. Negative or intermittently positive blood cultures§ plus all three of the following:
1. Fever
2. New regurgitant murmur, and
3. Vascular phenomena

Possible

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1. Predisposing heart disease, or
2. Vascular phenomena

B. Negative or intermittently positive blood cultures with all three of the following:
1. Fever
2. Predisposing heart disease, and
3. Vascular phenomena

C. For viridans streptococcal cases only: at least two positive blood cultures without an extra-cardiac source, and fever.

Rejected

A. Endocarditis unlikely, alternate diagnosis generally apparent
B. Endocarditis likely, empiric antibiotic therapy warranted
C. Culture negative endocarditis diagnosed clinically, but excluded by postmortem

New Criteria for Diagnosis of Infective Endocarditis: Utilization of Specific Echocardiographic Findings

DAVID T. DURACK, M.B., D.Phil., ANDREA S. LUKES, B.A. , DAVID K. BRIGHT, M.D., Pharm. D., and the DUKE ENDOCARDITIS SERVICE,* *Durham, North Carolina*

Proposed New Criteria for Diagnosis of Infective Endocarditis

Definite Infective Endocarditis

Pathologic criteria
- Microorganisms: demonstrated by culture or histology in a vegetation, *or* in a vegetation that has embolized, *or* in an intracardiac abscess, *or*
- Pathologic lesions: vegetation or intracardiac abscess present, confirmed by histology showing active endocarditis

Clinical criteria, using specific definitions listed in Table III
- 2 major criteria, *or*
- 1 major and 3 minor criteria, *or*
- 5 minor criteria

Possible Infective Endocarditis

Findings consistent with infective endocarditis that fall short of "definite," but not "rejected."

Rejected

Firm alternate diagnosis for manifestations of endocarditis, *or*

Resolution of manifestations of endocarditis, with antibiotic therapy for 4 days or less, *or*

No pathologic evidence of infective endocarditis at surgery or autopsy, after antibiotic therapy for 4 days or less

Year	Diagnostic Criteria	Improvement
1981	Von Reyn	1. Definite, Probable, Possible, Rejected
1994	Duke Criteria	1. Major & Minor Criteria 2. Clinical Definite Criteria 3. Add Echocardiography

