Second International Consensus on Periprosthetic Joint Infection
July 25-27, 2018
Javad Parvizi MD, FRCS
Thomas Jefferson University, Philadelphia
Bring together expert doctors and scientists from around the world to determine the state of art related to orthopedic infections
ICM 2018
Mission

- Improve musculoskeletal care of **patients** by preventing or better treating orthopedic infections
Why bother?
Literature is not definitive on many issues
Much of what we have is based on thin science, if any at all.
Challenges of Generating Evidence

- To do studies on infection, large sample sizes are needed
- $n=5,000$, $n=22,000$, $n=36,000$
Challenges of Generating Evidence

Not everything we do needs “randomized, prospective studies”
Scholar Innovators

Glove during surgery

Hand washing- sterile techniques

Antibiotics
Abstract
The ethics of clinical research requires equi-
pose, a state of genuine uncertainty on the part of
the clinical investigator regarding the relative
merits of treatment A and B. This uncertainty
is necessary for the clinical investigator to
avoid the ethical dilemma of preferring one
treatment while advocating the other. If a clini-
cian concludes that one treatment is of superior
merit, he or she is equipose, and a proper
clinical trial is required. The current understand-
ing of this requirement, which entails the invest-
gator uncertainty — not preference — throughout
the course of the trial, presents
results of trials needed to satisfy the require-
ment or completion of a controlled trial and may also con-
tribute to the termination of trials because of the failure
to enroll enough patients. This article proposes an alter-
native concept of equipose, which
would avoid the ethical dilemma of the clinical investigator's
preference for one treatment while advocating the other.
The paper argues that equipose is not a state of genuine
uncertainty but rather of genuine belief. A clinical
trial requirement is satisfied if there is genuine uncertain-
ty regarding the relative merits of A and B, as well as
in the patients' belief in the efficacy of the investiga-
tor's recommendations. This is more likely on the part of the individual investigator — about the
offered treatment. (N Engl J Med 1987; 317:
141-155.)

THERE is widespread agreement that ethics re-
quires that each clinical trial be based on equiv-
-frame null hypothesis, which states that the new treatment B is ineffective or only marginally
superior to the standard treatment A. It is neces-
sary that the clinical investigator be in a state of gen-
une uncertainty regarding the relative merits of the
treatments A and B for population P. If a physician
knows that these treatments are not equivalent, ethics
requires that the superior treatment be recommend-
ed. Following Fried, I call this state of uncertainty
about the relative merits of A and B “equipoise.”

Equipoise is an ethically necessary condition in all
cases of clinical research. In trials with several ar-
ms, equipoise must exist between all arms of the trial; otherwise the trial design should be modified to
ex-
clude the inferior treatment. If equipoise is disturbed
during the course of a trial, the trial may need to be
terminated and all subjects previously enrolled, as
cells, although equipoise has commonly been
described as a situation in which the investigator means
“no dominated clinical trials,” it is important to recog-
nize it as an ethical condition of all controlled clinical
trials, whether or not they are randomized, placebo-
controlled, or double-blind. The fact that equipoise is a
state of genuine uncertainty and not merely a circum-
cumstance of convenience means that equipoise is a
state of genuine uncertainty and not merely a circum-
cumstance of convenience means that equipoise is not
able to be achieved by simple randomization of sub-
jects. If equipoise is not achieved, the trial may be de-
termined to be unethical.

The recent increase in attention to the ethics of re-
search with human subjects has highlighted the
ethical dilemmas associated with equipoise. Yet, as I shall attempt to show, there is evidence that equipoise is attainable and that equipoise is a
state of genuine uncertainty.

Vol. 317 No. 3 EQUPOISE AND THE ETHICS OF CLINICAL RESEARCH — FREEDMAN 141

SPECIAL ARTICLE
EQUIPOISE AND THE ETHICS OF CLINICAL RESEARCH
Benjamin Freedman, Ph.D.

