

Second International Consensus
Meeting on Musculoskeletal Infection
Hip and Knee



Section 1: Prevention

- 1.1 - Host Related
- 1.2 - Risk Mitigation
- 1.3 - Antimicrobials (Systemic)
- 1.4 - Antimicrobials (Local)
- 1.5 - Operating Room Environment
- 1.6 - Surgical Technique
- 1.7 - Prosthesis Factors
- 1.8 - Postoperative Issues



1.1 - Prevention: Host Related



Question 1: What are the absolute and relative contraindications to elective primary total joint arthroplasty, with respect to SSI and PJI risk?

RESEARCHED BY:



Richard Iorio MD



Literature:

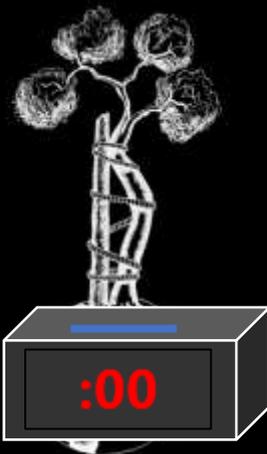
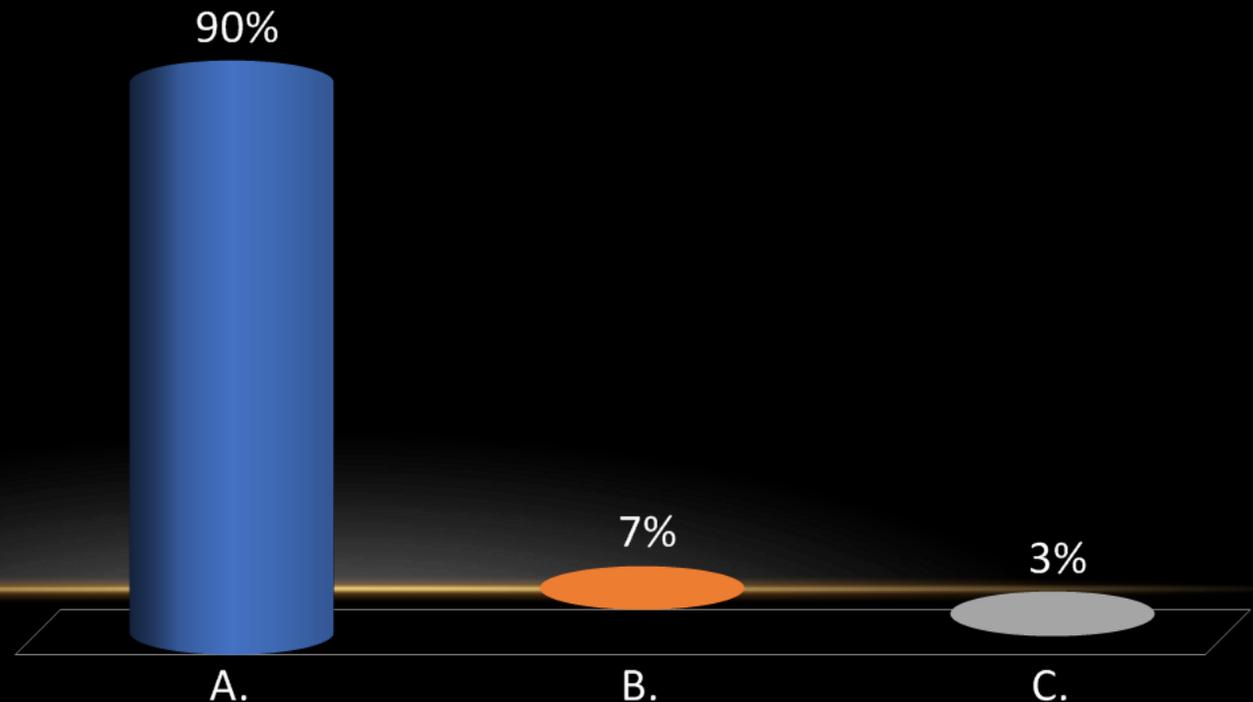
- **Meta-analysis 12, Prospective/Randomized 3, Retrospective 145**
- **Guidelines recommend discontinuing immunosuppressants prior to TJA.**
 - Data based primarily on studying transplant patients
- **Surgery must be delayed for 3 months following intraarticular steroid injection.**
- **Both low ($\leq 19 \text{ kg/m}^2$) and high ($> 30 \text{ kg/m}^2$) BMI are associated with increased SSI/PJI.**
 - Obesity and being underweight considered relative contraindications
- **There is strong evidence that links malnutrition to increased rates of SSI**
- Grammatico-Guillon et al. (2015) reported that patients with active ulcer sores preoperatively had significantly higher rates of SSI following TJA versus those without ulcer sores (HR 2.55; 95% CI 1.94-3.35).
- **Literature suggests optimizing patients medically in chronic conditions such as Diabetes, chronic kidney disease, and clotting disorders**



Recommendation: Elective joint arthroplasty is contraindicated in patients with an infectious lesion in the ipsilateral extremity until the infection is resolved. Total joint arthroplasty needs to be deferred in patients with uncontrolled conditions such as diabetes, malnutrition, chronic kidney disease as well as other diseases that are known to increase the risks of SSI/PJI.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Is the diagnosis of post-traumatic arthritis associated with an increased risk of subsequent SSI/PJI after joint arthroplasty?

RESEARCHED BY:



Usama H Saleh MD, Egypt



Neil Sheth MD, USA



Literature:

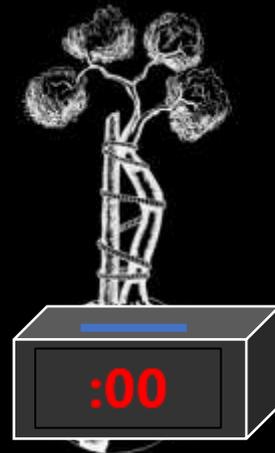
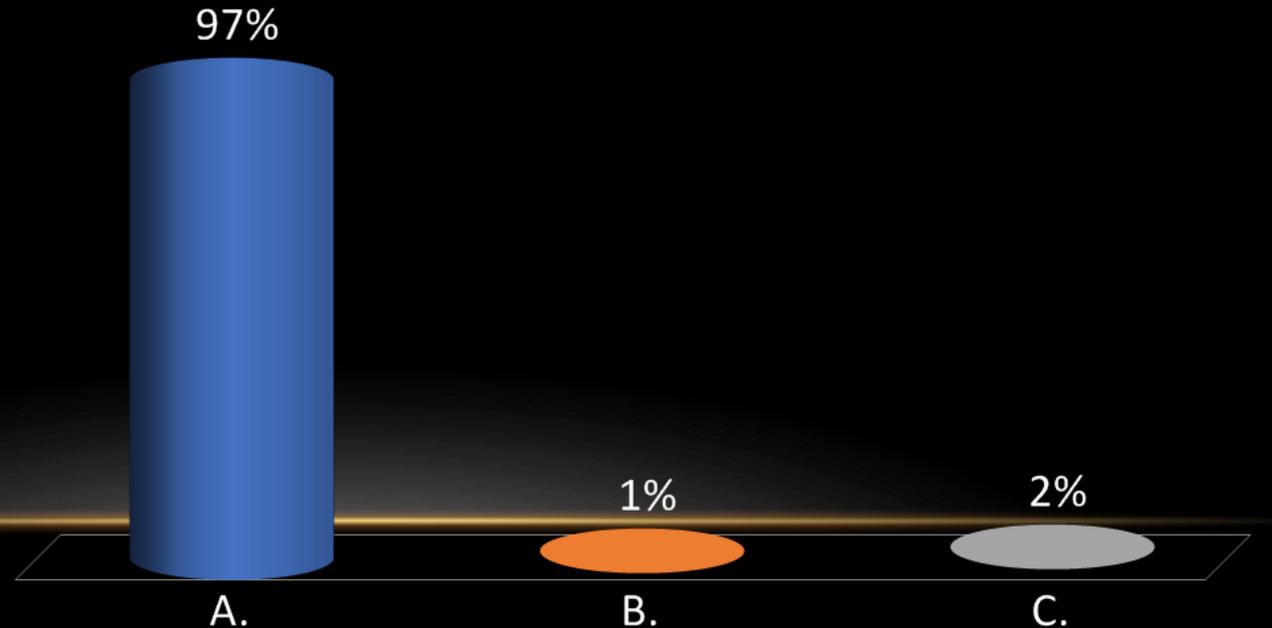
- **Meta-analysis/Systematic Review 1, Prospective 1, Retrospective 6**
- Among 3,509 patients there was a 4.93% risk of deep infection
 - 2.93% among the primary osteoarthritis group
- A systematic review (Saleh et al) reported infection rates in post-traumatic arthritis patients as higher than the general population



Recommendation: Yes. Total joint arthroplasty for patients with post-traumatic arthritis of the hip or knee carries higher risks of developing SSI/PJI. The incidence is markedly higher in patients with previous surgery and retained implants.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: What nutritional markers are the most sensitive and specific for SSI/PJI? Does improvement in nutritional status reduce the risk of SSI/PJI?

RESEARCHED BY:



Georgios Komnos MD,
Greece



Ronald Huang MD,
United States of America



Literature:

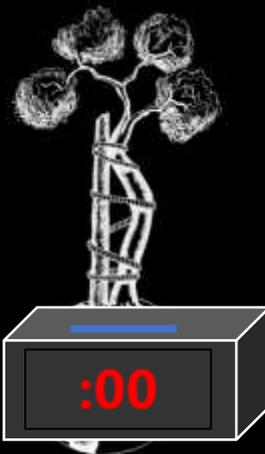
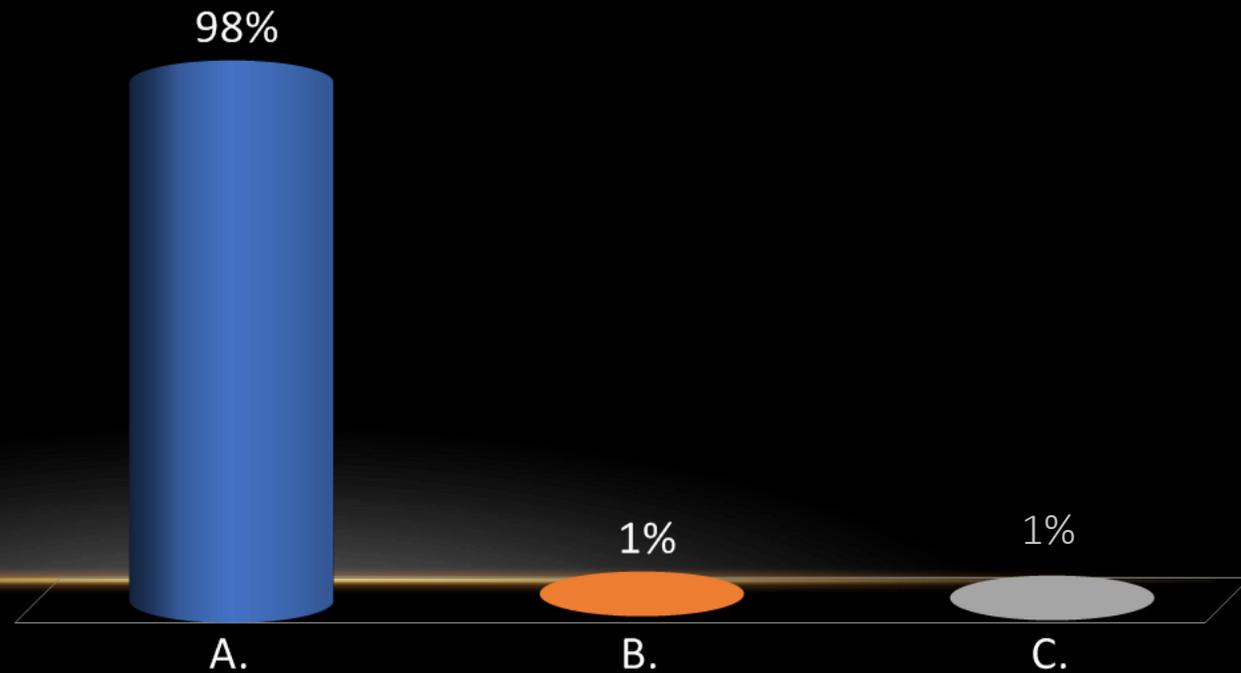
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 6**
- Several recent studies have identified serum albumin as an independent predictor of SSI and PJI
 - In the revision TJA setting, low serum albumin has also been found to be an independent risk factor for postoperative SSI and PJI (Yi et al. and Bohl et al.).
- Anthropometric measures such as calf circumference, arm muscle circumference, and triceps skinfold have been utilized to identify undernutrition in orthopedic patients, but cutoffs are poorly defined and correlation with SSI and PJI is not well studied



Recommendation: Serum albumin <3.5 g/dL has been demonstrated to be an independent risk factor for SSI/PJI after total joint arthroplasty in multiple large-scale studies. However, other nutritional markers are poorly studied. Currently, there is insufficient evidence to prove that correction of preoperative nutritional markers reduces the risk of subsequent SSI/PJI. Despite the absence of such evidence, we recognize the importance of an optimized nutritional status before TJA to reduce the risk of SSI/PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



1.2 - Prevention: Risk Mitigation



Question 1: What preoperative screening for infection should be performed in patients undergoing revision of hip or knee arthroplasty because of presumed aseptic failure?

RESEARCHED BY:



Matthew Austin MD



Mark Spangehl MD



Literature:

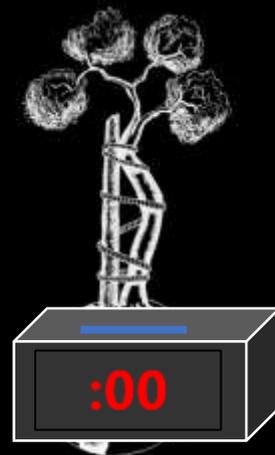
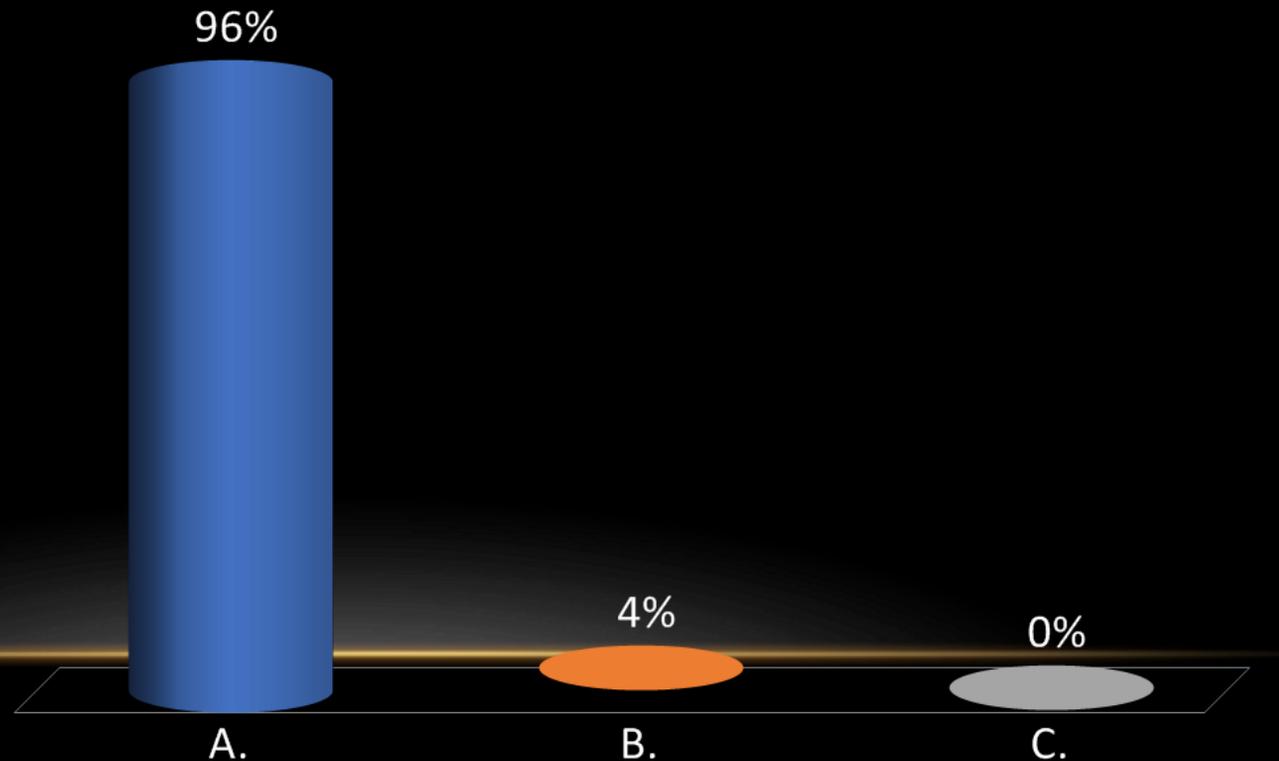
- **Meta-Analysis 2, Prospective/Randomized 2, Retrospective 24**
- According to the AAOS clinical practice guideline on the diagnosis of PJI of the hip and knee, patients are at higher risk of PJI if their medical history includes the following:
 - Recent bacteremia, multiple surgeries on the same joint, history of prior periprosthetic joint infection (PJI), history of surgical site infection of the same joint, comorbidities resulting in an immunocompromised state (i.e. diabetes mellitus, inflammatory arthropathy, etc.),
- A meta-analysis conducted by Berbari et al. showed that elevated levels of IL-6, CRP and ESR were shown to have high sensitivity for detecting PJI.



