Synovasure®

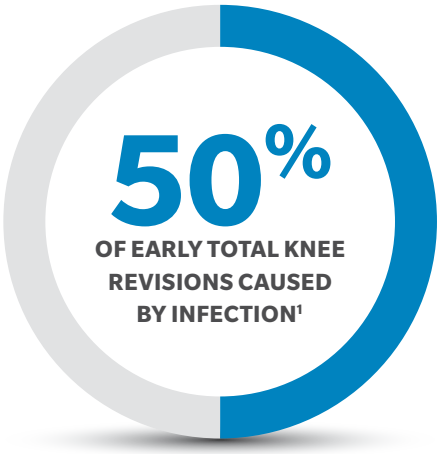
Comprehensive Infection Panel with SynTuition™

Laboratory Testing for Joint Infection

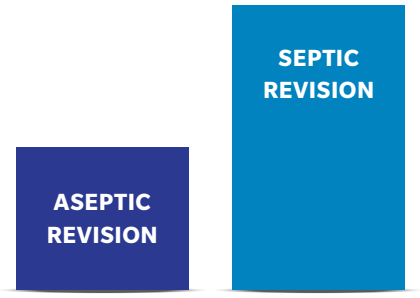
ZIMMER BIOMET

IMPACT OF PERIPROSTHETIC JOINT INFECTION

Periprosthetic Joint Infection (PJI) is one of the most common complications following total joint arthroplasty. Over 50% of early (<2 years) total knee arthroplasty revisions are caused by infection.[1] Additionally, the management costs of a septic revision are nearly double that of an aseptic revision.[2] Therefore, a comprehensive diagnosis of PJI is crucial.



MANAGEMENT COSTS NEARLY
2X HIGHER
FOR SEPTIC VS ASEPTIC REVISION[2]



Diagnosing PJI is Challenging

Currently, no single test exists to diagnose PJI, which can make diagnosing an infection difficult. However, there are a few industry-developed criteria used to support PJI diagnosis including:

- Musculoskeletal Infection Society (MSIS)[3]
- International Consensus Meeting (ICM)[4]
- European Bone & Joint Infection Society (EBJIS)[5]

2018 ICM PJI DIAGNOSIS CRITERIA[4]:

Major Criteria includes:	Decision
Two positive periprosthetic cultures with phenotypically identical organisms	Infected
A sinus tract communicating with the joint	

Test	Threshold		Score	Decision
	Acute*	Chronic		
Serum CRP (mg/L) **OR** D-Dimer (µg/L)	100 Unknown	10 860	2	Combined pre-operative and post-operative score: ≥ 6 = Infected 3-5 = Inconclusive** < 3 = Not Infected
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/µL) **OR** Leukocyte Esterase **OR** Positive Alpha Defensin (signal/cutoff)	10,000 ++ 1.0	3,000 ++ 1.0	3	
Elevated Synovial PMN (%)	90	70	2	
Single Positive Culture			2	
Positive Histology			3	
Positive Intra-operative Purulence***			3	

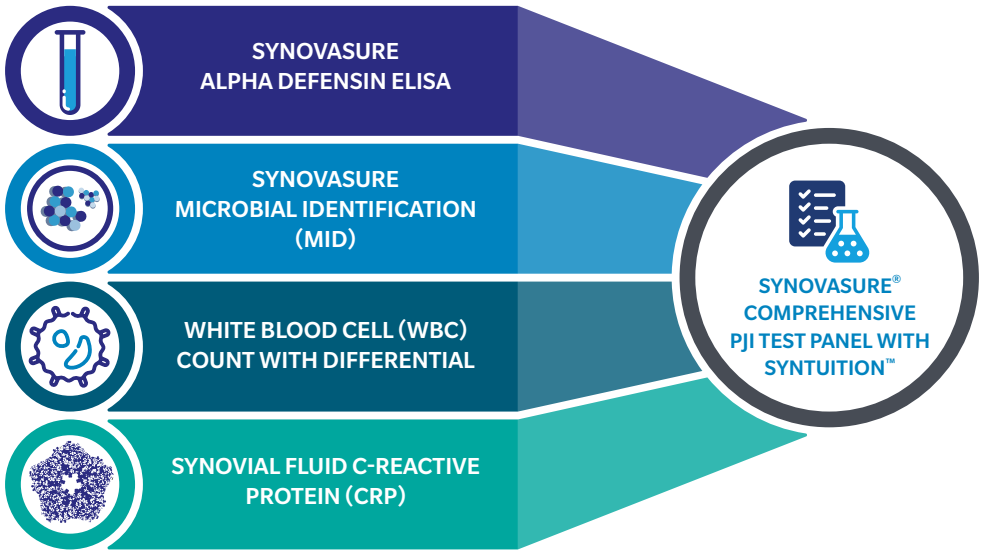
*Proceed with caution in: Adverse local tissue reaction, crystal deposition disease and slow growing organisms. *Further studies needed to validate a specific threshold. **Consider further molecular diagnostics such as next-generation sequencing. ***Has no role in patients with suspected adverse local tissue reaction.*

