■ ARTHROPLASTY

The EBJIS definition of periprosthetic joint infection

A PRACTICAL GUIDE FOR CLINICIANS

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Aims

The diagnosis of periprosthetic joint infection (PJI) can be difficult. All current diagnostic tests have problems with accuracy and interpretation of results. Many new tests have been proposed, but there is no consensus on the place of many of these in the diagnostic pathway. Previous attempts to develop a definition of PJI have not been universally accepted and there remains no reference standard definition.

Methods

This paper reports the outcome of a project developed by the European Bone and Joint Infection Society (EBJIS), and supported by the Musculoskeletal Infection Society (MSIS) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Implant-Associated Infections (ESGIAI). It comprised a comprehensive review of the literature, open discussion with Society members and conference delegates, and an expert panel assessment of the results to produce the final guidance.

Results

This process evolved a three-level approach to the diagnostic continuum, resulting in a definition set and guidance, which has been fully endorsed by EBJIS, MSIS, and ESGIAI.

Conclusion

The definition presents a novel three-level approach to diagnosis, based on the most robust evidence, which will be useful to clinicians in daily practice.

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Introduction

Periprosthetic joint infection (PJI) is a major burden for healthcare systems.[1-3] It is disabling for patients and may require invasive treatment with a risk of significant adverse events. Accurate diagnosis is the starting point for effective treatment.

There have been many attempts to define the criteria by which PJI is diagnosed. The Musculoskeletal Infection Society (MSIS) produced an initial definition in 2011,[4] modified and subjected to international consensus review (International Consensus on Musculoskeletal Infection (ICM)) in 2013.[5] Also in 2013, the Infectious Diseases Society of America (IDSA) published guidance on diagnosis from an international expert group.[6] More recently, a new definition has been produced using a weighted-score definition set, validated in a patient cohort.[7] This was discussed at the reconvened ICM in 2018, but was supported by only 68% of delegates.[8] It was not endorsed by the MSIS or the European Bone and Joint Infection Society (EBJIS).

These PJI definitions have allowed a clear focus on the need for accurate diagnosis and have provided reference standards for clinical and diagnostic studies. However, no single definition has gained acceptance as the reference standard for clinical practice. This may be due to many factors, including complexity, geographical variations in practice, the use of expensive tests, and disagreement over the accuracy of some of the included tests.[9]

Previous studies have used all of these definitions (MSIS, IDSA, or ICM) and others, making comparison of outcomes difficult. Perhaps the major concern with previous work involves the sensitivity of diagnosis.

There is now a greater understanding of low-grade infections which may have been missed in the past.[2,10-12] Underdiagnosis risks poor outcomes with inappropriate treatment aimed at aseptic revision, when infection is present.

This paper reports the outcome of a project developed by the EBJIS and supported by MSIS

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and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Study Group for Implant-Associated Infections (ESGIAI). It comprised a comprehensive review of the literature, open discussion with Society members and conference delegates, and an expert panel assessment of the results to produce the final guidance.

The purpose of a definition of PJI. Any diagnostic definition set has two distinct uses: firstly, and most importantly, it must give a clinician, who may or may not be an expert in the field, a clear set of investigations and outcomes which allow them to decide if an infection is present or not. If there was a diagnostic test with absolute accuracy, this would be a simple matter. We do not have such a test, so we must attribute levels of confidence to each test, in the context of the clinical picture. This will require the definition to distinguish between test results that are pathognomonic for infection (confirmed infection) and tests that are associated with infection, when positive, but cannot alone confirm that an infection is present (infection likely).

Secondly, the definition must facilitate researchers to perform studies in patients with or without an infection. The evaluation of a new treatment for PJI, for instance, will be misleading if it is applied to a group of patients in whom the diagnosis is not certain, and may include those with aseptic loosening. This problem may, in part, account for the varied reported treatment success rates from previous studies. This was recently highlighted by Renz et al.[13] In their study, the incidence of infection varied from 21% to 37%, depending on which definition set was studied.

