

Updating Duke/ESC 2015 Criteria:

Progress Report of the ISCVID Endocarditis Criteria Working Group

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Chair

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Disclosures

Nature of Relevant Financial Relationship	Commercial Interest
Grant or research support	Cerexa/Actavis, Pfizer, Advanced Liquid Logics, NIH, MedImmune, Cubist/Merck; Karius; Contrafect; Genentech; Regeneron
Paid consultant	Achaogen, Astellas, Arsanis; Affinergy; Basilea; Bayer; Cerexa, Contrafect; Cubist;Debiopharm, Destiny; Genentech/Roche; Integrated Biotherapeutics; MedImmune; Novartis, Theravance; Bii, Affinivax, Armata, ArcBio, Akagera, Aridis, Synermore,Zymeron
Speaker's Bureau	None
Employment	Duke University
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Other relevant financial interests	Patent pending in sepsis diagnostic, Predigen, Inc.
Royalties	UptoDate
Honoraria	IDSA for Assoc. Editor role, <i>Clinical Infectious Diseases</i>



6,000+ US flights canceled or delayed Friday after one of worst summer air travel days yet

ZACH WICHTER | USA TODAY

Updated 5:18 pm EDT Jun. 17, 2022

Travelers are facing a second day of misery at airports across the country.

More than 1,300 U.S. flights were canceled as of 5 p.m. ET Friday with over 5,000 more posting delays, according to FlightAware, which [tracks flights in real time](#).



Overall Point

- Significant advances have occurred in the field of endocarditis
- Diagnostic criteria have not kept up
- The field needs a way to periodically update endocarditis criteria to reflect new advances
- This task is best accomplished by an internationally representative professional society with appropriate expertise
- ISCVID is uniquely situated to provide this service

How Did this Start?

- **Fall 2021:** *I was designing clinical study of Microbial cell-free DNA in Diagnosis of Endocarditis*
- **Research problem:** *How do I incorporate advances that did not exist when Modified Duke Criteria (or ESC 2015) was invented?*

Advances in Diagnostics

Blood culture negative endocarditis in the modern era of 16S rRNA sequencing

Clinical Medicine 2020 Vol 20, No 4: 412–6

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Clinical Infectious Diseases

MAJOR ARTICLE

 IDSA
Infectious Diseases Society of America

 hivma
hiv medicine association

OXFORD

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

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 de Vries,² Vance G. Fowler Jr,^{1,●} and Asim A. Ahmed²

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Advances in Microbiology

Clinical Infectious Diseases

VIEWPOINTS



OXFORD

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;XX(XX):1–6

openheart Modified Duke/European Society of Cardiology 2015 clinical criteria for infective endocarditis: time for an update?

Open Heart 2022;**9**:e001856. doi:10.1136/openhrt-2021-001856

Alfonso Jan Kemp Pecoraro ¹, Philipus George Herbst,¹ Colette Pienaar,^{2,3} Jantjie Taljaard,⁴ Hans Prozesky ⁵, Jacques Janson,⁶ Anton Frans Doubell¹

Advances 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

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

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 Thébaud,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 Jung,^{1,2,3,4,a} and François Rouzet^{1,2,3,4,27,a}, for the AEPEI-TEPvENDO study group

Prediction Rules for Ruling Out Endocarditis in Patients With *Staphylococcus aureus* Bacteremia

Thomas W. van der Vaart,^{1,2,ⓐ} Jan M. Prins,² Robin Soetekouw,³ Gitte van Twillert,⁴ Jan Veenstra,⁵ Bjorn L. Herpers,⁶ Wouter Rozemeijer,⁷ Rogier R. Jansen,⁸ Marc J. M. Bonten,^{1,9} and Jan T. M. van der Meer²

Clinical Infectious Diseases® 2022;74(8):1442–9

SOLUTION:

Update Endocarditis Criteria

- **Short term goal:** *Update endocarditis criteria with contemporary advances to create an internationally generalizable diagnostic schema*
- **Long term goal:** *Create an online “Living Document” similar to HIV treatment guidelines*

Update Endocarditis Criteria: Approach

- Presented the idea to ISCVID Council for approval
- Identify an international professional society with unique expertise in IE to endorse criteria
- Create geographically diverse working group to identify consensus for updated diagnostic criteria
- Externally validate criteria in prospective cohort of IE patients

