

A global survey of diagnostic practices in prosthetic joint infections

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ABSTRACT

Prosthetic joint infections (PJIs) lead to significant morbidity, mortality and healthcare costs. A timely and accurate microbiological diagnosis is crucial for administering appropriate antimicrobial therapy. Periprosthetic tissue cultures are considered the 'gold standard' for microbiologically diagnosing PJIs. Though International guidelines provide some recommendations for achieving the aetiological diagnosis of PJI, many aspects remain unclear with local practices varying considerably. To better understand these practices, we conducted a global survey to evaluate microbiological diagnostic approaches for PJIs. One hundred and seven hospitals from 24 countries across six continents took part in the survey. Over half of the sites (51.4 %) were from Europe and the majority (79 %) were public hospitals. Nearly half of the sites (49.5 %) reported collecting 5-6 periprosthetic tissue samples for culture; however, 11 % collected fewer than 3 samples. Sonication on explanted joints were done in 46 (43 %) sites. It is noteworthy that 42 % of sites had a culture incubation period of 5 days or less, although 70 % of laboratories extended it under specific circumstances. Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) was the most used method for bacterial identification (74.8 %), and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) was the preferred method for susceptibility testing (64.5 % of sites), though notable differences were observed between continents. The availability of polymerase chain reaction (PCR) was limited to 46 (43 %) sites. These global variations in diagnostic practices may contribute to discrepancies in the reported aetiology and percentage of culture-negative PJIs reported in the literature.

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1. Introduction

Prosthetic joint infection (PJI) is a devastating complication of joint arthroplasty surgery with significant impact on the morbidity, quality of life and mortality of patients, as well as high healthcare and societal costs. Accurately estimating the global incidence and overall burden of PJI remains challenging due to inconsistencies in definitions, follow-up periods, and reporting practices [1–4]. In the United States, the economic burden of managing PJIs is estimated to be between \$60,000 and \$100,000 per patient, with hospital costs for hip and knee PJIs expected to reach \$1.85 billion annually by 2030 [5]. Different costs have been estimated for various countries and healthcare systems [1]. While the percentage of infected prosthetic joints appears to be low (typically 1–3 %), the large and growing number of joint replacements performed worldwide translates this percentage into a large and rising absolute number of PJIs. As a result, they are now recognised as a significant public health issue [6].

PJI can be caused by a wide variety of microorganisms [2,5,6] and accurate identification of the causative pathogen(s) is essential for effective management [2,4]. However, a significant proportion of patients, (ranging from 5 % to 45 %) are culture negative, complicating diagnosis and treatment. These culture-negative cases present challenges for antimicrobial stewardship, as they may lead to the use of prolonged or empirically chosen antimicrobials, increasing the risk of antimicrobial resistance. Despite these concerns, there remains a lack of standardised methodologies for the microbial diagnosis of PJI [7].

Diagnosis of PJI requires consideration of the number and types of sample types taken before and during surgery, as well as the duration of incubation of the cultures. Some sample types, such as blood cultures and synovial fluid can be obtained preoperatively. Although blood cultures are easy to obtain, their sensitivity, particularly in chronic PJIs is low [2,4]. Culture of periprosthetic tissue samples collected during surgery is usually considered the gold standard for diagnosing PJI [2,8]. While there is agreement that for optimal diagnostic yield multiple sites and tissue types must be sampled, there is no broad consensus on the exact number of samples to obtain, and this varies by guidelines (Table 1). Many laboratories use a range of tests or methods for PJI diagnosis, depending on the regional or international guidelines, cost, availability of skilled laboratory personnel, and laboratory infrastructure [8–10]. Regarding the incubation period, there is no clear consensus on the optimal number of days, in part due to the variability in data from different studies [11,12]. Sonication of the implant and culture of sonicate fluid may improve the microbial yield for PJI and is being increasingly adopted by many centres [13,14]. Molecular diagnostic methods are also sometimes used in conjunction with culture to enhance the diagnostic yield [2,15,16]. Molecular methods are appealing as they have a faster turnaround time, are unaffected by prior antimicrobial therapy, and have a higher sensitivity for microbial detection; however, they do not provide antimicrobial susceptibility [15], and the increased sensitivity can be at the cost of decreased specificity (by detecting organisms present in small numbers which may not be clinically significant). As such, molecular diagnostic methods are usually reserved for patients with suspected PJI and negative culture results [7,17–19].