Considerations on the design of a new definition set. The definition:

1. Must diagnose the large majority of infections based on the sensitivity of diagnostic tests. Underdiagnosing PJI leads to inadequate treatment with severe consequences.
2. Must not overdiagnose infection, resulting in inappropriate invasive treatment. Infection should only be regarded as definitely present, when confirmed with tests that have high specificity.
3. Must be simple in application.
4. Must help with decision-making at the time of use.
5. Must include widely available tests. There is no value in duplicating tests that are based on the same biochemical or pathological abnormalities.
6. Must be acceptable to a wide range of clinicians, in terms of the validity of its conclusions and the evidence base for the tests from which it is derived.
7. Must not be taken as an indication for any specific treatment. It is entirely reasonable for a surgeon and patient to agree to have no treatment, even when the definition suggests that an infection is present.
8. Must recognize that levels of confidence in any particular test will change with improving research and better understanding of disease mechanisms. This may change the place of that test within the definition over time.

Clinicians should be encouraged to apply the definition in the context of the information available on all aspects of the patient's health. This is difficult within a concise definition. For instance, a patient on immunosuppressive therapy will be less likely to produce high levels of inflammatory biomarkers, but is at higher risk of infection. Therefore, the clinician may wish to reduce the reliance on biomarkers and increase the significance of clinical, microbiological, or histological features. The decision to increase or reduce the significance of a diagnostic test should be considered within a multidisciplinary team, which can evaluate all aspects of the patient care.

Methods

In 2017, at the 36th annual meeting of the EBJIS, the production of a definition of PJI was discussed. In 2018, Renz et al[13] published a proposed EBJIS definition, which was presented to the 37th annual meeting of the EBJIS. The open discussion, with over 450 delegates present (including representatives of MSIS and ESGIAI), identified concerns over the choice of diagnostic cut-offs and the validity of the conclusions. The meeting recommended a reappraisal of the definition categories.

In 2018 to 2019, an extensive literature review was performed by three of the authors (RS, RH, MMcN), resulting in identification of over 250 studies with good methodology, on 27 diagnostic topics. Papers were selected with clear data on the sensitivity and specificity of diagnostic tests. Tests were only considered if there was more than one study group supporting accuracy and the test was widely available. Expert opinion alone was not used in the evaluation of any diagnostic test.

From this analysis, the EBJIS executive committee produced a draft definition which was circulated to the members of the MSIS and ESGIAI for comments before presentation at the 38th annual meeting of the EBJIS in 2019. At this meeting, the modified draft was approved and has since been endorsed by EBJIS, MSIS, and ESGIAI.

Results

In general, studies were compromised by a lack of rigour in defining the reference standard applied in each series, making comparison of tests difficult. However, there was a body of evidence which was useful in the definition of PJI and can be applied safely. It consisted of a range of simpler (and usually older) tests and newer, but often well studied tests. As expected, there was diversity in the conclusions of these papers and on the validity of the diagnostic tests.

It became clear that it was not practical to have a binary definition; infected or not infected. This problem has been previously identified in both PJI[14] and in fracture-related infection (FRI).[15] Currently available diagnostic tests cannot give us this, as each has significant false-positive and false-negative rates. Even combining tests (which has been reported in many papers) does not resolve this problem. At present, there are no tests that can definitively exclude infection. Therefore, a three-level definition is proposed. This is similar, in principle, to that published for FRI,[15] which has been adopted by the 2018 ICM[16] and used successfully in recent studies.[17]

The definition levels have been chosen to provide the most useful data for clinical decision-making for each scenario (Figure 1). We have allocated diagnostic tests to groups which indicated:

1. Infection unlikely.

	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 mg/l (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]
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[j]	

Summary Key

a. Infection is only likely if there is a positive clinical feature or raised serum C-reactive protein (CRP), together with another positive test (synovial fluid, microbiology, histology or nuclear imaging).

b. Except in adverse local tissue reaction (ALTR) and crystal arthropathy cases.

c. Should be interpreted with caution when other possible causes of inflammation are present: gout or other crystal arthropathy, metallosis, active inflammatory joint disease (e.g. rheumatoid arthritis), periprosthetic fracture, or the early postoperative period.