1990s: Changes in Microbiology

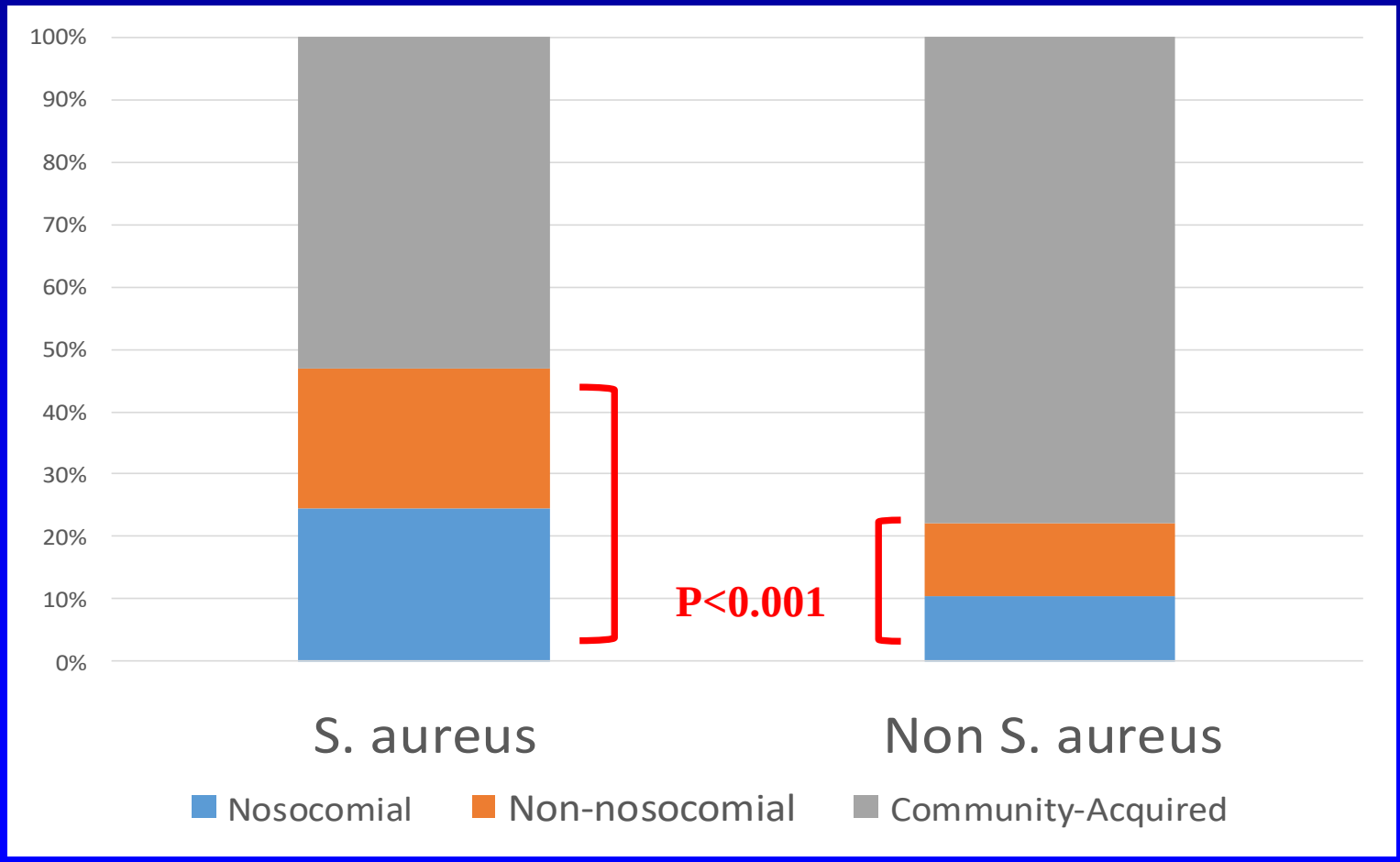
Staphylococcus aureus Endocarditis
A Consequence of Medical Progress

JAMA. 2005;293:3012-3021

Vance G. Fowler, Jr, MD, MHS
Jose M. Miro, MD, PhD
Bruno Hoen, MD, PhD
Christopher H. Cabell, MD, MHS

Context The global significance of infective endocarditis (IE) caused by *Staphylococcus aureus* is unknown.

Objectives To document the international emergence of health care–associated *S aureus* IE and methicillin-resistant *S aureus* (MRSA) IE and to evaluate regional variation in patients with *S aureus* IE.



Proposed Modifications to the Duke Criteria for the Diagnosis of Infective Endocarditis

Jennifer S. Li,[1,4] Daniel J. Sexton,[2,3] Nathan Mick,[3]
Richard Nettles,[3] Vance G. Fowler, Jr.,[2,3]
Thomas Ryan,[1,3] Thomas Bashore,[1,3]
and G. Ralph Corey[2,3]

From the Divisions of [1]Cardiology and [2]Infectious Diseases, and Departments of [3]Medicine and [4]Pediatrics, Duke University School of Medicine, Durham, North Carolina

Clinical Infectious Diseases 2000; 30:633–8

Major criteria

Blood culture positive for IE

Typical microorganisms consistent with IE from 2 separate blood cultures:

Viridans streptococci, *Streptococcus bovis,* HACEK group, *Staphylococcus aureus;* or

Community-acquired enterococci, in the absence of a primary focus; or

Microorganisms consistent with IE from persistently positive blood cultures, defined as follows:

At least 2 positive cultures of blood samples drawn >12 h apart; or

All of 3 or a majority of ≥4 separate cultures of blood (with first and last sample drawn at least 1 h apart)

Single positive blood culture for *Coxiella burnetii* or antiphase I IgG antibody titer >1 : 800

Evidence of endocardial involvement

Echocardiogram positive for IE **(TEE recommended in patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE [paravalvular abscess]; TTE as first test in other patients)**, defined as follows :

Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or

S. aureus bacteremia should be considered a major criterion in the Duke schema, regardless of whether the infection is nosocomially acquired or whether a removable source of infection is present.

Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor

Microbiological evidence: positive blood culture but does not meet a major criterion as noted above[a] or serological evidence of active infection with organism consistent with IE

Echocardiographic minor criteria eliminated

Year	Diagnostic Criteria	Improvement
1981	Von Reyn	1. Definite, Probable, Possible, Rejected
1994	Duke Criteria	1. Major & Minor Criteria 2. Clinical Definite Criteria 3. Add Echocardiography
2000	Modified Duke Criteria	1. Remove “Possible” Echo 2. Expand *S. aureus* inclusion

2000s: Changes in Imaging

Impact of Systematic Whole-body ^{18}F-Fluorodeoxyglucose PET/CT on the Management of Patients Suspected of Infective Endocarditis: The Prospective Multicenter TEPvENDO Study

Xavier Duval,[1,2,3,4] Vincent Le Moing,[5] Sarah Tubiana,[1,2,3] Marina Esposito-Farèse,[1,2,6] Emila Ilic-Habensus,[1,2] Florence Leclercq,[7] Aurélie Bourdon,[8] François Goehringer,[9] Christine Selton-Suty,[10] Elodie Chevalier,[11] David Boutoille,[12] Nicolas Piriou,[13,14] Thierry Le Tourneau,[13] Catherine Chirouze,[15] Marie-France Seronde,[16] Olivier Morel,[17] Lionel Piroth,[18] Jean-Christophe Eicher,[19] Olivier Humbert,[20] Matthieu Revest,[21,22] Elise Thébault,[22] Anne Devillers,[23] François Delahaye,[24] André Boibieux,[25] Bastien Grégoire,[26] Bruno Hoen,[9] Cédric Laouenan,[1,2,3,4,6,a] Bernard Iung,[1,2,3,4,a] and François Rouzet[1,2,3,4,27,a]; for the AEPEI-TEPvENDO study group

Clinical Infectious Diseases® 2021;73(3):393–403

Comparison of Cardiac Computed Tomography With Transesophageal Echocardiography for Identifying Vegetation and Intracardiac Complications in Patients With Infective Endocarditis in the Era of 3-Dimensional Images

Circ Cardiovasc Imaging. 2018;11:e006986

In-Cheol Kim, MD, PhD*; Suyon Chang, MD*; Geu-Ru Hong, MD, PhD; Seung Hyun Lee, MD, PhD; Sak Lee, MD, PhD; Jong-Won Ha, MD, PhD; Byung-Chul Chang, MD, PhD; Young Jin Kim, MD, PhD; Chi Young Shim, MD, PhD

2015 ESC Guidelines for the management of infective endocarditis

European Heart Journal (2015) **36**, 3075–3123

- Major Criteria
- Minor Criteria

2. Imaging positive for IE

a. Echocardiogram positive for IE:
- Vegetation;
- Abscess, pseudoaneurysm, intracardiac fistula;
- Valvular perforation or aneurysm;
- New partial dehiscence of prosthetic valve.

b. Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.

c. Definite paravalvular lesions by cardiac CT.

Year	Diagnostic Criteria	Improvement
1981	Von Reyn	1. Definite, Probable, Possible, Rejected
1994	Duke Criteria	1. Major & Minor Criteria 2. Clinical Definite Criteria 3. Add Echocardiography
2000	Modified Duke Criteria	1. Remove “Possible” Echo 2. Expand *S. aureus* inclusion
2015	ESC Criteria	1. Add PET-CT, Cardiac CT

Last 5 Years: Changes in Diagnostics

Pathogen Detection in Infective Endocarditis Using Targeted Metagenomics on Whole Blood and Plasma: a Prospective Pilot Study

