Second International Consensus on Periprosthetic Joint Infection

July 25-27, 2018

Thomas Jefferson University, Philadelphia

ICM 2018

Mission

- 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

International Consensus Group Discovery

Why bother?

International Consensus Group Discovery

Literature is not definitive on many issues

CDC Guidelines for SSI Prevention

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

Ran Equipose

SPECIAL ARTICLE

EQUIPOISE AND THE ETHICS OF CLINICAL RESEARCH

BENJAMIN FREEDMAN, PH.D.

Abstract The ethics of clinical research requires equipoise — a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial. Should the investigator discover that one treatment is of superior therapeutic merit, he or she is ethically obliged to offer that treatment. The current understanding of this requirement, which entails that the investigator have no "treatment preference" throughout the course of the trial, presents nearly insuperable obstacles to the ethical commencement or completion of a controlled trial and may also contribute to the termination of trials because of the failure to enroll enough patients.

I suggest an alternative concept of equipoise, which would be based on present or imminent controversy in the clinical community over the preferred treatment. According to this concept of "clinical equipoise," the requirement is satisfied if there is genuine uncertainty within the expert medical community — not necessarily on the part of the individual investigator — about the preferred treatment. (N Engl J Med 1987; 317: 141-5.)

THERE is widespread agreement that ethics requires that each clinical trial begin with an honest null hypothesis.[1,2] In the simplest model, testing a new treatment B on a defined patient population P for which the current accepted treatment is A, it is necessary that the clinical investigator be in a state of genuine uncertainty regarding the comparative merits of treatments A and B for population P. If a physician knows that these treatments are not equivalent, ethics requires that the superior treatment be recommended. Following Fried, I call this state of uncertainty about the relative merits of A and B "equipoise."[3]

Equipoise is an ethically necessary condition in all cases of clinical research. In trials with several arms, equipoise must exist between all arms of the trial; otherwise the trial design should be modified to exclude 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 well as other patients within the relevant population) may have to be offered the superior treatment. It has been rigorously argued that a trial with a placebo is ethical only in investigating conditions for which there is no known treatment[2]; this argument reflects a special application of the requirement for equipoise. Although equipoise has commonly been discussed in the special context of the ethics of randomized clinical trials,[4,5] it is important to recognize it as an ethical condition of all controlled clinical trials, whether or not they are randomized, placebo-controlled, or blinded.

The recent increase in attention to the ethics of research with human subjects has highlighted problems associated with equipoise. Yet, as I shall attempt to show, contemporary literature, if anything, minimizes those difficulties. Moreover, there is evidence that concern on the part of investigators about failure to satisfy the requirements for equipoise can doom a trial as a result of the consequent failure to enroll a sufficient number of subjects.

The solutions that have been offered to date fail to resolve these problems in a way that would permit clinical trials to proceed. This paper argues that these problems are predicated on a faulty concept of equipoise itself. An alternative understanding of equipoise as an ethical requirement of clinical trials is proposed, and its implications are explored.

Many of the problems raised by the requirement for equipoise are familiar. Shaw and Chalmers have written that a clinician who "knows, or has good reason to believe," that one arm of the trial is superior may not ethically participate.[6] But the reasoning or preliminary results that prompt the trial (and that may themselves be ethically mandatory)[7] may jolt the investigator (if not his or her colleagues) out of equipoise before the trial begins. Even if the investigator is undecided between A and B in terms of gross measures such as mortality and morbidity, equipoise may be disturbed because evident differences in the quality of life (as in the case of two surgical approaches) tip the balance.[3-5,8] In either case, in saying "we do not know" whether A or B is better, the investigator may create a false impression in prospective subjects, who hear him or her as saying "no evidence leans either way," when the investigator means "no controlled study has yet had results that reach statistical significance."

Late in the study — when P values are between 0.05 and 0.06 — the moral issue of equipoise is most readily apparent,[9,10] but the same problem arises when the earliest comparative results are analyzed.[11] Within the closed statistical universe of the clinical trial, each result that demonstrates a difference between the arms of the trial contributes exactly as much to the statistical conclusion that a difference exists as does any other. The contribution of the last pair of cases in the trial is no greater than that of the first. If, therefore, equipoise is a condition that reflects equivalent evidence for alternative hypotheses, it is jeopardized by the first pair of cases as much as by the last. The investigator who is concerned about the ethics of recruitment after

From the McGill Centre for Medicine, Ethics and Law, McGill University, Lady Meredith Bldg., 1110 Pine Ave. W., Montreal, PQ H3A 1A3, Canada, where reprint requests should be addressed to Dr. Freedman.

Supported in part by a research grant from the Social Sciences and Humanities Research Council of Canada.

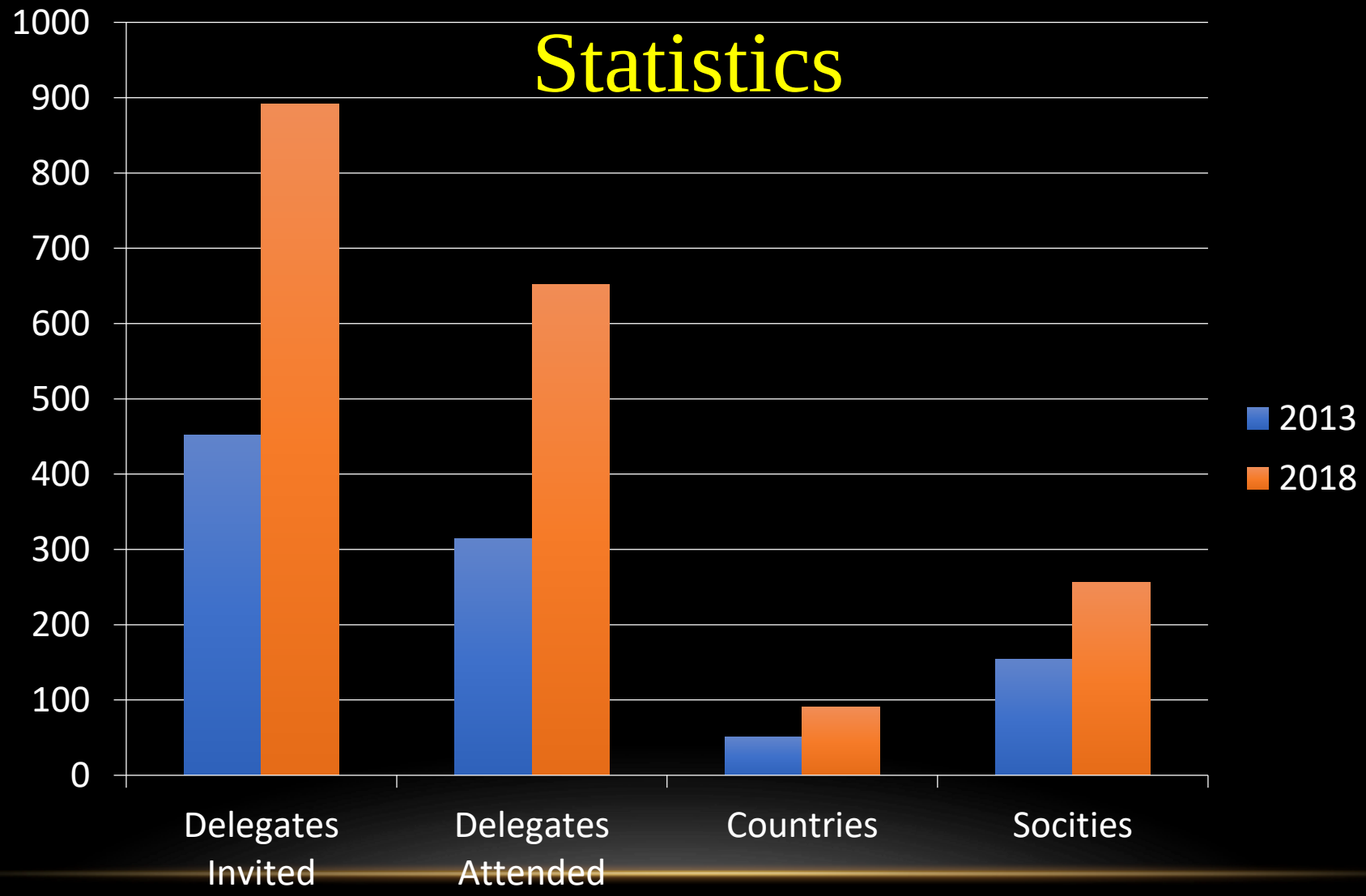
First International Consensus on Periprosthetic Joint Infection
August 1-3, 2013