d. These values are valid for hips and knee periprosthetic joint infection (PJI). Parameters are only valid when clear fluid is obtained and no lavage has been performed. Volume for the analysis should be > 250 µL, ideally 1 ml, collected in an EDTA containing tube and analyzed in <1h, preferentially using automated techniques. For viscous samples, pre-treatment with hyaluronidase improves the accuracy of optical or automated techniques. In case of bloody samples, the adjusted synovial WBC= synovial $WBC_{observed}$ – [WBC_{blood} / RBC blood x $RBC_{synovial\ fluid}$] should be used.

e. Not valid in cases of ALTR, haematomas, or acute inflammatory arthritis or gout.

f. If antibiotic treatment has been given (not simple prophylaxis), the results of microbiological analysis may be compromised. In these cases, molecular techniques may have a place. Results of culture may be obtained from preoperative synovial aspiration, preoperative synovial biopsies or (preferred) from intraoperative tissue samples.

g. Interpretation of single positive culture (or < 50 UFC/ml in sonication fluid) must be cautious and taken together with other evidence. If a preoperative aspiration identified the same microorganism, they should be considered as two positive confirmatory samples. Uncommon contaminants or virulent organisms (e.g. *Staphylococcus aureus* or Gram negative rods) are more likely to represent infection than common contaminants (such as coagulase-negative staphylococci, micrococci, or *Cutibacterium acnes*).

h. If centrifugation is applied, then the suggested cut-off is 200 CFU/ml to confirm infection. If other variations to the protocol are used, the published cut-offs for each protocol must be applied.

i. Histological analysis may be from preoperative biopsy, intraoperative tissue samples with either paraffin, or frozen section preparation.

j. WBC scintigraphy is regarded as positive if the uptake is increased at the 20-hour scan, compared to the earlier scans (especially when combined with complementary bone marrow scan).

Fig. 1

EBJIS criteria for the diagnosis of clinically-suspected periprosthetic joint infection.

2. Infection likely.
3. Infection confirmed.

It is important to note that the significance of each test is different in each group. If a confirmatory test is positive, this test alone can define the presence of an infection (infection confirmed). Such a test must have very high specificity. Conversely, in order to conclude that infection is not present (infection unlikely), there must be no positive tests which suggest or confirm an infection. There are also patients who may have some positive diagnostic tests (clinical signs, raised biomarkers, imaging) which are associated with infection but are not of sufficient specificity to confirm an infection. This group may include patients with low grade infections, which may be missed in the classical bimodal definitions.

In this proposal, a middle group (infection likely) is defined, which should alert the clinician that there is a significant risk that an infection may be present and further comprehensive investigation should be considered. In this group, the presence of a single positive test does not imply that an infection is likely. However, if there is a clinical sign or raised serum C-reactive protein (CRP), together with another positive test, this indicates that an infection is likely. It should be noted that multiple positive suggestive tests in this group do not confirm infection. This can only be done with identification of a positive test from the confirmatory criteria.

Figure 1 summarizes the elements of the proposed three-level definition. It should be noted that many of the elements have specific caveats applied to their use or interpretation, as listed in the legends.

Diagnostic categories

Clinical signs. PJI can present in many ways, ranging from fulminant joint sepsis with clear signs of infection to more indolent symptoms, such as pain or joint dysfunction. The mode of clinical presentation relates to the pathogenesis (planktonic bacteria vs biofilm) and microbial aetiology of the infection (high vs low virulence microorganisms). While fever and erythema are quite specific, they are also insensitive for diagnosing PJI.[18] Pain and reduced range of movement are the most sensitive clinical findings in infected cases, but they greatly overlap with aseptic failures.[18] Correctly distinguishing PJI from aseptic failure is a real problem in clinical practice and, above all, it depends on keen clinical awareness and suspicion.