Journal of Clinical Microbiology September 2022 Volume 60 Issue 9

Laure Flurin,[a,b] Matthew J. Wolf,[a] Cody R. Fisher,[a] Edison J. Cano Cevallos,[c,d] James J. Vaillant,[a,c] Bobbi S. Pritt,[a,c] Daniel C. DeSimone,[c,e] Robin Patel[a,c]

Microbial Cell-Free DNA Identifies the Causative Pathogen in Infective Endocarditis and Remains Detectable Longer Than Conventional Blood Culture in Patients with Prior Antibiotic Therapy

Clinical Infectious Diseases® 2023;76(3):e1492–e500

Emily M. Eichenberger,[1] Nicholas Degner,[2] Erick R. Scott,[2] Felicia Ruffin,[1] John Franzone,[1] Batu Sharma-Kuinkel,[1] Pratik Shah,[1] David Hong,[2] Sudeb C. Dalai,[2] Lily Blair,[2] Desiree Hollemon,[2] Eliza Chang,[2] Carine Ho,[2] Lisa Wanda,[1] Christiaan R. de Vries,[2] Vance G. Fowler Jr,[1] and Asim A. Ahmed[2]

New Perspectives for Prosthetic Valve Endocarditis: Impact of Molecular Imaging by FISHseq Diagnostics

Maria M. Hajduczenia,[1,2] Frank R. Klefisch,[3] Alexander G. M. Hopf,[1] Herko Grubitzsch,[4,a] Miriam S. Stegemann,[5,a] Frieder Pfäfflin,[5,a] Birgit Puhlmann,[6] Michele Ocken,[6] Lucie Kretzler,[7,a] Dinah von Schöning,[8,a] Volkmar Falk,[4] Annette Moter,[1,9,10,a] and Judith Kikhney[1,9,a]

Clinical Infectious Diseases® 2023;76(6):1050–8

Last 5 Years: Changes in Microbiology

Recognition of Healthcare-Associated *E. faecalis* IE

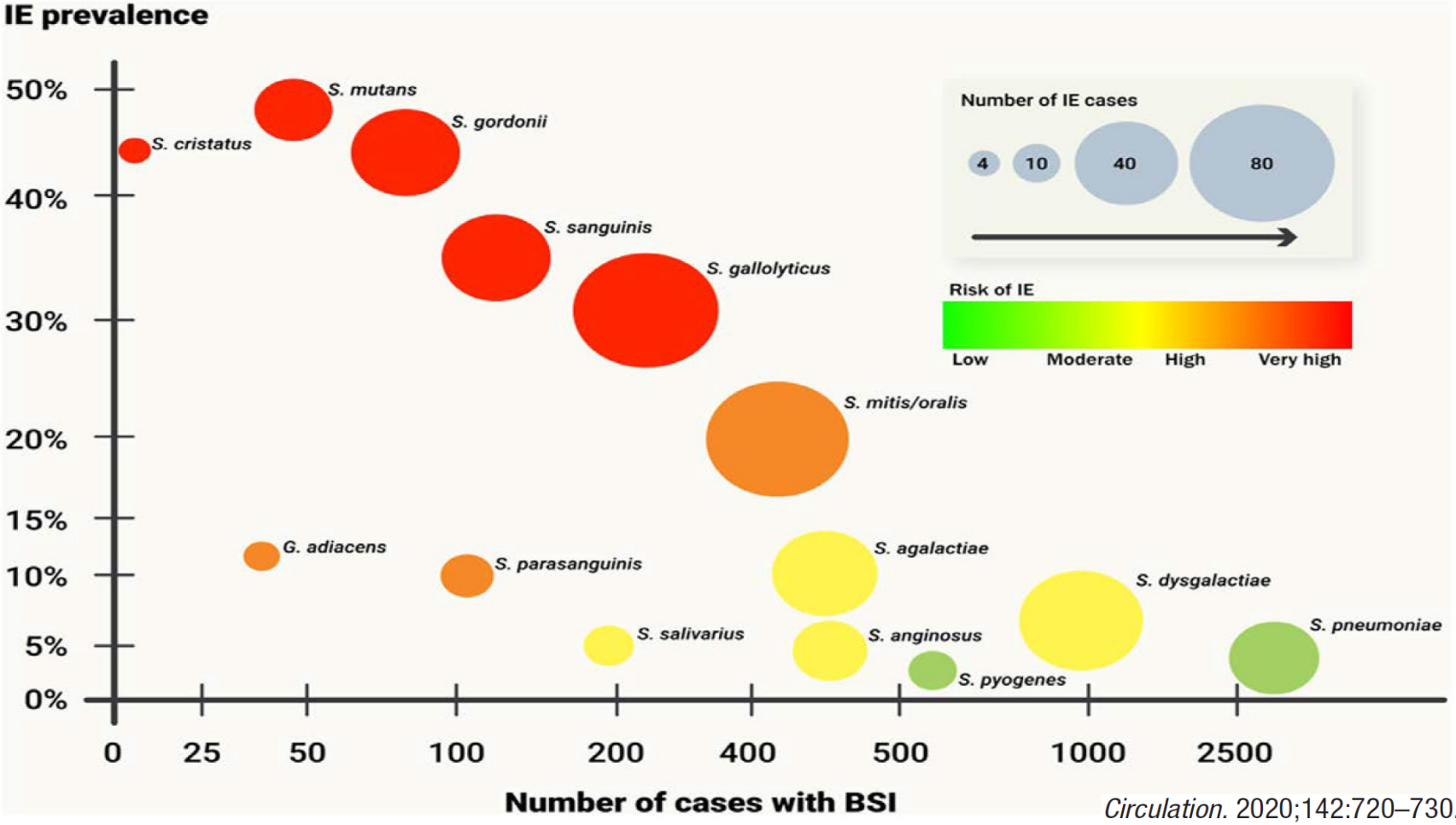
Sign of the Times: Updating Infective Endocarditis Diagnostic Criteria to Recognize *Enterococcus faecalis* as a Typical Endocarditis Bacterium

