X REUNIÓN CIENTÍFICA
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Criterios Diagnósticos Actuales: ¿Novedades a la vista?

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GEIO
GRUPO DE ESTUDIO DE LA INFECCIÓN OSTEOARTICULAR
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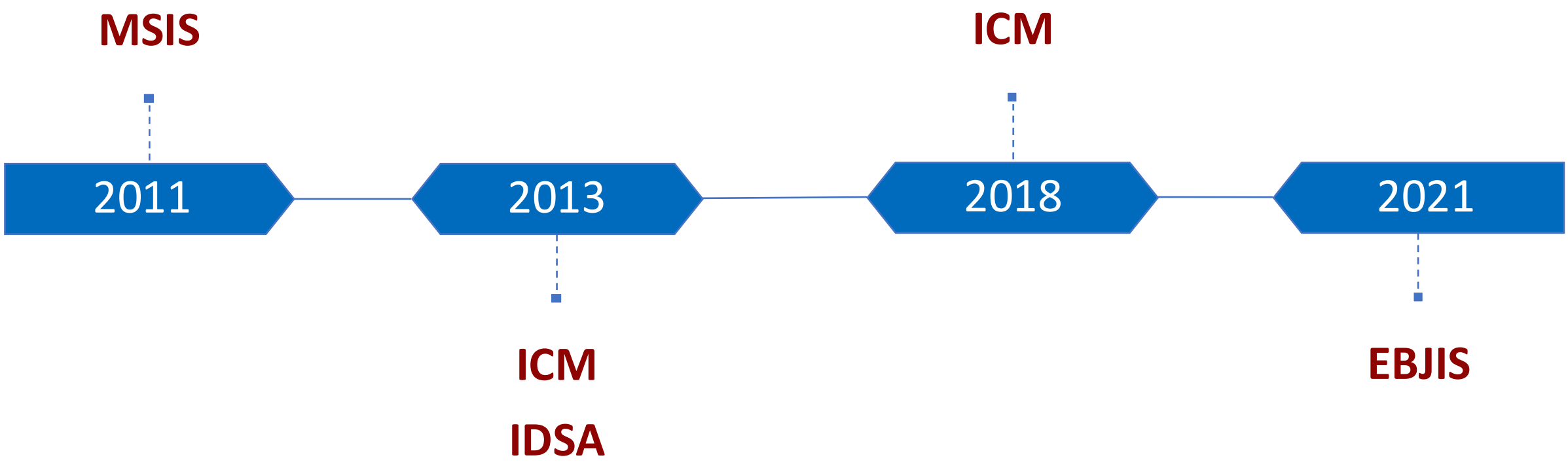
PJI definitions



MSIS definition 2011

major criteria

Definition of Periprosthetic Joint Infection

Based on the proposed criteria, definite PJI exists when:

(1) There is a sinus tract communicating with the prosthesis; or

(2) A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or

minor criteria

(3) Four of the following six criteria exist:

(a) Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration,

(b) Elevated synovial leukocyte count,

(c) Elevated synovial neutrophil percentage (PMN%),

(d) Presence of purulence in the affected joint,

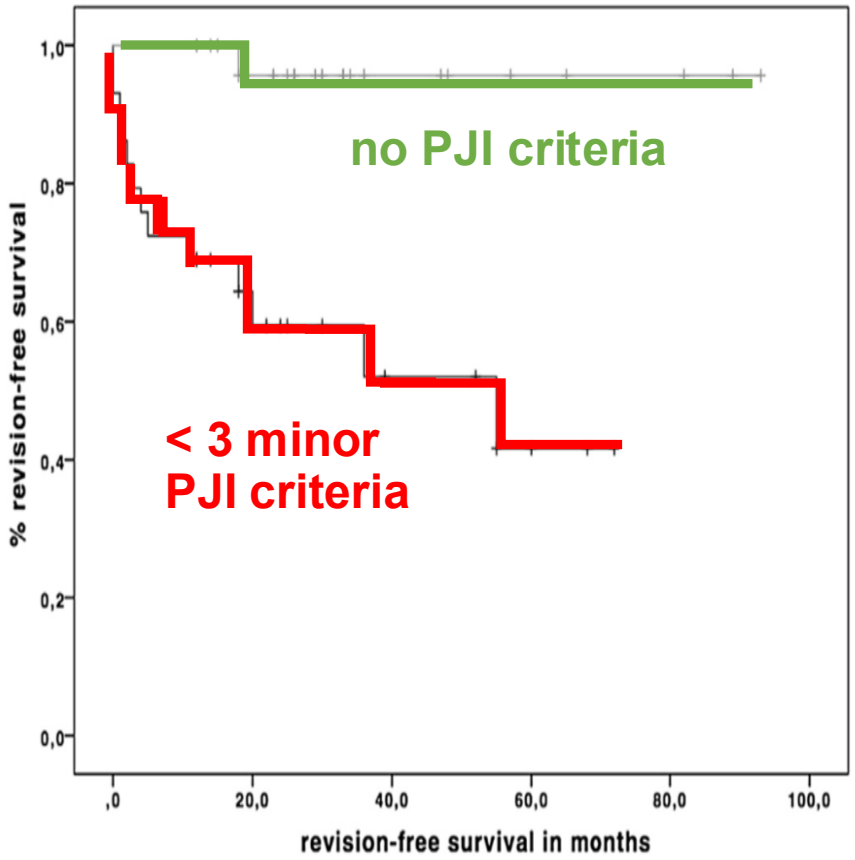
(e) Isolation of a microorganism in one culture of periprosthetic tissue or fluid, or

(f) Greater than five neutrophils per high-power field in five high-power fields observed from histologic analysis of periprosthetic tissue at ×400 magnification.