Recommendation: In addition to taking a thorough history, obtaining radiographs, and performing a physical examination, all patients with a failed hip or knee arthroplasty awaiting revision surgery at minimum should have their serum erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) measured. Patients with high index of suspicion for infection should be considered for further work up.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does prior septic arthritis (aerobic, anaerobic, fungal, tuberculosis) of a native joint predispose the patients to an increased risk of subsequent PJI in the same joint receiving arthroplasty? If yes, how soon after a prior septic arthritis can elective arthroplasty be performed in the same joint?

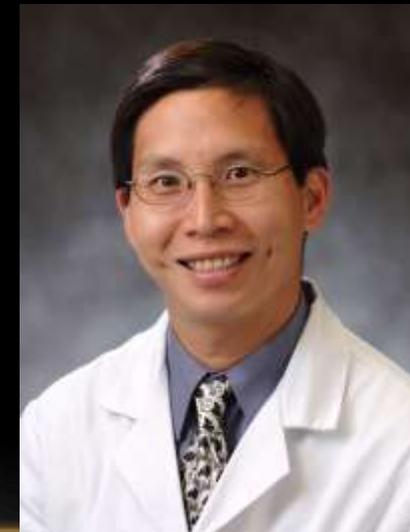
RESEARCHED BY:



Saravanan Sankaranarayanan Arumugam
MD, Russia



Elie Ghanem MD,
USA

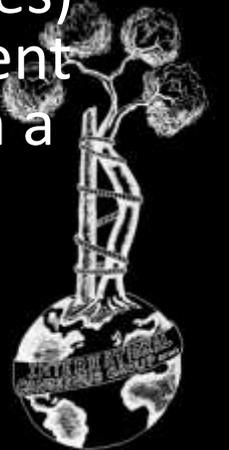


Gwo-Chin Lee MD,
USA



Literature:

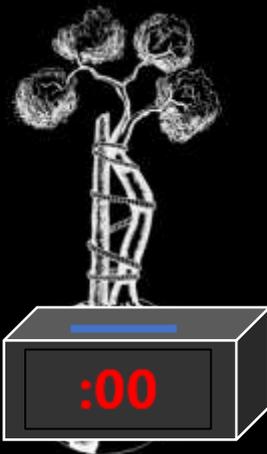
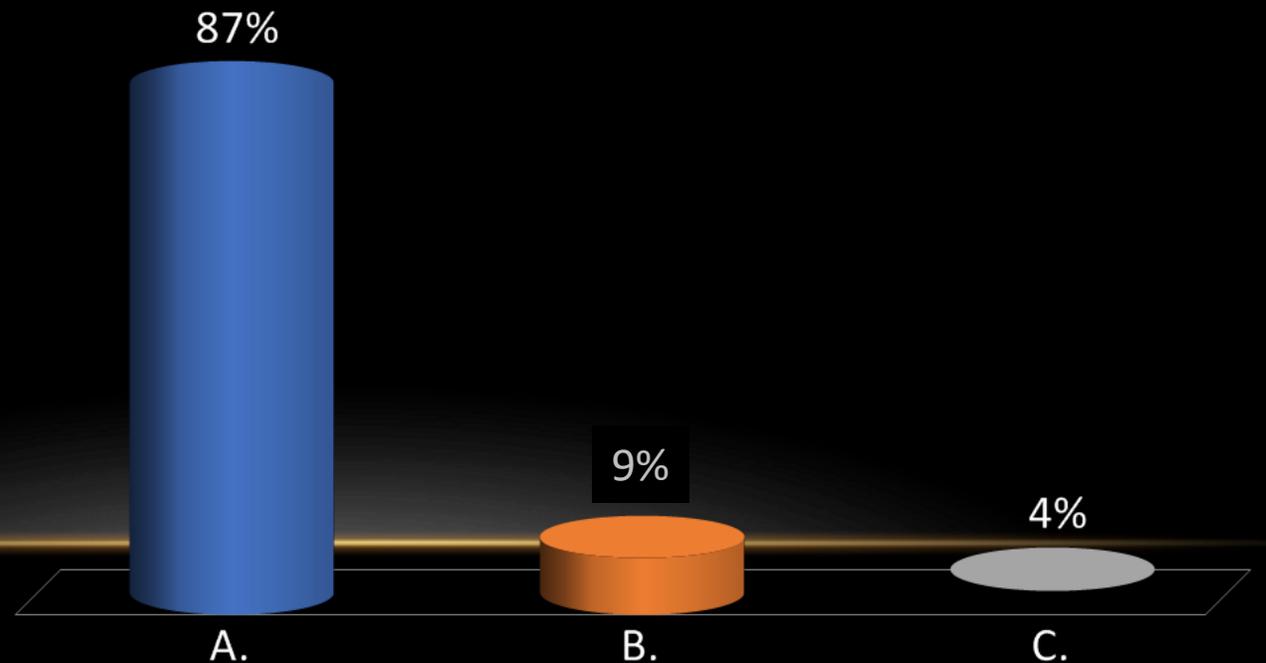
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 50**
- Kim et al reviewed 170 patients undergoing 1-stage total hip arthroplasty (THA) with quiescent infection (mean 32.7 years post-infection). All patients except for one (2 hips) had THA at least 10 years after septic arthritis, and the only hips that were complicated by PJI after THA were those two hips that had a quiescent period of only 7 years.
- Seo et al. reported on 62 patients (42% methicillin-resistant Staph. species) undergoing one-stage total knee arthroplasty (TKA) after a mean quiescent period of only 4.3 years, all of which had adult-onset septic arthritis with a PJI rate of 9.7%.



Recommendation: Yes. A prior septic arthritis in a joint does predispose the same joint to subsequent PJI after arthroplasty. In the absence of concrete evidence, we recommend that arthroplasty be delayed at least until completion of antibiotic treatment and resolution of clinical signs of infection but no earlier than three months from the inciting event.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: What indicators/metrics would compel a surgeon to perform resection arthroplasty and antibiotic spacer insertion, delaying the arthroplasty to a later date, in a patient with prior septic arthritis undergoing primary arthroplasty?

RESEARCHED BY:



Jean-Yves-Jenny MD

Yale Fillingham MD



Literature:

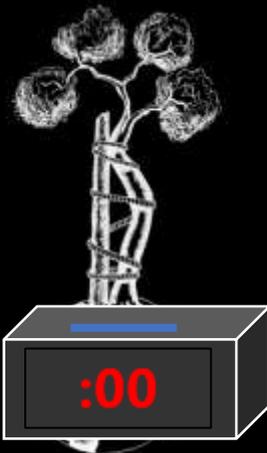
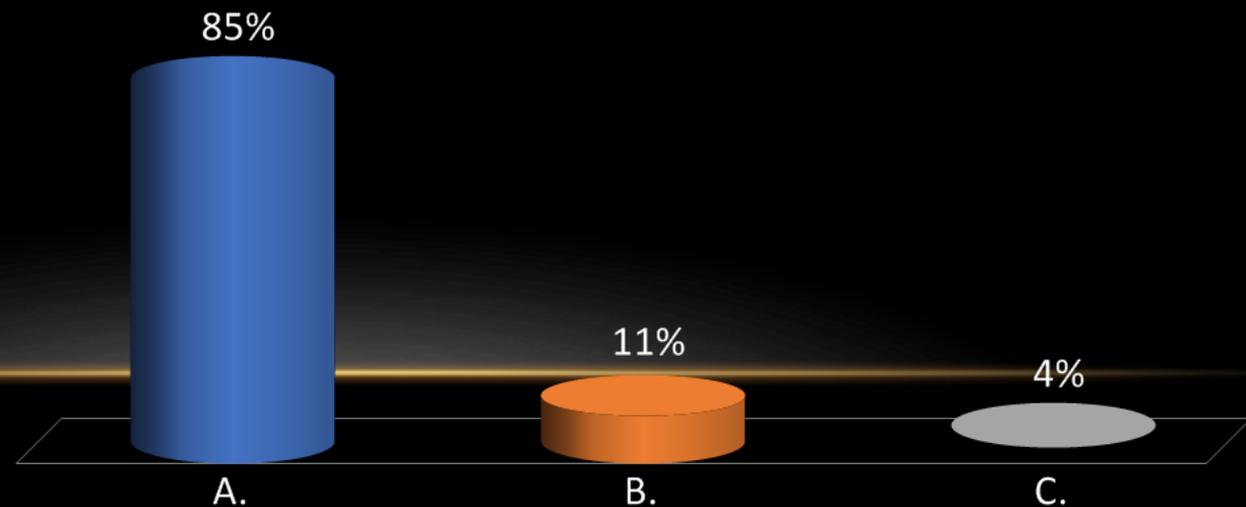
- **Meta-Analysis 0, Prospective/Randomized 0, Retrospective 23**
- In THA, 7 publications with 98 hips and 9 publications with 398 hips were identified as reporting on active or quiescent hip septic arthritis/osteomyelitis, respectively
- All reports of active hip infections were only treated with a two-stage arthroplasty, which demonstrated a 10.2% recurrence of infection.
- Unlike the active hip infections, all quiescent hip infections were treated with a one-stage arthroplasty with a 1.5% recurrence of infection.
- Even fewer publications were available on total knee arthroplasties (TKA), (7 publications with 46 knees and 5 publications with 89 knees reporting on active and quiescent knee septic arthritis/osteomyelitis, respectively).
- Among the reports of active knee infections, all but three knees were treated with a two-stage arthroplasty demonstrating a 4.7% recurrence of infection, while the three knees treated with a one-stage arthroplasty had no recurrence.
- Similar to quiescent hip infections, all quiescent knee infections were treated with a one-stage arthroplasty and had a 4.5% recurrence of infection.



Recommendation: Patients with active septic arthritis or chronic osteomyelitis of the hip or knee may be best treated with a two-stage arthroplasty. Evidence would suggest a limited risk of infection recurrence following a one-stage arthroplasty in the presence of a quiescent septic arthritis.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Does a prior arthroscopy of the hip joint increase the risks of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs) in patients undergoing elective total hip arthroplasty?

RESEARCHED BY:

Arash Aalirezaie

Nirav K. Patel

Zoran Bozinovski

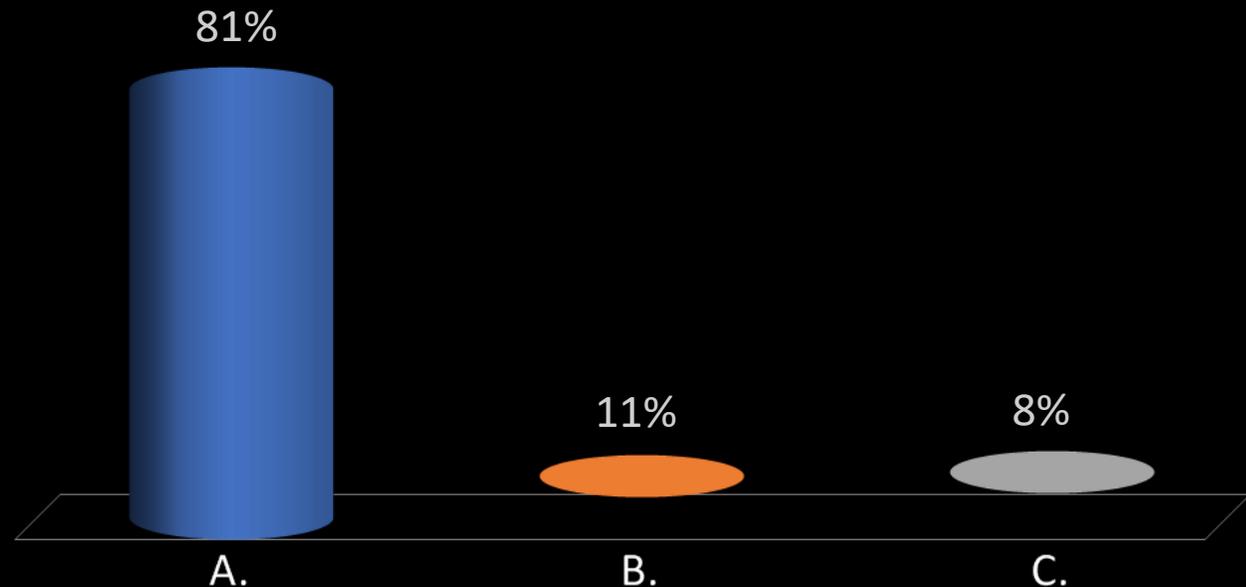
Hamed vahedi

Perica Iazarovski

Recommendation: There is no evidence to suggest that a prior arthroscopy of the hip increases the risk of subsequent SSIs/PJIs.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Does a prior arthroscopy of the knee increase the risk of a subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs) in patients undergoing elective arthroplasty?

RESEARCHED BY:

Arash Aalirezaie

Nirav K. Patel

Zoran Bozinovski

Hamed Vahedi

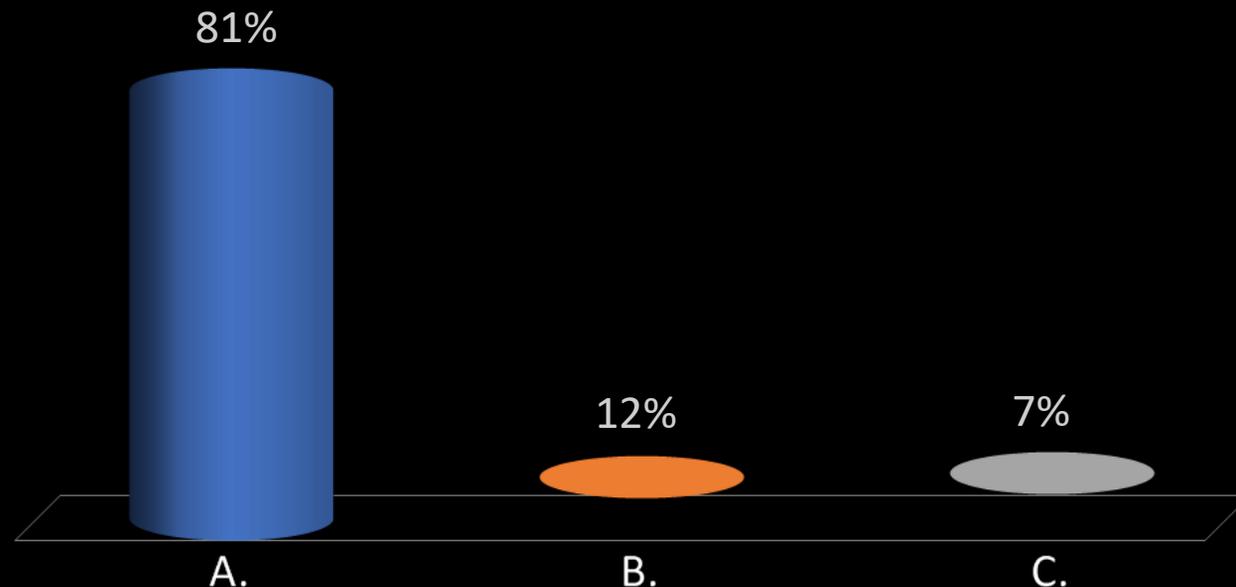
Perica

Lazarowski

Recommendation: There is no evidence to suggest that a prior arthroscopy of the knee increases the risk of subsequent SSIs/PJIs in patients undergoing total knee arthroplasty (TKA).

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain

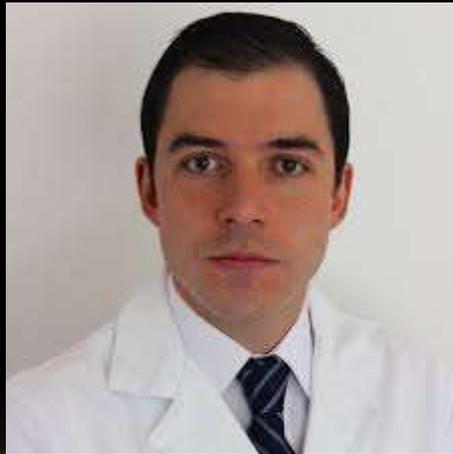


Question 6: Do patients undergoing outpatient total joint arthroplasty have a higher incidence of SSI/PJI?

RESEARCHED BY:



Francisco Reyes
MD, Colombia



Jorge Manrique
MD, Colombia



Mojieb Manzary
MD, Saudi Arabia



Wei Huang
MD, China



Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 14**
- Nelson et al. examined 2005-2014 the ACS9 NSQIP database of patients who underwent THA as outpatient
 - 63,844 THA patients were identified out of which 420 (0.66%) were outpatients.
 - Patients undergoing outpatient THA (LOS 0 days) were not at increased risk of 30-day adverse events or readmission compared to inpatient procedures, including infection.
 - Deep SSI in patients with LOS between 1-5 days was 0.23% and in outpatients was 0% (p=0.319).
 - Rates of superficial SSI lower in outpatient TJA 0.48% vs. 0.64% (p = 0.821)
- Springer et al. compared 30d hospital readmission rates in patients undergoing outpatient TJA (n=137) and inpatient TJA (n=105).
 - No statistical difference in 30-day readmission was associated with outpatient TJA
- Courtney et al. found no significant difference in the rates of complications (including superficial and deep SSI) associated with outpatient vs. inpatient TJA, in the NSQIP database.