We conducted a survey study on the diagnostic methods and tests for the microbiological diagnosis of PJI among hospitals interested in participating in a worldwide study on the microbial aetiology of PJI. Using these data, the current study aims to compare the microbiological diagnostic workup used in various geographic areas around the world and investigate factors that may influence these differences.

2. Method

As part of an ongoing study on the global microbial aetiology of PJIs, we first conducted a prospective survey with 138 questions to collect data on hospital characteristics and patient populations (patients

undergoing arthroplasty surgery and those with PJI), as well as 16 questions about the microbiologic diagnosis of PJI, which are shown in table S1. The survey questionnaire’s initial draft was written by NB, an infectious diseases physician. A clinical microbiologist (PH) developed the specific survey questions regarding the workup to diagnose the microbial aetiology of PJI. The questionnaire was reviewed and piloted by all members of the study’s steering committee, which includes specialists in infectious diseases, clinical microbiologists, and orthopaedic surgeons with expertise in managing PJIs. The clarity and accuracy of the questions, the simplicity of the format, and the appropriateness of the answer coding were assessed during the pilot test of the survey. Ultimately, one version was approved by all members of the committee. The study’s steering committee included at least one representative from each continent (MW-B-Europe, LM-Africa, PYL-Asia, JD and PC—Oceania, AC—North America, and MS-South America). For the pilot of the approved survey version, each representative extended an invitation to at least one site from their respective continents with PJI multidisciplinary teams (MDTs). The respondents were also requested to propose modifications to enhance question understanding and response precision. The steering committee developed and approved a new version in response to the results and recommendations of the pilot test. The final survey version was validated by requesting that at least two MDT members from the piloted sites complete the survey. The validation process demonstrated that over 95 % of survey responses were consistent.

The steering committee’s representatives from each continent invited sites on their respective continents that had expressed an interest in participating in the global study of PJI aetiology to complete the survey. The questionnaire was conducted in English using an online REDCap database hosted by the Institut de Recerca del Hospital de la Santa Creu i Sant Pau (IIB Sant Pau) in Barcelona, Spain, which sponsored the study. The survey was completed in 2022.

Table 1
Microbiologic diagnostic criteria of prosthetic joint infection according to different scientific societies.

Criteria	Infectious Diseases Society of America (IDSA) 2013 [9]	Musculoskeletal Infection Society (MSIS) 2018 I [10]	European Bone and Joint Infection Society (EBJIS) 2021 [8]
Recommended no of intraoperative samples to be sent for culture	At least 3, optimally 5 or 6 intraoperative periprosthetic tissue samples	No recommendation done	In addition to synovial fluid, at least 5 solid tissue samples
No of tissue cultures that need to be positive for a definitive diagnosis	At least 2 positive cultures of same organism. Only 1 positive culture with a “virulent” organism (such as <i>Staphylococcus aureus</i>), needs to be evaluated in the contexts of other results	At least 2 positive cultures with the same organism	At least 2 positive cultures of the same organism- Only 1 positive culture needs to be evaluated with other criteria.
Incubation period	The optimal duration of incubation of peri-prosthetic tissue specimen is unknown, but prolonged incubation of up to 14 days may help with pathogen isolation, particularly <i>Cutibacterium</i> species	Not stipulated.	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

2.1. Statistical analysis

Survey results were extracted into a Microsoft Excel spreadsheet. Categorical variables were summarised using frequencies and percentages, while continuous variables were described using means and standard deviations (SD) or medians and interquartile ranges (IQR), depending on data normality. To compare categorical variables, the Chi-square or Fisher's exact test was applied. For quantitative variables, the t-test or Mann-Whitney test was used. The independent factors associated with the implementation of specific diagnostic practices were identified using multivariate logistic regression. The continent of placement and the characteristics of each centre, including the number of beds, whether it was a tertiary or university hospital, public or private, and whether PJIs were diagnosed and treated by an MDT, were potential independent variables that were analysed. Statistical significance was defined as p-values <0.05. The statistical analysis was conducted using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY)

3. Results

3.1. Participant site characteristics

A total of 118 participant sites from 24 different countries across six continents took part in the survey. Participants who submitted incomplete responses received a reminder email and were given a two-week deadline to respond. The final dataset comprised 107 sites with complete responses to the most relevant survey questions.