PJI may be present if fewer than four of these criteria are met.

Missed PJI diagnosis?

Lower rate of revision free survival when <3 minor criteria are present

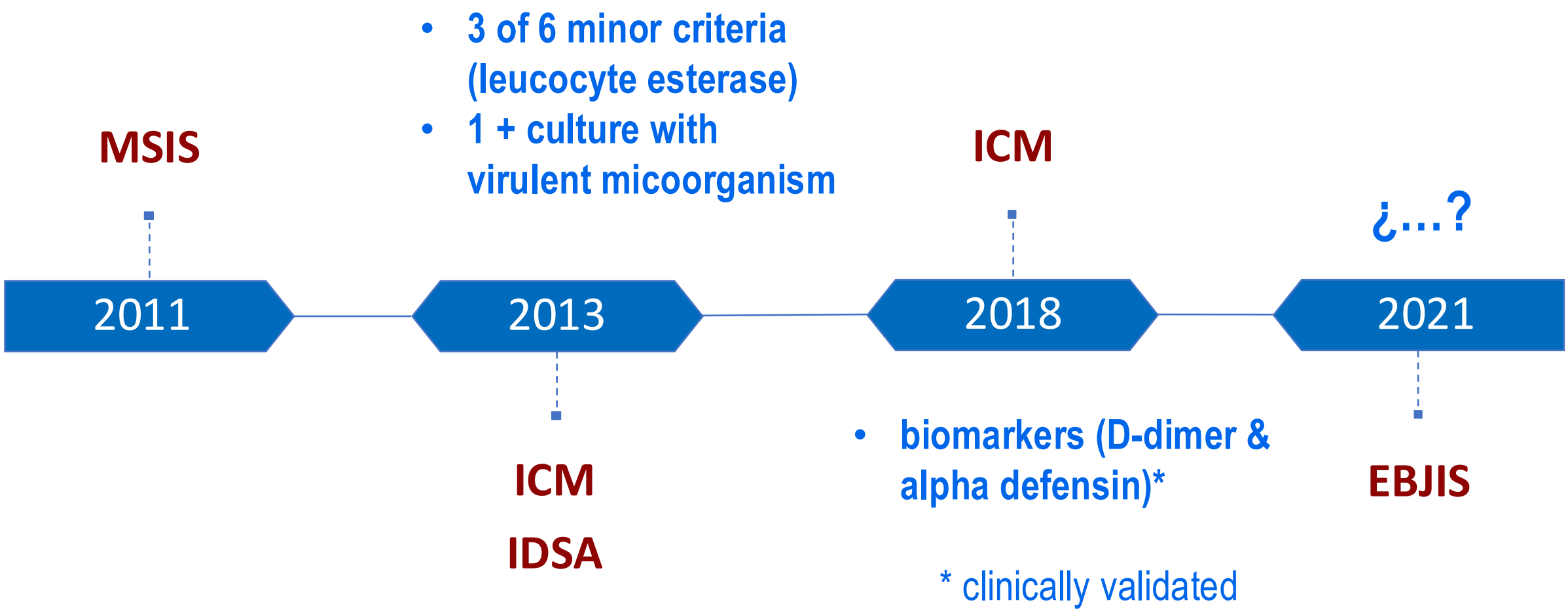


Outcome of Total Hip and Total Knee Revision Arthroplasty With Minor Infection Criteria: A Retrospective Matched-Pair Analysis

Kevin Staats, MD, BSc, Paul Kolbitsch, MD, Irene K. Sigmund, MD, Gerhard M. Hobusch, MD, Johannes Holinka, MD, Reinhard Windhager, MD *

The Journal of Arthroplasty 32 (2017) 1266–1271

PJI definitions



McNally M, et al. The EBJIS definition of periprosthetic joint infection.

Bone Joint J 2021

250 studies with good methodology, on 27 diagnostic topics. Papers were selected with clear data on the sensitivity and specificity of diagnostic tests.

	Infection Unlikely (all findings negative)	Infection Likely (two positive findings)[a]	Infection Confirmed (any positive finding)
Clinical and blood workup			
Clinical features	Clear alternative reason for implant dysfunction (e.g. fracture, implant breakage, malposition, tumour)	1) Radiological signs of loosening within the first five years after implantation 2) Previous wound healing problems 3) History of recent fever or bacteraemia 4) Purulence around the prosthesis[b]	Sinus tract with evidence of communication to the joint or visualization of the prosthesis
C-reactive protein		10 mgl (1 mg/dl)[c]	
Synovial fluid cytological analysis[d]			
Leukocyte count[c] (cells/µl)	≤ 1,500	> 1,500	>3,000
PMN (%)[c]	≤ 65%	> 65%	> 80%
Synovial fluid biomarkers			
Alpha-defensin[e]			Positive immunoassay or lateral-flow assay[e]

McNally M, et al. The EBJIS definition of periprosthetic joint infection.