SYNOVASURE
COMPREHENSIVE PJI TEST PANEL

A SINGLE SOURCE FOR JOINT INFECTION DIAGNOSIS*

The Synovasure Comprehensive PJI Test Panel with SynTuition™ combines laboratory diagnostic tests including proprietary tests only available through Zimmer Biomet into a validated, machine-learning algorithm to aid in PJI diagnosis.[1]

Results include an easy-to-understand score based on the proprietary SynTuition algorithm along with individual test results.



Proprietary Testing Included
Synovasure Alpha Defensin and Synovasure Microbial Identification testing are included as part of the panel.

Integrity Assessments on All Specimens
Approximately 8% of specimens are affected by specimen integrity, impacting the accuracy of tests.[6] As part of the panel, every specimen is tested for Absorbance at 280 nm (A280) and Red Blood Cell Count to ensure the specimen is not diluted by added fluid or blood.

Fulfills Industry-Developed Criteria
Panel includes tests that fulfill MSIS, ICM and EBJIS criterias.

Quick Results Turnaround
Providers receive results report within 24 hours of receipt at CD Laboratories**

* Final patient diagnosis responsibility lies with the medical professional.
**Cultures are held for 7 days (14 days for shoulders) and sent in subsequent report.

BRINGING THE POWER OF AI TO PJI DIAGNOSTICS

Providing an accurate interpretation of multiple diagnostic tests is key to a proper treatment plan for patients with pain and inflammation following total joint replacement. A 2023 study found that the complexity of diagnostic criteria such as the 2018 ICM demonstrated poor interobserver agreement and increased inconclusive diagnosis rates.[7]

INTRODUCING SYNTUITION™

The SynTuition™ Score is a machine-learning, algorithmic interpretation of multiple tests results to aid in the diagnosis of PJI. Utilizing the vast synovial fluid testing database only available at CD Laboratories, SynTuition is aiding providers with added information to make a final diagnosis.

Developed Specifically to Aid PJI Diagnosis

Using unsupervised clustering with biomarker data from over 83,000 specimens, SynTuition clearly defined PJI-positive and PJI-negative clusters.

Accurate Interpretation[8,9]

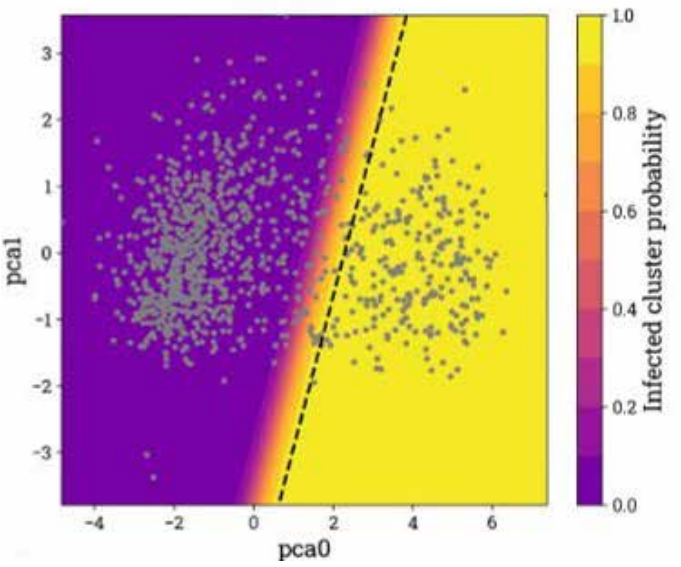
Validated against the 2018 ICM PJI Definition with high accuracy of 98.1% Sensitivity and 97.6% Specificity. Additionally, SynTuition minimizes inconclusive rates to a 0.6% rate[8,9] vs. published rates of the ICM definition ranging from 7.5% to 26.0%.[10,11]

Easy-to-Understand Interpretation

The SynTuition Score is delivered as part of the results report as a visual representation of the combined algorithmic results that is available within 24 hours of specimen receipt at CD Laboratories.