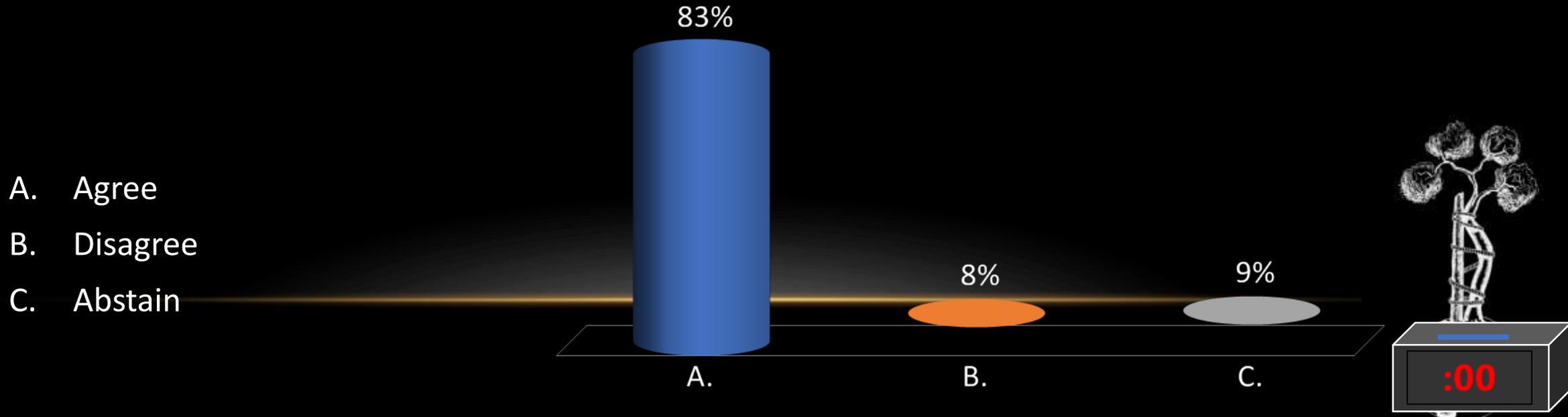
SSI	Outpatient: N=1,220	Inpatient: N=168,186
Superficial	6 (0.5%)	1,053 (0.6%)
Deep	4 (0.3%)	354 (0.2%)

Table 1. NSQIP database comparison of Complications Within 30 d of Surgery Between the Outpatient and Inpatient TJA Groups (7).



Recommendation: No. Patients undergoing outpatient total joint arthroplasty do not have a higher incidence of SSI/PJI.

Level of Evidence: Moderate



1.3 - Prevention: Antimicrobials (Systemic)



Question 1: What is the most appropriate perioperative prophylactic antibiotic (agent, route and number of doses) for patients undergoing primary total joint arthroplasty to reduce the risk of subsequent SSI/PJI?

RESEARCHED BY:



Francisco Reyes



Arthur Malkani

Jorge Manrique



Literature:

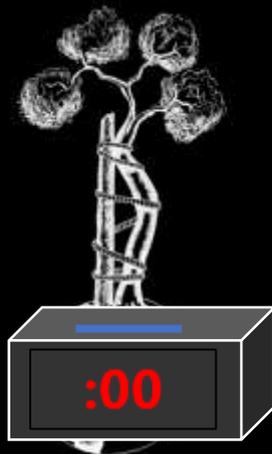
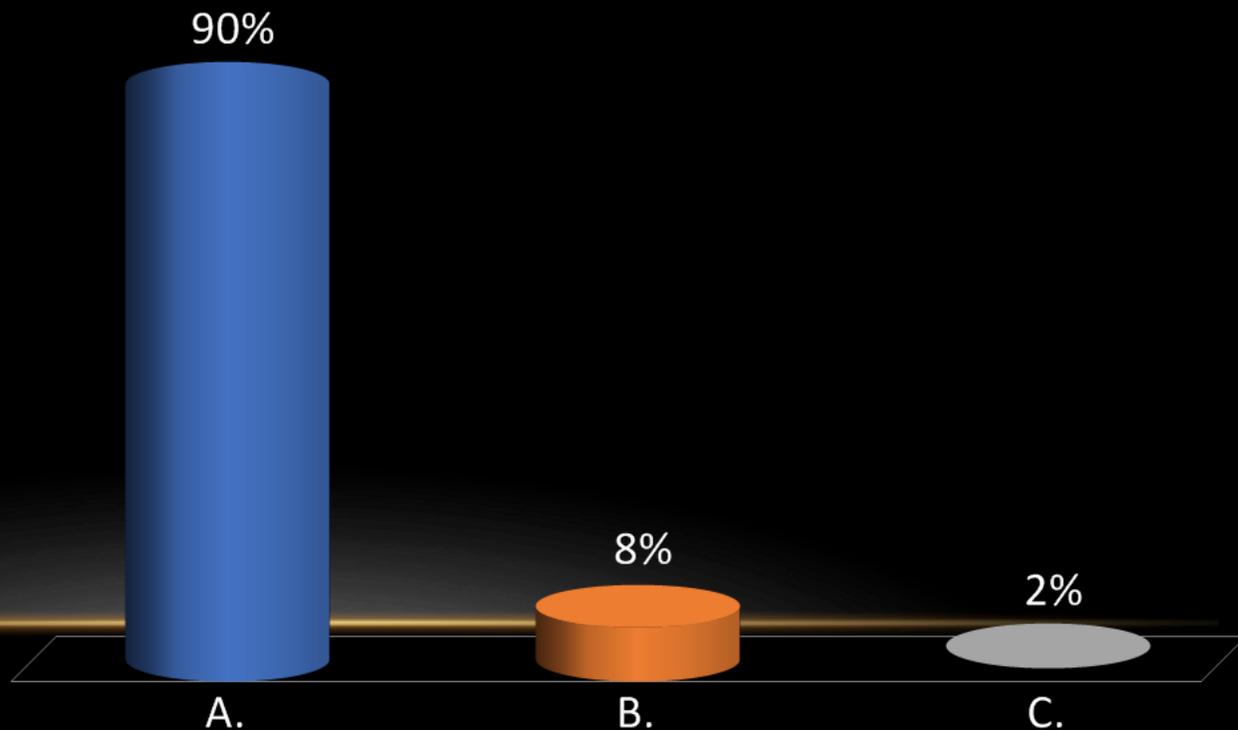
- Meta-Analysis 1, Prospective/Randomized 4, Retrospective 23
- The American Academy of Orthopaedic surgery Recommends the use of either a first- or second-generation cephalosporin in routine perioperative prophylaxis in patients undergoing any orthopaedic procedure, including TJA.
- A multicenter study by Illingworth et al. recommends that when selecting antibiotic prophylaxis, the appropriate agent should be able to cover the most common organisms in the surgical site while avoiding the usage of broad-spectrum therapy.



Recommendation: The most appropriate perioperative prophylactic antibiotic is a first or second generation cephalosporin (i.e. cefazolin or cefuroxime) administered intravenously within 60 to 30 minutes prior to incision as a single and weight adjusted dose.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Question 2: What are the appropriate weight-adjusted prophylactic antibiotic dosages?

RESEARCHED BY:



Craig A Aboltins MD

Timothy L. Tan MD

Robert Townsend MD



Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 15**
- The dosing of Cefazolin, according to the ASHP clinical practice guideline is 2g as a standard dose and 3g for patients weighing 120kg or greater (Bratzler et al. 2013).
 - Studies have shown that even 2g can exceed MIC of common pathogens, even in obese women undergoing C-Section (Young et al. 2015).
- Kheir et al. (2017) performed a retrospective study on 1828 patients who received vancomycin prior to TJA.
 - 64% of patients with fixed-dose (1g) vancomycin were underdosed (<15 mg/kg).
 - 10% of PJIs in the vancomycin underdosed group were due to MRSA
 - No patients with adequate dosing or overdosing of vancomycin developed PJI with MRSA.
- Multiple studies have shown that standard dosing (600-900mg) of clindamycin produces adequate penetration into bone and other deep tissues (Panzer et al. 1972, Schurman et al. 1975, Nicholas et al. 1975)



Recommendation: The recommended weight-adjusted doses of antimicrobials for prophylaxis of hip and knee arthroplasty in adults are shown in Table 1.

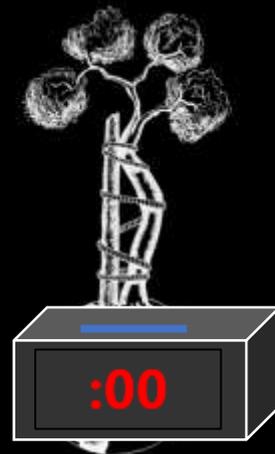
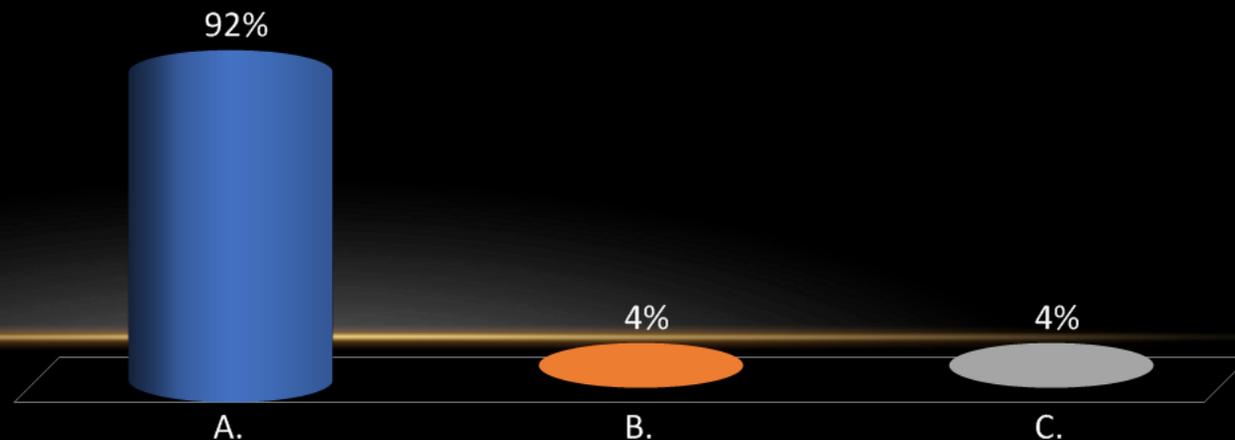
ANTIMICROBIAL	RECOMMENDED DOSE	RE-DOSING INTERVAL
Cefazolin	2 g (consider 3g if patient weight $\geq 120\text{kg}^*$) 1g (consider in patients $< 60\text{kg}$)	4 hours
Vancomycin	15-20 mg/kg*	Not applicable
Clindamycin	600-900 mg [#]	6 hours

*Actual body weight.

[#]No recommended adjustment for weight.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Is one dose of preoperative antibiotic adequate for patients undergoing total joint arthroplasty?

RESEARCHED BY:



Timothy L. Tan MD, USA



Wei Huang MD, China



Thorsten Seyler MD, USA

Literature:

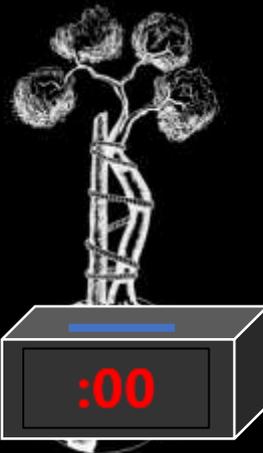
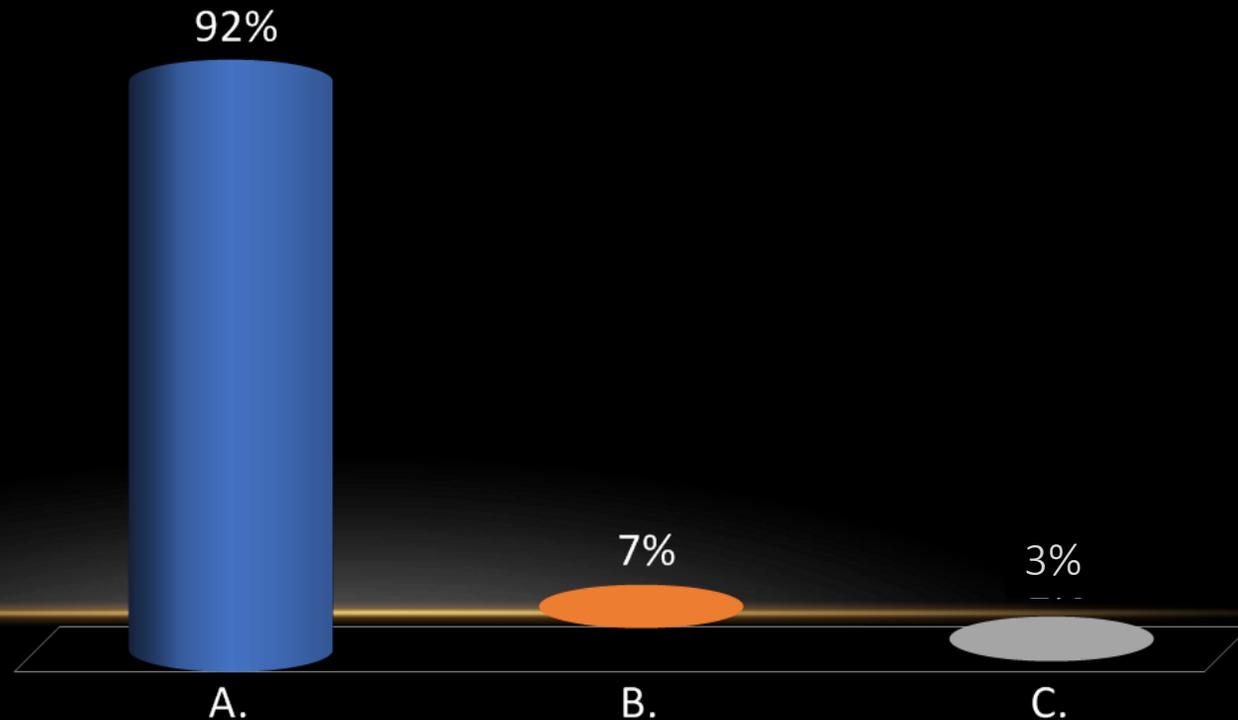
- **Meta-analysis 1, Prospective/Randomized 1, Retrospective 23**
- WHO and CDC recommend for single preoperative antibiotic dosing
 - There is insufficient arthroplasty literature to support this recommendation
- A meta-analysis concluded that postoperative antibiotics did not reduce the rate of infection,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

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Should patients undergoing outpatient total joint arthroplasty receive additional post-operative prophylactic antibiotics?

RESEARCHED BY:

O'Byrne, John



Literature:

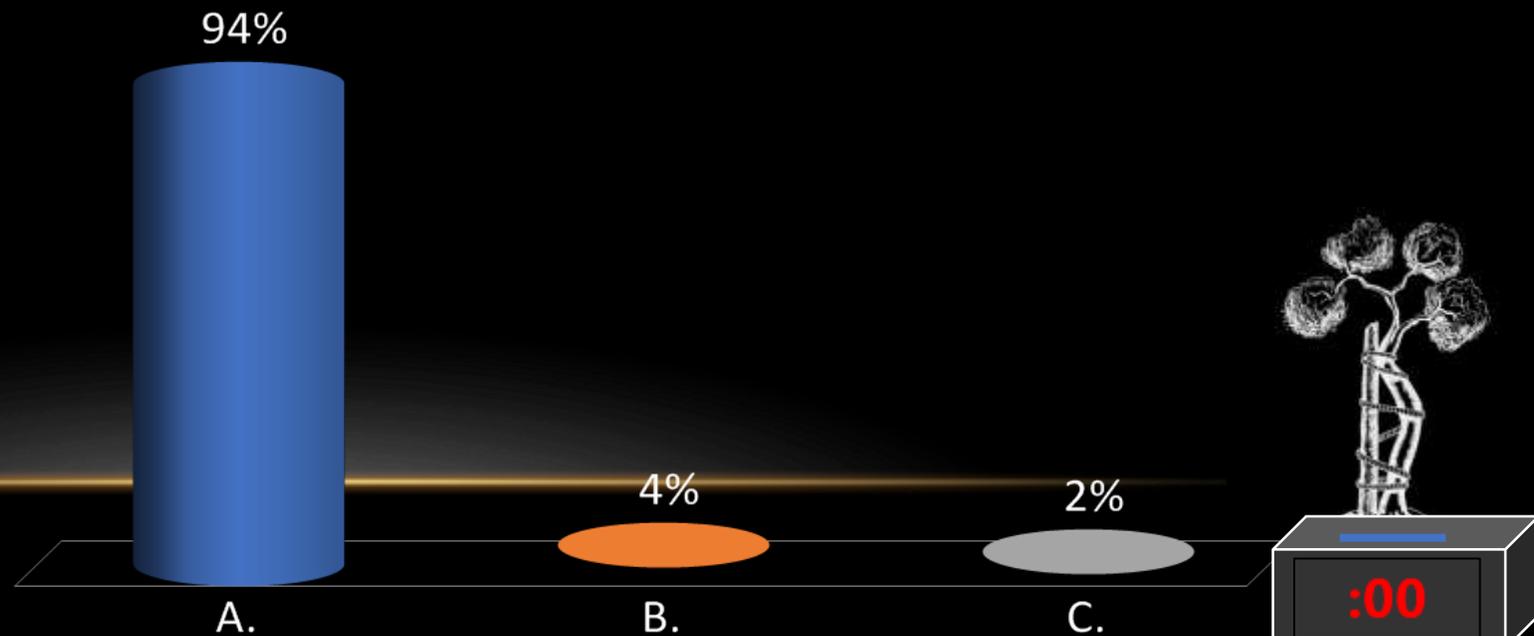
- Meta-analysis 1, Prospective/Randomized 4, Retrospective 15
- Recent guidelines for prevention of SSI issued by the WHO and CDC recommend against the administration of additional postoperative antibiotics.
- One systematic review has shown an incidence of infection of 3.1% following multiple postoperative antibiotics and 2.3% following a single dose. Four RCTs found similar results that favoured single dose regimens, however, were underpowered.
- One registry study did report a higher revision rate in patients receiving a single dose of antibiotics compared to four doses



Recommendation: Despite the current guidelines from The Centers for Disease Control and Prevention (CDC) advocating for a single dose of perioperative antibiotics, the studies utilized to form these guidelines are underpowered and primarily in specialties outside orthopaedics. The limited evidence suggests that a single perioperative dose of antibiotics, compared to multiple doses, does not increase the rates of subsequent SSIs/PJIs. A randomized prospective study in patients undergoing elective arthroplasty is underway, which should help answer this question definitively.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Does extended prophylactic antibiotics therapy for patients undergoing aseptic revision help reduce the risk of subsequent SSI/PJI?