A sinus tract communicating with the joint or exposed prosthesis are the only fully specific clinical findings. A history of problems with wound healing (such as prolonged wound leakage, wound dehiscence, or superficial infection) after primary implantation,[19-21] or a recent bacteraemia[22,23] (which may be a consequence of, or cause, the PJI), should suggest that an infection is likely. The timing of failure is relevant information to consider as there is an inverse correlation between prosthesis-age and positive microbiological findings. Early loosening is more often caused by hidden PJI than late loosening.[24,25]

Intraoperative finding of purulent fluid around a prosthesis is a subjective assessment by the surgeon. It is difficult to distinguish between pus and other turbid fluids present in other conditions, such as adverse local tissue reaction (ALTR) and crystal arthropathy, and virtually impossible to describe the features defining each.[26] As such, although its presence may raise suspicion of infection, it should be considered suggestive of PJI but not a confirmatory sign.

Blood biomarkers. Erythrocyte sedimentation rate, white cell count, percentage of polymorph neutrophils (PMN), and CRP are the most widely available and studied.[27] They are all a reflection of general inflammation and are affected by non-infective inflammatory conditions and may be normal in low-grade infections.[10,11,28]

CRP is especially useful in gauging the systemic severity of any infection, and is often recommended for septic screening. In the absence of other causes of raised inflammatory markers, which are often easy to exclude (e.g. crystal arthropathy, active inflammatory joint disease, periprosthetic fracture, or in the first few postoperative weeks), CRP level above 10 mg/l has sufficient specificity to be associated with PJI in the majority of cases. It cannot be used alone to confirm or exclude PJI,[11] but a raised CRP without other cause should prompt the clinician to think about the likelihood of PJI. A normal CRP does not exclude infection.

Synovial fluid cytology. Synovial fluid aspiration in suspected PJI is a central part of the diagnostic pathway. It not only allows assessment of the degree of local inflammation, but also enables limited microbiological analysis. Synovial white blood cell (WBC) count has been included in all of the major definitions.[4-6] The diagnostic cut-offs proposed in the literature vary between 1,500 and 4,000 cells/µL and the percentage of polymorphonuclear cells (PMN) between 65% and 80%.[29]

This variation highlights the difficulty for a bimodal definition set. In most analyses, sensitivities and specificities are around 90% and largely depend on the definition used to diagnose PJI. Levels for WBC count and PMNs below the lowest reported cut-offs can be used to indicate that an infection is unlikely. Values above this threshold may suggest infection, especially in PJI of the knee.[30] In addition, there is a high level of consensus and literature support for a cut-off value of 3,000 cells/µl and a percentage of PMNs above 80% to confirm a PJI in the hip and knee.[30] It must be noted that these cut-off levels can be affected by other conditions,[30] and may not be appropriate for other joints, particularly in the upper limbs. Future studies are necessary to define the best cut-off level in these joints.

Synovial fluid biomarkers. Synovial fluid can be further investigated to assess biomarkers involved in the host/bacteria interaction.[27,29] Among them, alpha-defensin has recently been added to the 2018 ICM definition.[8] Laboratory-based alpha-defensin testing presents good diagnostic accuracy.[27,29,31] It may be helpful in specific circumstances, such as after prior antibiotic administration[32] or with low virulence microorganisms,[33] and is not affected by contamination with blood.[13]

Current evidence, from independent studies, shows that it has demonstrated consistently high specificity and so can confirm infection.[13,34–36] However, non-infectious inflammatory conditions, such as metallosis, gout, or inflammatory diseases, may lead to false-positives and their presence may invalidate the use of this test.[37–39] A negative test should not be used to rule out PJI due to low sensitivity.[13,40]

It should be noted that the lateral-flow test has a significantly lower diagnostic accuracy (especially lower sensitivity) compared to the enzyme-linked immunosorbent assay (ELISA) in the laboratory.[40,41]

Microbiology. The sensitivity of preoperative synovial fluid culture in chronic infections is low and cannot be used as a screening test to rule out PJI. A positive preoperative culture is suggestive of infection.[42,43]

During revision surgery, in addition to synovial fluid, at least five reliable tissue samples must be obtained using separate instruments and immediately transferred to the laboratory.[44,45] Anatomically representative solid tissue samples should be taken, particularly from the bone-implant interface membrane.[46-48] The patient should be off antibiotics for at least two weeks, but antibiotic prophylaxis need not be withheld, and should be given prior to surgical incision.[49] Cultures should be incubated for at least 14 days, unless enrichment techniques are used, like sonication and/or incubation of samples in blood culture bottles.[50,51] Phenotypically indistinguishable microorganisms with identical antibiotic susceptibility pattern, ideally in all positive samples, but in at least two different samples clearly define infection.[44,45]