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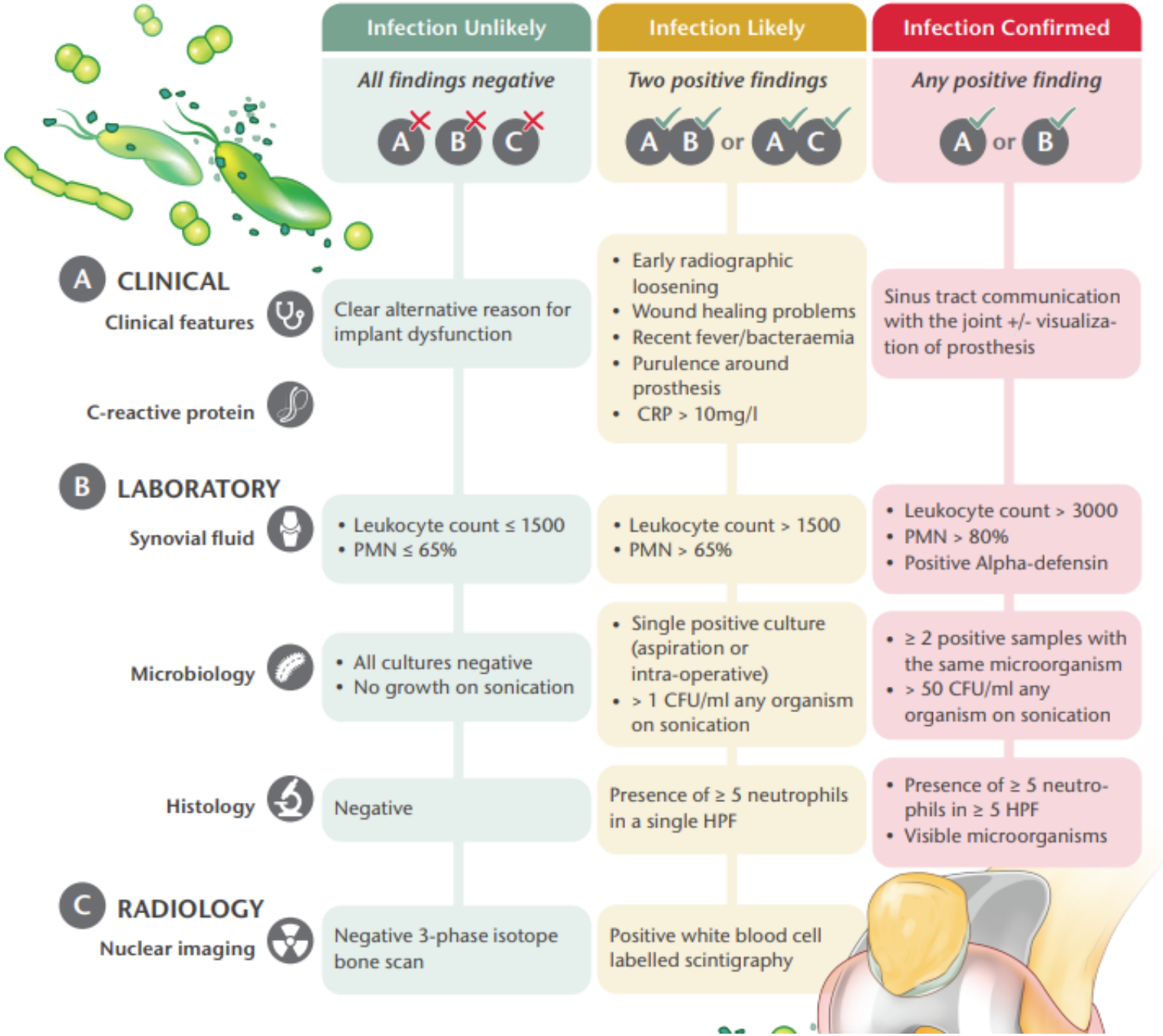
	Infection Unlikely (all findings negative)	Infection Likely (two positive findings)[a]	Infection Confirmed (any positive finding)
Microbiology[f]			
Aspiration fluid		Positive culture	
Intraoperative (fluid and tissue)	All cultures negative	Single positive culture[g]	≥ two positive samples with the same microorganism
Sonication[h] (CFU/ml)	No growth	> 1 CFU/ml of any organism[g]	> 50 CFU/ml of any organism
Histology[c,i]			
High-power field (400x magnification)	Negative	Presence of ≥ five neutrophils in a single HPF	Presence of ≥ five neutrophils in ≥ five HPF
			Presence of visible microorganisms
Others			
Nuclear imaging	Negative three-phase isotope bone scan[c]	Positive WBC scintigraphy[i]	