There is widespread agreement that ethics require-
that each clinical trial be based on an equiva-

From the Medical Center for Medical Ethics and Law, McGill University,
Montreal, Quebec, Canada.
11. Fried, R. Controlled clinical trials. In Medical Ethics: The
12. Abraham, H., and Cohen, M. Ethics of clinical research:
13. Cohen, M., and Abraham, H. Ethics of clinical research: The
privileged position of the investigator. JAMA 1973; 226:
1370-1371.
15. Freedman, B., and Selim, R. The ethics of clinical research:
Criteria for controlling and randomizing subjects in clini-

First International Consensus on Periprosthetic Joint Infection
August 1-3, 2013
Javad Parvizi MD, FRCS
Thomas Jefferson University, Philadelphia
Delegates

- 890 Delegates
- 98 Countries
- Over 200 societies
- 98 Presidents
Step VI: Systematic Review

- Over 200,000 publications reviewed
Step XII
Voting
July 26-27, 2018
ICM 2018

Subspecialties:

- General (171)
- Hip and knee (157)
- Shoulder (77)
- Spine (65)
- Trauma (52)
- Foot and ankle (42)
- Oncology (34)
- Sports (20)
- Biofilm (20)
- Elbow (16)
ICM 2018

- Class 1: Clinically important, high evidence
- Class 2: Clinically important, low evidence
- Class 3: Clinically less important, high evidence
- Class 4: Clinically less important, low evidence
**HK-39: What is the definition of PJI of the knee and the hip? Can the same criteria be used for both joints?**

**RESEARCHED BY:**

<table>
<thead>
<tr>
<th>Noam Shohat MD</th>
<th>Jean-Yves Jenny MD</th>
<th>Ricardo Sousa MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thomas Bauer MD</td>
<td>Per Kjaersgaard-Andersen, MD</td>
<td>Mark Spanghel MD</td>
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<tr>
<td>Martin Bhuttaro MD</td>
<td>Mel Lee MD</td>
<td>Rashid Tikilov MD</td>
</tr>
<tr>
<td>Nicolaas Budhiparma MD</td>
<td>Adolfo Lina MD</td>
<td>Ibrahim Tuncay MD</td>
</tr>
<tr>
<td>Craig Della Valle MD</td>
<td>Konstantinos Malizos MD</td>
<td>Eivind Witso MD</td>
</tr>
<tr>
<td>Thorsten Gehrke MD</td>
<td>Rhidian Morgan Jones MD</td>
<td>Marjan Wouthuyzen-Bakker MD</td>
</tr>
<tr>
<td>Luiz S Marcelino Gomes MD</td>
<td>Javad Parvizi MD</td>
<td>Simon Young MD</td>
</tr>
<tr>
<td>Seung Beom Han MD</td>
<td>Patricia Peel MD</td>
<td>Xianlong Zhang MD</td>
</tr>
<tr>
<td>Yutaka Inaba MD</td>
<td>Salvador Rivero-Boschert MD</td>
<td>Yixin Zhou MD</td>
</tr>
<tr>
<td></td>
<td>John Segreti MD</td>
<td>Werner Zimmerli MD</td>
</tr>
</tbody>
</table>
Literature:

• Meta-Analysis 2, Prospective/Randomized 0, Retrospective 17

• Parvizi et al. introduced an updated set of criteria in their paper in 2018. With the advent of new literature and diagnostic tests, the new 2018 MSIS criteria integrated these new discoveries to better characterize the diagnosis of PJI.

• Sousa et al, demonstrated in a prospective study in 2017 that biomarkers in synovial fluid, such as CRP, ADA, and α2M, have high sensitivity and specificity in diagnosing the presence of PJI.
### Major criteria (at least one of the following)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Decision</th>
</tr>
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<tbody>
<tr>
<td>Two positive growth of the same organism using standard culture methods</td>
<td>Infected</td>
</tr>
<tr>
<td>Sinus tract with evidence of communication to the joint or visualization of the prosthesis</td>
<td></td>
</tr>
</tbody>
</table>