Interpretation of a single positive culture (in either preoperative aspiration or tissue culture) must be cautious and taken together with other evidence. When uncommon contaminants or virulent organisms (such as *Staphylococcus aureus* or Gram-negative rods) are found, this suggests an infection is likely. A single positive culture of a common contaminant (such as coagulase-negative staphylococci or *Cutibacterium acnes*) does not confirm the presence of infection, but should prompt further investigation.

Ideally, the implant should also be collected and processed using validated methods for biofilm disruption. Sonication of implants increases the yield of cultured organisms in chronic infections, in particular when the patient was on prior antibiotic treatment.[44,52,53] Sonication can be performed with or without a concentration centrifugation step. Any positive culture from sonication fluid must be considered as a potential infection,[52] but > 50 colony-forming units/ml (CFU/ml) confirms infection.[52,53] The proposed cut-offs refer to a non-concentrated technique.[52] If the concentration technique is applied, the suggested cut-off is 200 CFU/ml to confirm an infection.[54] If other variations to the protocol are used, validated cut-offs for each protocol must be applied.

Histology. The presence of acute inflammatory cells in tissue is highly specific for PJI.[54-60] This can be determined from preoperative biopsies or intraoperative tissue samples. However, the inflammatory infiltrate may not be uniformly distributed throughout the joint. It is essential to take at least three deep samples, favouring the bone-implant interface membrane, synovium/pseudo capsule, or other abnormal tissue.[48] Five to ten high-power fields (× 400 magnification) should be evaluated.

Various diagnostic criteria have been published, again demonstrating the difficulty of a bimodal definition. The most common criterion for confirmation of infection is the presence of five or more neutrophils in each of five high-powered fields.[4,60-62] A lower number of neutrophils or a lower number of positive high-powered fields has also been reported with good specificity,[57-59,63-65] making it reasonable to conclude that infection is likely if at least one high-power field contains at least five neutrophils. Regardless of the criterion proposed, histology has lower sensitivity than specificity (especially with microorganisms like coagulase-negative staphylococci and *C. acnes*).[59]

The presence of visible microorganisms with appropriate histological stains (Gram stain, Zeihl-Neelsen, fungal stains) has low sensitivity but is specific,[45,66] especially for identification of atypical organisms, which may not be cultured on routine microbiological protocols (e.g. fungi, filamentous bacteria, and mycobacteria).

Interpretation criteria are valid both for paraffin and frozen sections. Although interpretation of cell morphology in the latter may be more difficult, it can be applied when a specialist pathologist is available.[63,67,68]

Nuclear imaging. The role of nuclear imaging in the diagnosis of PJI is emerging. False-positive isotope uptake can occur around loose aseptic implants and in the postoperative period. For this reason, three phase bone scintigraphy is only reliable two years after hip arthroplasty and five years after knee arthroplasty.[69] A negative isotope scan in this regard has a high negative predictive value and makes an infection unlikely. In addition, improved protocols for nuclear imaging, particularly for WBC scintigraphy, have recently allowed better diagnostic evaluation of infected implants. A positive WBC scintigraphy, defined as an increasing accumulation of labelled leucocytes over time (after three to four hours and 20 hours), is suggestive of infection, especially when combined with bone marrow scintigraphy by reducing the number of false-positive cases.[70,71] Currently, no standardized interpretation criteria exist for FDG-PET CT in the diagnosis of PJI.[18]

Discussion

This project draws together the work of previous groups and adds new insights from recent studies. We have retained parts of the MSIS, IDSA, and ICM definitions, which are validated in multiple publications. This new EBJIS definition will be more sensitive due to upgrading of some diagnostics from minor criteria to full confirmatory tests. We aimed to include well-studied, validated tests and to avoid duplicating tests which address the same biochemical or pathological pathways. For instance, other serum biomarkers included in previous definitions, such as ESR or D-dimer, were judged to offer no added value over CRP.[72] We also avoided overdiagnosis by including only tests with high specificity in the confirmatory category.