Anders Dahl,[1,2] Vance G. Fowler,[3] José M. Miro,[2,4] and Niels E. Bruun[5,6]

Clinical Infectious Diseases® 2022;75(6):1097–102

Last 5 Years: Changes in Microbiology

Risk of Streptococcal IE is Species Specific



Circulation. 2020;142:720–730.

The 2023 Duke-ISCVID Criteria for Infective Endocarditis:

Updating the Modified Duke Criteria

Vance G. Fowler, Jr[1,2*], David T. Durack[1], Christine Selton-Suty[3], Eugene Athan[4], Arnold S. Bayer[5], Anna Lisa Chamis[1], Anders Dahl[6], Louis DiBernardo[1], Emanuele Durante-Mangoni[7], Xavier Duval[8], Claudio Fortes[9], Emil Fosbøl[10], Margaret M. Hannan[11], Barbara Hasse[12], Bruno Hoen[13], Adolf W. Karchmer[14], Carlos A. Mestres[15], Cathy A. Petti[1,16], María Nazarena Pizzi[17], Stephen D. Preston[18], Albert Roque[19], Francois Vandenesch[20], Jan T. M. van der Meer[21], Thomas W. van der Vaart[21], and Jose M. Miro[, 22,23]

6 Specialties: *ID, Cardiac Surgery, Radiology, Pathology, Cardiology, Clinical Microbiology*

5 Continents, 13 Countries

Clinical Infectious Diseases in press

Timeline

- 12/21 to 1/23, multiple versions of draft were circulated within the ISCVID Council and IE Criteria Writing Group

- 6/ 2022: Draft presented in open forum of attendees at 16th ISCVID Conference for vote on unresolved issues.