Note: SynTuition is available as a laboratory-developed test (LDT), except in NY State.

Gaussian Mixture Model (GMM)[9]



Gaussian Mixture Model (GMM) demonstrating the clustering of specimens into non-infected and infected clusters.[9]

SYNOVASURE ALPHA DEFENSIN ELISA TEST

Alpha defensin is an antimicrobial peptide released by neutrophils in response to pathogens and has been well published as a biomarker to aid in PJI diagnosis. The Synovasure Alpha Defensin ELISA Test is a laboratory-based test that detects elevated levels of the alpha defensin biomarker in synovial fluid. The Synovasure Alpha Defensin ELISA Test can be ordered individually or as part of the Synovasure Comprehensive PJI Test Panel with SynTuition.

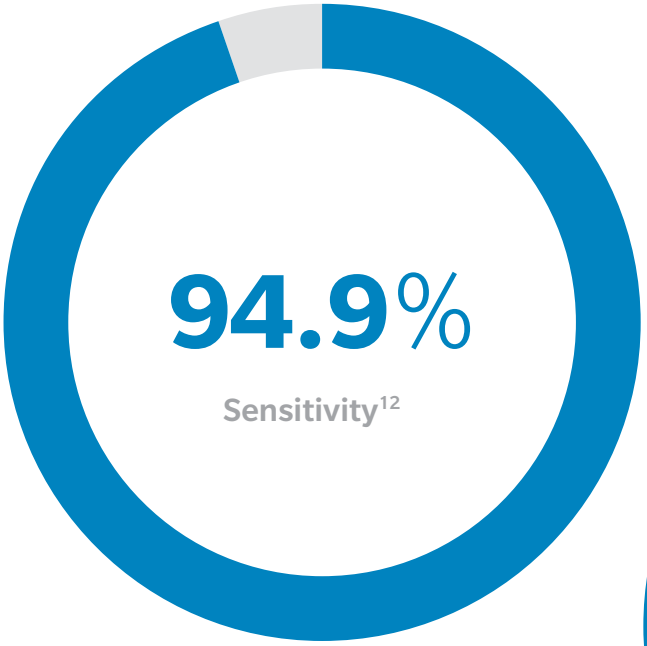
First and Only Test Specifically Designed and Validated to Aid in the Diagnosis of PJI

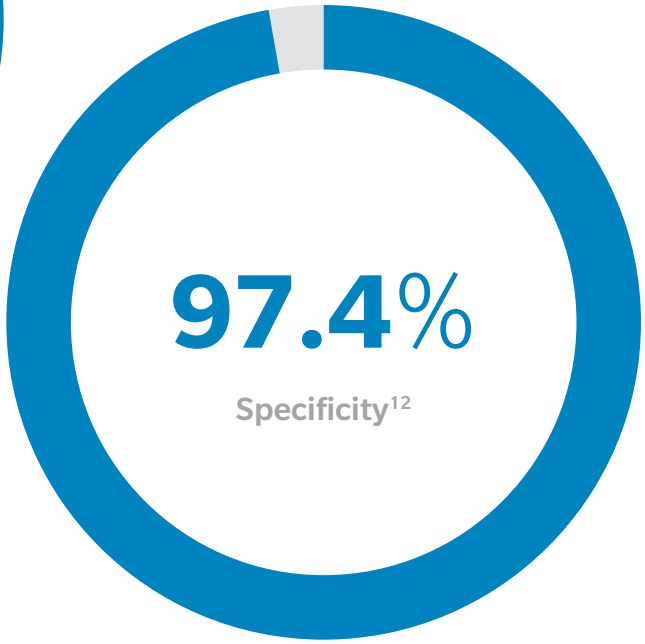
Highly Sensitive and Specific Based on 2013 MSIS Criteria for PJI[12]

- 94.9% Sensitivity
- 97.4% Specificity

Performance Unaffected by:

- Prior antibiotic administration [13, 14]
- Comorbidities related to inflammation [13, 15]
- Type and/or virulence of organism [13, 16]





SYNOVASURE MICROBIAL IDENTIFICATION (MID)

The Synovasure MID Test* utilizes a novel bead-based technology for early detection (typically within 24 hours) of microbial antigen in synovial fluid by binding genera-specific antibodies to a corresponding antigen. The Synovasure MID Test can be ordered individually or as part of the Synovasure Comprehensive PJI Test Panel.