RESEARCHED BY:



Feng Chih Kuo MD,
Taiwan



Marjan Wouthuyzen-Bakker MD,
Netherlands



Edward Hendershot MD,
USA



Literature:

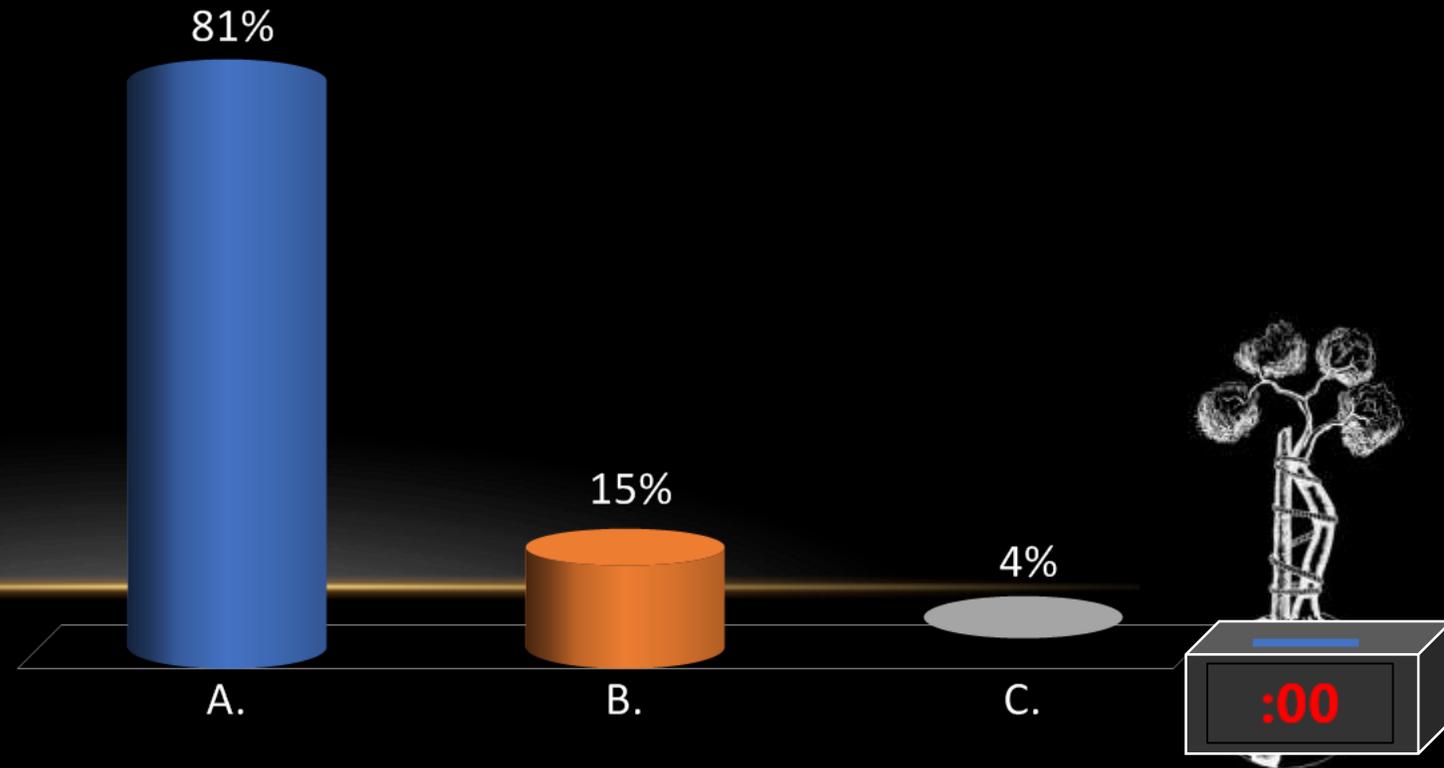
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 1**
- Only a single retrospective study (Claret et al) has examined the utility of extended antibiotic prophylaxis (5 days) in revision arthroplasty (n=341)
 - PJI rates were significantly lower within the 3-months of revision surgery in the extended antibiotic prophylaxis group vs. the short-prophylaxis group (2.2% vs. 6.9%, $p=0.049$).
- However several studies have been conducted in primary TKA and THA, indicating no difference SSI rates in patients who received antibiotic prophylaxis for 24 hours vs. those receiving longer prophylaxis
- Further evidence is needed – the PARITY trial, an international prospective RCT currently conducted in the field of orthopedic oncology, may provide us additional evidence about the potential benefit of extended antibiotic prophylaxis in high risk patients undergoing TJA



Recommendation: In the absence of concrete evidence we recommend the use of routine antibiotic prophylaxis (maximum 24 hours) for patients undergoing revision arthroplasty as long as infection has been properly ruled out prior to revision surgery.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 6: Should duration and the type of antibiotic prophylaxis be altered in patients with a prior PJI?

RESEARCHED BY:



Pablo S Corona, MD



Akos Zahar, MD



Matteo Carlo Ferrari, MD



Literature:

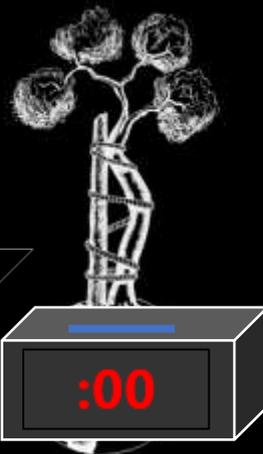
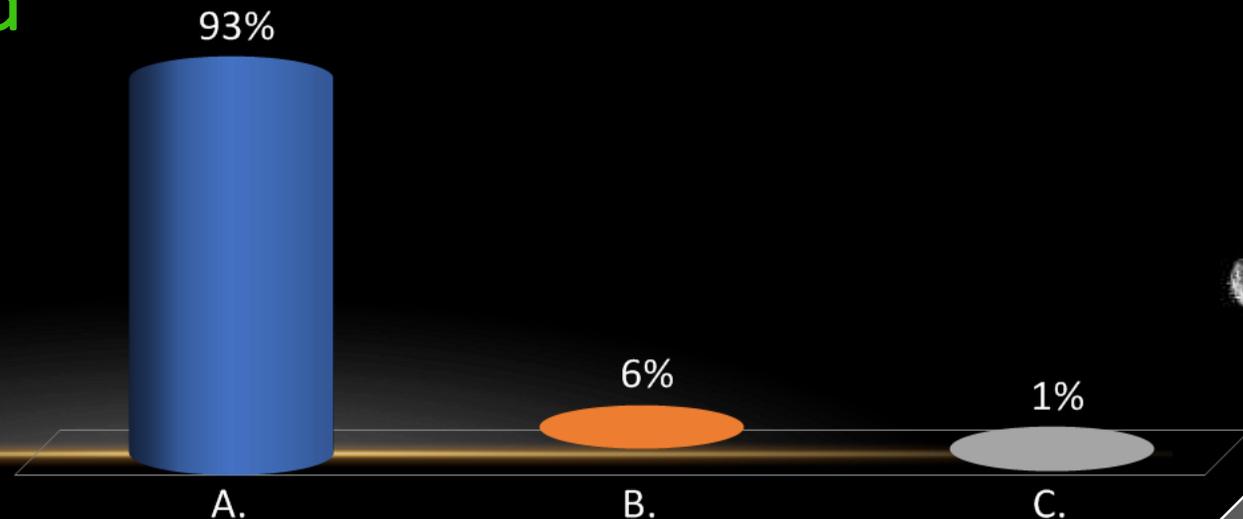
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 7
- Patients with prior PJI at higher risk of subsequent infection by same organism
- No evidence regarding duration of antibiotic treatment and impact of subsequent PJI



Recommendation: Antibiotic prophylaxis should be tailored in patients with prior PJIs who are undergoing another subsequent elective primary or revision joint arthroplasty. Antibiotic prophylaxis should cover the initial causative organism(s) as well as the most common pathogens that can cause periprosthetic joint infection (PJI) with either single or dual antibiotics.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 7: Should prophylactic antibiotic therapy be administered for an extended duration in patients admitted to the Intensive Care Unit (ICU)?

RESEARCHED BY:

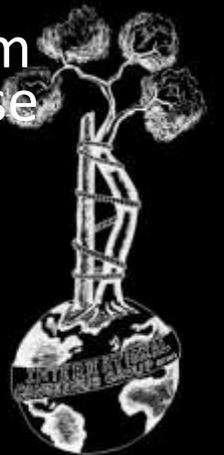
Berdal, Jan Erik

Tuncay, Ibrahim



Literature:

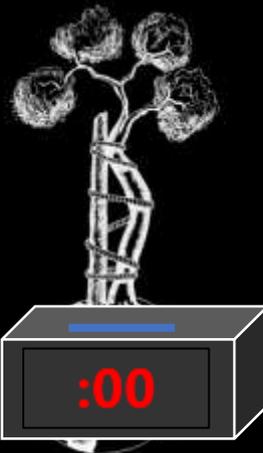
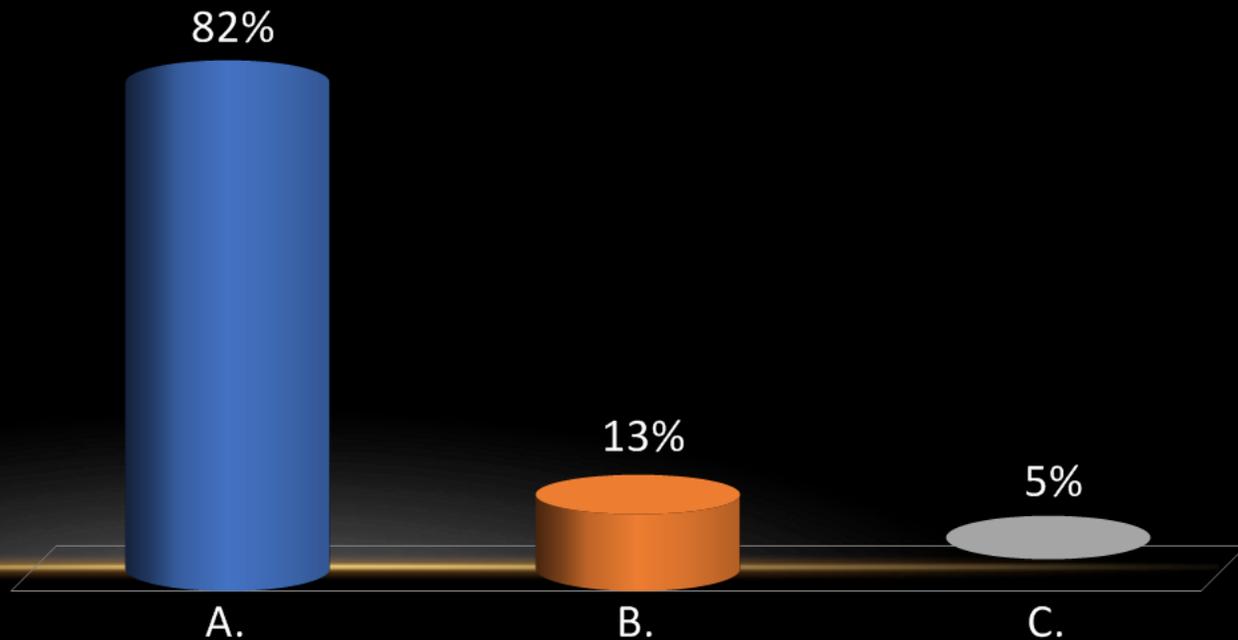
- Meta-analysis 1, Prospective/Randomized 3, Retrospective 19
- The CDC and WHO guidelines concur on not exceeding prophylaxis past wound closure based on a comprehensive systematic literature review, though strength of the supporting literature has been questioned
- A meta-analysis did not find evidence to show efficacy of extended antibiotic prophylaxis in TJA for the prevention of SSI.
- The continuation of a narrow-acting antibiotic therapy from the operating room into the ICU may give a false sense of security and both obscure and delay these interventions, or even harm patients by promoting anti-microbial resistant bacteria



Recommendation: Surgical prophylactic antibiotic therapy should not be administered for an extended duration in patients admitted to the ICU.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 8: Does the use of allografts alter the recommended duration of prophylactic antibiotics?

RESEARCHED BY:



Heinz Winkler MD,
Austria



Oleg Safir MD,
Canada



Sergio Rudelli MD,
Brazil



Literature:

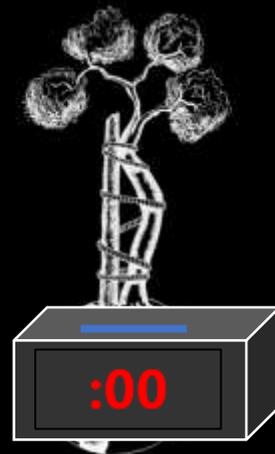
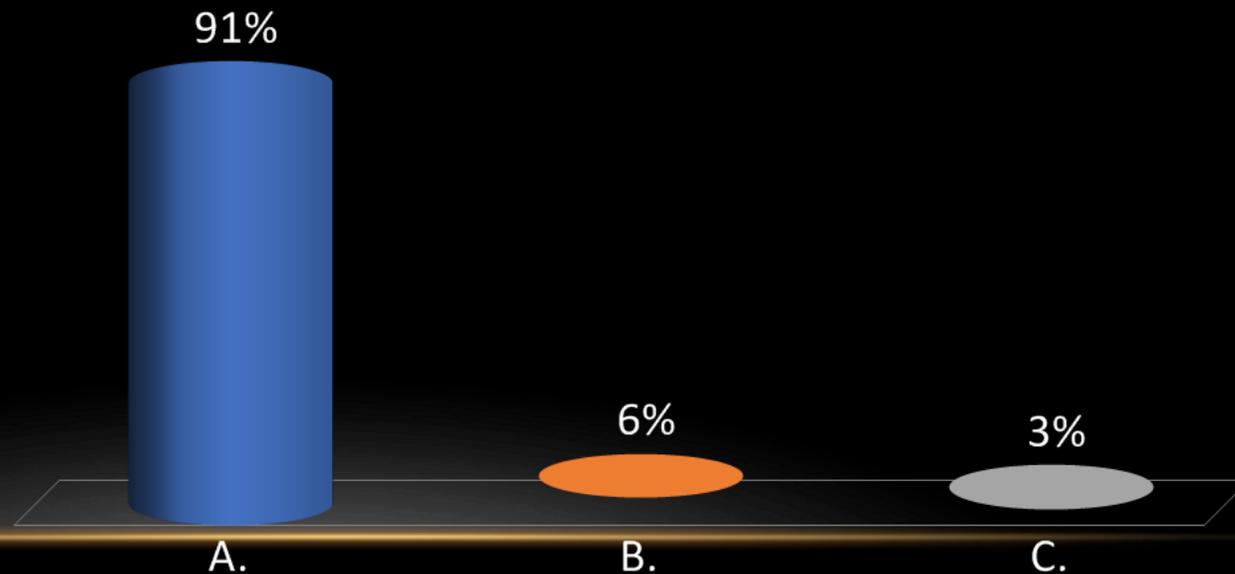
- Meta-analysis 2, Prospective/Randomized 0, Retrospective 8
- Limited evidence as there are no high-quality studies available comparing differences between the duration of systemic antibiotic prophylaxis with and without allograft use in primary or revision total joint arthroplasty.