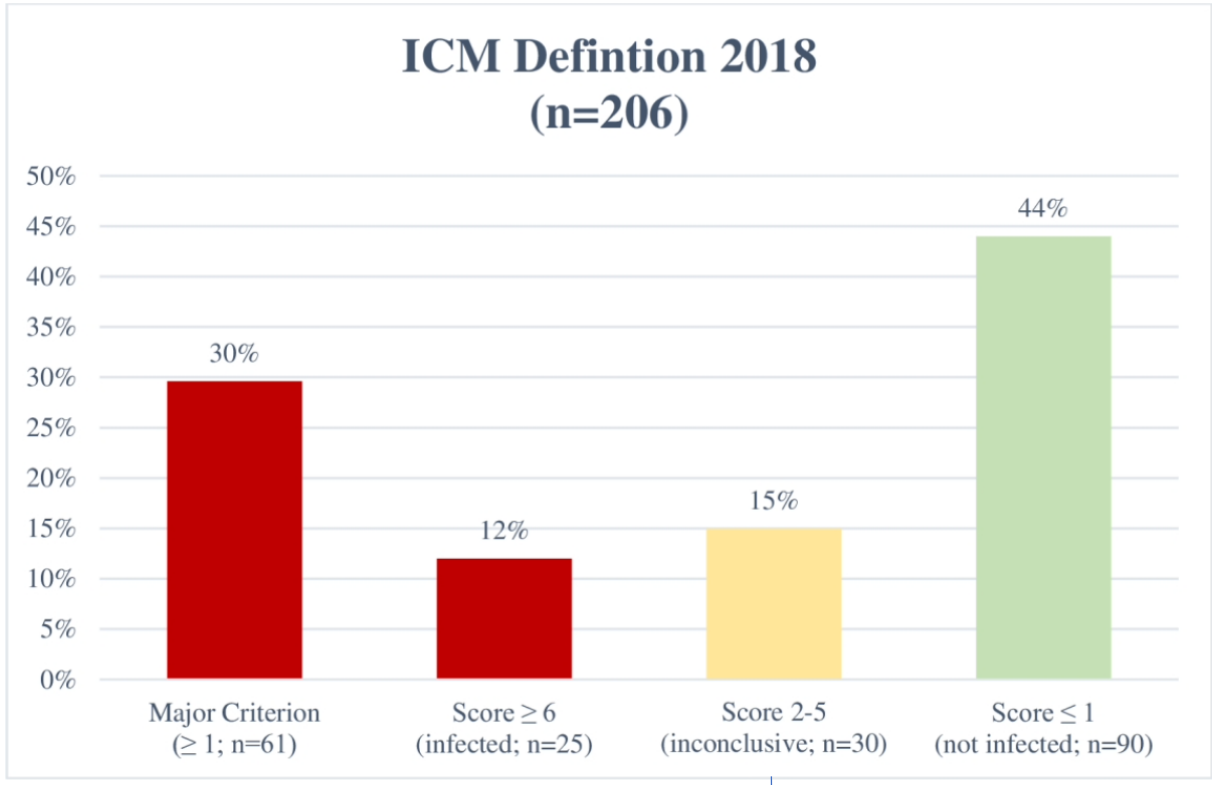
EBJIS criteria

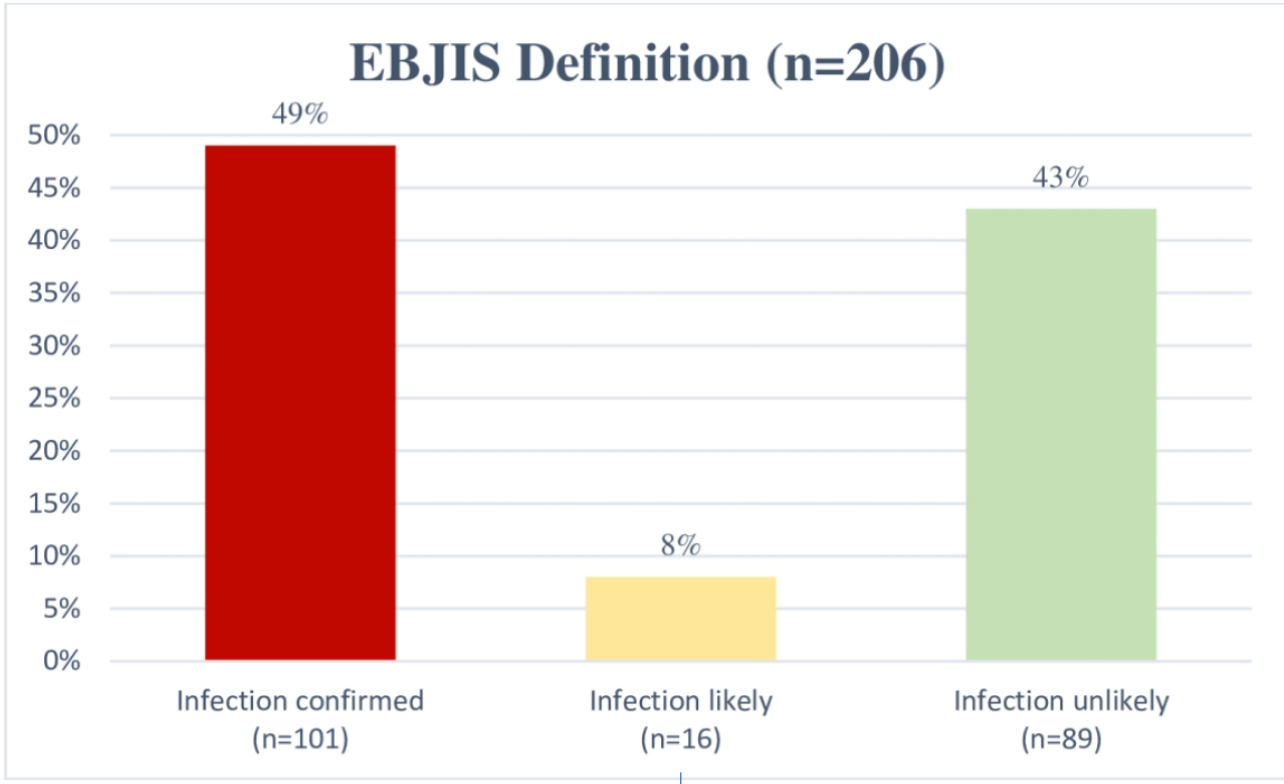
THE BONE & JOINT JOURNAL EST. 1948

**M. McNally,
R. Sousa,
M. Wouthuyzen-Bakker,
A. F. Chen,
A. Soriano,
H. C. Vogely,
M. Clauss,
C. A. Higuera,
R. Trebše**

Sigmund I, et al. Diagnosing PJI: a comparison of infection definitions: EBJIS 2021, ICM 2018 and IDSA 2013. ***Bone & Joint Res 2022***