More than half of the respondents, were from Europe (51.4 %), followed by Asia (21.5 %), Oceania (9.3 %), Africa (7.5 %), South America (6.5 %), and North America (2.8 %). Participants from Europe, Oceania and North America were more likely to be from a high-income country as per the World Bank classification (Table 2). The five countries with most participants were Spain, Australia, Taiwan, South Africa and Brazil, 60 % of those representing high income countries. In all continents, except for North and South America, most participating hospitals were public. Specifically, 91 % of hospitals in Europe and 100 % in

Oceania were public hospitals, while in Africa and Asia, the proportion was 63 % in both regions. A total of 85 (79.4 %) were university hospitals. The median number of beds across the participating hospitals was 796 (IQR 372-1172).

The most performed joint replacement surgery in the participating hospitals was total knee arthroplasty, reported in 45 sites (42 %), where >200 procedures were performed annually, followed by total and partial hip arthroplasties (Fig. 1). Overall, 56 % of hospitals reported an incidence of PJI ranging from 1 % to 2 %, with this percentage being significantly more common in European countries compared to other continents (Table 3). Nearly 90 % of sites had MDTs for managing PJIs; however, this percentage was notably lower in Asia and Africa.

3.2. Microbial aetiology workup

Most sites (97.2 %) reported taking more than one intraoperative sample for culture. In almost half of sites, an average of 5-6 samples were collected (Fig. 2). However, 11 % of hospitals collected <3 samples (Table 3). Factors associated with this low number of samples in the multivariate analysis were non-university affiliated hospitals and continent. Sonication was available in 43 % of hospitals, most of them in Europe. The sole factor that was independently associated with the availability of sonication in the hospital was the presence of an MDT.

An on-site microbiology laboratory and medical microbiologist were present in nearly all hospitals. As for solid culture media, blood agar was the most used (in >90 % of sites), followed by chocolate and MacConkey agar. Nutrient broth was utilised in almost 60 % of sites and anaerobic cultures were performed in 64 %. In >70 % of sites, 3 or more culture media were used. Of the 103 sites that responded to the question regarding the incubation duration of culture plates, the median duration of incubation period was 5 days (IQR 3-7). A total of 42 % of sites opted for a shorter incubation period of 5 days or less routinely. In the multivariate analysis, the continent was the only variable linked to this short incubation time. Asia and Oceania reported significantly more often incubation durations of 5 days or less than the other continents, with prevalence rates reaching >75 % of hospitals (Table 3). It is worth

Table 2
Characteristics of participant sites from different continents.

Characteristics	Europe	Asia	Oceania	Africa	South America	North America	P value	Overall
Number of sites- n (%)	55 (51.4)	24 (21.5)	10 (9.3)	8 (7.5)	7 (6.5)	3 (2.8)	0.001	107
Number of countries- n (%)	Spain 38 (35.8 %)	Taiwan 9 (8.4)	Australia 10 (9.3)	South Africa 8 (7.5)	Brazil 7 (6.5)	USA 2 (1.9)		24
	Italy 3 (2.8)	China 5 (4.7)				Canada 1 (0.9)		
	France 3 (2.8)	India 4 (3.7)						
	Switzerland 2 (1.9)	Singapore 2 (1.9)						
	Germany 2 (1.9)	Korea 1 (0.9)						
	Romania 2 (1.9)	Thailand 1 (0.9)						
	Lithuania 1 (0.9)	Malaysia 1 (0.9)						
	Norway 1 (0.9)	Turkey 1 (0.9)						
	Denmark 1 (0.9)							
	UK 1 (0.9)							
	Slovenia 1 (0.9)							
World Bank Income Classification n (%)	High income 11 (100)	High income 3 (38)	High income 1 (100)	Upper middle 1 (100)	Upper middle 1 (100)	High income 2 (100)		
		Upper middle income 5 (63)						
Public hospitals (%)	50 (90.9)	15 (62.5)	10 (100)	5 (62.5)	3 (42.9)	1 (33.3)	0.01	85 (79.4)
Private hospitals (%)	5 (9.1)	8 (33.3)	0	3 (37.5)	4 (57.1)	2 (66.7)	0.02	22 (20.6)
Specialty orthopaedics hospital (%)	4 (7.2)	0	0	1 (12.5)	1 (14.3)	1 (33.3)	0.93	7 (6.5)
Median no of beds (IQR)	819 (450-1028)-	1,125 (425-1606)-	748 (597-975)-	285 (142-473)	250 (136-381)	1,200 (230-1275)	<0.001	796 (372-1172)
PJI incidence <1 % (%)	5 (9.1)	17 (70.8)	2 (8.3)	2 (25)	0	3 (100)	<0.001	29 (27.1)
PJI incidence 1-2 % (%)	41 (74.5)	6 (25)	5 (20.8)	5 (62.5)	3 (42.9)	0	0.004	60 (56.1)
PJI incidence >3 % (%)	4 (7.2)	0	1 (4.2)	1 (12.5)	4 (57.1)	0	<0.001	10 (9.3)
Annual PJI prevalence, unsure: n (%)	5 (9.1)	1 (4.2)	2 (8.3)	0	0	0	0.93	8 (7.5)
MDT team availability: n (%)	53 (96.3)	19 (79.2)	9 (90)	4 (50)	7 (100)	3 (100)	0.02	95 (88.8)