### Minor Criteria

<table>
<thead>
<tr>
<th>Minor Criteria</th>
<th>Threshold</th>
<th>Score</th>
<th>Decision</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum CRP (mg/L)</td>
<td>Acute: 100</td>
<td>Chronic: 10</td>
<td>2</td>
</tr>
<tr>
<td>or D-Dimer (ug/L)</td>
<td>Unknown</td>
<td>860</td>
<td>1</td>
</tr>
<tr>
<td>Elevated Serum ESR (mm/hr)</td>
<td>No role</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Elevated Synovial WBC (cells/µL)</td>
<td>Acute: 10,000</td>
<td>Chronic: 3,000</td>
<td>3</td>
</tr>
<tr>
<td>or Leukocyte Esterase</td>
<td>++</td>
<td>++</td>
<td>3</td>
</tr>
<tr>
<td>or Positive Alpha-defensin (signal/cutoff)</td>
<td>1.0</td>
<td>1.0</td>
<td>3</td>
</tr>
<tr>
<td>Elevated Synovial PMN (%)</td>
<td>90</td>
<td>70</td>
<td>2</td>
</tr>
<tr>
<td>Single Positive Culture</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Histology</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Intraoperative Purulence*</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*This criteria was never validated on acute infections.

*No role in suspected adverse local tissue reaction.
Recommendation: This is the proposed 2018 ICM criteria for PJI:

Level of Evidence: Moderate

A. Agree 68%
B. Disagree 28%
C. Abstain 4%
HK-49: Do you agree with the American Academy of Orthopaedic Surgeons’ algorithm for diagnosis of Periprosthetic Joint Infection?

RESEARCHED BY:

Timothy Tan MD, United States of America
Javad Parvizi MD, United States of America
Craig Della Valle MD, United States of America
Literature:

• While the existing algorithms are widely accepted, they are not completely evidence based and have not been validated.

• Several new synovial, serum and molecular biomarkers have been introduced in recent years which has increased confusion regarding a potential diagnostic algorithm.

• There is no role for certain tests e.g. Gram staining
Proposed 2018 ICM Algorithm for PJI:

Sinus Tract

- All negative
- Any Positive
  - Serum ESR, CRP, D-dimer
  - Clinical Suspicion
  - Low
  - High

Synovial Fluid Testing
- Synovial WBC
- Synovial LE
- Alpha Defensin
- Synovial PMN %
- Cultures

Surgery Planned

- Intraoperative Findings
  - Histology
  - Purulence
  - Cultures
  - NGS

Surgery Unplanned

- Dry Tap
  - Repeat Aspiration

- Consider further testing with:
  - Biopsy, Bone Scan, PET scan

Doesn’t Meet ICM Definition

- Doesn’t Meet ICM Definition
- Synovial Fluid Testing

Not Infected

* At any time - 2 positive cultures or sinus tract are major criteria for infection

Infected*
**Recommendation:** Yes. However, since the introduction of the AAOS’s algorithm for diagnosis of PJI numerous new tests and diagnostic modalities have become available. The proposed evidence-based and validated algorithm includes the guidelines from AAOS and the 2013 International Consensus Meeting on PJI. A stepwise algorithm first using serological markers followed by more specific and invasive tests continues to be recommended.

**Level of Evidence:** Strong

A. Agree

B. Disagree

C. Abstain
PJIDX App
Question: What modifiable and non-modifiable host related factors contribute to an increased risk of SSI/PJI?

RESEARCHED BY:

Setor Kunutsor
Literature:

• In pooled analysis of 14 studies, Kerkhoffs and colleagues reported an increased risk of infection following total knee arthroplasty (TKA) when obese were compared to non-obese patients.

• In pooled analysis of eight studies, age (as a continuous exposure) was not associated with the risk of PJI. However, findings from two studies suggested that patients aged 75 years and above had an increased risk of SSI following primary THA.

• In pooled analysis of eight studies, Chen and colleagues demonstrated that males had a higher risk of infection after TKA than females. Recent pooled multivariate analysis of 28 studies confirms the emerging evidence.

• Pooled analysis shows that black populations (compared with the white race) have an increased risk of PJI/SSI.
Recommendation: Modifiable host related factors such as BMI, smoking, alcohol consumption, diabetes, malnutrition and other and certain medical co-morbidities have been shown to increase the risk of SSI/PJI. Non-modifiable factors such as increasing age, male gender, and low-socioeconomic status have also been shown to increase the risk if SSI/PJI.