Javad Parvizi MD, FRCS

Thomas Jefferson University, Philadelphia

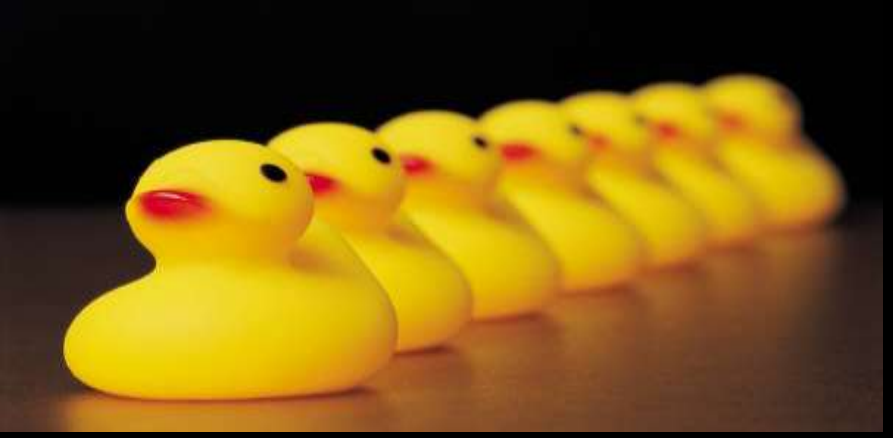
ICM 2013

Statistics



Delegates

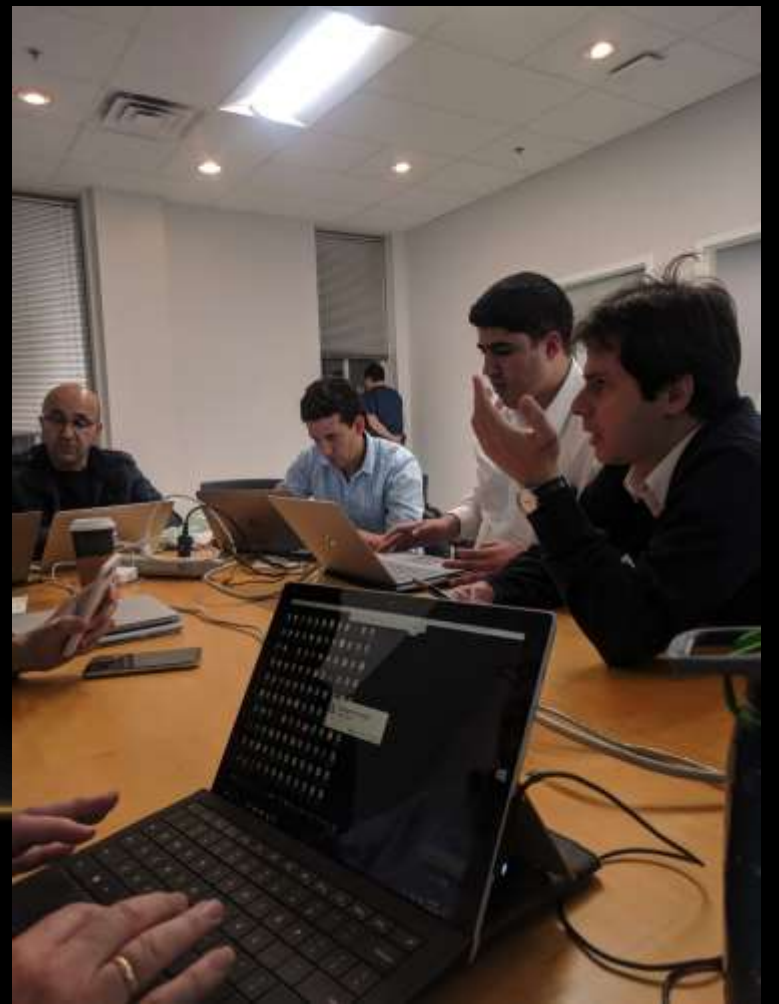
- 890 Delegates
- 98 Countries
- Over 200 societies
- 98 Presidents

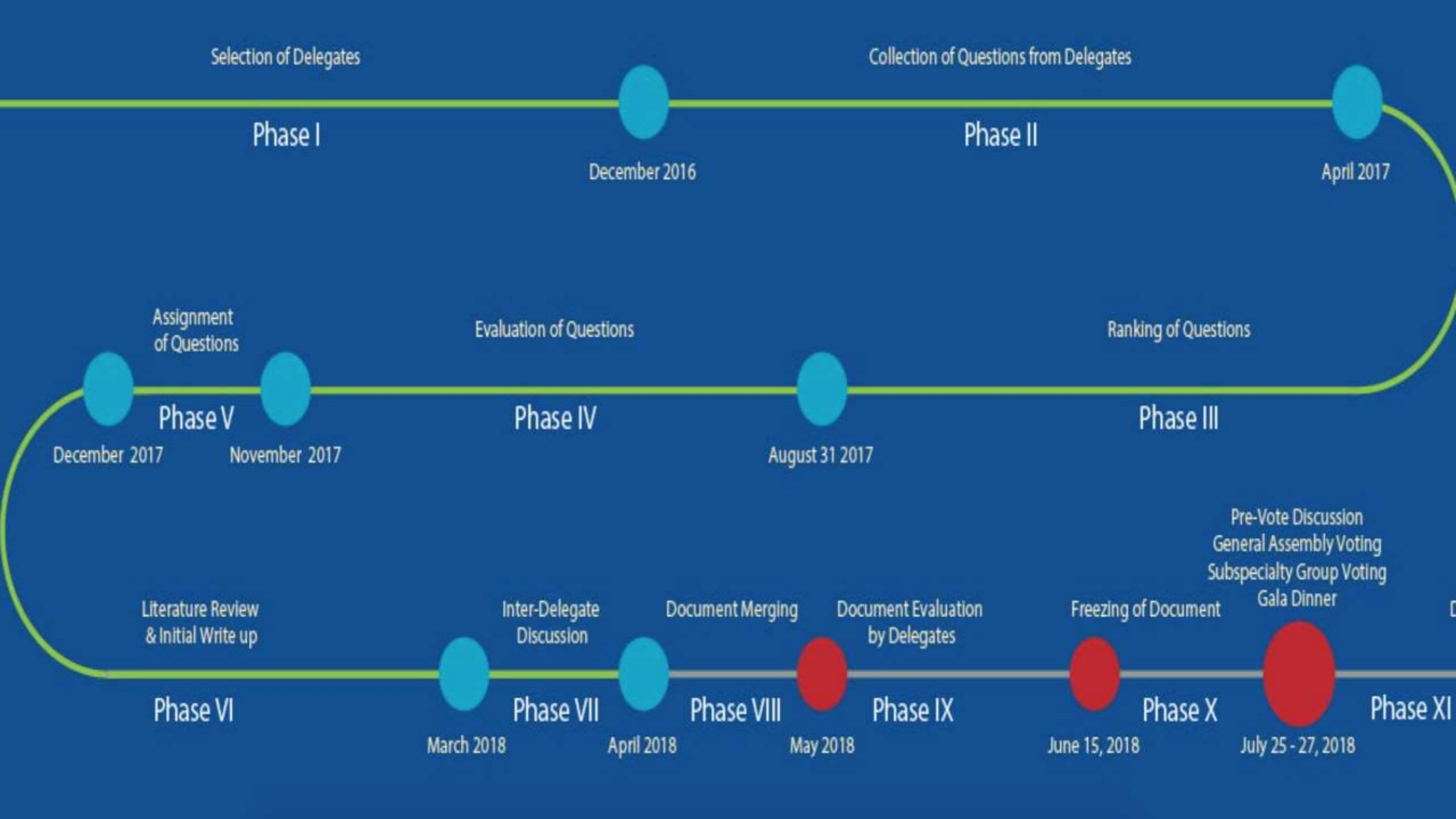


ICM 2018

Delphi Steps

Thorsten On Skype




Selection of Delegates
Phase I
December 2016
Collection of Questions from Delegates
Phase II
April 2017
Assignment of Questions
December 2017
Phase V
November 2017
Evaluation of Questions
Phase IV
August 31 2017
Ranking of Questions
Phase III
Literature Review & Initial Write up
Phase VI
March 2018
Inter-Delegate Discussion
Phase VII
April 2018
Document Merging
Phase VIII
May 2018
Document Evaluation by Delegates
Phase IX
Freezing of Document
Phase X
June 15, 2018
Pre-Vote Discussion
General Assembly Voting
Subspecialty Group Voting
Gala Dinner
July 25 - 27, 2018
Phase XI

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)

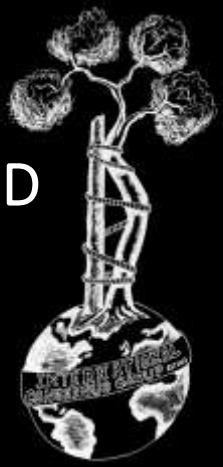
ICM 2018

- 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:

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



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)	Decision
Two positive growth of the same organism using standard culture methods	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