IQR= interquartile range; MDT= multidisciplinary team; PJI= prosthetic joint infection; UK= United Kingdom; USA= United States of America.

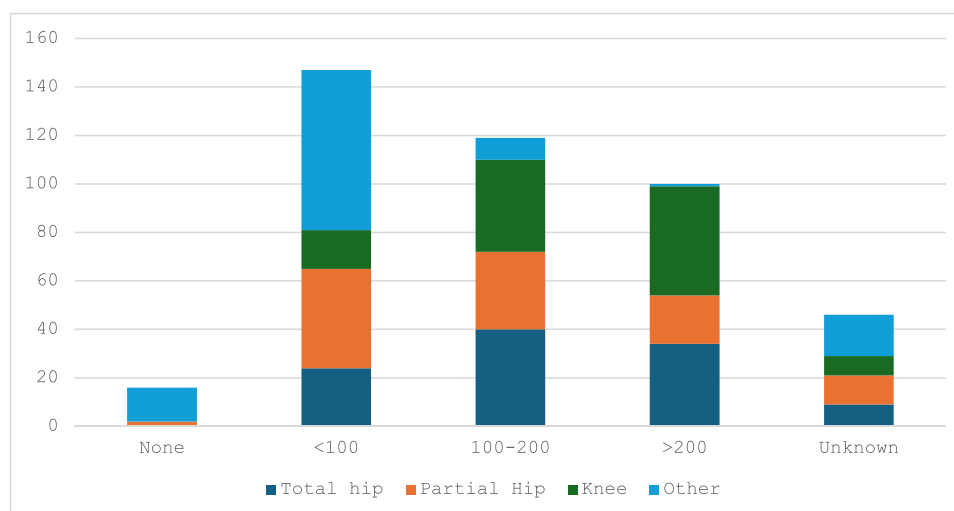


Fig. 1. Total no of arthroplasties by type.

noting that an incubation period of 5 days or less may result in lower diagnostic yield, with the possibility of missing pathogens such as *Cutibacterium* species. However, while all the Oceanic sites with short incubation extended culture incubation in some cases, 7 sites in Asia (29.2 %) did not extend incubation in any case, as did one centre in South America (14.3 %) and two centres in Europe (3.6 %). In total, 70 % of laboratories extended the incubation time in some circumstances, with the duration ranging from 7 to 30 days (median 14 days). A total of 33 (30.8 %) extended the culture incubation period for infections suspected to be caused by *Cutibacterium acnes*, atypical or fastidious organisms, or chronic PJIs, 17 (15.9 %) extended culture incubation period based on “clinical request” or “high clinical suspicion of PJI documented on request form”, 12 (11.2 %) extended the incubation period for all suspected PJIs and 9 (8.4 %) cited other reasons.

Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) was the most used method for bacterial identification (>70 % of sites). Vitek or Vitek 2 (bioMérieux, Marcy-l'Etoile, France) was the most common method of antimicrobial susceptibility testing (60 %), followed by agar plate disc diffusion (43 %). More than 1 susceptibility testing method was used in 36 % of sites. Overall, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines was used as the reference susceptibility testing method in most of the sites, but significantly more often in Europe and Oceania than elsewhere. Clinical and Laboratory Standards Institute (CLSI) reference (developed in the USA) was more commonly in Asia and North America.

Regarding molecular diagnosis, polymerase chain reaction (PCR) assays were available in 43 % of laboratories and bacterial genome sequencing in 41 %, with statistically significant differences among continents. Of the sites that mentioned the type of PCR used, GeneXpert (Cepheid, Sunnyvale, California) was used in 6 sites, BioFire Joint Infection panel (bioMérieux, Marcy-l'Etoile, France) in 6 sites, Unyvero i60 cartridge system (U-ITI; Curetis AG, Germany) in 2 sites and 16S rRNA sequencing in 12 sites. The remaining 26 laboratories did not mention the type of PCR used.