N=206 knee (102) or hip (104) revisions





P=0.041

Clinical validation PJI definitions

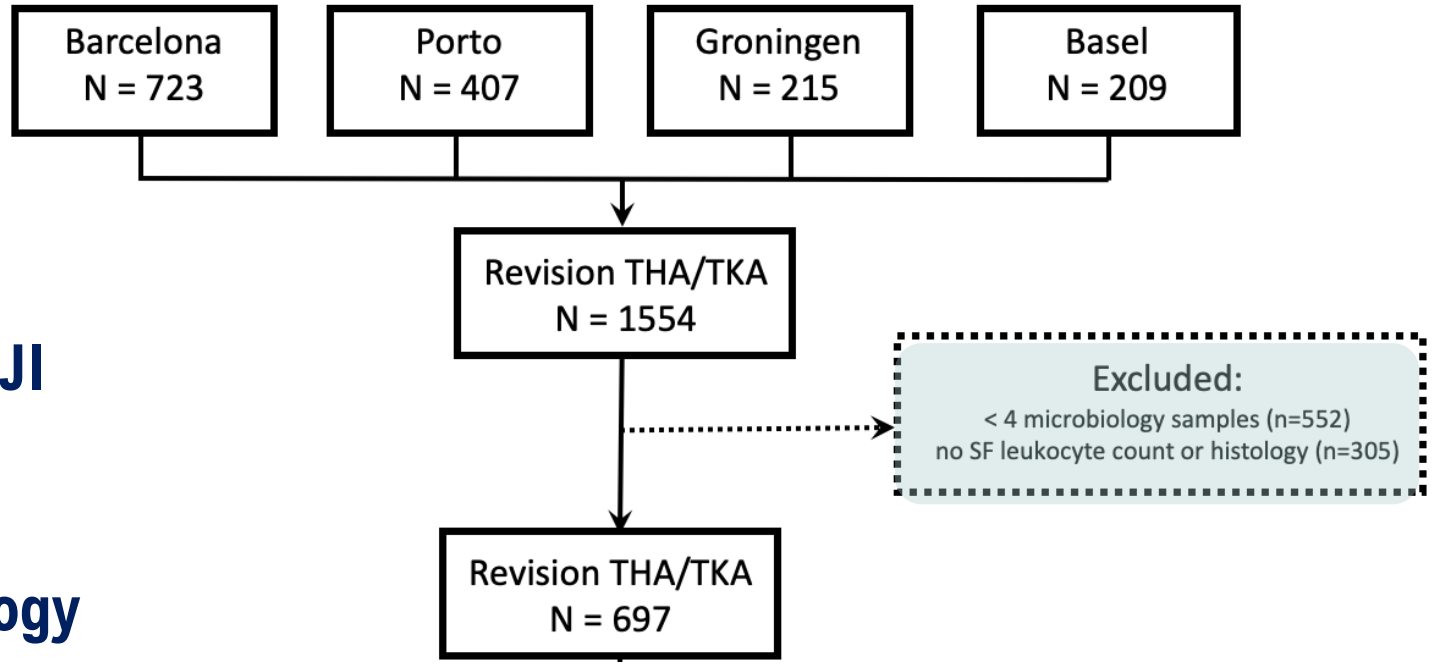
The European Bone and Joint Infection Society definition of periprosthetic joint infection is meaningful in clinical practice: a multicentric validation study with comparison with previous definitions

Ricardo SOUSA [1], Ana RIBAU [2], Pedro ALFARO [3], Marc-Antoine BURCH [4], Joris PLOEGMAKERS [5], Martin MCNALLY [6], Martin CLAUSS [4,7], Marjan WOUTHUYZEN-BAKKER [8], and Alex SORIANO [9]

Acta Orthopaedica 2023; 94: 8–18

Sousa R, et al. EBJIS definition of PJI- a multicentric validation study and comparison to previous definitions. ***Acta Orthop 2022***

- ✓ **Multicentric retrospective study**
- ✓ **Revision THA/TKA (2013-2018)**
- ✓ **Minimum diagnostics to rule out PJI**
  - ○ **≥ 4 microbiology samples**
  - ○ **SF leukocyte count / histology**



Sousa R, et al. EBJIS definition of PJI- a multicentric validation study and comparison to previous definitions. ***Acta Orthop 2022***

Final Diagnosis Classification According to Different Definitions			
EBJIS 2021	*Infection Unlikely*	*Infection Likely*	*Infection Confirmed*
	255 (54.0%)	**22 (4.7%)**	**195 (41.3%)**
ICM 2018	*Not Infected*	*Inconclusive*	*Infected*
	258 (54.7%)	**42 (8.9%)**	**172 (36.4%)**
IDSA	*Not Infected*		*Infected*
	284 (60.2%)		**188 (39.8%)**
MSIS 2013	*Not Infected*		*Infected*
	327 (69.3%)		**145 (30.7%)**

Disadvantages development of PJI definitions

- Different reference standards used in PJI research
- Confusion amongst physicians which criteria to use

Steering committee unified PJI definition

First meeting November 2023

It was agreed that none of the societies can claim the credits for the definition.