1. Enter Answer Text

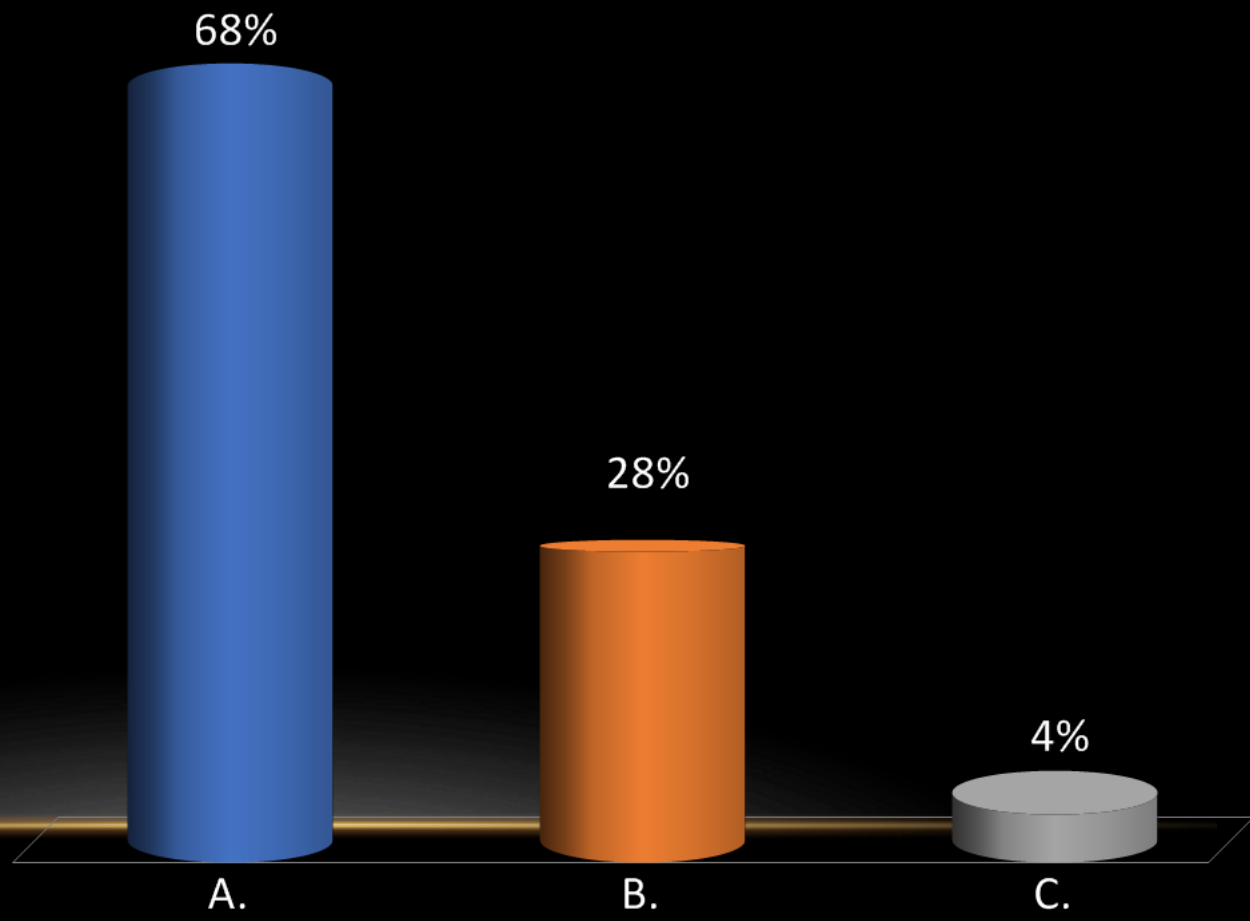
Minor Criteria	Threshold		Score	Decision
	Acute€	Chronic		
Serum CRP (mg/L) *or* D-Dimer (ug/L)	100 Unknown	10 860	2	Combined preoperative and postoperative score: ≥6 Infected 4-5 Inconclusive* ≤3 Not Infected
Elevated Serum ESR (mm/hr)	No role	30	1	
Elevated Synovial WBC (cells/µL) *or* Leukocyte Esterase *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 Intraoperative Purulence¥			3	

€ 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
B. Disagree
C. Abstain



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

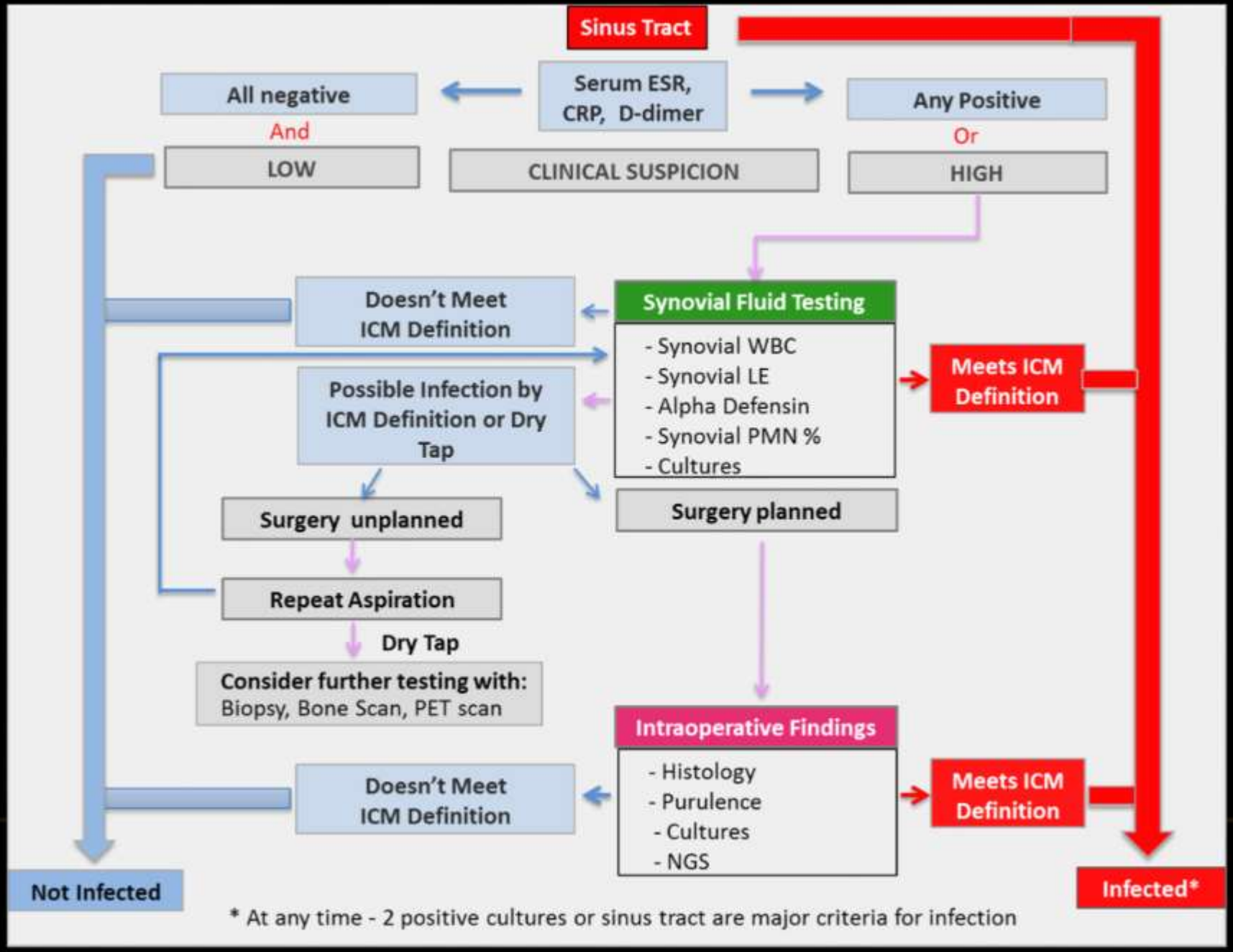
Literature:

- 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

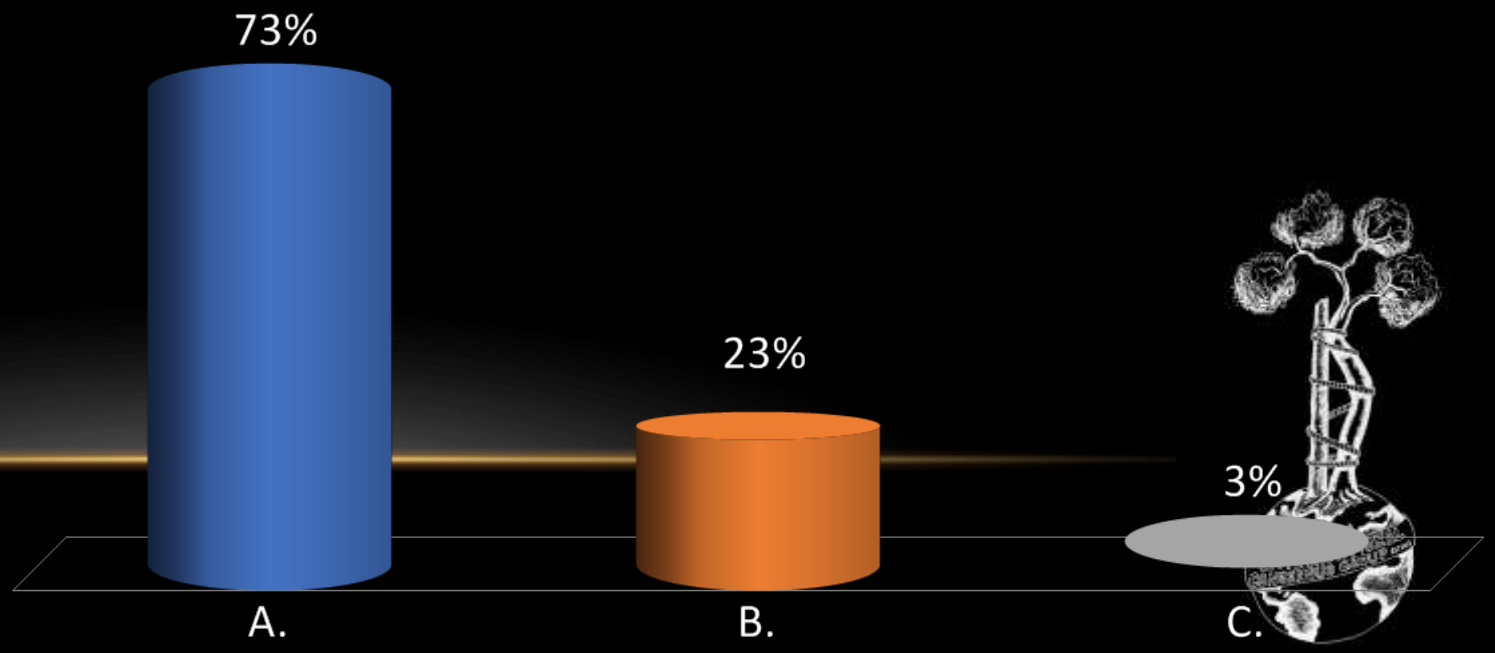
Proposed 2018 ICM Algorithm for PJI:



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

Available on the App Store

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

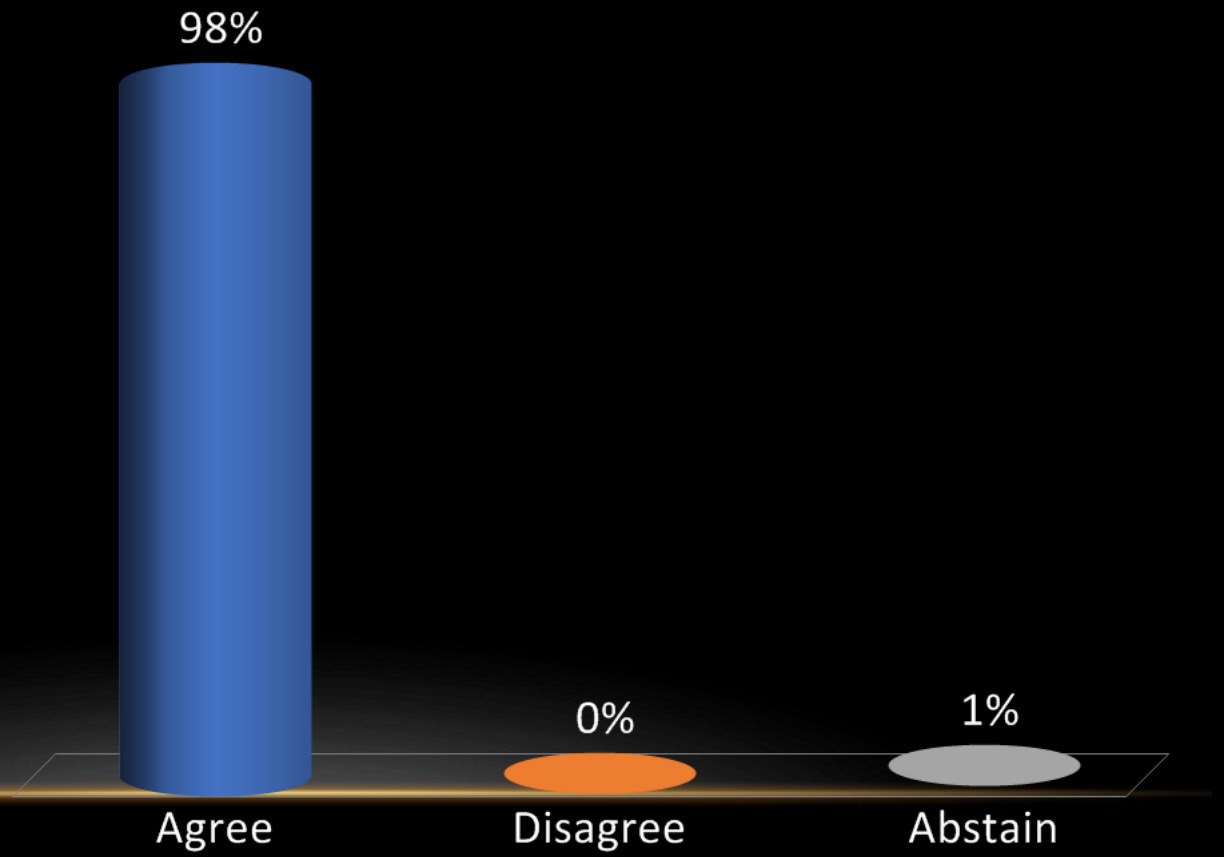
- In pooled analysis of eight studies, Chen and colleagues demonstrated that males had a higher risk of infection after TKA than females. Recent pooled multivariate analysis of 28 studies confirms the emerging evidence

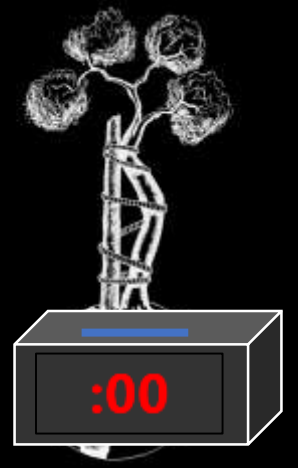
- Pooled analysis shows that black populations (compared with the white race) have an increased risk of PJI/SSI

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

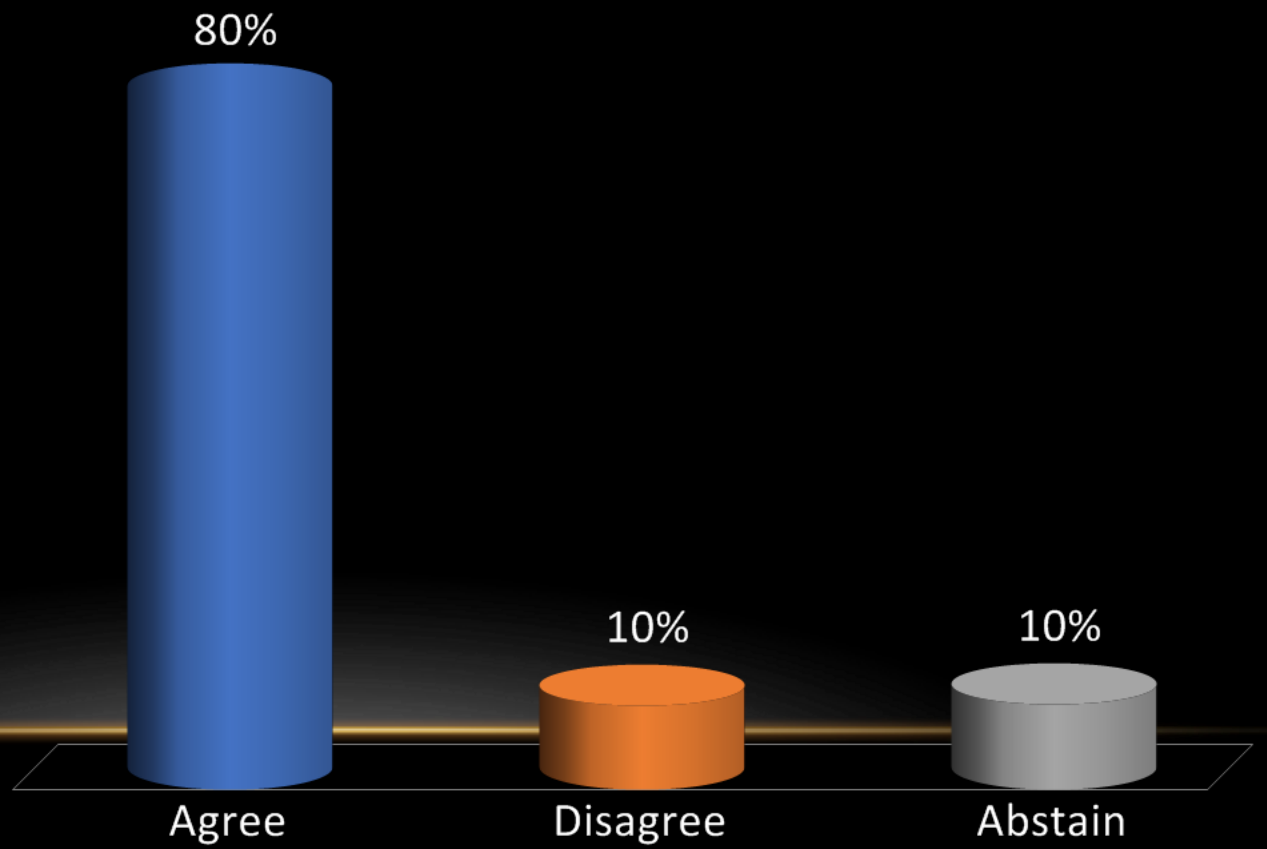
- A prospective cohort study showed a significantly higher rate of surgical site infections in patients receiving LMWH prophylaxis dosing compared with patients receiving therapeutic warfarin with or without bridging therapy .

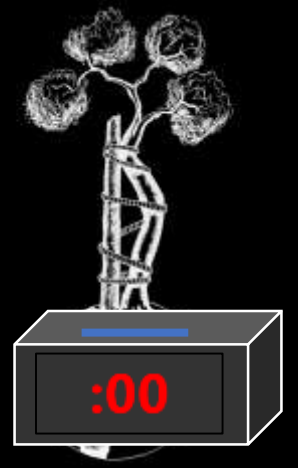
- Two recent meta-analyses of RCTs found no difference in SSI/PJI rates in TJA patients receiving rivaroxaban versus enoxaparin
-
- Randomized trial demonstrated that n patients receiving enoxaparin, there was nearly eight times the number of wound complications compared to other modalities

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

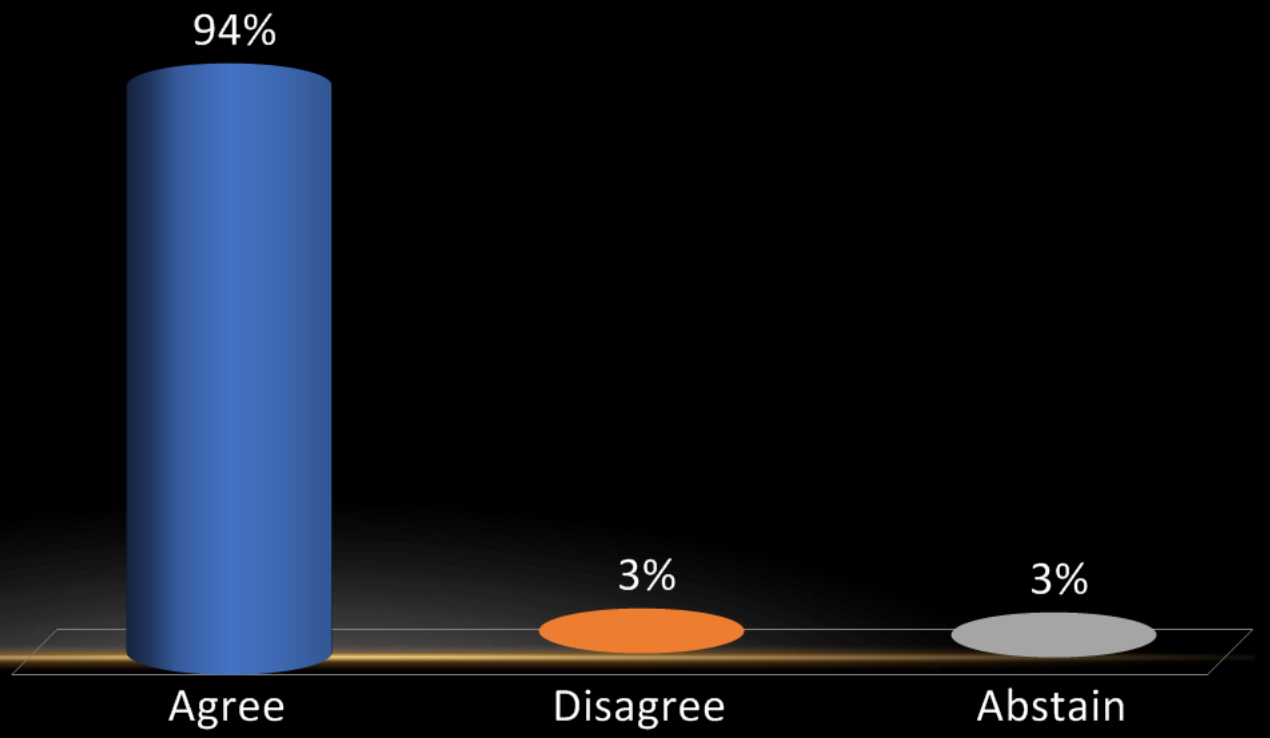
Literature:

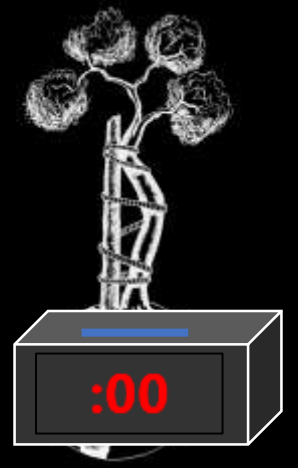
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 22
- Many studies consistently demonstrate that allogenic blood transfusion is a risk factor for PJI.
- Five studies demonstrate that allogenic transfusion increases infection rate compared to autologous transfusion

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

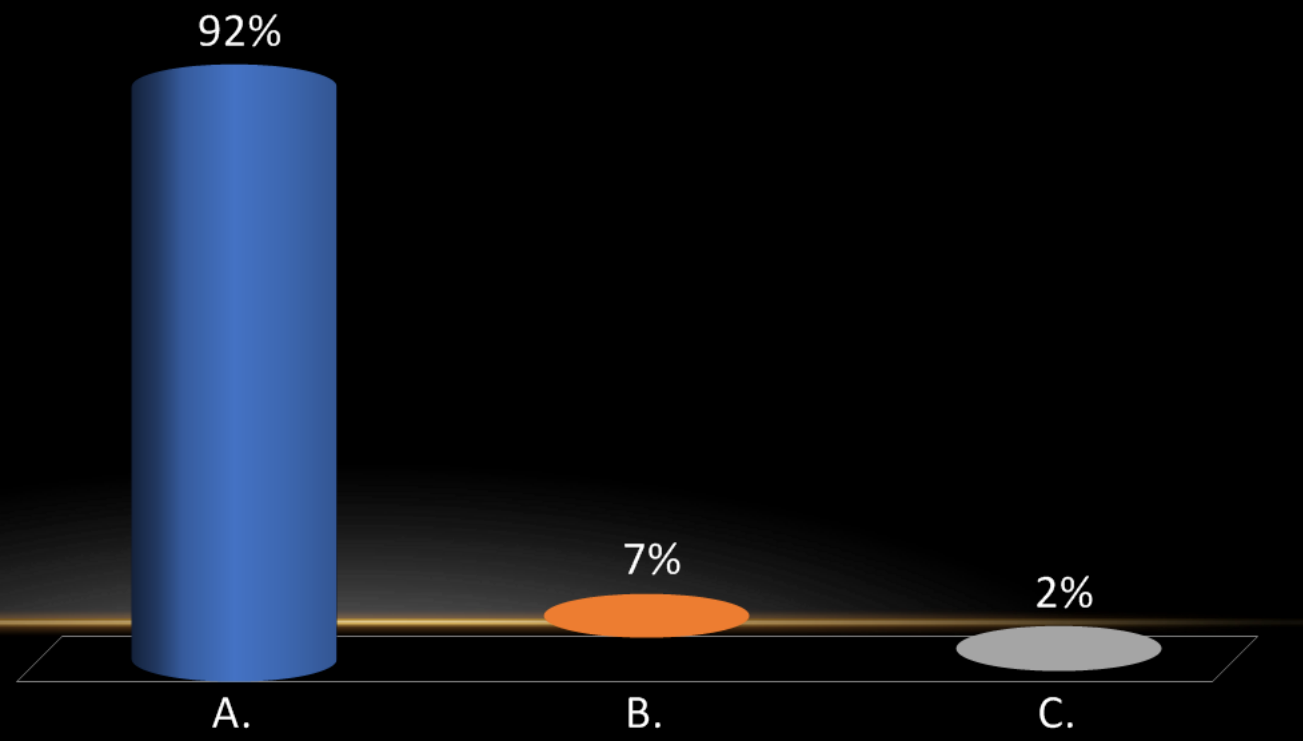
Literature:

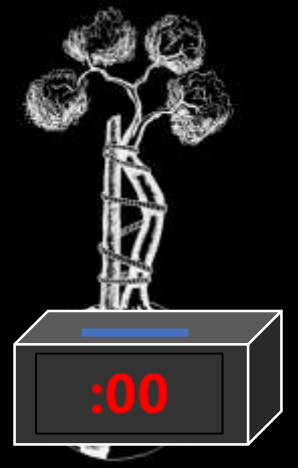
- **Meta-analysis 1, Prospective/Randomized 1, Retrospective 23**
- WHO and CDC recommend for single preoperative antibiotic dosing
  - There is insufficient arthroplasty literature to support this recommendation
- A meta-analysis concluded that postoperative antibiotics did not reduce the rate of infection, 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

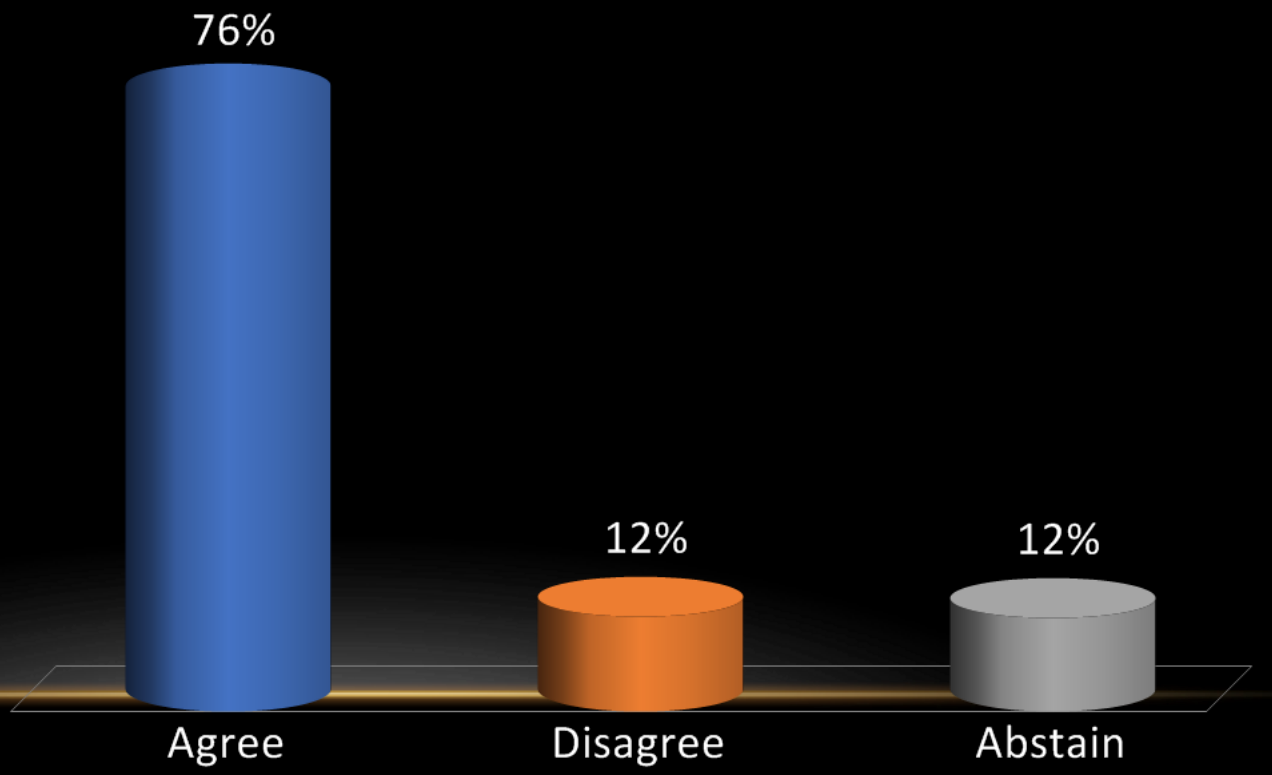
Literature:

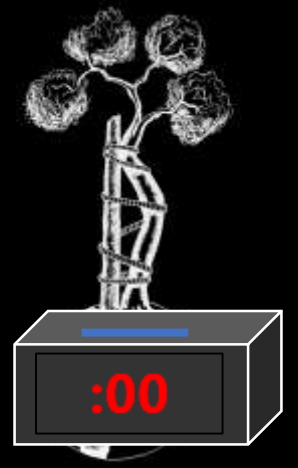
- Meta-analysis 2, Prospective/Randomized 0, Retrospective 16
- Several retrospective, and meta-analysis have demonstrated that general anesthesia has a higher rate of infection and wound complications than neuraxial anesthesia.
- Large database and registry studies also demonstrate increased infection 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





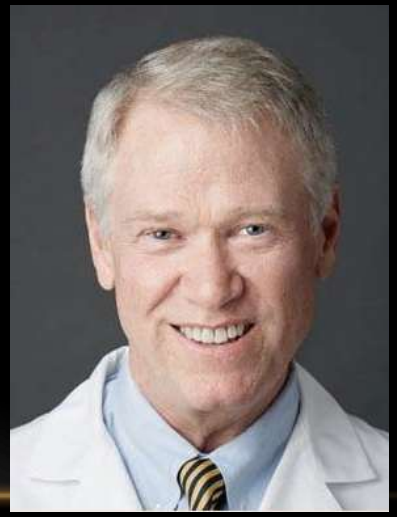
G-49: Does the use of laminar flow in the operating room reduce the risk of subsequent SSI/PJI in patients undergoing orthopedic procedures?