Validated Test Panel for Common Species

Designed to identify the organisms in synovial fluid responsible for more than 70% of PJIs[17] including:

- *Staphylococcus* species
- *Enterococcus* species
- *Candida* species
- *Cutibacterium acnes* (formerly *P. acnes*)

Performance Backed by Data

Highly sensitive and specific compared to synovial fluid culture techniques

Organism genus	Sensitivity[18]	Specificity[18]
Staphylococcus species	94%	99%
Enterococcus species	97%	99%
Candida species	90%	99%

Note: *Due to difficult nature of culturing C. acnes, sensitivity and specificity data is unavailable*

Performance in Culture-negative Specimens[11]

A 2023 clinical study showed the panel's ability to detect a microorganism in >49% of culture-negative PJI samples.

Note: MID is not available in NY state.

SYNOVIAL FLUID C-REACTIVE PROTEIN (CRP)

The Synovial Fluid CRP test measures the levels of the c-reactive protein biomarker within a specimen.

Clinically Validated Performance[19]

A 2024 clinical study demonstrated 86.1% Sensitivity and 87.1% Specificity compared to the 2018 ICM Definition of PJI, outperforming published Serum CRP diagnostic performance.

STANDARD OF CARE TESTING

In addition to the proprietary tests offered only through Zimmer Biomet, the Synovasure Comprehensive PJI Test Panel also includes standard of care (SoC) tests:

Synovial Fluid Culture

Aerobic and anaerobic culture is performed on synovial specimens to determine identity and susceptibility of organisms. Cultures are held for seven (7) days on all samples and 14 days for shoulder specimens.

White Blood Cell Count w/ Differential

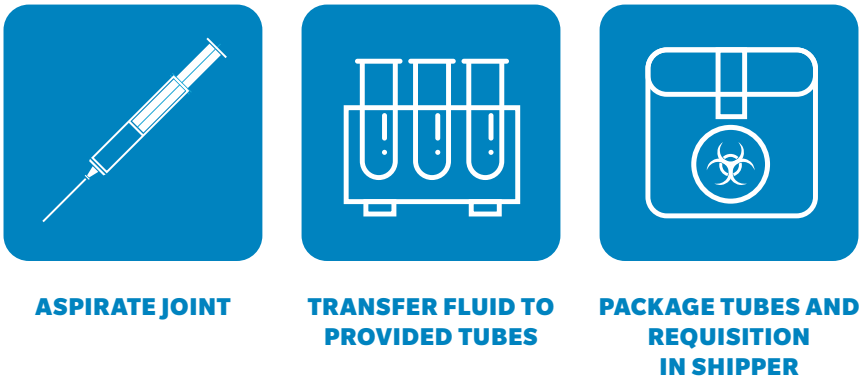
An automated, high-performance cell count that provides the overall number of white blood cells, as well as the percentage breakdown of white blood cell type in synovial fluid. There is evidence that an automated WBC count can be affected by the presence of total joint arthroplasty, leading to higher rates of false-positive results[20] ; therefore, elevated white blood cells (>3000 cells/uL) are confirmed by a manual count as part of the PJI comprehensive panel testing.

Crystal Analysis

Specimens are tested with polarized microscopy to detect monosodium urate (MSU) and calcium pyrophosphate dihydrate (CPPD) crystals to aid in identifying the presence of gout and pseudogout/CPPD disease. Crystal analysis is available as an optional add-on test to Synovasure Comprehensive PJI Panel with SynTuition.

A STREAMLINED PROCESS

Submitting synovial specimens to CD Laboratories uses a simple, streamlined process from aspiration to results reporting.



ASPIRATE JOINT

TRANSFER FLUID TO PROVIDED TUBES

PACKAGE TUBES AND REQUISITION IN SHIPPER

OVERNIGHT SHIPMENT TO CD LABORATORIES

TESTS PERFORMED AND RESULTS SENT TO PROVIDER

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3178.6-US-en Issue Date 2025-03

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