Workings groups

Topic	Participants
Leucocyte count synovial fluid. (including % PMN and ratios of different leucocytes)	Ricardo Sousa Martin Clauss
Other biomarkers synovial fluid (including leucocyte esterase, CRP, calprotectin, alpha-defensin)	Andy Miller Alex Soriano Thorsten Seyler
Serum markers (Including CRP, ESR, D-dimer, IL-6, procalcitonin)	Irene Sigmund Nicolas Cortes-Penfield Matthew Dietz
Cultures (Synovial fluid, tissue, sonication)	Jaime Esteban Robin Patel Sandra Nelson
Histology (Including frozen section, paraffin)	Martin McNally Thomas Bauer
Imaging (including (PET)CT, MRI, WBC-scintigraphy, bonescan)	Andor Glaudemans Javad Parvizi
Clinical features (including sinus tract, pus, early loosening)	Thorsten Gehrke Tristan Ferry
Molecular techniques (including 16S PCR, targeted PCRs / film arrays, NGS)	Marjan Wouthuyzen-Bakker Holger Rohde Elie Berbari

- **No financial conflict of interest of the evaluated test was allowed**
- **Systematic reviews & meta-analyses 2000-2024**
- **Unified literature search & grading of evidence**

Delphi recommendations

- Recommendation about the position of the diagnostic test in the **unified PJI definition**
- Recommendation about the position of the diagnostic test in the **diagnostic flowchart** of a patient with suspected PJI
- Recommendations basic principles
- Recommendations were entered into an anonymous Delphi round

Unified Criteria for Periprosthetic Joint Infections (PJI)

Standalone criteria

Clinical features

- A sinus tract communicating from the joint to the outside environment that develops or persists after the incision has or should have healed

Microbiology

- Two positive cultures with a phenotypically indistinguishable organism from periprosthetic tissue
- One positive culture from synovial fluid or sonicate fluid PLUS one positive culture from periprosthetic tissue with a phenotypically indistinguishable organism

Inflammatory markers and histology

- Synovial leucocyte count >3000 cells/µL
- Synovial polymorphonuclear cells >75%
- Positive histology: 5 or more neutrophils in each of 5 or more high power fields (400x)

All without any alternative explanation[1]

Specificity >95%

Supportive criteria

Microbiology

- A single positive synovial fluid, sonicate fluid or periprosthetic tissue culture
- A positive molecular test of any organism in synovial fluid, tissue or sonication fluid

Imaging

- A positive WBC-scintigraphy[3]
- A positive [^{18}F]-FDG-PET/CT when performed more than 6 months after the index arthroplasty[4]

Inflammatory markers

- Synovial leucocyte count 1500 - 2999 cells/µL
- Synovial polymorphonuclear cells 65 - 74%
- Any alternative positive synovial fluid biomarker[5]

All without any alternative explanation[1]