- 4/2023: In press, *Clinical Infectious Diseases*

2023 Duke ISCVID Criteria

- **DEFINITE**
  - Pathologic
  - Clinical
    - 2 Major
    - 1 Major + 3 Minor
    - 5 Minor
- **POSSIBLE**
  - 1 Major + 1 Minor
  - 3 Minor
- **REJECTED**

DEFINITE: Pathologic

I. DEFINITE ENDOCARDITIS

A. Pathologic Criteria

(1) **Microorganisms identified* in the context of clinical signs of active endocarditis in a vegetation; from cardiac tissue; from an explanted prosthetic valve or sewing ring; from an ascending aortic graft (with concomitant evidence of valve involvement); from an endovascular intracardiac implantable electronic device (CIED); or from an arterial embolus**

or

(2) **Active endocarditis† (may be acute¶ or subacute/ chronic§) identified in or on a vegetation; from cardiac tissue; from an explanted prosthetic valve or sewing ring; from an ascending aortic graft (with concomitant evidence of valve involvement); from a CIED; or from an embolus**

**** by culture, staining, immunologic techniques, PCR or other nucleic acid based tests including amplicon (16S, 18S, internal transcribed spacers) sequencing, metagenomic (shotgun) sequencing, or in situ hybridization on fresh or paraffin-fixed tissue. Molecular techniques and tissue staining (Gram stain, Periodic acid Schiff with diastase [PASD], Grocott, or silver stains such as Warthin-Starry, Steiner, or Dieterle) should be interpreted cautiously, particularly in patients with a prior episode of IE since such tests can remain positive for extended periods following successful treatment. Antibiotic therapy prior to tissue procurement may also significantly alter microorganism morphology and staining characteristics. Test specificity is influenced by several factors and false positives can occur. Test interpretation should always be in the context of clinical and histological evidence of active endocarditis.*** **A single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence should be regarded as Minor Criterion and not Definite IE[51]**

DEFINITE: Clinical

No Change

B. CLINICAL CRITERIA*

(1) 2 major criteria; or

(2) 1 major criterion and 3 minor criteria; or

(3) 5 minor criteria

POSSIBLE IE:
No Change

POSSIBLE IE

A. 1 MAJOR CRITERION AND 1 MINOR CRITERION, OR

B. 3 MINOR CRITERIA

REJECTED

III. REJECTED ENDOCARDITIS

A. Firm alternate diagnosis explaining signs/symptoms‡

or

B. Lack of recurrence despite antibiotic therapy for less than 4 days.

or

C. No pathologic or macroscopic evidence of IE at surgery or autopsy, with antibiotic therapy for less than 4 days

or

D. Does not meet criteria for possible IE, as above

‡ "Firm alternate diagnosis explaining IE signs and symptoms consists of either microbiologic or non-microbiologic causes. Firm alternate microbiologic diagnosis includes a) identifiable source for bloodstream infection with a nontypical IE pathogen; b) rapid resolution of bloodstream infection; and c) absence of evidence for IE on cardiac imaging. Firm alternate non-microbiologic diagnosis includes a) presence of non-IE cause for cardiac imaging findings (e.g., marantic or nonbacterial thrombotic endocarditis); and b) absence of microbiologic evidence for IE.

Major Criteria
Clinical Categories

- Microbiological
- Imaging
- Surgical

Microbiologic Criteria

A. Microbiologic Major Criteria

(1) Positive blood cultures

i. **Microorganisms that commonly cause IE* isolated from two or more separate blood culture sets¶**

or

ii. **Microorganisms that occasionally or rarely cause IE isolated from three or more separate blood culture sets¶**

(2) Positive laboratory tests

i. Positive PCR or other nucleic acid-based technique† for *Coxiella burnetii*, *Bartonella* species, or *Tropheryma whipplei* from blood

or

ii. *Coxiella burnetii* antiphase I IgG antibody titer > 1:800[24] ††††, or isolated from a single blood culture

or

iii. Indirect immunofluorescence assays (IFA) for detection of IgM and IgG antibodies to *Bartonella henselae* or *Bartonella quintana* with IgG titer ≥ 1:800 [24, 25] ††††