RESEARCHED BY:

Arash Aalireazaie

Everth Merida

Kelly Vince



Greg Stocks

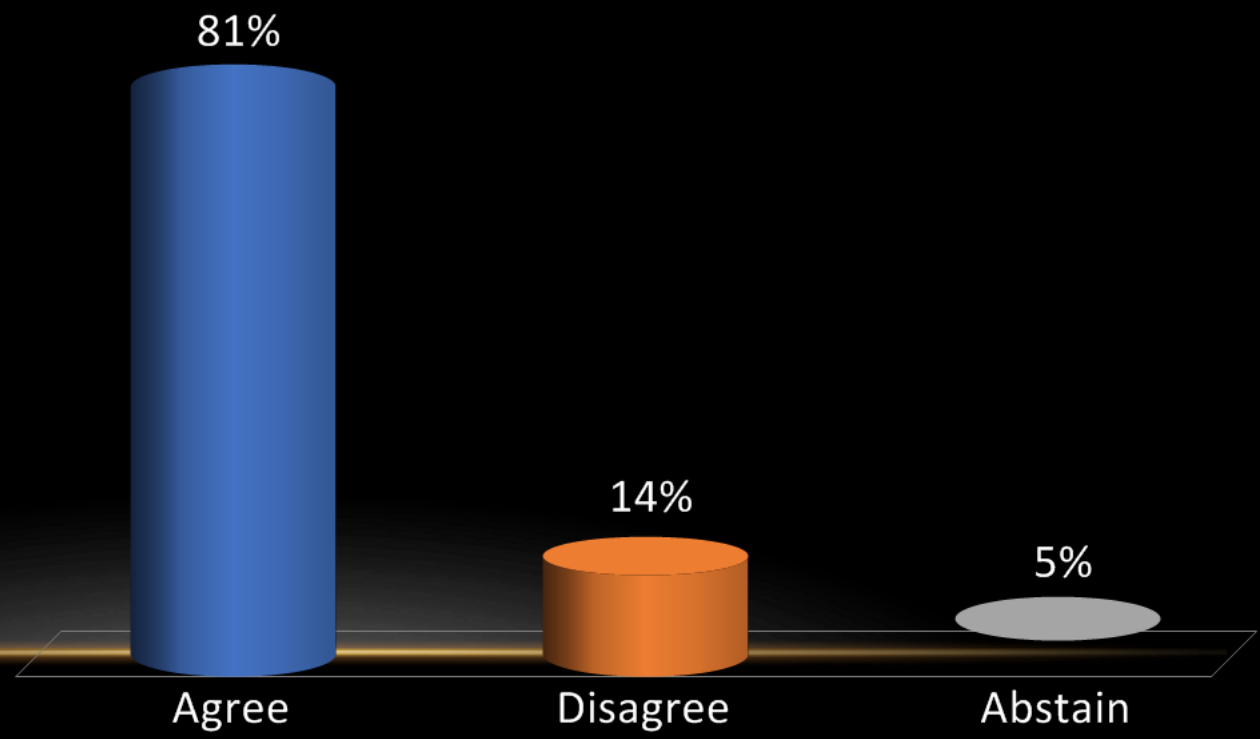
Literature:

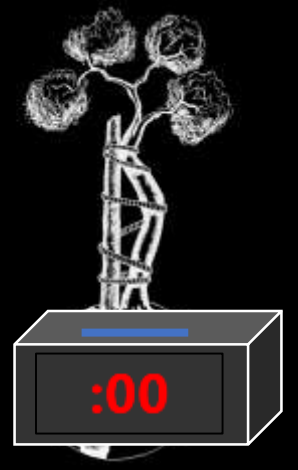
- Meta-analysis 0, Prospective/Randomized 1, Retrospective 20
- Early studies suggested LAF was effective in reducing SSI/PJI
- 6 retrospective studies found no difference in rate of SSI/PJI with use of LAF
- 3 recent studies linked use of LAF to increase in rate of SSI/PJI

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, 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
B. Disagree
C. Abstain





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

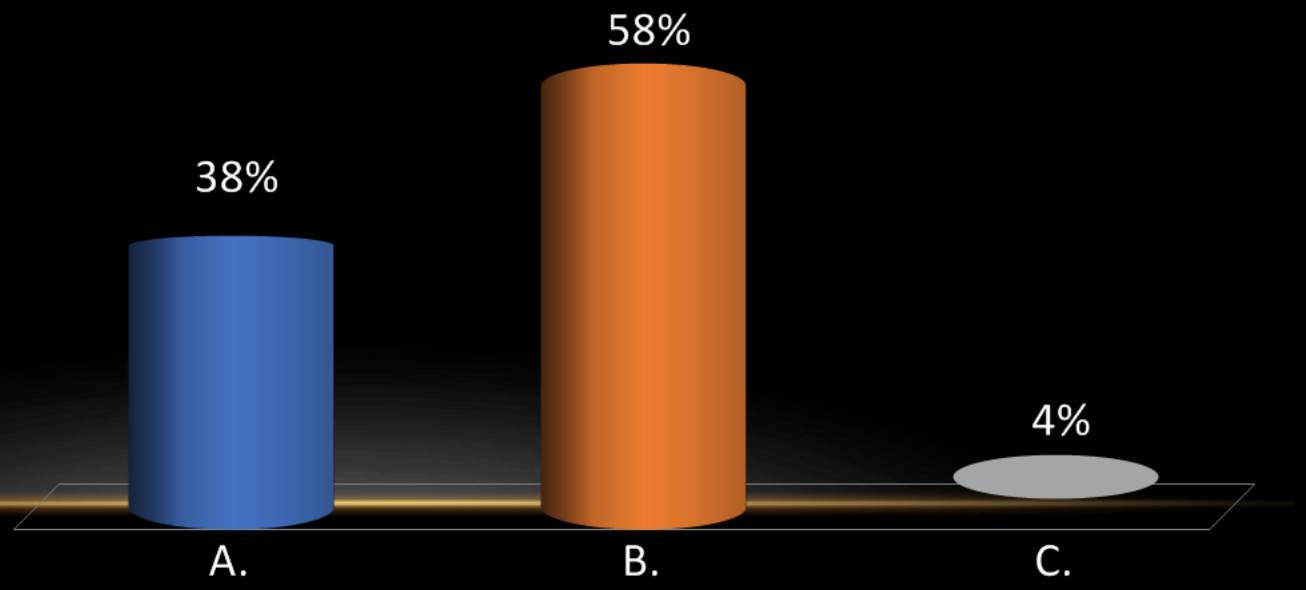
Literature:

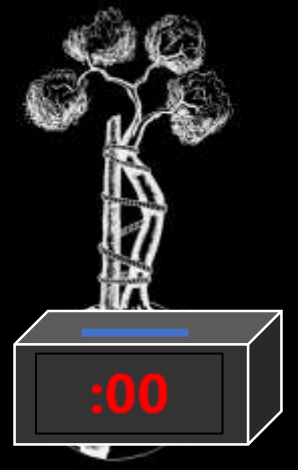
- Meta-analysis 1, Prospective/Randomized 0, Retrospective 26
- A number of retrospective studies have correlated use of antibiotic-loaded cement with lower rates of wound infection and failure in THA and TKA, whereas others show no difference
- No evidence exists demonstrating that use of antibiotic-loaded 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
B. Disagree
C. Abstain





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

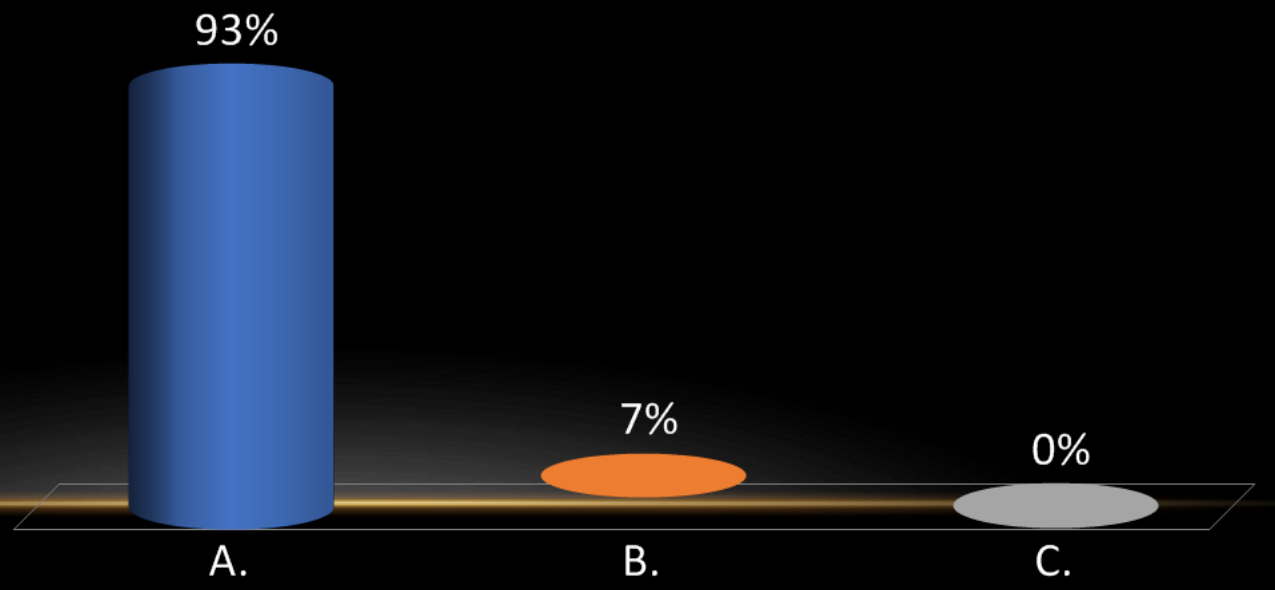
Literature:

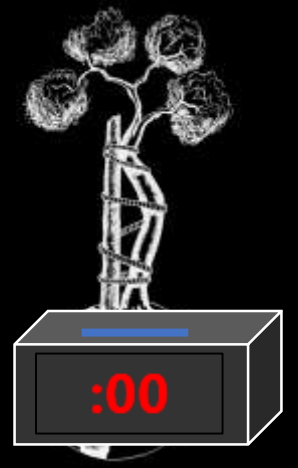
- Meta-analysis 1, Prospective/Randomized 0, Retrospective 26
- A number of retrospective studies have correlated use of antibiotic-loaded cement with lower rates of wound infection and failure in THA and TKA, whereas others show no difference
- No evidence exists demonstrating that use of antibiotic-loaded cement reduces incident 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

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-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

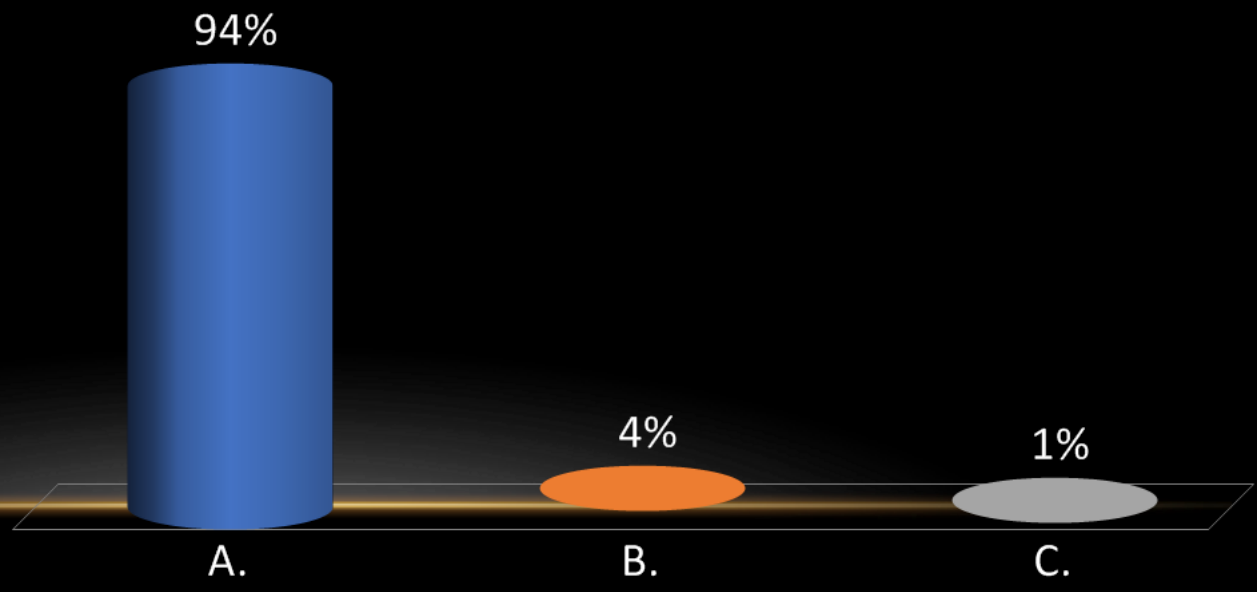
Literature:

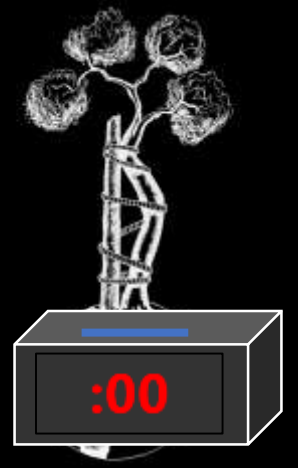
- There are no studies that assess the impact of changing the drapes during DAIR.
- After a literature review of 51 papers, only one study was identified that indirectly mentioned the use of clean draping during the surgical procedure.
- Changing the drapes during DAIR can be performed at the surgeon’s 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
B. Disagree
C. Abstain





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:

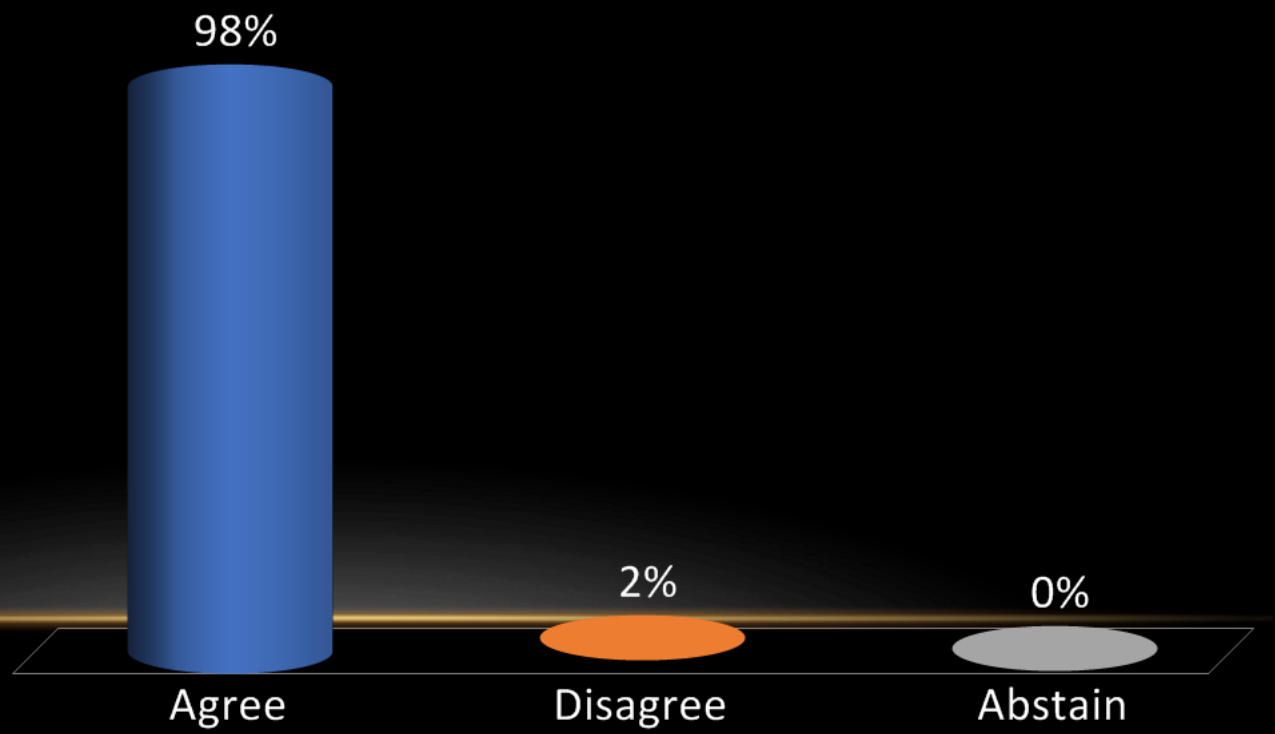
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 29

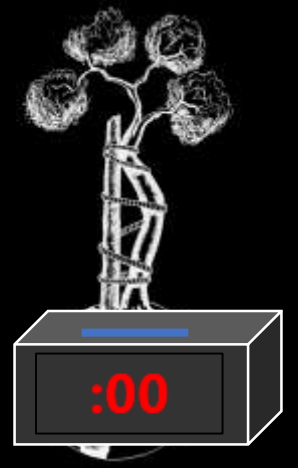
- Multiple studies show an increased trend in PJI associated with high OR traffic and increased rate of door opening.
-
- Systemic and behavioural measures in the OR have been shown to significantly reduce the incidence of superficial PJI and a non-significant decrease in the deep PJI.