Specificity >80%

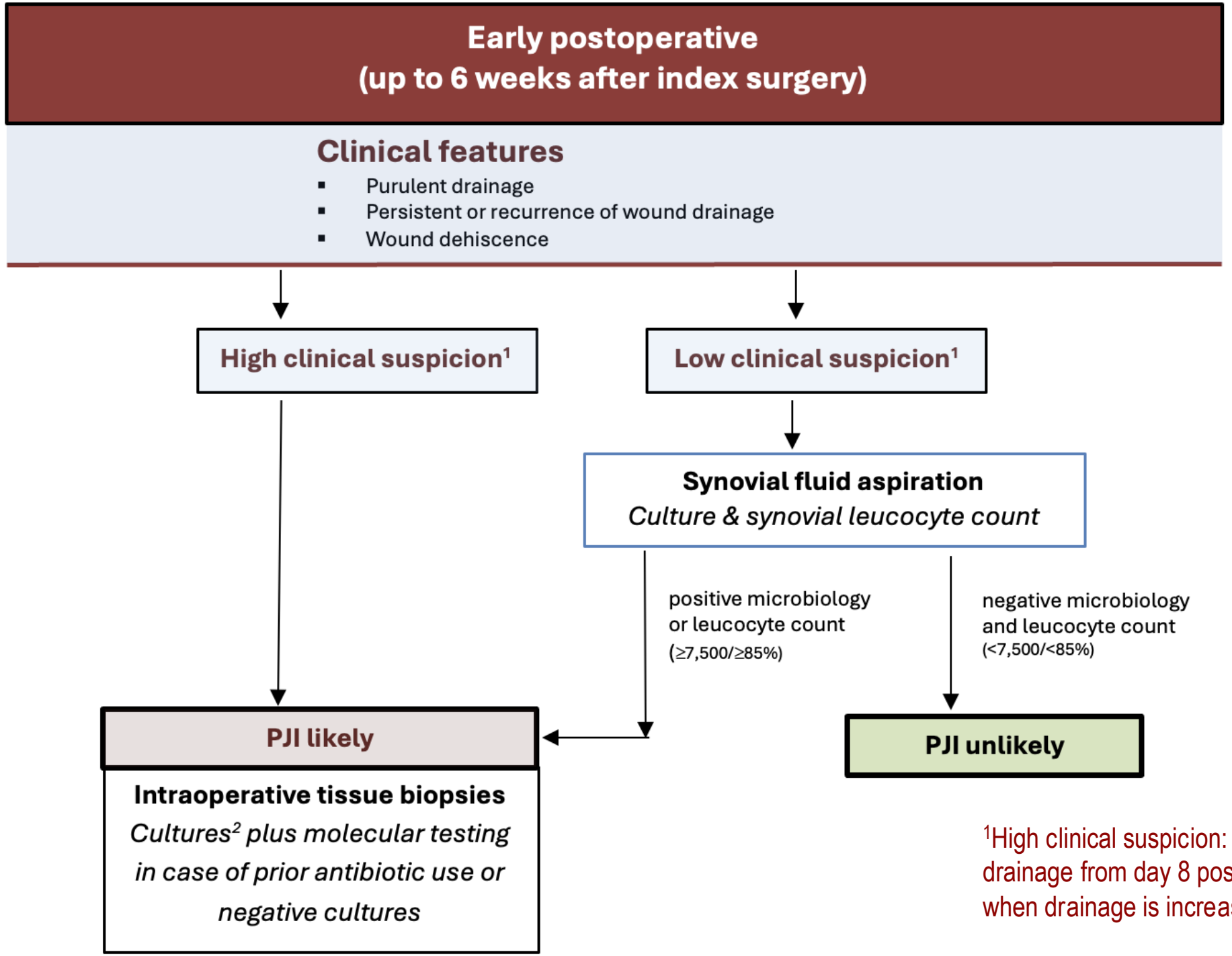
Confirmed PJI

One standalone criterion in any category

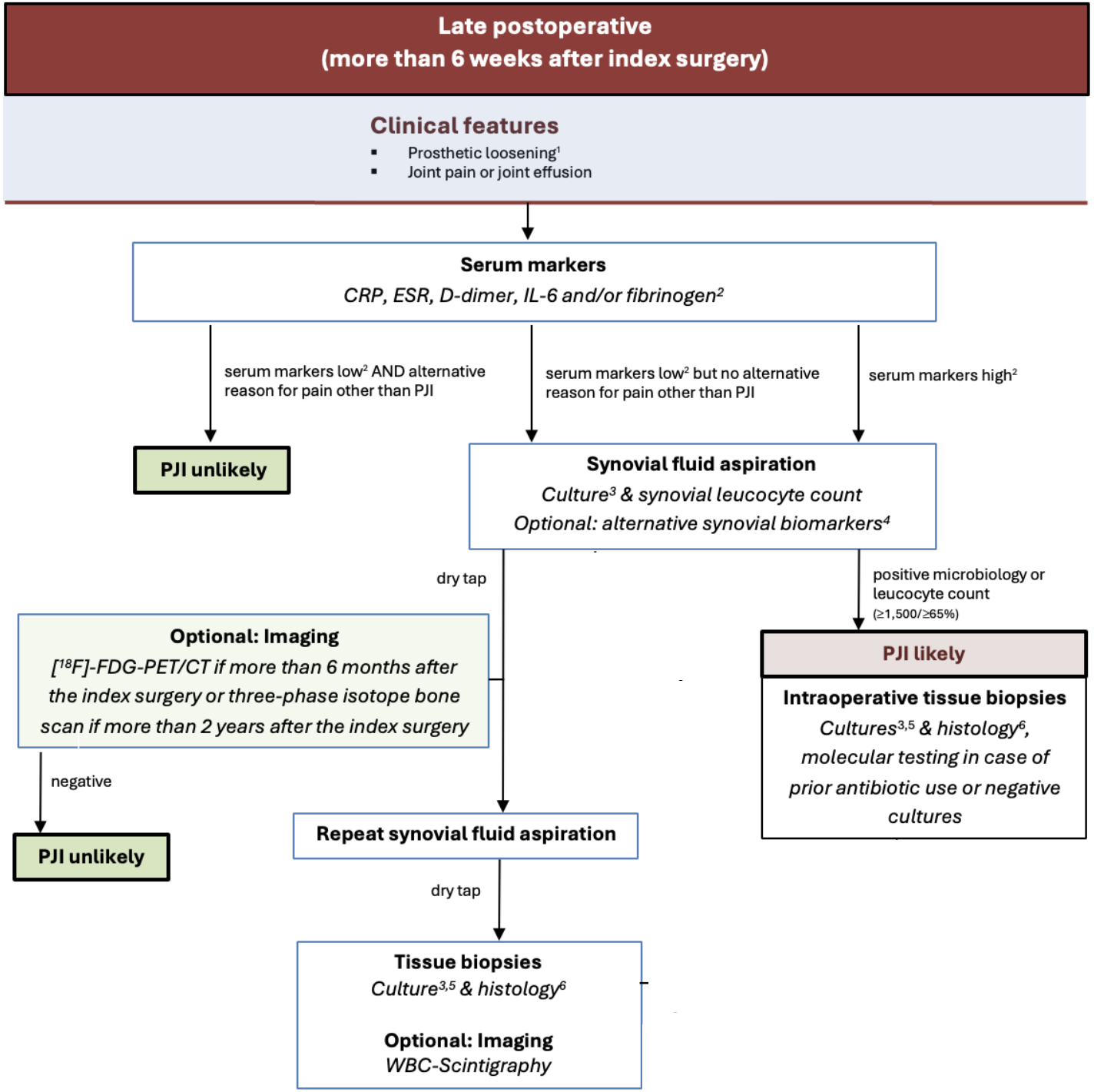
Probable PJI

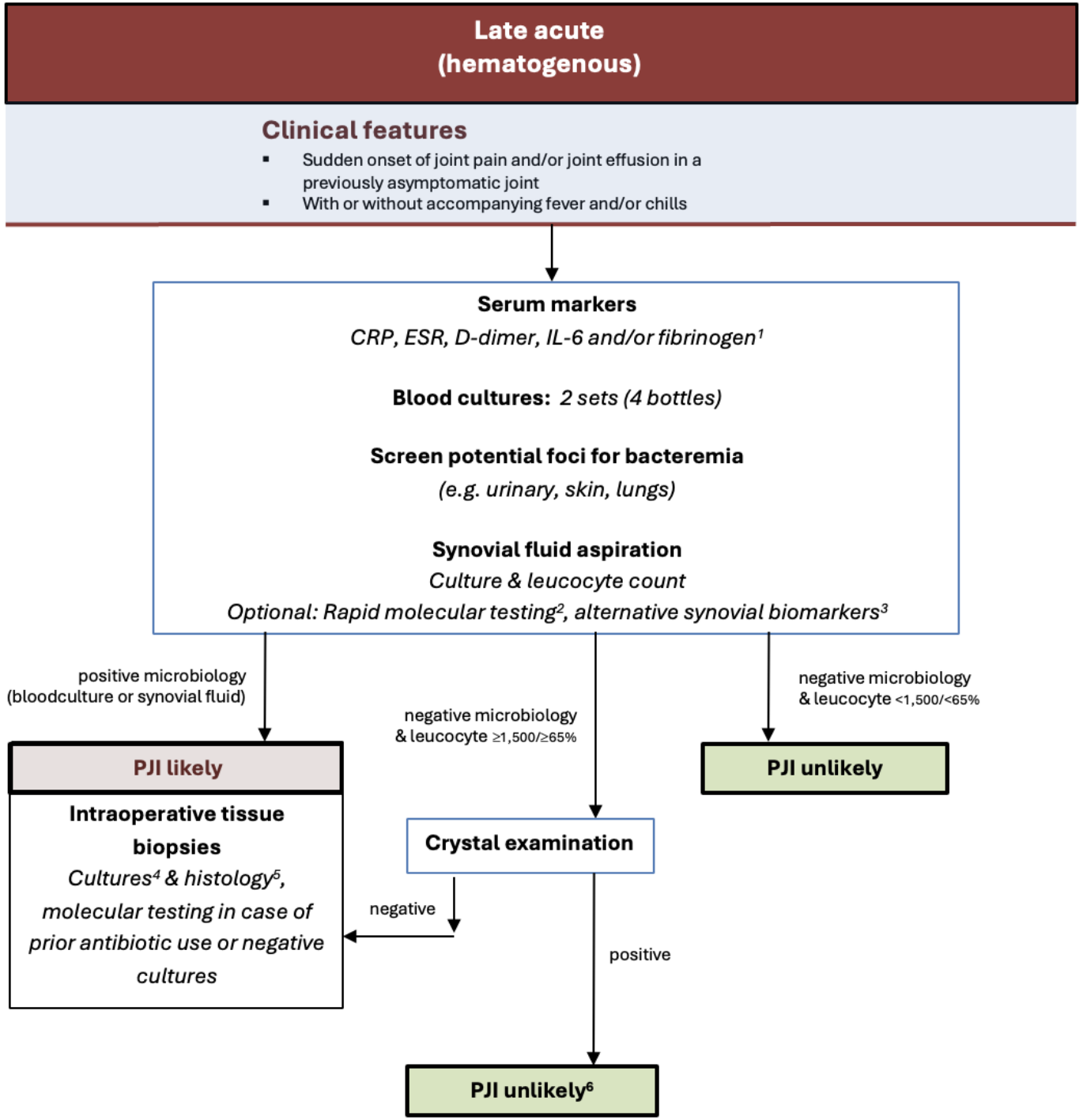
One supportive microbiology criterion PLUS one supportive inflammatory criterion or imaging criterion

[5] Synovial fluid leucocyte esterase (2+), C-reactive protein (> 6.9 mg/L), alpha defensin (positive lateral flow assay or ELISA > 5.2 mg/L), or calprotectin (> 50 mg/L). The threshold for a positive test may vary based on the selected test and the manufacturer guide should be consulted.



[1]High clinical suspicion: purulent drainage or any drainage from day 8 post-operatively, especially when drainage is increasing or reoccurs


Late postoperative
(more than 6 weeks after index surgery)
Clinical features
Prosthetic loosening[1]
Joint pain or joint effusion
Serum markers
CRP, ESR, D-dimer, IL-6 and/or fibrinogen[2]
serum markers low[2] AND alternative reason for pain other than PJI
serum markers low[2] but no alternative reason for pain other than PJI
serum markers high[2]
PJI unlikely
Synovial fluid aspiration
Culture[3] & synovial leucocyte count
Optional: alternative synovial biomarkers[4]
dry tap
positive microbiology or leucocyte count
(≥1,500/≥65%)
PJI likely
Intraoperative tissue biopsies