4. Discussion

This is the first international survey with a large geographic scope to highlight the diversity of methods used to diagnose the microbial aetiology of PJIs around the world. Our study reveals deviations from recommendations in diagnosing PJIs across different geographic regions. Many factors can influence the culture yield of periprosthetic tissues in PJI cases, including the number of samples collected, the type of media used for culture, the incubation time, and whether the explanted

implants are sonicated [2,4,9,7]. Thus, a low number of samples or the underutilisation of extended incubation, anaerobic cultures, or sonication, as observed in our study, may result in a higher percentage of “false negative cultures” or under detection of certain pathogens. It is difficult to determine the exact impact of each of these factors, or their combination, on these results, but they may all have an effect [2,4,9,7]. Some PJIs reported as “culture-negative PJIs” in some studies could ultimately be the result of insufficient diagnostic workup. We should consider using the term “culture-negative PJI” only when an extensive microbiological study of appropriate samples fails to identify an infectious agent.

In the present study, more than half of sites indicated that it was routine to collect 5-6 intraoperative samples, and 27 % usually collected 3-4 samples. These numbers are in line with the Infectious Diseases Society of America guidelines, (which recommend collecting a minimum of 3 and optimally 5 to 6 periprosthetic specimens) [9] and other guidelines (Table 1). Surprisingly, 11 % of sites reported collecting <3 samples, representing a significant deviation from the recommendations of all diagnostic criteria. Since detection of the same microorganism in two or more specimens establishes the microbiologic diagnosis, it is reasonable to assume that more than two samples must be obtained [2]. According to a recent review, 4 tissue samples should be cultured if standard plate and broth cultures are used, and 3 tissue samples should be cultured if blood culture bottles are used [2]. We did not ask specifically about the possible practice of culturing tissue samples in blood culture bottles in our study.

To improve diagnostic yield, various types of agar media are commonly used to enhance the likelihood of detecting these organisms [20,21]. Though the use of nutrient broth increases sensitivity of picking of microbial growth in PJIs [21], only 60 % of sites used this to set up their culture. Moreover, only 65.4 % sites reported setting their culture plates in anaerobic agar and conditions. This could significantly affect the detection of low-burden or anaerobic organisms such as *Cutibacterium* spp. However, the optimal media for culturing periprosthetic tissue biopsies are not well standardised, and the discussion of how different culture media may affect the microbiological diagnosis of PJI is beyond the scope of this study.

Due to the costs associated with species identification of bacteria, many laboratories have historically only reported genus-level identifications for many bacteria, including coagulase-negative Staphylococci and *Corynebacterium* species. MALDI-TOF allows for the rapid and accurate identification of bacteria to the species level in routine clinical practice. Given that current definitions of PJI include isolation of the same microorganisms from two or more specimens, the ability to

Table 3
Microbial aetiology work-up across different continents.