Recommendation: No. Allografts are avascular materials that are prone to contamination and may serve as a scaffold for bacterial colonization and biofilm production, similar to a prosthesis or osteosynthetic material. However, it is difficult to establish a causal relationship between the use of an allograft and subsequent infection. Thus, there is no evidence to support the use of extended antibiotic prophylaxis.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



1.4 - Prevention: Antimicrobials (Local)



Question 1: 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:

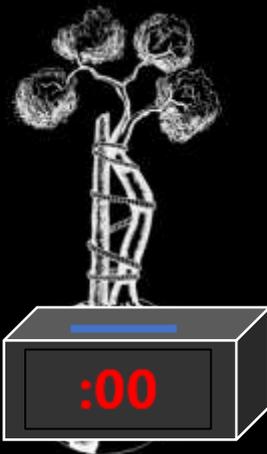
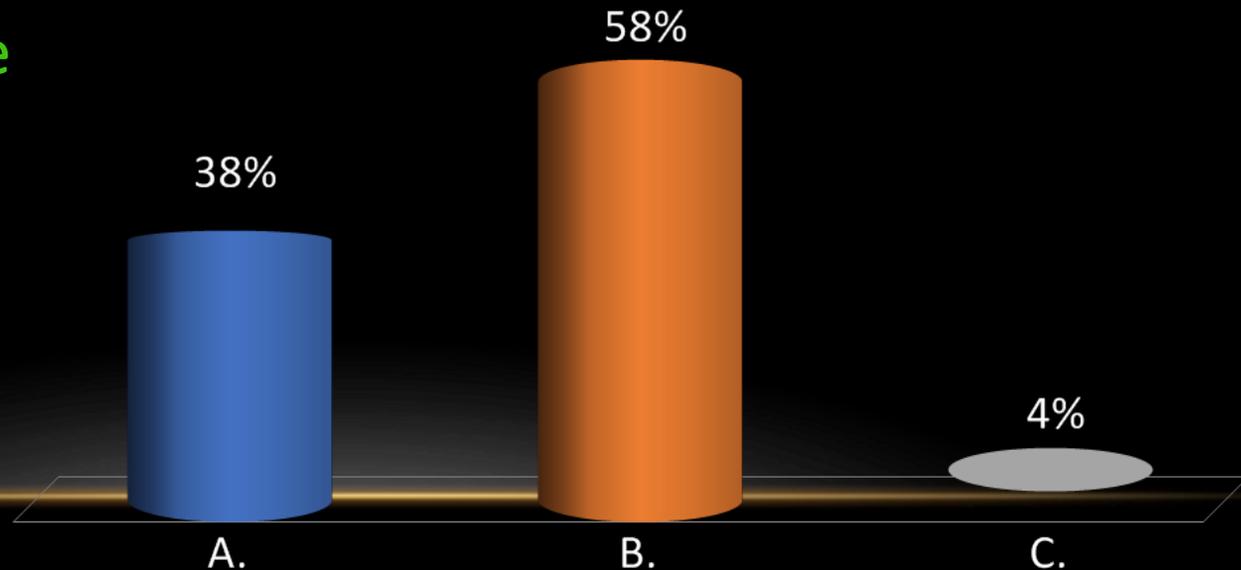
- Meta-analysis 1, Prospective/Randomized 0, Retrospective 26
- A number of retrospective studies have correlated use of antibiotic-loaded cement with lower rates of wound infection and failure in THA and TKA, whereas others show no difference
- No evidence exists demonstrating that use of antibiotic-loaded 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 SSIs/PJIs. Recent high level evidence and registry data has not demonstrated a reduction in SSI/PJIs. Furthermore, the added cost, the potential for the 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: Moderate

- A. Agree
- B. Disagree
- C. Abstain

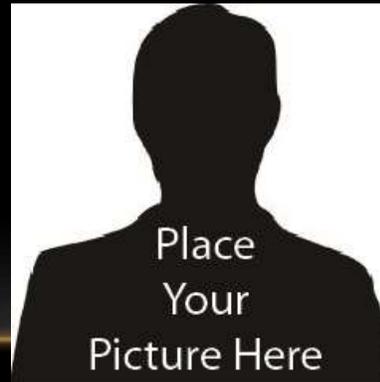


Question 2: Is there a role for the use of antibiotic-impregnated cement in primary total joint arthroplasty?

RESEARCHED BY:



Yale Fillingham, MD



Sergei Oshkukov, MD



Ali Parsa, MD



Literature:

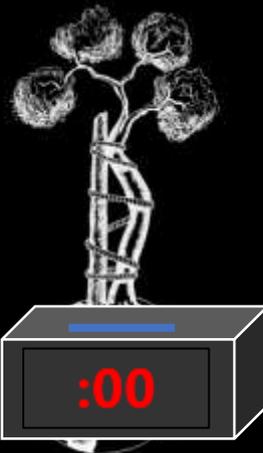
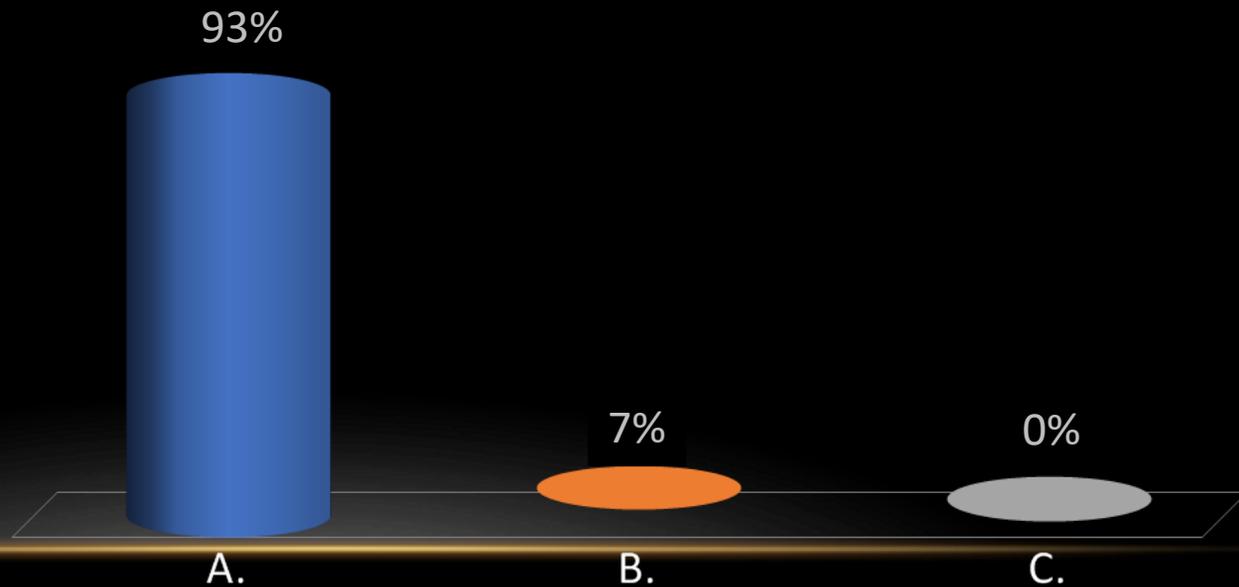
- Meta-analysis 1, Prospective/Randomized 0, Retrospective 26
- A number of retrospective studies have correlated use of antibiotic-loaded cement with lower rates of wound infection and failure in THA and TKA, whereas others show no difference.
- No evidence exists demonstrating that use of antibiotic-loaded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



Recommendation: Antibiotic-impregnated cement may be used during primary TJA to reduce the risk of surgical site infections/periprosthetic joint infections (SSIs/PJIs). 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: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: What is the optimal antibiotic(s) dosage to be used in cement during reimplantation that does not significantly interfere with the mechanical strength of cement used for fixation?

RESEARCHED BY:



Andrew Porteous MD,
United Kingdom



Matthew Squire MD, United
States of America



Literature:

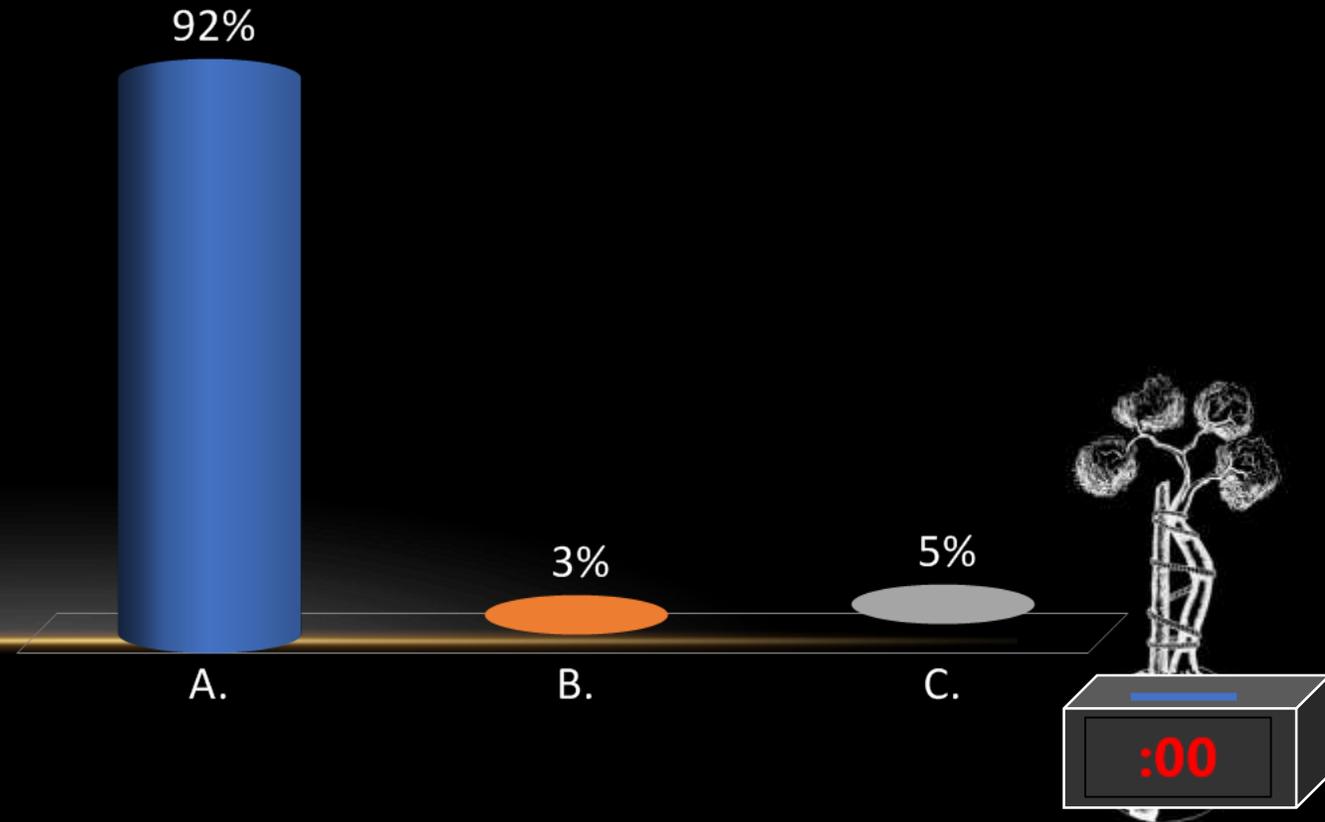
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 12**
- Investigations examining the mechanical properties of ALBC are all *in vitro* investigations
 - Loading conditions for revision THA and TKA modeled *in vitro* do not translate adequately to *in vivo* environments
- A recent (2017) investigation quantifying the mechanical properties of dual-antibiotic loaded PMMA demonstrated that up to 3g total of powdered antibiotics can be included into a 40g pack of PMMA before compressive strength is decreased below the ISO standard.
- At this time, there is no definitive conclusion on what prosthetic reimplantation antibiotic-loaded bone cement formulation provides the best eradication of PJI and/or is most protective against subsequent prosthetic aseptic loosening



Recommendation: The mechanical strength of most cement is maintained if $\leq 5\%$ (w/w) of antibiotics is added (equating to 2g in a 40g packet).

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain

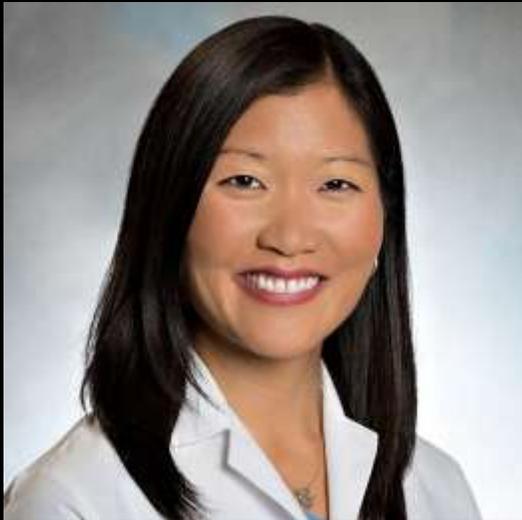


1.5 - Prevention: Operating Room Environment



Question 1: Does performing a primary total joint arthroplasty after a dirty case (infection or open abdomen) in the same operating room increase the risk of SSI/PJI?

RESEARCHED BY:



Antonia Chen MD,
USA



Michael Kheir MD, USA

Francisco Montilla MD,
Spain



Literature:

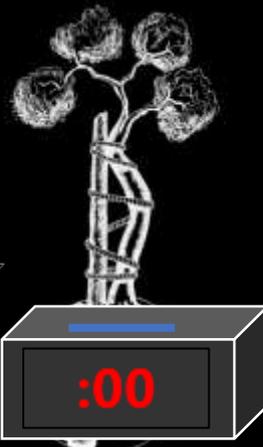
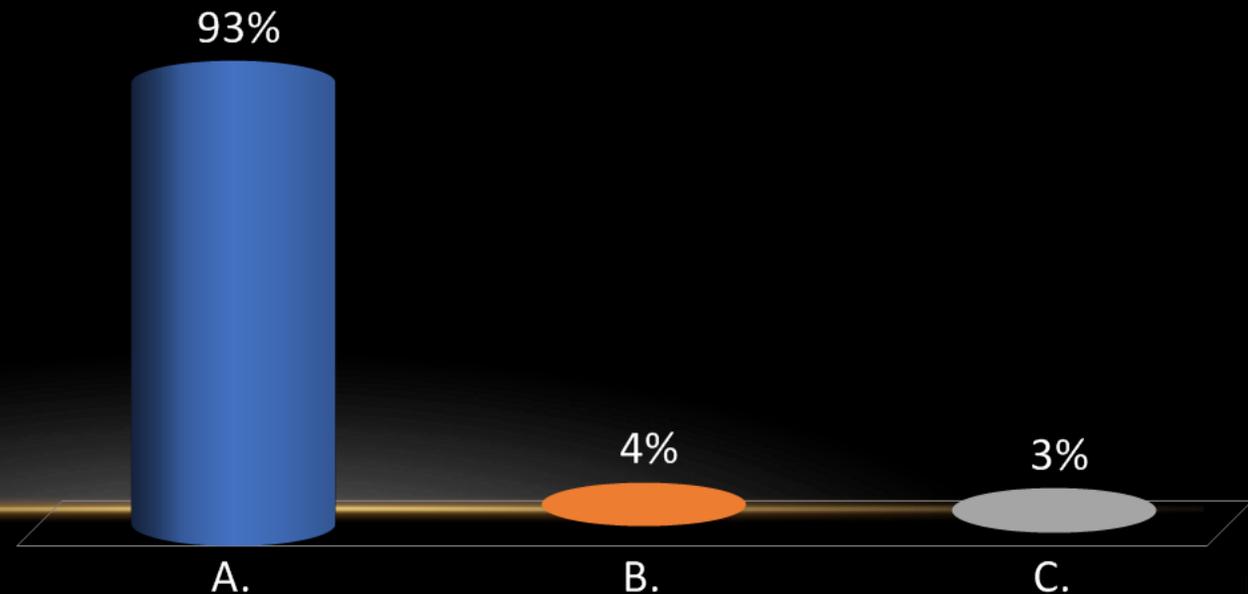
- **Systematic review 1, Prospective/Randomized 0, Retrospective 3**
- Limited data in literature specific to infection risk when performing primary total joint arthroplasty (TJA) after a contaminated case
- In a systematic review, Kramer et al. showed that nosocomial pathogens persist on inanimate surfaces for several days, with many Gram-positive, Gram-negative and fungal pathogens remaining for months.
- Chen et al. showed that infection risk increased by 2.4 times if a TJA case followed an infected case in the same room on the same operative day.



Recommendation: The little data on this subject suggests that the risk of PJI may be higher when an elective arthroplasty follows a contaminated case. The risk may be reduced if terminal cleaning of the operating room can be done after the dirty case. Further studies are necessary to elucidate this connection.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does the use of sterile surgical vests decrease the risk of contamination or incidence of infection following total joint arthroplasty?

RESEARCHED BY:



Dominic Meek MD, UK

Mike Reed MD, UK



Literature:

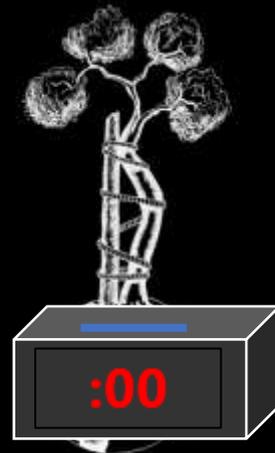
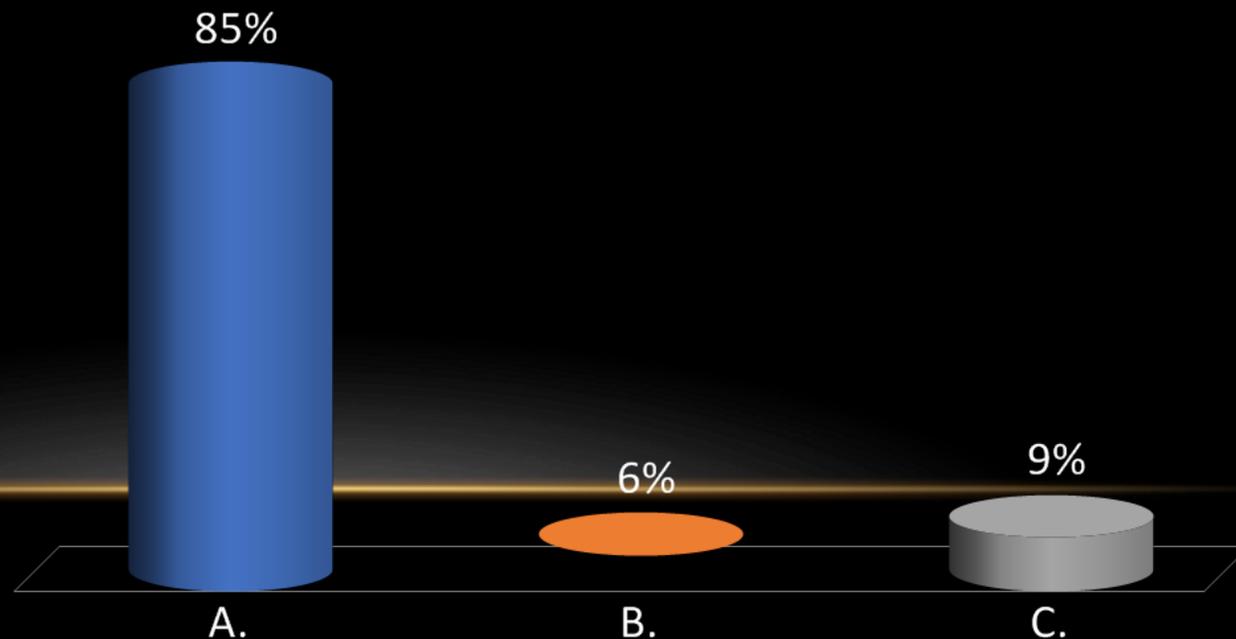
- Meta-analysis 0, Prospective/Randomized 6, Retrospective 19
- Randomized study of standard surgical gowns and positive-pressure surgical helmet systems, with and without cuff/glove taping (Singh et al.)
 - More positive surgical site cultures with helmets and tape, but this was not statistically significant
- Positive pressure systems show more contamination in this area, even compared to conventional sterile gowns (Merollini et al.)