Cultures[3,5] & histology[6], molecular testing in case of prior antibiotic use or negative cultures
Optional: Imaging
[18F]-FDG-PET/CT if more than 6 months after the index surgery or three-phase isotope bone scan if more than 2 years after the index surgery
negative
PJI unlikely
Repeat synovial fluid aspiration
dry tap
Tissue biopsies
Culture[3,5] & histology[6]
Optional: Imaging
WBC-Scintigraphy


Late acute
(hematogenous)
Clinical features
Sudden onset of joint pain and/or joint effusion in a previously asymptomatic joint
With or without accompanying fever and/or chills
Serum markers
CRP, ESR, D-dimer, IL-6 and/or fibrinogen1
Blood cultures: 2 sets (4 bottles)
Screen potential foci for bacteremia
(e.g. urinary, skin, lungs)
Synovial fluid aspiration
Culture & leucocyte count
Optional: Rapid molecular testing2, alternative synovial biomarkers3
positive microbiology (bloodculture or synovial fluid)
negative microbiology & leucocyte ≥1,500/≥65%
negative microbiology & leucocyte <1,500/<65%
PJI likely
Intraoperative tissue biopsies
Cultures4 & histology5, molecular testing in case of prior antibiotic use or negative cultures
Crystal examination
negative
positive
PJI unlikely
PJI unlikely6

Current status

- Endorsed by the executive committees of EBJIS, MSIS, ESCMID study group on implant associated infections (ESGIAI), ICM and IDSA
- Submitted to NEJM
- Future perspective: clinical validation