Characteristics	Europe <i>N</i> = 55	Asia <i>N</i> = 24	Oceania <i>N</i> = 10	North America <i>N</i> = 3	South America <i>N</i> = 7	Africa <i>N</i> = 8	<i>p</i> value	Overall
Average number of samples: <i>n</i> (%)								
<3	0	10 (41.7)	1 (10)	0	1 (14.3)	0	<0.001	12 (11.2)
3-4	12 (21.8)	8 (33.3)	3 (30)	2 (66.7)	0	4 (50)		29 (27.1)
5-6	36 (65.5)	4 (16.7)	5 (50)	1 (33.3)	6 (85.7)	3 (37.5)		55 (51.4)
>6	7 (12.7)	2 (8.3)	1 (10)	0	0	1 (12.5)		11 (10.3)
Sonication performed	30 (54.5)	8 (33.3)	3 (30)	0	5 (62.5)	0	0.08	46 (43)
Identification method: <i>n</i> (%)								
MALDI-TOF	49 (89.1)	12 (50)	10 (100)	1 (33.3)	5 (71.4)	3 (37.5)	0.001	80 (74.8)
Vitek/Vitek 2	2 (3.6)	9 (37.5)	1 (10)	0	2 (28.6)	1 (12.5)		15 (14)
>1 method	7 (12.7)	4 (16.7)	1 (10)	0	1 (14.3)	0		13 (12.1)
Don't know	0	0	0	2 (66.7)	0	4 (50)		6 (5.6)
Susceptibility method: <i>n</i> (%)								
Vitek/Vitek 2	30 (54.5)	16 (66.7)	10 (100)	1 (33.3)	4 (57.1)	3 (37.5)		64 (59.8)
Disc Diffusion	26 (47.2)	10 (41.7)	3 (30)	0	5 (71.4)	2 (25)		46 (43)
E-tests	9 (16.4)	0	1 (10)	0	3 (42.9)	0		13 (12.1)
MicroScan	9 (16.4)	0	0	0	0	0		9 (8.4)
>1 method	23 (41.8)	5 (20.8)	3 (30)	0	6 (75)	2 (25)		39 (36.4)
Don't know	0	0	0	2 (66.7)	0	4 (50)		6 (5.6)
Standard of susceptibility interpretation: <i>n</i> (%)								
EUCAST	52 (94.5)	1 (4.2)	9 (90)	1 (33.3)	1 (14.3)	5 (62.5)	<0.001	69 (64.5)
CLSI	0	22 (91.7)	1 (10)	2 (66.7)	1 (14.3)	2 (25)	<0.001	28 (26.2)
Both	2 (3.6)	0	0	0	0	0		2 (1.9)
Other	1 (1.8)	1 (4.2)			5 (71.4)	1 (12.5)		8 (7.5)
Media: <i>n</i> (%)								
Blood	51 (92.7)	21 (87.5)	9 (90)	3 (100)	6 (75)	7 (87.5)		97 (90.7)
Chocolate	35 (63.6)	13 (54.2)	10 (100)	3 (100)	5 (85.7)	5 (62.5)		71 (63.3)
MacConkey	24 (43.6)	14 (58.3)	5 (50)	2 (66.7)	5 (71.4)	4 (50)		54 (50.5)
Nutrient broth	35 (63.6)	11 (45.8)	8 (80)	1 (33.3)	4 (57.1)	4 (50)		63 (58.9)
Anaerobic	43 (78.2)	12 (50)	5 (50)	2 (66.7)	3 (42.8)	3 (37.5)		68 (63.6)
Other	10 (18.2)	8 (33.3)	1 (10)	0 (0)	3 (37.5)	1 (12.5)		23 (21.5)
>/=3 media	41 (74.5)	15 (62.5)	8 (80)	2 (66.7)	5 (62.5)	5 (62.5)		76 (71)
Culture duration and extension								
Median duration of incubationdays (IQR)	6 (5-9.5)	4 (3-5)	5 (5-6)	14 (5-21)	11 (12.25-14)	6.5 (2.25-11)		5 (3-7)
</=5 days (%)	12 (22.2)	16 (76.2)	8 (80)	1 (33.3)	3 (42.9)	3 (37.5)	<0.001	43 (41.7)
7 days (%)	20 (38.5)	4 (19)	1 (10)	0	3 (42.8)	0		28 (27.2)
>7 days (%)	20 (38.5)	1 (4.8)	1 (10)	2 (66.7)	1 (14.3)	5 (62.5)		30 (29.4)
Culture extension: <i>n</i> (%)	38 (73.1)	14 (66.7)	9 (90)	3 (100)	4 (57.1)	7 (87.5)		75 (72.8)
Median extension of cultures, days (range)	14 (7-30)	14 (7-28)	12 (10-14)	21 (10-28)	14 (14-14)	21 (7-42)		14 (7-30)
Molecular diagnostics: <i>n</i> (%)								
PCR	30 (54.5)	7 (29.2)	2 (20)	2 (66.7)	1 (14.3)	4 (50)	0.061	46 (43)
Sequencing (16 s rDNA or metagenomics)	23 (41.8)	5 (20.8)	10 (100)	1 (33.3)	1 (14.3)	4 (50)	<0.001	44 (41.1)

CLSI= Clinical and Laboratory Standards Institute; EUCAST= European Committee on Antimicrobial Susceptibility Testing; MALDI-TOF= Matrix-assisted laser desorption ionisation-time of flight; PCR= Polymerase chain reaction.