Recommendation: The use of sterile surgical vests has no bearing on the incidence of subsequent SSI/PJI following orthopedic procedures.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Does the use of personal protection suits (space suits) influence the rate of SSI/PJI in patients undergoing joint arthroplasty?

RESEARCHED BY:



Mark Spangehl MD,
USA



Xianlong Zhang MD,
China



Literature:

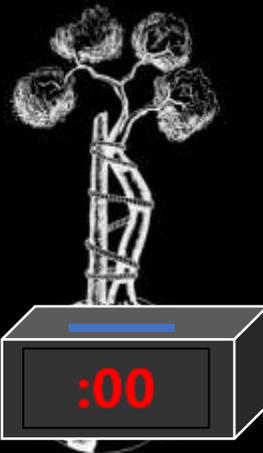
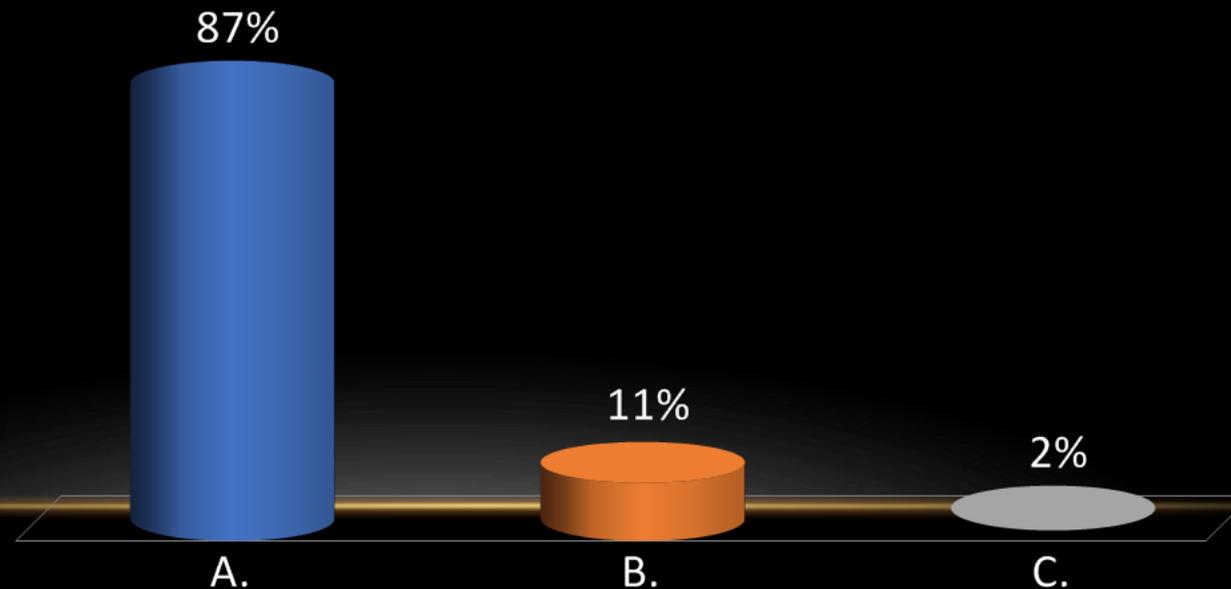
- Meta-analysis 1, Prospective/Randomized 3, Retrospective 17
- Meta-analysis of body exhaust suits (Blomgren et al.)
 - Body exhaust suits were associated with a significant reduction in deep infection rates (RR 0.11, 95% CI 0.09-0.46)



Recommendation: In the absence of strong evidence, we believe the use of personal protection suits (space suits) does not reduce the rate of subsequent SSI / PJI in patients undergoing joint arthroplasty.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4: 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:

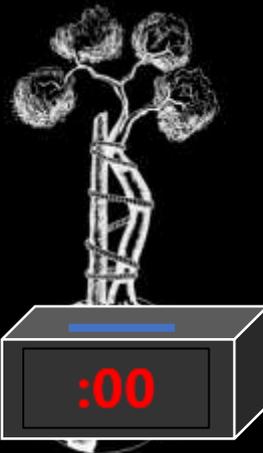
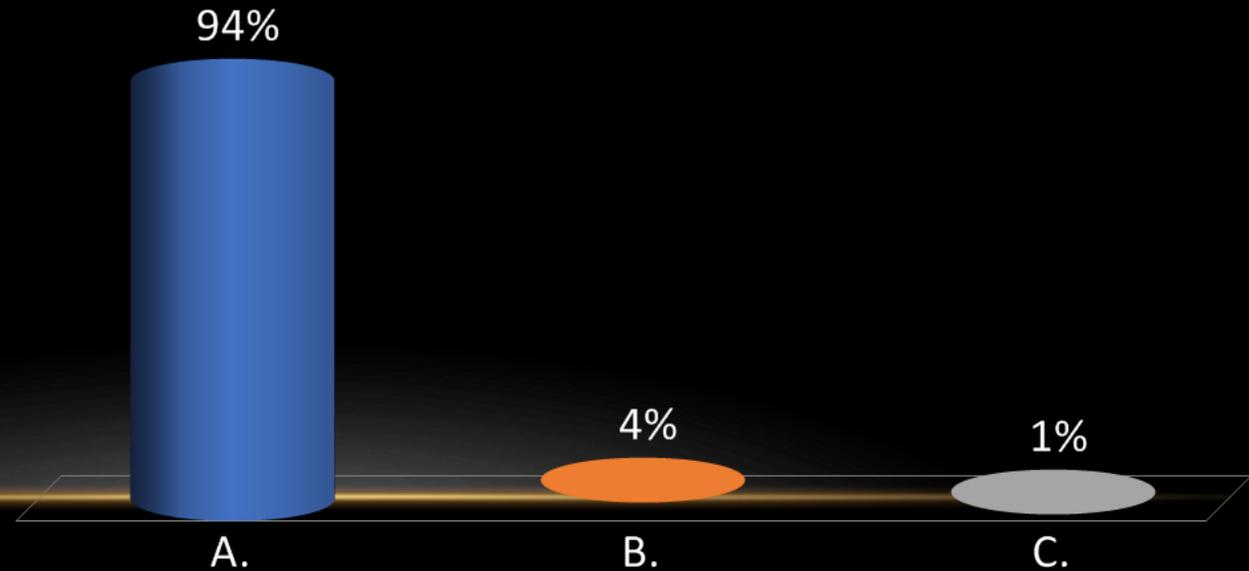
- There are no studies that assess the impact of changing the drapes during DAIR.
- After a literature review of 51 papers, only one study was identified that indirectly mentioned the use of clean draping during the surgical procedure.
- Changing the drapes during DAIR can be performed at the surgeon's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



Question 5: Does the use of separate instruments for each side reduce the rate of subsequent SSI/PJI in patients undergoing simultaneous bilateral hip or knee arthroplasties?

RESEARCHED BY:



Jeffrey Granger MD,
USA



Gustavo Garcia MD,
Venezuela



Michel Malo MD,
Canada



Literature:

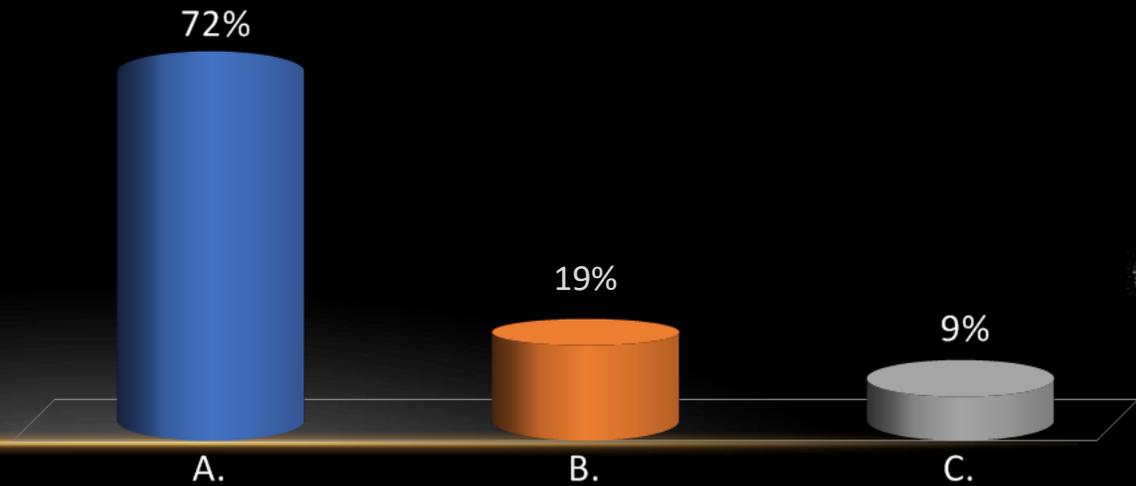
- **Meta-analysis 0, Prospective/Randomized 3, Retrospective 28**
- **Retrospective studies TKA (Dimitris et al. and Leonard et al.)**
Using separate instrument sets in bilateral procedures, he observed infection rates of 0% in 227 patients and 2.7% in 92 patients
- **Retrospective study (Gonzalez Della Valle et al.)**
No difference in infection rates between same and separate instrument procedures, its retrospective nature and lack of statistical power are not strong enough



Recommendation: No. The use of separate instruments for each side does not appear to reduce the rate of subsequent SSI/PJI in patients undergoing simultaneous bilateral hip or knee arthroplasties.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 6: Does routine use of a new set of surgical instruments and equipment following debridement and before reimplantation reduce the risk of SSI/PJI recurrence? Is it necessary to change all surgical fields before the final reimplantation in septic revision surgery?

RESEARCHED BY:



Marie-Jacque Reisener MD,
Germany



Adrian van der Rijt MD,
Australia

Jorge Manrique MD,
Colombia



Literature:

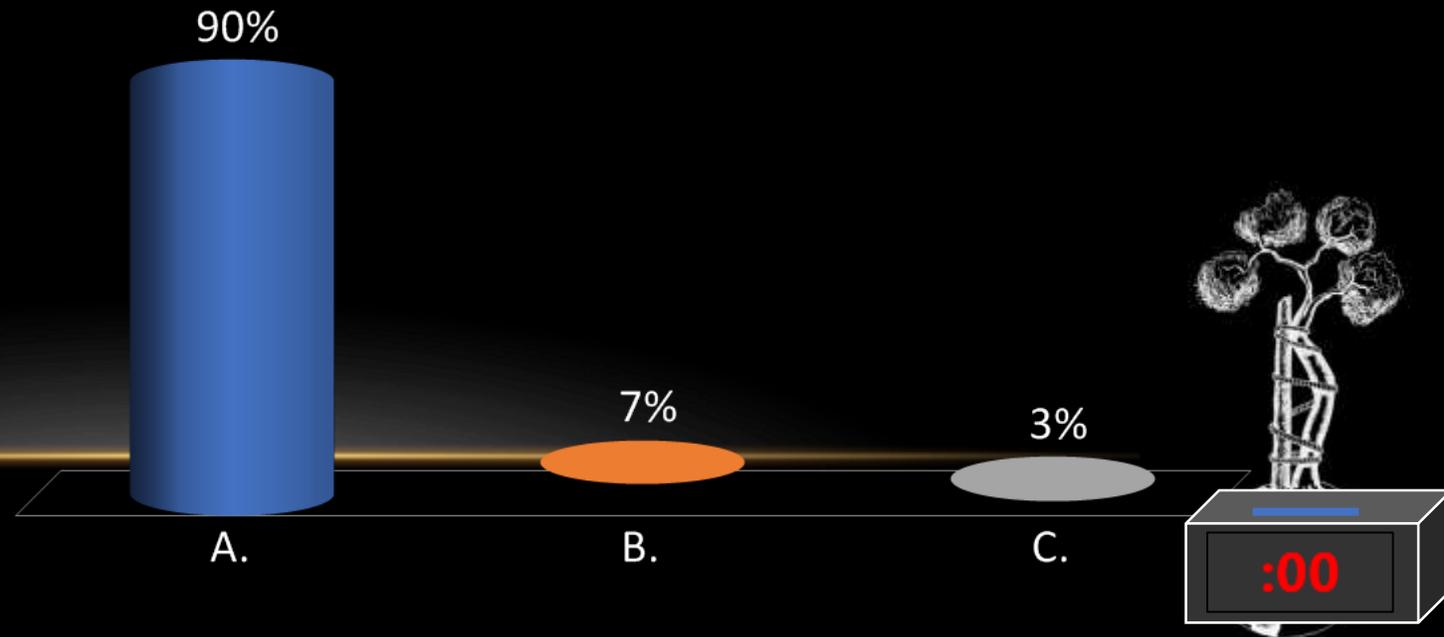
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 11**
- Pinto et al showed that in clean orthopaedic surgeries, 47% of the instruments were contaminated. In the same study, an even higher rate of 70% had positive cultures in contaminated surgeries and up to 80% in infected cases
- Davis et al showed that in 100 consecutive primary hip and knee arthroplasty operations, under laminar flow, instruments get contaminated. 11.4% of suction tips, 14.5% of light handles, 9.4% of skin blades and 3.2% of deep blades were seen to have positive cultures



Recommendation: The change of the surgical field following debridement of an infected joint leads to a reduction in the bioburden and stands to improve outcome of surgical intervention and should be considered.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 7: Is there a concern for contamination of the surgical field by particles, such as cement, that may escape the wound intraoperatively by coming into contact with the ceiling light or facial masks and fall back into the wound?

RESEARCHED BY:



Greg Stocks MD, USA



Abtin Alvand MD, UK



Literature:

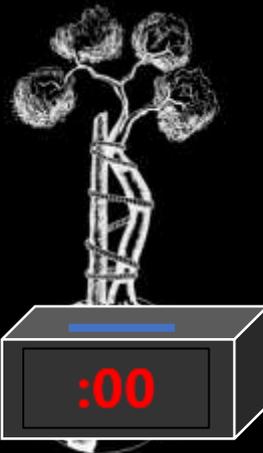
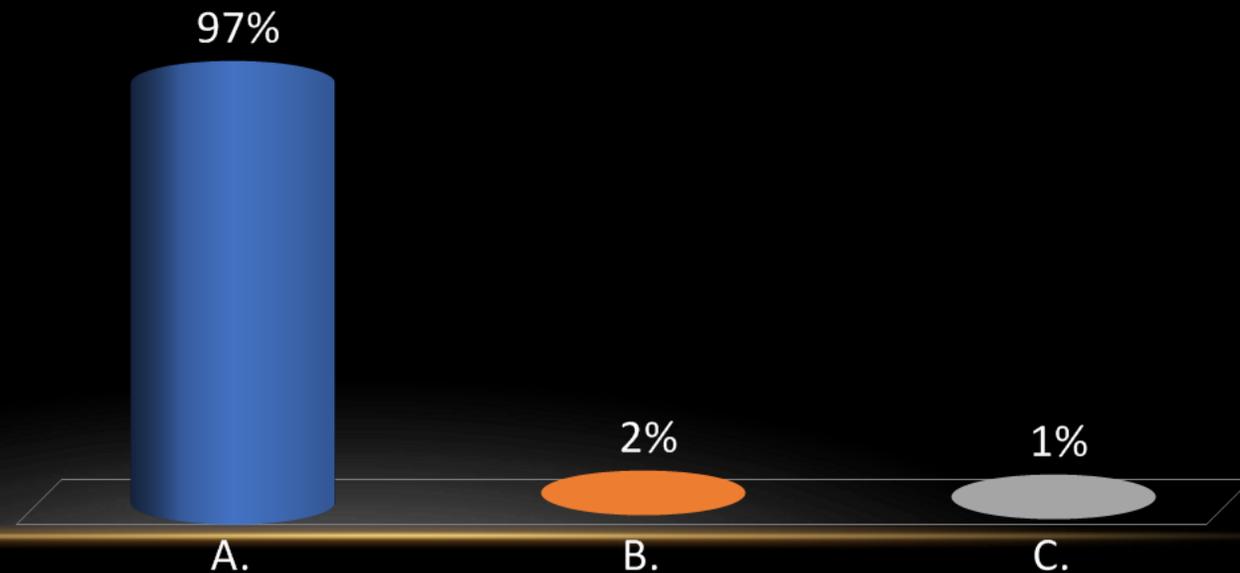
- **Systematic review 0, Prospective/Randomized 0, Retrospective 16**
- Several studies have shown that high-speed cutters in primary hip arthroplasty and spinal surgery can produce aerosols
- There are no studies in the literature evaluating the effect of debris that come in contact with an unsterile surface and fall back into the wound
- Airborne particles are a source of bacterial inoculation of the wound and can result in post-operative SSI/PJI
 - Debris would presumably act similarly and therefore should be protected against



Recommendation: There is logically a high risk that particles which fall into the wound after coming into contact with unsterile equipment (e.g. ceiling lights / facial masks) will contaminate the surgical field. However, no studies investigating this hypothesis directly exist in the current literature. We recommend that surgeons must be conscious of, and take precautions, to prevent particles fall into the surgical field, and when such scenario arises, to use copious antiseptic solutions, such as dilute betadine, to irrigate the wound.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



1.6 - Prevention: Surgical Technique



Question 1: Does the use of a tourniquet influence the rate of SSI/PJI in primary or revision TKA?