Level of Evidence: Strong

A. Agree
B. Disagree
C. Abstain
**Question:** Does the type of venous thromboembolic (VTE) prophylaxis influence the risk of SSI/PJI in patients undergoing orthopedic procedures?

**RESEARCHED BY:**

Ronald Huang

James J Purtill

I. Remzi Tozun
Literature:

• Meta-analysis 2, Prospective/Randomized 2, Retrospective 30

• A prospective cohort study showed a significantly higher rate of surgical site infections in patients receiving LMWH prophylaxis dosing compared with patients receiving therapeutic warfarin with or without bridging therapy.

• Two recent meta-analyses of RCTs found no difference in SSI/PJI rates in TJA patients receiving rivaroxaban versus enoxaparin.

• Randomized trial demonstrated that in patients receiving enoxaparin, there was nearly eight times the number of wound complications compared to other modalities.
**Recommendation:** Yes. In a majority of studies evaluating venous thromboembolic (VTE) prophylaxis in patients undergoing total joint arthroplasty (TJA), aspirin appears to result in a lower risk of SSI/PJI than anticoagulants (vitamin K antagonists, heparin-based products, factor Xa inhibitors, and direct thrombin inhibitors).

**Level of Evidence:** Moderate

A. Agree
B. Disagree
C. Abstain
G-75: Does allogeneic blood transfusion increase the risk of SSI/PJI?

RESEARCHED BY:

Trisha Peel  Luis Pulido  Kalin Mihov
Literature:

• Meta-analysis 0, Prospective/Randomized 0, Retrospective 22

• Many studies consistently demonstrate that allogenic blood transfusion is a risk factor for PJI.

• Five studies demonstrate that allogenic transfusion increases infection rate compared to autologous transfusion
**Recommendation:** Yes. Allogenic blood transfusion is associated with an increased risk of SSI / PJI.

**Level of Evidence:** Strong

A. Agree
B. Disagree
C. Abstain
ICM 2018

- Class 1: Clinically important, high evidence
- Class 2: Clinically important, low evidence
- Class 3: Clinically less important, high evidence
- Class 4: Clinically less important, low evidence
HK-7: Is one dose of preoperative antibiotic adequate for patients undergoing total joint arthroplasty?

RESEARCHED BY:

Timothy Tan MD, USA
Wei Huang MD, China
Thorsten Seyler MD, USA
Literature:

- Meta-analysis 1, Prospective/Randomized 1, Retrospective 23

- WHO and CDC recommend for single preoperative antibiotic dosing
  - There is insufficient arthroplasty literature to support this recommendation

- A meta-analysis concluded that postoperative antibiotics did not reduce the rate of infection, however, they reported that the quality of evidence was very low
**Recommendation:** Despite the current guidelines from CDC advocating for a single dose of perioperative antibiotics, these studies are underpowered and primarily in specialties outside orthopaedics. From the limited evidence available, it does appear that a single preoperative dose of antibiotics, compared to multiple doses, does not increase the rate of subsequent SSI/PJI. A randomized prospective study in patients undergoing elective arthroplasty in underway that should answer this question definitively.

**Level of Evidence:** Limited

A. Agree
B. Disagree
C. Abstain
G-65: Does the type of anesthesia (general vs. neuraxial) influence the risk of subsequent SSI/PJI?

RESEARCHED BY:

Andrew Fleischman
Stavros G Memtsoudis
Literature:

- Meta-analysis 2, Prospective/Randomized 0, Retrospective 16

- Several retrospective, and meta-analysis have demonstrated that general anesthesia has a higher rate of infection and wound complications than neuraxial anesthesia.

- Large database and registry studies also demonstrate increased infection with general anesthesia

- There are no high quality randomized studies available
**Recommendation:** Compared to general anesthesia (GA), neuraxial anesthesia (NA) appears to be associated with reduced risk of SSI/PJI after total hip arthroplasty (THA) and total knee arthroplasty (TKA).

**Level of Evidence:** Limited

- A. Agree
- B. Disagree
- C. Abstain
G-49: Does the use of laminar flow in the operating room reduce the risk of subsequent SSI/PJI in patients undergoing orthopedic procedures?