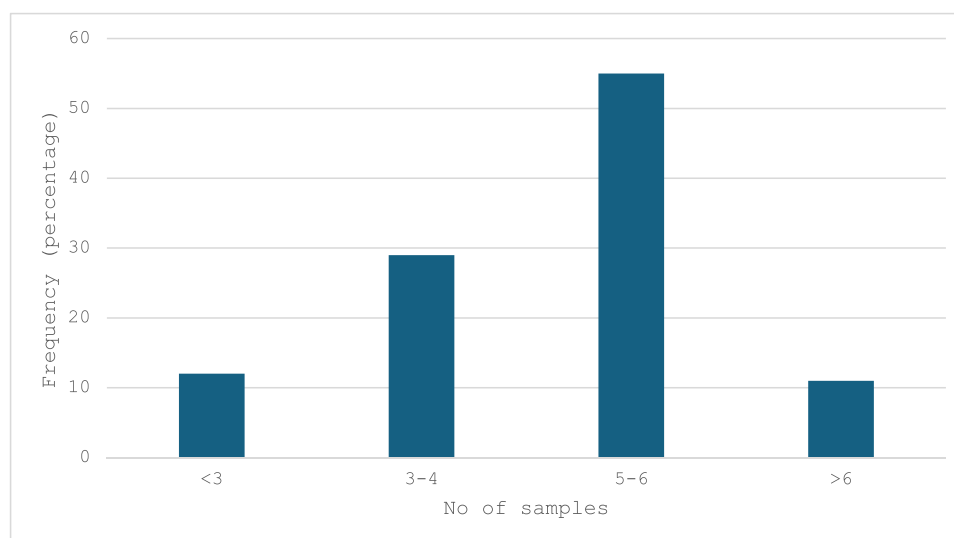


Fig. 2. Number of intraoperative samples collected for culture.

confirm species may improve diagnostic certainty, though the performance of this newer method for diagnosing PJI in comparison to traditional techniques has yet to be established. In the present study, MALDI-TOF was the most common method used for bacterial identification from culture. However, the percentage in the present study (74.8 %) was lower compared to a survey published by Yusuf E et al., which only included sites in Europe [22]. In that study, 94.3 % of sites used MALDI-TOF for bacterial identification. Like their findings, our study demonstrated that European sites were more likely to use MALDI-TOF for bacterial identification from culture plates at 89 % vs non-European sites at 57.8 %. This difference may be partially explained by the income categories of the countries that participated in the survey, with all European sites classified as high-income according to the World Bank classification (Table 2).

Duration of incubation of 7 days or more is often required for certain slow growing organisms that cause PJIs such as *Cutibacterium* spp. However, extending incubation beyond 14 days may not necessarily improve yield [20]. Remarkably, 42 % of the sites incubated cultures for 5 days or less, which may be insufficient for detecting slow growing or fastidious organisms. According to our findings, sites reporting short incubation durations would be more likely to be in resource-limited settings, as was the case in Asia (Table 2); however, the situation in Oceania would suggest that typical short incubation durations, which were extended in some circumstances, adhered to specific guidelines. Our survey did not differentiate between duration of incubation for acute PJI (where longer incubation might not be needed) versus chronic PJIs.

Regarding antimicrobial susceptibility test interpretation, EUCAST was most used, particularly in Europe and Oceania, while CLSI was more frequently used in Asia and North America. Clinical breakpoint differences between CLSI and EUCAST have a significant impact on interpreting susceptibility in clinical isolates. This affects antimicrobial resistance surveillance when data is compared within and between countries using different systems, and it may have implications for antimicrobial stewardship. As a result, the use of these different systems may account for some variations in reported PJI antimicrobial resistance rates in the literature.

Sonication of explanted joints, that has been shown to increase the microbial yield when used in conjunction with periprosthetic tissue culture (particularly when preoperative antibiotics are used), was implemented at fewer than half of the sites, mainly in Europe, and not used by respondents from North America and Africa. This aligns with findings from other published literature, including the PIANO study

(performed in Oceania), where only 1 out of 32 sites reported using sonication [23].

Due to the limitations of culture-based methods, newer methods such as polymerase chain reaction techniques (PCR) and next-generation sequencing (NGS) are increasingly being used to complement existing methods for the microbiological diagnosis of PJI. These techniques are a valuable supplemental tool in patients with culture-negative PJI caused by fastidious or slow-growing microorganisms and in patients who have previously been on antibiotics [7]. There are different techniques of PCR with different diagnostic applications and varying diagnostic performance. Generally, molecular-based methodologies are more cost-intensive and, depending on the platform, may necessitate specialised infrastructure along with associated operational expenses. Clinical metagenomics (CMG), a process that extracts and sequences every DNA fragment in a sample, has shown promising results in detecting PJI pathogens [7,16,24,25]. In addition to better detecting traditional bacterial pathogens that cause PJIs, CMG will also help detect less common pathogens such as fungi and mycobacteria and can detect pathogens in culture-negative PJIs. CMG can also provide information on antimicrobial resistance and virulence genes [7,26,27]. In our study, four sites reported using CMG, but mostly for research purposes only. Despite some advantages, these newer molecular diagnostic techniques have several limitations, including their cost and accessibility; currently they can only be regarded as complementary techniques but not a substitute for traditional cultures.