ISCVID IE Criteria Working Group

5 Specialties from 8 Countries on 4 Continents

Francois Vandenesch	<i>France</i>	Eugene Athan	<i>Australia</i>
Barbara Hasse	<i>Switzerland</i>	Jan van der Meer	<i>Netherlands</i>
Xavier Duval	<i>France</i>	Claudio Fortes	<i>Brazil</i>
Christine Suty-Selton	<i>France</i>	David Durack	<i>USA</i>
Mohamad Ramadan	<i>Italy</i>	AW Karchmer	<i>USA</i>
Bruno Hoen	<i>France</i>	Jose Miro	<i>Spain</i>
T. van der Vaart	<i>Netherlands</i>	Arnold Bayer	<i>USA</i>
Carlos Mestres	<i>Spain</i>	Vance Fowler	<i>USA</i>
		Louis Dibernardo	<i>USA</i>

Review and approval by ISCVID Council

Methods

- From 12/21 to 5/22, multiple versions of draft were circulated within the ISCVID Council and IE Criteria Writing Group
- Points of disagreement discussed.
- Current draft presented today
- Unresolved items identified for vote and ISCVID membership commentary

Current Draft Updated IE Criteria

- **DEFINITE**

- Pathologic

- Clinical

- 2 Major

- 1 Major + 3 Minor

- 5 Minor

- **POSSIBLE**

- 1 Major + 1 Minor

- 3 Minor

- **REJECTED**

- Firm alternate diagnosis or resolution with < 4d therapy

- Neg path or macroscopic evidence surgery/autopsy

DEFINITE: Pathologic

A. PATHOLOGIC CRITERIA

- (1) Microorganisms identified* in a vegetation, cardiac tissue, embolus, or reconstructive graft of the ascending aorta in the context of current clinical disease without recent prior IE with histologic examination showing **active endocarditis**[†]

1. Question for Attendees: Which of the following results from a resected cardiac valve should constitute “Definite” IE, *with and without associated Active endocarditis by histopathology?*

	<i>With Active endocarditis</i>	<i>Without active endocarditis</i>
16s rRNA sequencing	Yes/No?	Yes/No?
Next Gen sequencing	Yes/No?	Yes/No?
PCR	Yes/No?	Yes/No?
Any other DNA-based assay	Yes/No?	Yes/No?

Rationale (text field): _____

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:

No Change

REJECTED IE

- A. FIRM ALTERNATE DIAGNOSIS EXPLAINING SIGNS/SYMPTOMS OR
- B. RESOLUTION OF ALL IE SYMPTOMS AND SIGNS WITH ANTIBIOTIC THERAPY FOR 4 DAYS OR LESS; OR
- C. NO PATHOLOGIC OR MACROSCOPIC EVIDENCE OF IE AT SURGERY OR AUTOPSY, WITH ANTIBIOTIC THERAPY FOR 4 DAYS OR LESS; OR
- D. DOES NOT MEET CRITERIA FOR POSSIBLE IE, AS ABOVE

Major Criteria

Categories Unchanged

- Microbiological
- Imaging
- Physical Examination

Microbiologic Criteria

A. MICROBIOLOGIC CRITERIA

(1) Positive blood cultures

- i. Microorganisms that commonly cause IE* isolated from two or more blood cultures, each obtained by separate blood draws
- ii. Microorganisms that occasionally or rarely cause IE isolated from three or more blood cultures, each obtained by separate blood draws

(2) Positive laboratory tests

i. Positive nucleic acid-based techniques† for *Coxiella burnetii*, *Bartonella* species, or *Tropheryma whippelii* from blood

or

ii. *Coxiella burnetii* antiphase I IgG antibody titer greater than 1:800

or

iii. indirect immunofluorescence assays (IFA) for detection of IgM and IgG antibodies to *Bartonella henselae* and *Bartonella quintana* with IgG titre above 1:128 and/or IgM titre above 1:40**

**Staphylococcus aureus*; *Staphylococcus lugdunensis*; *Enterococcus faecalis*; streptococci of the following groups or species: *S. mitis/oralis* (excluding *S. pneumoniae*), *S. bovis/equinus* (including *S. gallolyticus* and *S. infantarius*), *S. sanguinis/parasanguinis*, *S. salivarius*, *S. mutans*, *S. gordonii*, *S. cristatus/sinensis*, *Granulicatella spp.*, *Abiotrophia defectiva*; HACEK group organisms (*Haemophilus* species, *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*)

† such as broad range rRNA (16S/18S), microbial cell free DNA, or specific PCR

** PMID: 35534094

Imaging Criteria

B. IMAGING CRITERIA

(1) Echocardiographic criteria

i. Vegetation*, valvular perforation†, valvular aneurysm §, abscess ¶, pseudoaneurysm‡, or intracardiac fistula**