RESEARCHED BY:



Bin Shen MD,
China



Goran Bicanic MD,
Croatia

Rahul Goel MD,
USA



Literature:

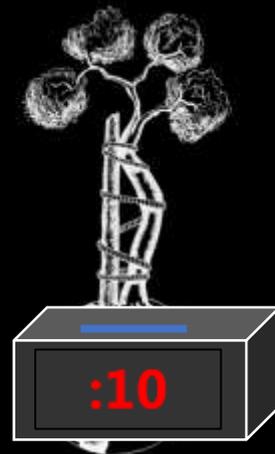
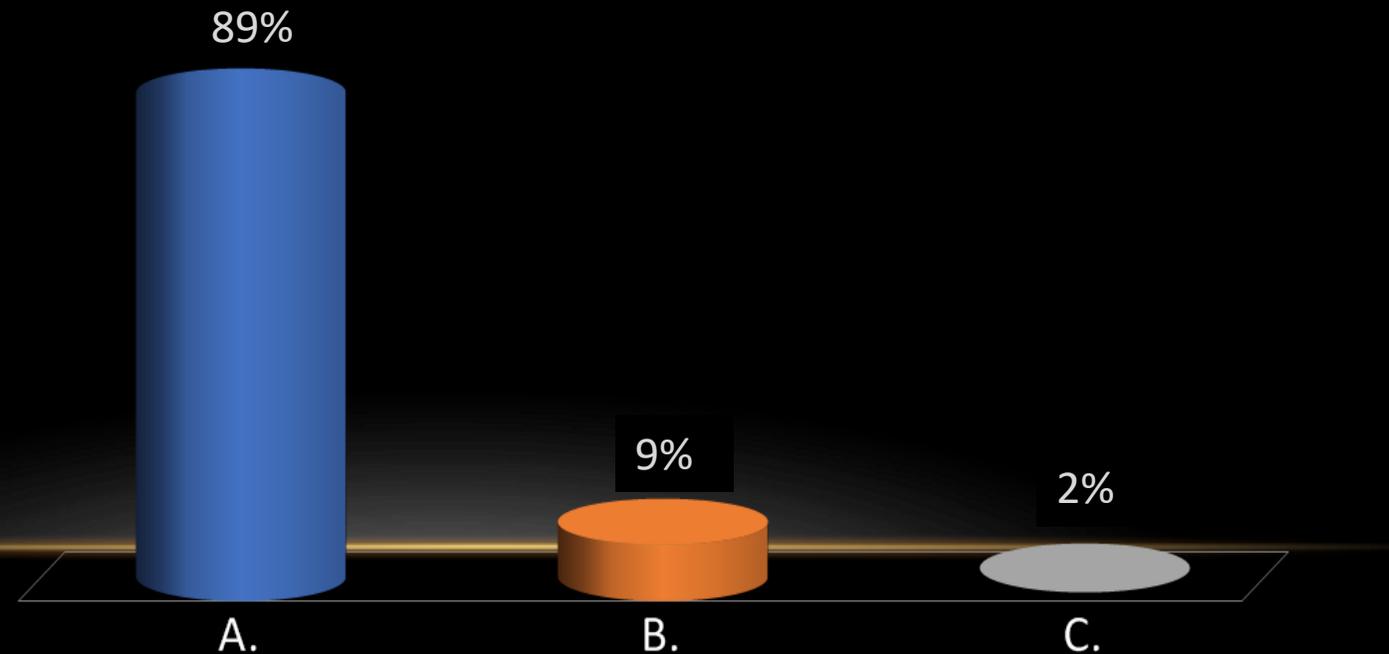
- **Meta-analysis 7, Prospective/Randomized 3, Retrospective 12**
- **Moderate evidence suggesting that the effect of a tourniquet has on the incidence of SSI and PJI following TKA has not been fully evaluated.**
- **The randomized controlled trials of this subject have been of small cohorts of patients that lack the power to evaluate these complications.**



Recommendation: The literature is inconclusive regarding the use of a tourniquet during TKA and its potential to increase the risks for SSIs/PJIs in TKAs. Tourniquet times and pressures should be minimized to reduce this risk.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does the surgical approach (parapatellar vs. subvastus) during primary TKA affect the incidence of subsequent SSI/PJI?

RESEARCHED BY:



Nicholas Giori MD,
USA



Giovanni Balato MD,
Italy



Michael Hirschmann MD,
Switzerland



Literature:

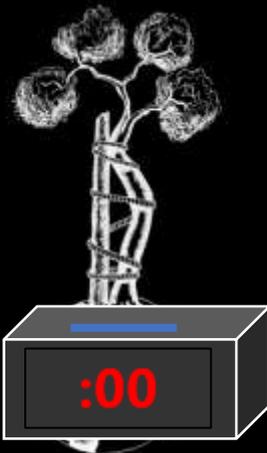
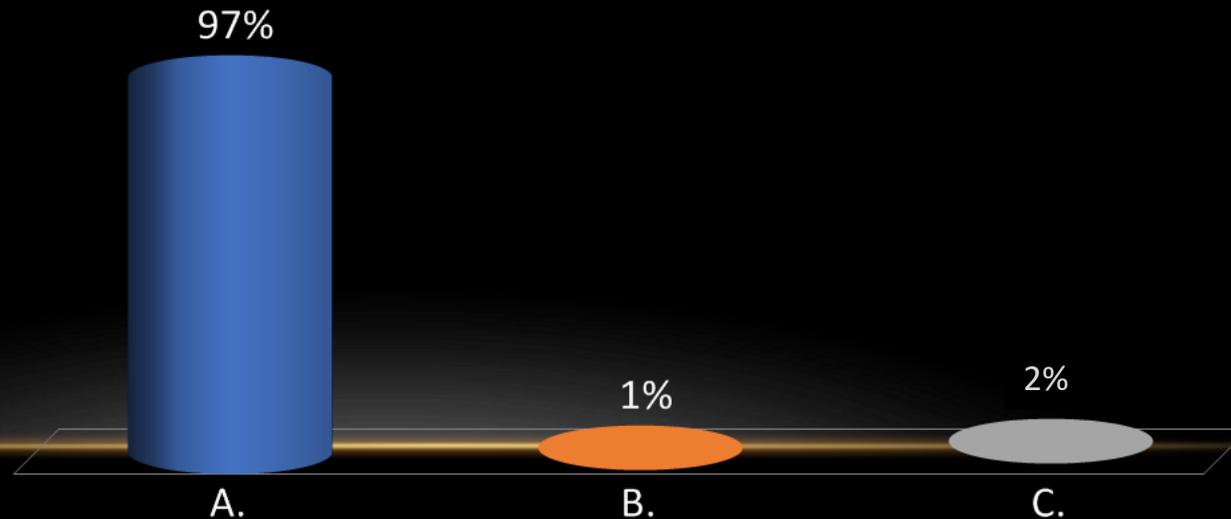
- **Meta-analysis 3, Prospective/Randomized 0, Retrospective 2**
- **Strong evidence suggesting no difference between parapatellar approach and the subvastus approach.**



Recommendation: The incidence of surgical site infections (SSI) or periprosthetic joint infections (PJI) after primary total knee arthroplasty (TKA) is not influenced by the surgical approach (parapatellar or subvastus).

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Does the surgical approach of primary THA affect the incidence of subsequent SSI/PJI?

RESEARCHED BY:



Eleftherios Tsiridis MD,
Greece



Stefano Bini MD,
USA



Majd Tarabichi MD,
USA



Literature:

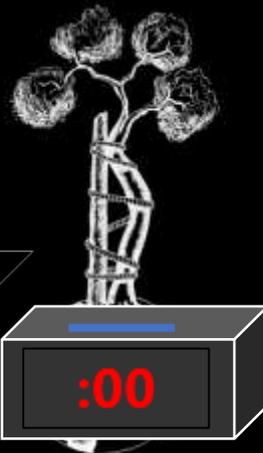
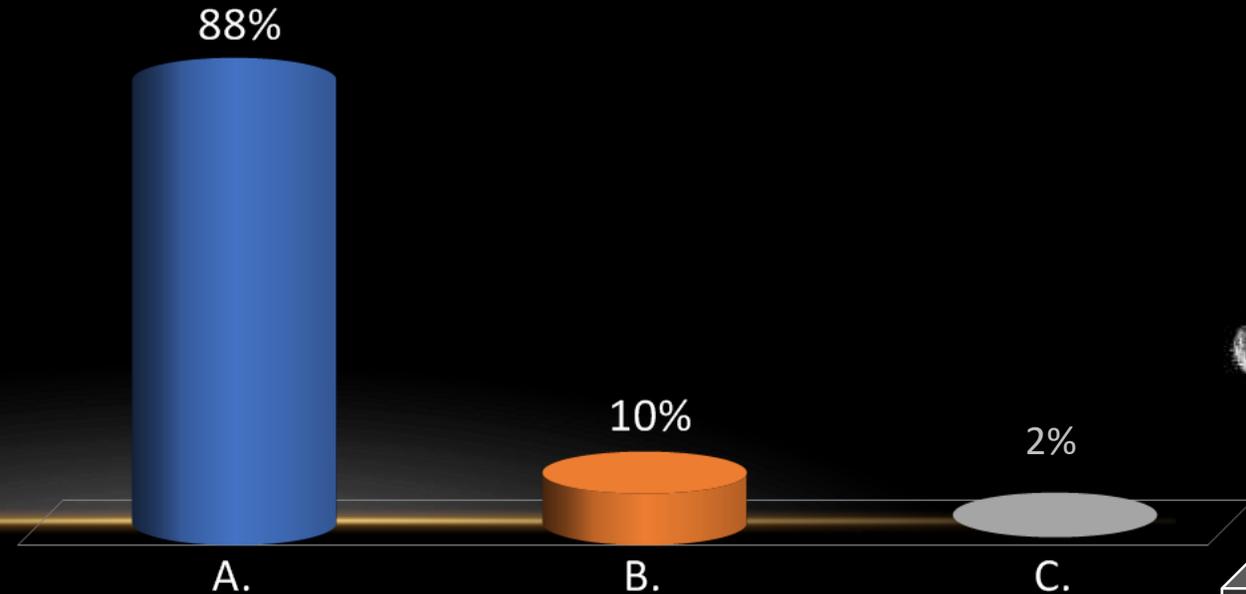
- **Meta-analysis 8, Randomised/Prospective 3, Retrospective 13**
- One RCT: No SSI/PJI in standard PL approach, 1 SSI and 1 PJI in MIS group
 - All studies underpowered to associate relationship between approach and SSI/PJI
- 2 of the 8 meta-analyses specifically examined THA approach and infection:
 - PL has lowest risk for overall complications, incl. infection
 - PJI rate of 0.2/100-person-years for DA and 0.4/100-person-years for PL (RR=0.55, $p=0.002$)
- Registry data: contradictory findings or no association found



Recommendation: The surgical approach in primary THA does not affect the incidence of subsequent SSI/PJI.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Does the use of periarticular injections affect the rate of SSI/PJI recurrence in reimplantation?

RESEARCHED BY:



Denis Nam MD, USA



Hongyi Shao MD,
China



Maurilio Marcacci
MD, Italy



Literature:

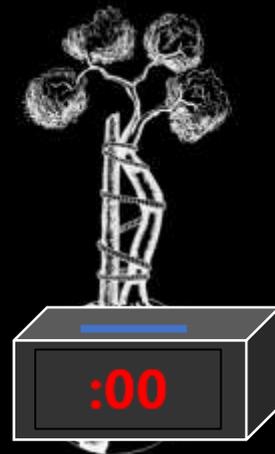
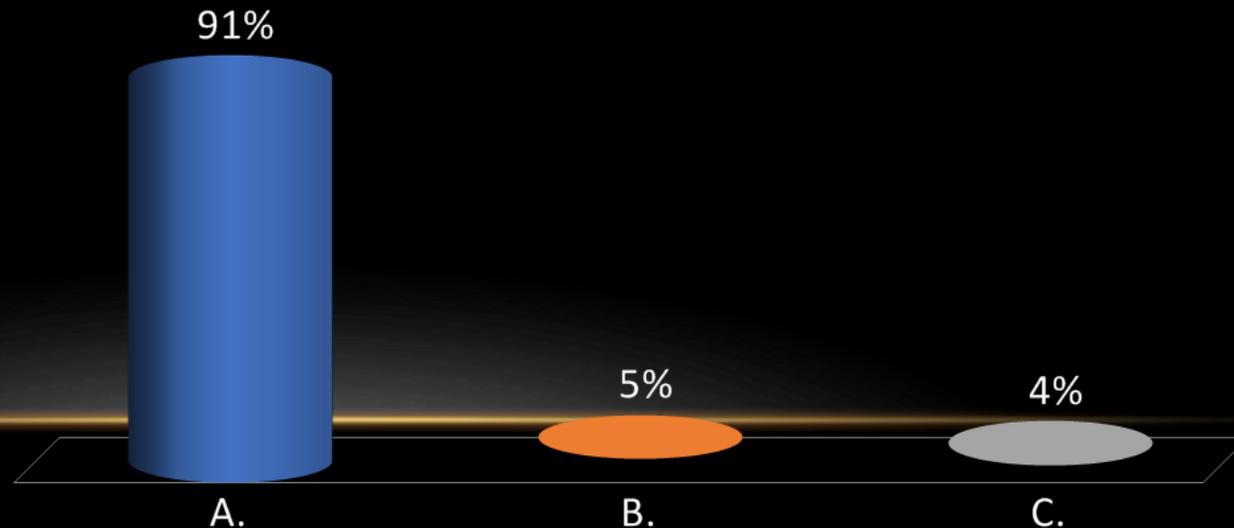
- **Meta-analysis 2, Prospective/Randomized 9, Retrospective 5**
- **Systematic Review of THA patients (Marques et al.)**
 - patients receiving local anesthetic infiltration to have a greater reduction in pain at 24 and 48 hours postoperatively



Recommendation: Unknown. PAls are an effective adjunct treatment for pain control following primary total joint arthroplasty (TJA), but their effectiveness and impact on the rates of SSIs/PJIs in the revision setting has not been investigated. The use of periarticular injections at the time of reimplantation can be performed at the surgeon's discretion.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Does simultaneous bilateral hip or knee arthroplasty (SBTHA or SBTKA) increase the risk of subsequent surgical site infections/periprosthetic joint infections (SSIs/PJIs) compared to unilateral or staged bilateral arthroplasty?

RESEARCHED BY:



Carles Amat Mateu MD,
Spain



Jiyong Chen MD,
China

Samih Tarabichi MD,
UAE



Literature:

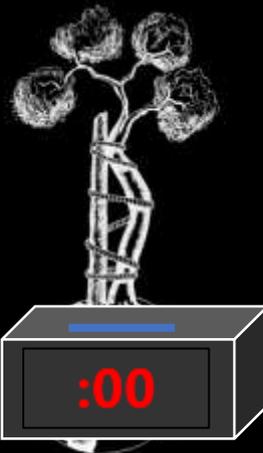
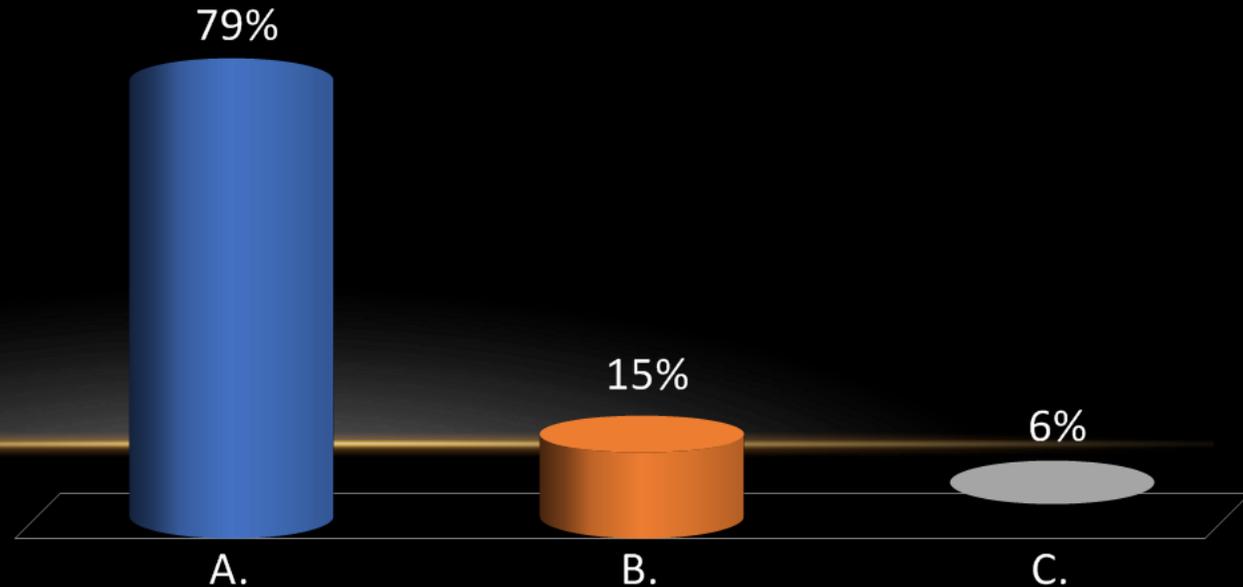
- **Meta-analysis 3, Prospective/Randomized 2, Retrospective 36**
- Meta-analyses: Hu et al. and Hussain et al. concluded that the infection rates were similar between the two groups.
- Other studies did not observe differences in the infection rate between simultaneous and unilateral or staged bilateral TKA.
- Fu et al.(16) in another meta-analysis concluded that simultaneous bilateral total knee arthroplasty was associated with a lower infection rate.
- There is only one prospective, randomized, controlled study in literature comparing simultaneous bilateral and staged hip arthroplasties, and no significant difference was found in the incidence of infection between the two hip replacement groups.