*Staphylococcus aureus; ***Staphylococcus lugdunensis; Enterococcus faecalis; all streptococcal species (except for S. pneumoniae and S. pyogenes), Granulicatella and Abiotrophia spp., Gemella spp.,*** *HACEK group microorganisms (Haemophilus species, Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae).* **In the setting of intracardiac prosthetic material, the following additional bacteria should be included as "typical" pathogens: coagulase negative staphylococci, *Corynebacterium striatum* and *C. jeikeium*, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Cutibacterium acnes*, non-tuberculous mycobacteria (especially *M chimaerae*), and *Candida* spp.**

¶ *"Blood culture set" is defined as a simultaneously drawn pair of one aerobic and one anaerobic bottle. "Positive" blood culture set is defined as microbial growth from at least one of the bottles. Blood cultures from separate venipuncture sites are strongly recommended whenever possible for evaluating suspected IE.*

† ***Amplicon (16S or 18S) or metagenomic (shotgun) sequencing***

Imaging Criteria

B. Imaging Major Criteria

(1) Echocardiography and **Cardiac Computed Tomography** Imaging

i. Echocardiography and/or **Cardiac CT** showing vegetation[§], valvular/leaflet perforation[‡], valvular/leaflet aneurysm[**], abscess[¶¶], pseudoaneurysm[††], or intracardiac fistula[§§]

or

ii. Significant new valvular regurgitation on echocardiography as compared to previous imaging. Worsening or changing of pre-existing regurgitation is not sufficient.

or

iii. New partial dehiscence of prosthetic valve as compared to previous imaging[52]

(2) [18F]FDG PET/CT Imaging

Abnormal metabolic activity[‡‡] involving a native or prosthetic valve, ascending aortic graft (with concomitant evidence of valve involvement), intracardiac device leads or other prosthetic material [* ¶¶¶,]**

New Major Criteria: Surgical

C. Surgical Major Criteria

Evidence of IE documented by direct inspection during heart surgery neither Major Imaging Criteria nor subsequent histologic or microbiologic confirmation[§§§§]

Minor Criteria

A. Predisposition

- **Previous history of IE**
- Prosthetic valve†††

- Previous valve repair†††
- Congenital heart disease§§§
- More than mild regurgitation or stenosis of any etiology
- **Endovascular CIED**
- Hypertrophic obstructive cardiomyopathy
- Injection drug use

Minor Criteria:

B. Fever

Unchanged

B. Fever

Documented temperature greater than 38.0 degrees Centigrade (100.4 degrees Fahrenheit)

Minor Criteria:
C. Vascular & Embolic Phenomenona

- Combined Vascular & Embolic Phenomena

- Added 2 new embolic criteria

Clinical or radiological evidence of arterial emboli, septic pulmonary infarcts, ***cerebral*** **or** ***splenic abscess*****,** *mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions, purulent purpura*

Minor Criteria:

D. Immunologic Phenomena

Positive rheumatoid factor, Osler's nodes, Roth's spots, or immune complex-mediated glomerulonephritis###

1) unexplained presence of either acute kidney injury (AKI, defined below) or acute on chronic kidney injury (defined below) plus two of the following: *hematuria, proteinuria,* cellular casts on inspection of urinary sediment, *or serologic perturbations (hypocomplementemia, cryoglobulinemia, and/or presence of circulating immune complexes);*

or

2) renal biopsy consistent with immune complex-mediated renal disease.

Minor Criteria:

E. Microbiologic Criteria

1) Positive blood cultures for a microorganism consistent with IE but not meeting the requirements for Major Criterion[****]
2) Positive culture, PCR or other nucleic acid based test (amplicon or shotgun sequencing, *in situ* hybridization) for an organism consistent with IE [****] from a sterile body site other than cardiac tissue, cardiac prosthesis, or embolus; or a single finding of a skin bacterium by PCR on a valve or wire without additional clinical or microbiological supporting evidence[51]

Minor Criteria:

F. Imaging Criteria

Abnormal metabolic activity as detected by [18F]FDG PET/CT within 3 months of implantation of prosthetic valve, ascending aortic graft (with concomitant evidence of valve involvement), *intracardiac device leads or other prosthetic material*