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:

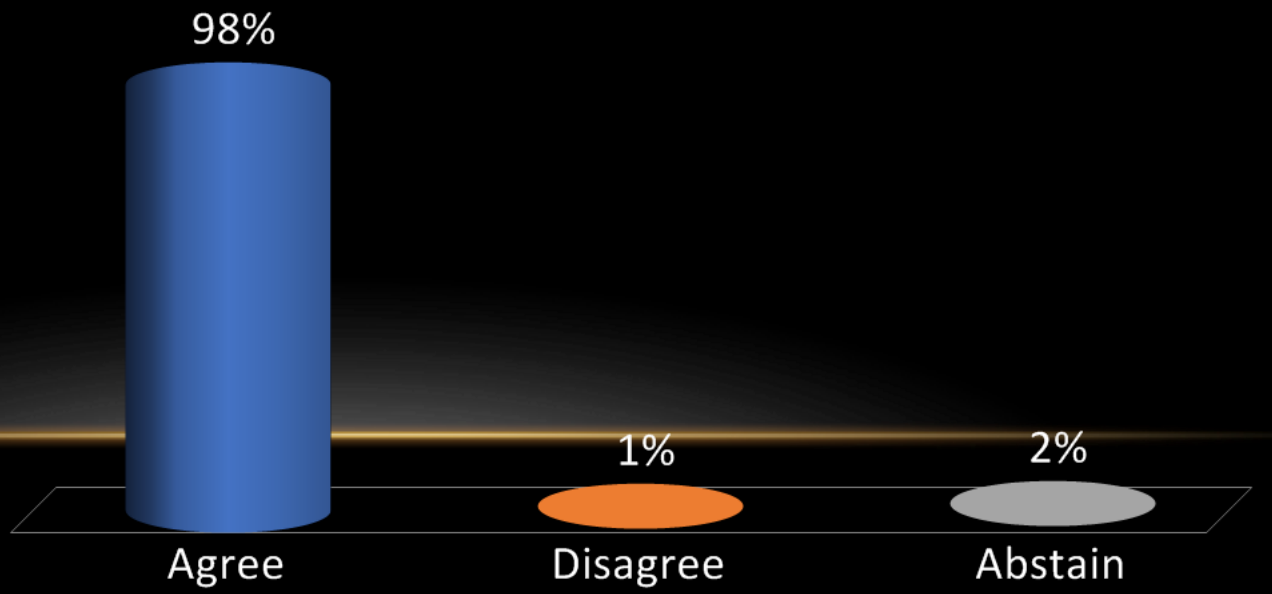
- Meta-analysis/Systematic review 2, Prospective/Randomized 0, Retrospective 12

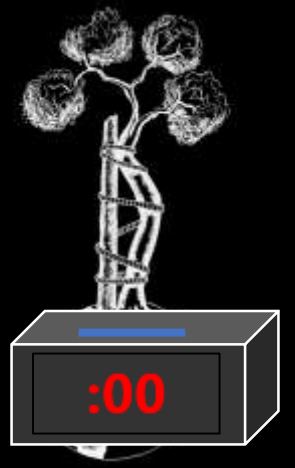
- Multiple systematic reviews found that the evidence regarding the efficacy of surgical facemasks in preventing postoperative wound infection is inconclusive

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

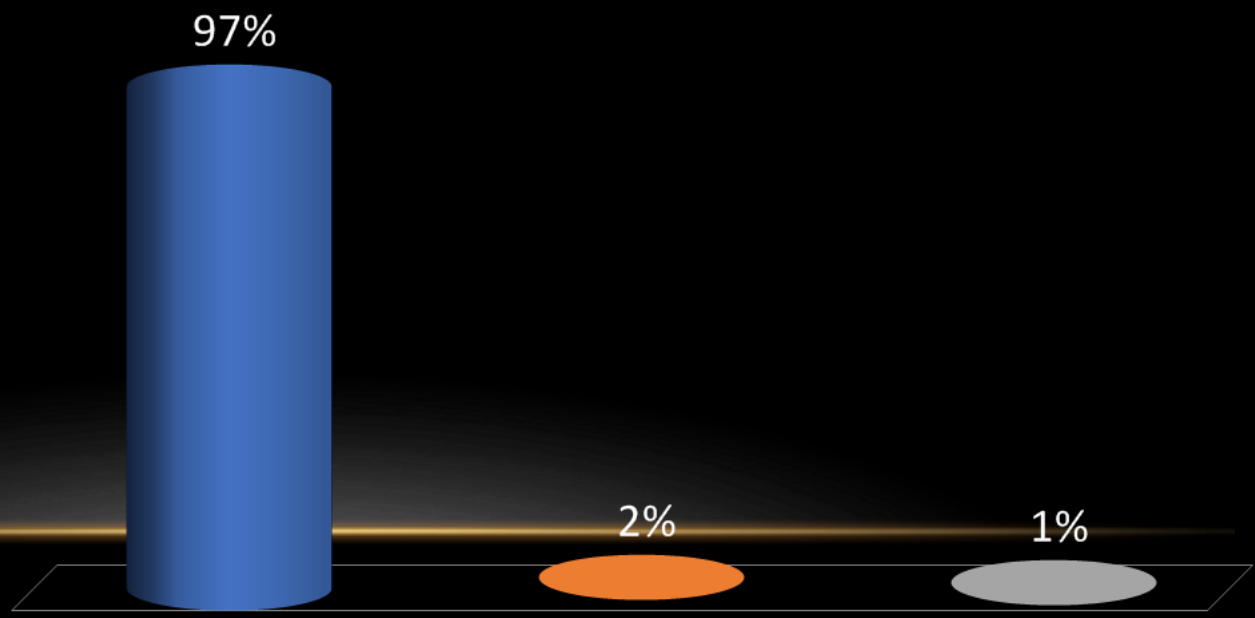
Literature:

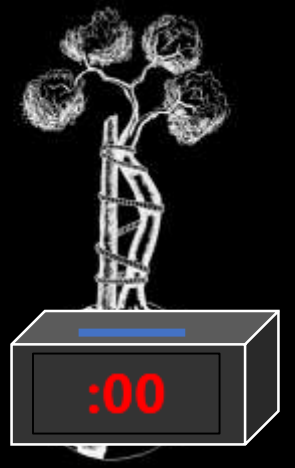
- **A sinus tract (latin: hollow, cavity) is an abnormal channel connecting a cavity lined with granulation tissue to an epithelial surface.**
- **Historically described by Edwin-Smith Papyrus, Hippocrates, Richard Wiseman**
- **Classifications made by Ger and Cierny-Mader**

Recommendation: A sinus tract has the following characteristics:
1) It is an abnormal channel through the soft tissues that allows communication between ajoint 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





Step XIII

Dissemination of the Information

OREF
ORTHOPAEDIC RESEARCH
AND EDUCATION FOUNDATION

AAHKS
AMERICAN ASSOCIATION OF
HIP AND KNEE SURGEONS

Second INTERNATIONAL CONSENSUS MEETING (ICM) on MUSCULOSKELETAL INFECTION

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!

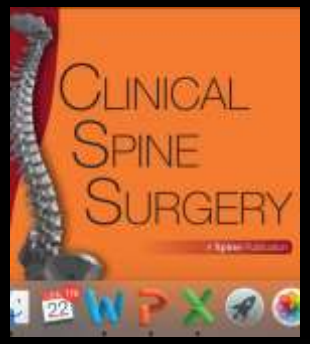
Step XIII

Dissemination of the Information

- J. of Shoulder and Elbow Surg

- Foot and Ankle Int.

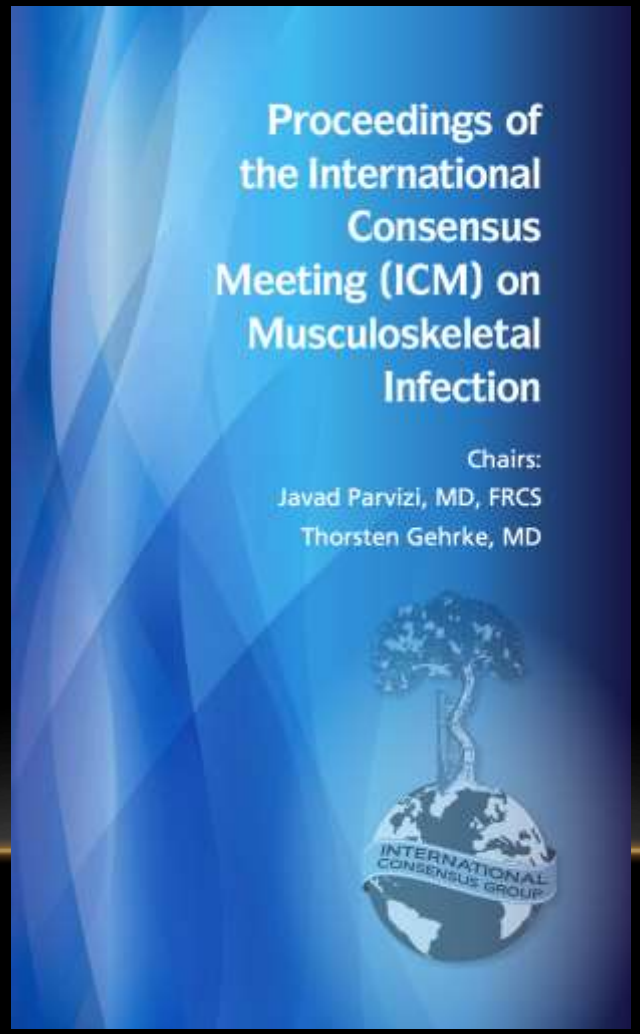
- Spine



- Trauma

Step XIII

Dissemination of the Information: **December 2018**

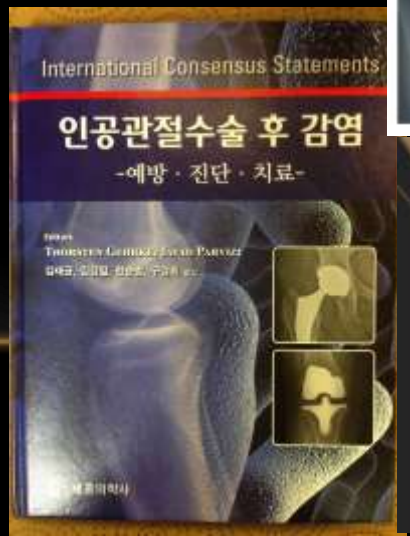


Step XIII

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



ICM Philly app

Available on the App Store

Get it on Google play

Windows Mobile

Download the ICMPhilly app at:

Download on the App Store

GET IT ON Google Play