RESEARCHED BY:

Arash Aalireazaie  Everth Merida  Kelly Vince  Greg Stocks
Literature:

• Meta-analysis 0, Prospective/Randomized 1, Retrospective 20

• Early studies suggested LAF was effective in reducing SSI/PJI

• 6 retrospective studies found no difference in rate of SSI/PJI with use of LAF

• 3 recent studies linked use of LAF to increase in rate of SSI/PJI
**Recommendation:** Recent orthopedic literature has not demonstrated that the use of laminar flow systems (LAF) reduces surgical site infection (SSI) or periprosthetic joint infection (PJI) in orthopedic surgery. At this time, it is not necessary to perform a clean orthopedic surgery procedure, including elective joint replacement surgery, in an operating theatre equipped with LAF systems.

**Level of Evidence:** Moderate

A. Agree 81%
B. Disagree 14%
C. Abstain 5%
HK-12: Is there sufficient evidence to support the use of antibiotic-loaded cement in primary TKA or THA to reduce the risk of SSI/PJI?

RESEARCHED BY:

Yale Fillingham, MD
Sergei Oshkukov, MD
Ali Parsa, MD
Literature:

• Meta-analysis 1, Prospective/Randomized 0, Retrospective 26

• A number of retrospective studies have correlated use of antibiotic-loaded cement with lower rates of wound infection and failure in THA and TKA, whereas others show no difference

• No evidence exists demonstrating that use of antibiotic-loaded cement reduces incident of SSI/PJI in primary hip or knee arthroplasty
**Recommendation:** There is no conclusive evidence to demonstrate that routine use of antibiotic-loaded cement in primary TKA or THA reduces the risk of subsequent SSI/PJI. Recent high level evidence and registry data has not demonstrated a reduction in SSI/PJI. Furthermore, the added cost, the potential for emergence of resistant organisms, and the potential adverse effect of antibiotics on the host provide adequate reasons to refrain from routine use of antibiotic loaded cement during primary total joint arthroplasty.

**Level of Evidence: Limited**

A. Agree  38%
B. Disagree  58%
C. Abstain  4%
HK-12: Is there a role for the use of antibiotic-impregnated cement in primary TJA? (To vote upon now)

RESEARCHED BY:

Yale Fillingham, MD
Sergei Oshkukov, MD
Ali Parsa, MD
Literature:

• Meta-analysis 1, Prospective/Randomized 0, Retrospective 26

• A number of retrospective studies have correlated use of antibiotic-loaded cement with lower rates of wound infection and failure in THA and TKA, whereas others show no difference

• No evidence exists demonstrating that use of antibiotic-loaded cement reduces incidence of SSI/PJI in primary hip or knee arthroplasty
Recommendation: (To vote upon now) Antibiotic impregnated cement may be used during primary total joint arthroplasty to reduce the risk of SSI/PJI. The benefits of antibiotic impregnated cement versus its cost and other potential adverse effects may be most justified in patients at high risk of infection

Level of Evidence: Limited
ICM 2018

- Class 1: Clinically important, high evidence
- Class 2: Clinically important, low evidence
- Class 3: Clinically less important, high evidence
- Class 4: Clinically less important, low evidence
HK-29 : Does changing the drapes during debridement, antibiotics, and implant retention affect the rate of success?

RESEARCHED BY:

Plamen Kinov MD, Bulgaria
Akos Zahar MD, Germany
Thorsten Gehrke MD, Germany
Literature:

• There are no studies that assess the impact of changing the drapes during DAIR.

• After a literature review of 51 papers, only one study was identified that indirectly mentioned the use of clean draping during the surgical procedure.

• Changing the drapes during DAIR can be performed at the surgeon’s discretion.
**Recommendation:** The impact and effectiveness of changing the drapes during debridement, antibiotics, and implant retention (DAIR) has not been investigated and therefore it can be performed at the surgeon’s discretion.

**Level of Evidence:** Consensus

A. Agree - 94%
B. Disagree - 4%
C. Abstain - 1%
G-35: Does the number of individuals in the operating room affect the rate of SSI/PJI? If so, what strategies should be implemented to reduce traffic in the operating room?