** - oscillating intracardiac mass on valve or other cardiac tissue, intracardiac implantable electronic devices (CIED) or other implanted material in the absence of an alternative anatomic explanation*

† - interruption of valvular endocardial tissue continuity

§- Saccular outpouching of valvular tissue

¶ - Perivalvular cavity not communicating with the cardiovascular lumen, as per PMID: 20223755

‡ - Perivalvular cavity communicating with the cardiovascular lumen

*** - Communication between two neighboring cavities through a perforation*

ii. – Significant new (not worsening) valvular regurgitation at echocardiography as compared to previous imaging

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

(2) Functional Imaging criteria

heterogeneous or focal, non physiological uptake involving prosthetic valve, aortic graft, native cardiac valve, perivalvular or periprosthetic area or intracardiac leads as detected by 18F-FDG PET/CT *

** performed after 3 months of surgery for prosthetic valves (PMID: 32488236)*

(3) Other imaging criteria

Positive cardiac CT or MRI, indicating either presence of perivalvular abscess or pseudoaneurysm, or infection of aortic graft.

Physical Examination Criteria:

C. PHYSICAL EXAMINATION CRITERIA

New valvular regurgitation (worsening of pre-existing murmur not sufficient)

2. Question for Attendees: Should the physical examination finding of “new valvular regurgitation (worsening of pre-existing murmur not sufficient)” remain as a Major Criteria?

Yes/No? Yes: 20% vs. No: 80%

Minor Criteria: Predisposition

V. MINOR CRITERIA

A. PREDISPOSITION

- Previous history of IE
- Prosthetic valve*
- Valve repair*
- Congenital heart disease[†]
- Underlying rheumatic and non rheumatic Valvular Heart Disease with more than mild regurgitation
- CIED recipients[§]
- Hypertrophic obstructive cardiomyopathy

3. Question for Attendees: Are cardiac predispositions acceptable as defined??

Yes/ No?

Yes: 70%

Text: _____

4. Question for Attendees: Is inclusion of hemodialysis as predisposition acceptable as defined??

Yes/ No?

No: 60%

Text: _____

5. Question for Attendees: Is inclusion of central venous catheter as predisposition acceptable as defined??

Yes/ No?

No: 70%

Text: _____

Minor Criteria: Fever

Unchanged

B. FEVER

measured body temperature, including temperature reading performed by patient, greater than 38 degrees Centigrade (101.4 degrees Fahrenheit)

Minor Criteria: Vascular & Embolic Phenomena

6. Question for Attendees: Is inclusion of hematogenous spondylodiscitis brain abscess, intracranial hemorrhage, splenic abscess as vascular phenomena acceptable as defined??

Yes/ No?

Yes: 70%

Question for Attendees: Agree with combining vascular and immunologic phenomena?

Yes/ No?

No: 70%

Text: _____

C. VASCULAR OR IMMUNOLOGIC PHENOMENA

identified by clinical symptoms, examination or diagnostic imaging: arterial emboli, septic pulmonary infarcts, cerebral or splenic abscess, hematogenous spondylodiscitis, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions, purulent purpura; positive rheumatoid factor, immune- complex glomerulonephritis, Osler's nodes, Roth's spots

Minor Criteria: Microbiologic Criteria

D. MICROBIOLOGIC EVIDENCE, FALLING SHORT OF A MAJOR CRITERION*

- 1) Positive blood cultures for an organism consistent with IE but not meeting the requirements for Major Criterion[†]
- 2) Microbiologic evidence (e.g., serology, urine or serum antigen testing, etc.) indicating active infection with an organism not listed above
- 3) Positive cell-free DNA sequencing assay from venipuncture specimen for an organism consistent with IE
** when accompanied by additional evidence of cardiac involvement (e.g., histopathology, cardiac imaging, etc)*

Minor Criteria: Microbiologic Criteria

New

E. OPERATIVE CRITERIA

Vegetations, abscess, valvular destruction, dehiscence or loosening of prosthetic valve, or other evidence of endocarditis demonstrated at time of surgery but without histologic or microbiologic confirmation

Validation

- **Options**

- 1. Existing dataset*

- + Immediately available
 - Variables collected ? (e.g., mcfDNA)

- 2. Prospective dataset*

- + Specific
 - Time, €

- **“Gold Standard”**

- 1. Histopathologically confirmed (+ and -)*

- 2. Adjudication Committee (+ and -)*

Next Steps

- Revise based on ISCVID feedback
- Consider validation options
- Publication strategy

(e.g., *Clinical Infectious Diseases* Opinion Piece vs. accompanying validation cohort)

- ISCVID website upload
- Funding