Minor Criteria:

G. Physical Exam Criteria

Moved from Major to Minor Criteria

New valvular regurgitation identified on auscultation, if echocardiography is not available. Worsening or changing of pre-existing murmur not sufficient

PATHOLOGIC CRITERIA	Change
Microorganism identification	Microorganisms identified in appropriate sample by PCR, amplicon or metagenomic sequencing, or *in situ* hybridization
MAJOR CLINICAL CRITERIA	Change
Microbiology	
Blood cultures	Removed requirements for timing and separate venipunctures for blood cultures.
Definition of typical organisms	Added typical pathogens: 1) *S. lugdunensis*; *E. faecalis;* all streptococci except *S. pneumoniae* and *S. pyogenes*; *Granulicatella spp.; Abiotrophia spp.; & Gemella* spp. 2) Organisms to be considered "typical" IE pathogens in the setting of intracardiac prosthetic material: coagulase negative staphylococci, *Corynebacterium striatum; C. jeikeium*, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Cutibacterium acnes*, non-tuberculous mycobacteria, and *Candida* spp.
Other Microbiologic tests	Added new Major Criteria for fastidious pathogens: 1) PCR or amplicon/metagenomic sequencing identifies *C. burnetii*, *Bartonella* sp., or *T. whipplei* from blood; or 2) IFA $\geq$ 1:800 for IgG antibodies identifies *B. henselae* or *B. quintana*.
Imaging	
Echocardiography	Similar to earlier versions. Cornerstone of imaging criterion.
Cardiac Computerized Tomography	Added new Major Criterion. Findings equivalent to echocardiography.
[18F]FDG PET/CT	Added new Major Criterion. Findings for native valve, cardiac device, or prosthetic valve > 3 months after cardiac surgery are equivalent to echocardiography.
Surgical	Added new Major Criterion. Intraoperative inspection constitutes Major Criterion in absence of Major Criterion by cardiac imaging or histopathology.
MINOR CLINICAL CRITERIA	
Predisposition	Added Transcatheter valve implant/ repair, endovascular CIED, and prior diagnosis of IE.
Fever	Unchanged.
Vascular phenomena	Added splenic and cerebral abscess.
Immunologic phenomena	Added definition for immune complex mediated glomerulonephritis.
Microbiological	Added PCR or amplicon/metagenomic sequencing evidence of typical pathogen.
Imaging	Added PET/CT evidence < 3 months of cardiac surgery.
Physical examination	New auscultation of regurgitant murmur when echocardiography is unavailable.

Year	Diagnostic Criteria	Improvement
1981	Von Reyn	1. Definite, Probable, Possible, Rejected
1994	Duke Criteria	1. Major & Minor Criteria 2. Clinical Definite Criteria 3. Add Echocardiography
2000	Modified Duke Criteria	1. Remove "Possible" Echo 2. Expand *S. aureus* inclusion
2015	ESC Criteria	1. Add PET-CT, Cardiac CT
2023	Duke ISCVID Criteria	1. Expand Microbiology *- E. faecalis, most Streptococci* *- Add "Typical" PVE Pathogens* 2. Add Molecular Diagnostics *- 16S rRNA PCR, FISHseq from valve* *- next generation sequencing from blood* 3. Add Surgical Major Criteria 4. Remove Blood culture Restrictions *- Timing & Separate Venipunctures*

Future

- "Living Document"
  - (~ HIV & Hepatitis C treatment guidelines)
- Annual review of literature by *ad hoc* ISCVID committee
- Updates on ISCVID website
- Updates submitted for peer-review and publication every 4-5y

Conclusions

- **After > 20y, Modified Duke Criteria have been updated**
- **2023 Duke ISCVID Criteria Updates**
  - ***Microbiology***
  - ***Imaging***
  - ***Diagnostics***
  - ***Technical details***
- **Validation Studies are Underway in Multiple Countries**
- **ISCVID will perform “Living Document” updates**

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