RESEARCHED BY:

Eleftherios Tsiridis
Daniel Del Gaizo
Literature:

• Meta-analysis 0, Prospective/Randomized 0, Retrospective 29

• Multiple studies show an increased trend in PJI associated with high OR traffic and increased rate of door opening.

• Systemic and behavioural measures in the OR have been shown to significantly reduce the incidence of superficial PJI and a non-significant decrease in the deep PJI.
**Recommendation:** Yes. The number of individuals in the operating room (OR) and door openings (DO) during total joint arthroplasty (TJA) are correlated to the number of airborne particles in the OR. Elevated airborne particles in the OR can predispose to subsequent periprosthetic joint infection (PJI). Therefore, operating room traffic should be kept to a minimum. Multiple strategies, outlined below, should be implemented to reduce traffic in the OR during orthopaedic procedures.

**Level of Evidence:** Moderate

A. Agree
B. Disagree
C. Abstain
ICM 2018

- Class 1: Clinically important, high evidence
- Class 2: Clinically important, low evidence
- Class 3: Clinically less important, high evidence
- Class 4: Clinically less important, low evidence
G-37: Should surgeons and personnel in the OR wear a mask and a cap in the operating room?

RESEARCHED BY:

Kevin Tetsworth
Rajendra Shetty
Literature:

- Meta-analysis/Systematic review 2, Prospective/Randomized 0, Retrospective 12

- Multiple systematic reviews found that the evidence regarding the efficacy of surgical facemasks in preventing postoperative wound infection is inconclusive
Recommendation: Yes. The use of surgical facemasks and caps by staff in the operating room is presumed to reduce the frequency of surgical site infections. There is a paucity of data with few studies addressing this topic. The long-standing established standard of surgical facemasks and caps in the operating room should continue despite the lack of strong evidence demonstrating clinical efficacy and a lack of persuasive evidence for altering current clinical practice. Evidence for the potential role for surgical facemasks in protecting staff from infectious material encountered in the operating room is also controversial. In the absence of convincing clinical evidence either for or against wearing masks and caps in the OR, it is advisable at this time to continue to follow local or national health and safety regulations.

Level of Evidence: Limited

A. Agree
B. Disagree
C. Abstain
G-125: What is the definition of a sinus tract?

RESEARCHED BY:

Jeffrey Lange, MD  Jesse Otero, MD
Literature:

• A sinus tract (latin: hollow, cavity) is an abnormal channel connecting a cavity lined with granulation tissue to an epithelial surface.

• Historically described by Edwin-Smith Papyrus, Hippocrates, Richard Wiseman

• Classifications made by Ger and Cierny-Mader
**Recommendation:** A sinus tract has the following characteristics:

1) It is an abnormal channel through the soft tissues that allows communication between a joint prosthesis and the outside environment, known or presumed to be colonized by bacteria.

2) Its presence may be confirmed with direct visualization of an underlying prosthesis, evidence of communication with fistulogram, ultrasound, computed tomography, or MRI.

**Level of Evidence: Consensus**

A. Agree  
B. Disagree  
C. Abstain

![Agreement Chart]

- Agree: 97%
- Disagree: 2%
- Abstain: 1%
Step XIII
Dissemination of the Information
ICM Philly Comes to JOA

For the first time, the proceedings of the Second International Consensus Meeting on Musculoskeletal Infection held July 25-27, 2018 in Philadelphia is published in the Journal of Arthroplasty. Prosthetic joint infection articles are now available "in-press" online at

www.ArthroplastyJournal.org/prosthetic-joint-infection

The journal will be in the mail soon!
Step XIII
Dissemination of the Information

- J. of Shoulder and Elbow Surg
- Foot and Ankle Int.
- Spine
- Trauma
Step XIII

Dissemination of the Information: December 2018

Proceedings of the International Consensus Meeting (ICM) on Musculoskeletal Infection

Chairs:
Javad Parvizi, MD, FRCS
Thorsten Gehrke, MD
Step XIII
Dissemination of the Information
Translations

- Spanish
- Chinese
- Japanese
- Italian
- Korean
- Portuguese
- Russian
- Turkish
- Farsi
- Czech
- Indonesian
- German
- Polish
- Arabic
- Ukrainian
- French
- Greek
- Bulgarian
- Romanian
- Dutch/Africaans