The development of the middle 'infection likely' group is novel and was the most difficult to define. It is perhaps the most important because it directs clinicians to think again about cases which traditionally would not be classed as infected, but which may be. This more flexible approach may increase the face validity.[14] The inclusion of nuclear imaging reflects the increasing knowledge in this field and the wider availability of this modality.[69]

It is crucial to acknowledge that most PJI cases can be accurately diagnosed using simple, inexpensive, and widely available tests. Sharp clinical suspicion, basic synovial fluid analysis, and consistent intraoperative tissue investigation are key for successful diagnosis and treatment and are

recommended. This guide does not dictate which tests are mandatory for diagnosis, as availability and expertise vary around the world. There is little published evidence on the minimum set of diagnostic investigations, which is required to diagnose or exclude PJI. Expensive or laborious tests are not essential and should be reserved for selected cases where their potential benefits outweigh their limitations.[73]

Many researchers prefer to focus diagnostic investigations on changes which occur within the synovial cavity. Leucocyte esterase has shown good results[27,74] and was included in previous PJI definitions.[5,8] However, it is a qualitative estimation of leucocyte count and there are practical limitations, such as bloody taps or intermediate results, that limit its interpretation.[75,76] It was tempting to include many novel diagnostic molecules, such as synovial CRP,[77,78] calprotectin,[79] D-lactate,[80] adenosine deaminase,[78] or even synovial cytokines (e.g. IL-6).[27,29] These show early promise, but are neither as widely studied nor readily available and, as such, are not practical at this time.

Microbiological investigation, especially after revision surgery, remains a important cornerstone for PJI management. Not only does it clarify diagnosis, but also guides targeted antibiotic treatment. All efforts should be made to ensure adequate and reliable sampling and laboratory processing including biofilm disruption techniques. Notwithstanding, a proportion of cases remain culture-negative.[44,45,49,53,54,81] Molecular techniques are gaining momentum and promise to be useful, especially in such cases, but the lack of clear interpretative criteria make it difficult to include them in a definition set at this point.[12,82-85]

A plethora of other diagnostic tests and techniques have been proposed. We considered many at length, but concluded that they either duplicated the place of other tests, were expensive, did not add to the precision of diagnosis, or required expertise which was not generally available.[63,73,86,87] However, all can be supported in terms of their accuracy in some clinical studies.

This definition does not distinguish PJI on the basis of the duration of the infection (acute or chronic) or the time of onset from implantation (early or late). These terms are not defined with any degree of certainty with time-dependant cut-offs, and so cannot be included in a definition of PJI. We support the view that infection occurs as a continuum over time.[8,9] The criteria we have presented are valid, with the stated caveats, at all time points, although special care must be taken to interpret tests which quantify inflammation in the early postoperative period.

The concept of a three-level 'traffic light' definition allows the clinician to consider the place of test results or clinical signs which are commonly found, but are not specific for infection (such as a raised CRP) (Figure 1). This problem is recognized in the 2018 ICM definition[8] and is partly addressed with a scoring system from a single clinical series.[7] This was also suggested by Oussedik et al[14] (2012), who advocated a multilevel definition with scores based on statistical analysis of parameters. We did not apply scores to our test criteria as the literature is highly heterogenous and scores would be arbitrary at best. The three-level concept has been applied in fracture-related infection[15,16,88] and requires similar consideration in PJI.

The need for a unified definition is clear, and this offers a practical way forward which can be used immediately in many clinics around the world. As stated above, it is likely that the place of each element will change over time with new diagnostic tests and more robust evaluation of existing tests.

Take home message

- Diagnosis of periprosthetic joint infection (PJI) can be difficult. Low-grade infections can be missed and overdiagnosis is a risk with false-positive tests.
- A PJI definition must recognise the limitations of existing tests, and the need to interpret these in the clinical context.
- This new EBJIS definition proposes a three-level approach, which can be applied now with patients around the world.

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