The strengths of our study lie in its large geographic reach, covering 6 continents and 24 countries. Our study has several limitations. There could be a reporting bias (social desirability bias), as respondents may have reported practices that reflect guidelines rather than actual day-to-day operations. Self-selection of participating centres likely resulted in overrepresentation of well-resourced sites. In fact, the sampling frame predominantly consists of large tertiary or university-affiliated hospitals with an on-site microbiologist and microbiology laboratory. Moreover, although sites from six continents participated in the survey, >50 % were from Europe, so the survey results are skewed to represent well-resourced sites. Thus, our results may not reflect practices in smaller or resource-limited settings, affecting consequently, the generalisability of the findings. This is however the case with most studies reported in the literature, in which the respondents are likely to be sites with the capacity to participate in a large international study, and smaller or less-resourced sites are likely to be underrepresented [21]. Nonetheless, it should be noted that management at hospitals where specialists in orthopaedic surgery, microbiology, and infectious diseases can directly

collaborate in an MDT (as is more common in large tertiary or university hospitals) may improve the diagnosis, treatment, and, ultimately, outcomes of patients with PJI. Finally, due to the lack of outcome data in our study, we are unable to establish associations between procedures performed and microbiological diagnosis or patient outcomes.

5. Conclusion

Our study highlights significant variability in the diagnostic practices for microbiological diagnosis of PJI worldwide, which may contribute to discrepancies in the reported aetiology of PJIs in the literature. This underscores the need for global consensus-building efforts and the harmonisation of diagnostic protocols to reduce culture-negative PJIs and improve international surveillance of antimicrobial resistance. As more data on emerging diagnostic methods, such as PCR and NGS become available, these techniques will need to be integrated into diagnostic algorithms of PJI. Furthermore, there is a pressing need for outcome-focused research that directly links diagnostic practices to patient-level outcomes, to ensure that advances in diagnostic methodology translate into meaningful clinical benefit.

CRediT authorship contribution statement

Shradha Subedi: Writing – original draft, Formal analysis, Data curation. **Patrick NA Harris:** Writing – review & editing, Validation, Methodology, Data curation. **Paul Chapman:** Writing – review & editing, Project administration, Conceptualization. **Antonia F Chen:** Writing – review & editing, Project administration. **Joshua S Davis:** Writing – review & editing, Project administration. **Po-Yu Liu:** Writing – review & editing, Project administration. **Leonard C Marais:** Writing – review & editing, Project administration. **Mauro J Salles:** Writing – review & editing, Project administration. **Jason A Roberts:** Writing – review & editing. **Jesus Rodriguez-Bano:** Writing – review & editing, Validation, Methodology, Data curation. **Marjan Wouthuyzen-Bakker:** Writing – review & editing, Project administration, Conceptualization. **David L Paterson:** Writing – review & editing. **Natividad Benito:** Writing – review & editing, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

PH has received research grants from Gilead unrelated to this project and research contract from Mutabilis and Microbio unrelated to this project; Speaker fees paid to Institution from BioMérieux and Gilead; advisory board for OpGen and Sandoz. LM has received grant from South African National Research Foundation- not used for this project, SS has received grant from GSK not used for this project and speaker fees and testing kits from BioMérieux unrelated to this project, MW-B has received a grant from Heraeus which was paid to the institution, honoraria from Heraeus, BioMérieux and Zimmerbiomet paid to the institution and sits on the board member of EBJIS and Board member of ESGIAI, DLP has received grants from Shinongi, Pfizer, Merck and BioMérieux not related to this project and consulting fees from Pfizer, Entasis, Shinongi, BioMérieux, Cepheid, GSK, Menarini, Aurobac, JAR has received grants from BioMérieux, Pfizer, QPEX, British society of antimicrobial chemotherapy not related to this project, consulting fees from Sandoz, Wolters Kluwer, Qpex, Gilead, Advanz Pharma, Pfizer, Summit Pharma, MSD, Speaker Honoraria fees from Sandoz, Pfizer, MSD, Gilead, Cipla unrelated to this project, NB has received consulting fees from MSD, Honoraria from MSD and Menarini unrelated to this work, Support for attending meetings from MSD, Menarini and Pfizer, AC has received grant from Foundation for arthroplasty Research and Education not related to this project, Royalties from Stryker, UpToDate,

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.diagmicrobio.2025.116919.

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Further reading

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