Recommendation: SBTHA or SBTKA does not increase the risks of SSIs/PJIs compared to unilateral or staged bilateral arthroplasty.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



1.7 - Prevention: Prosthesis Factors



Question 1: Are there implant materials that mitigate the risk for SSI/PJI after total joint arthroplasty?

RESEARCHED BY:

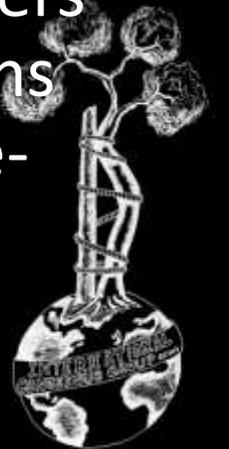
Paul Ducheyne MD, United States of America

Nusret Kose MD, Turkey



Literature:

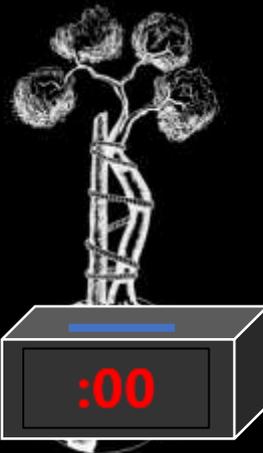
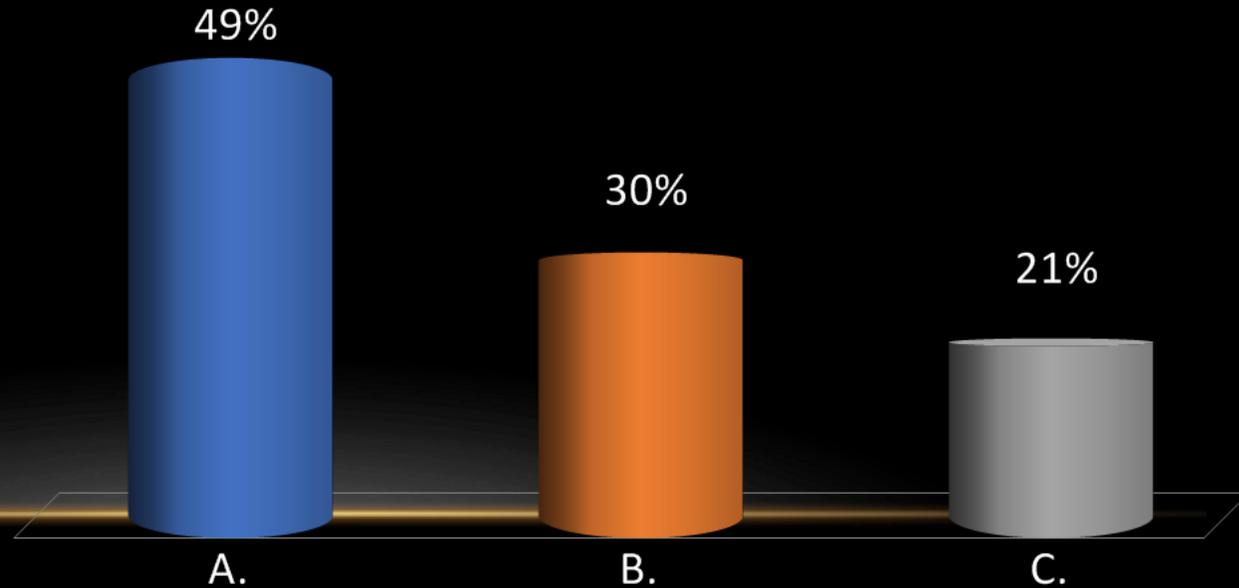
- Several types of metal coating are available, however more prospective randomized controlled trials that investigate postoperative infection rates of the reviewed coatings vs. uncoated control implants are needed
- Chemical modification of the implant surface has shown promise
 - Current immobilization studies focus mainly on binding of vancomycin
- Local delivery of antibiotics using antibiotic-loaded resorbable carriers is a very attractive strategy and the local antibiotic treatment options have the potential to become major tools in the treatment of bone-associated and implant-associated infections



Recommendation: There are various implant materials that can be utilized to reduce the chance for SSI/PJI in patients undergoing total joint arthroplasty.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does the type of fixation of an arthroplasty component influence the incidence of subsequent SSI/PJI?

RESEARCHED BY:



Mel Lee MD,
Taiwan



Philip Mitchell MD,
United Kingdom



Craig A. Aboltins MD,
Australia



Literature:

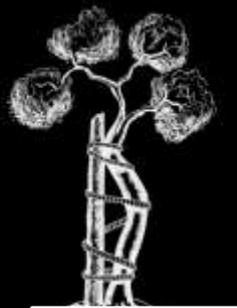
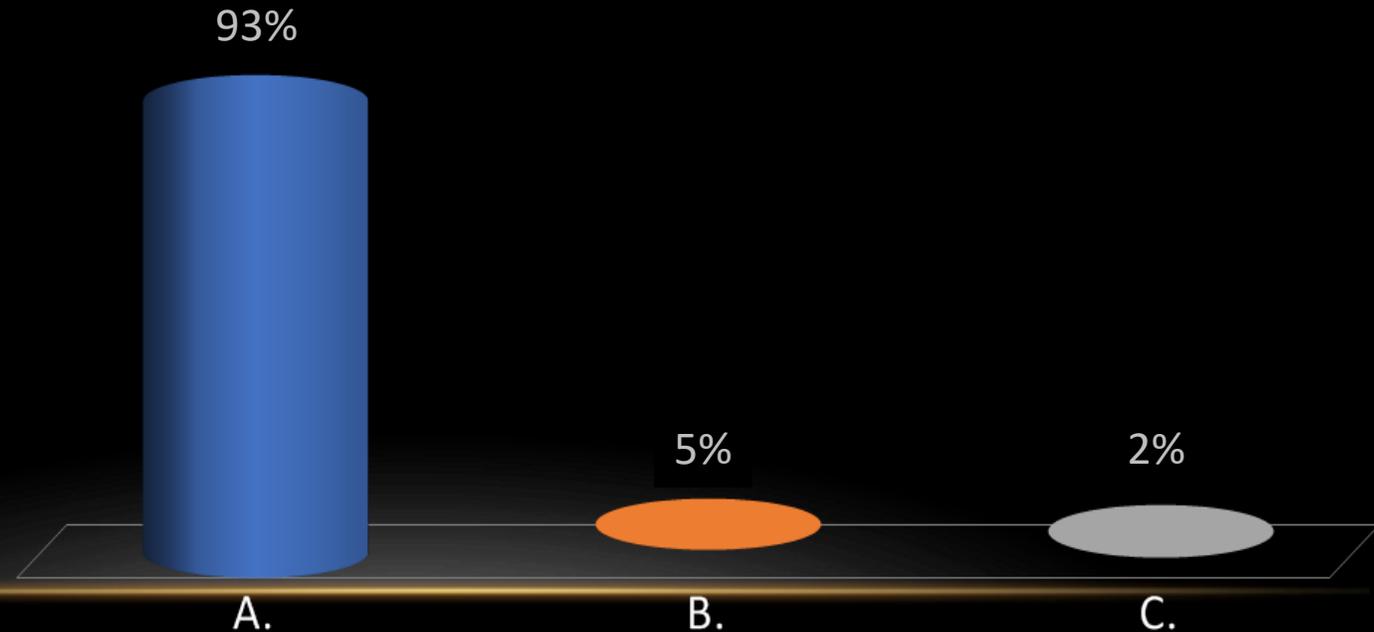
- **Meta-analysis 6, Prospective/Randomized 6, Retrospective 14**
- **Moderate evidence suggesting most of the studies were unable to reach a conclusion on the risk of PJI based on the type of fixation due to the infrequent occurrence of SSI/PJI and low number of subjects in the cohort.**



Recommendation: There is no difference in the rates of SSIs/PJIs after total hip arthroplasty (THA) or total knee arthroplasty (TKA) based on fixation of the prosthesis.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Does the surface (grit blasted, plasma sprayed, porous metal, porous beaded and hydroxyapatite coated) of uncemented THA components influence the rate of subsequent SSI/PJI?

RESEARCHED BY:



Valentin Antoci MD, Moldova

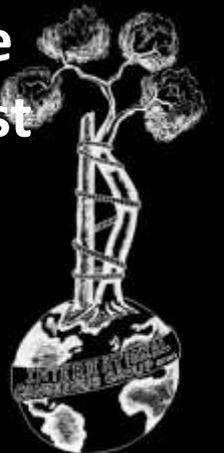


Constantinos Ketonis MD, USA



Literature:

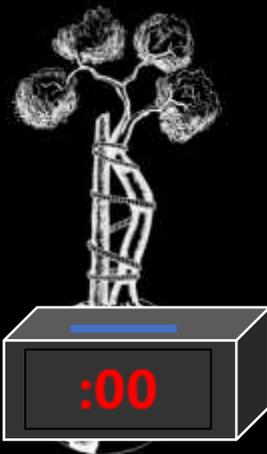
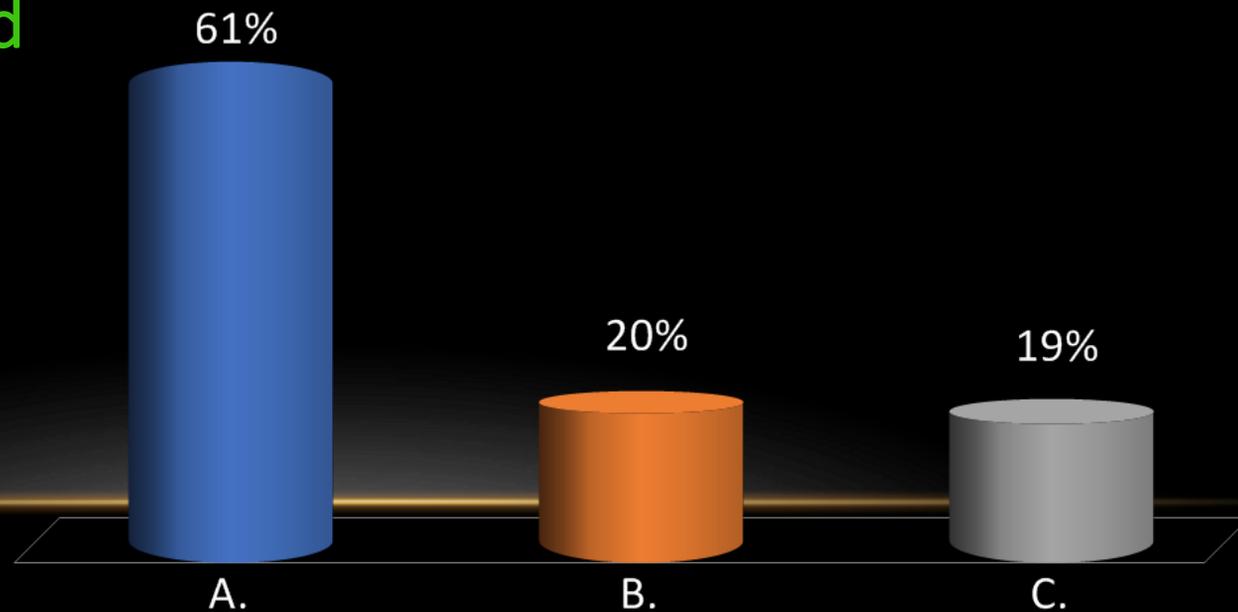
- **Meta-analysis 0, Prospective/Randomized 12, Retrospective 6**
 - **Grit blasting of titanium with zirconia has lower bacterial adhesion.**
 - **No difference was seen in bacterial colonization between polished and blasted surfaces**
 - **Plasma spray exhibits highest surface roughness (3.43um)**
 - **Registry data has shown no difference in revision rate comparing HA, uncemented porous or rough sand-blasted stems**
 - **“Race for the surface” theory postulates that roughened titanium provide an osteoconductive advantage , and hence, competitive advantage against infection**



Recommendation: The surface roughness, including porosity size, geometry and symmetry determines biocompatibility. Several studies have shown that the surface material influences bacterial adherence, with an ideal pore size dependent on bacterial size. Too small a pore size does not allow bacterial lodging. In recent studies, nanotexture of material has been found to be important with some surfaces with nanotubules showing anti-infective properties.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Does the type of bearing surface influence the incidence of SSI/PJI after total hip arthroplasty?

RESEARCHED BY:



Rihard Trebse MD,
Greece



Sumon Nandi MD,
USA



Literature:

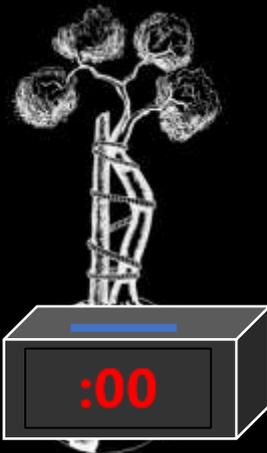
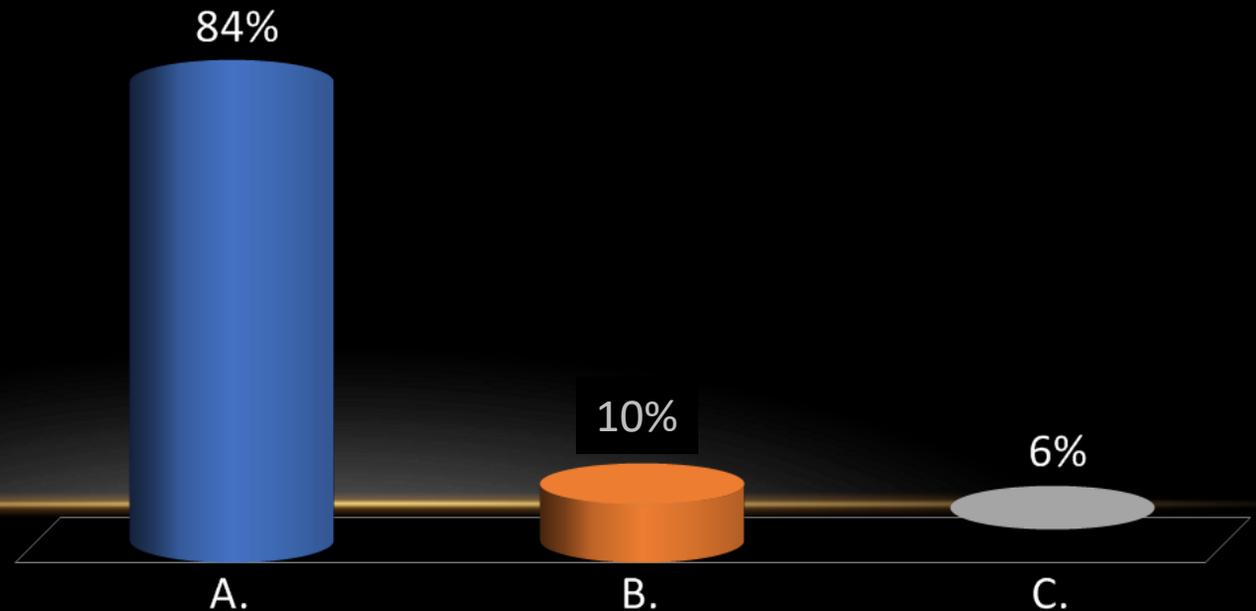
- **Meta-analysis 2, Prospective/Randomized 2, Retrospective 7**
- **Moderate to strong evidence suggesting higher infection rate with metal on metal but no difference in infection rate between metal-on-polyethylene, ceramic-on-ceramic, and ceramic-on-polyethylene bearings.**



Recommendation: There is a higher incidence of periprosthetic joint infection (PJI) with metal-on-metal total hip arthroplasty; however, there is no difference in risk of PJI among other bearing surfaces.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Does the use of a modular femoral neck during primary THA affect the risk of subsequent SSI/PJI?

RESEARCHED BY:



Hernan Prieto MD,
USA



Nils Hailer MD,
Sweden



Michael Cross MD,
USA



Mitchell Klement MD,
USA



Literature:

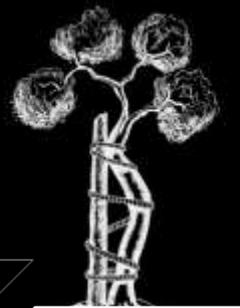
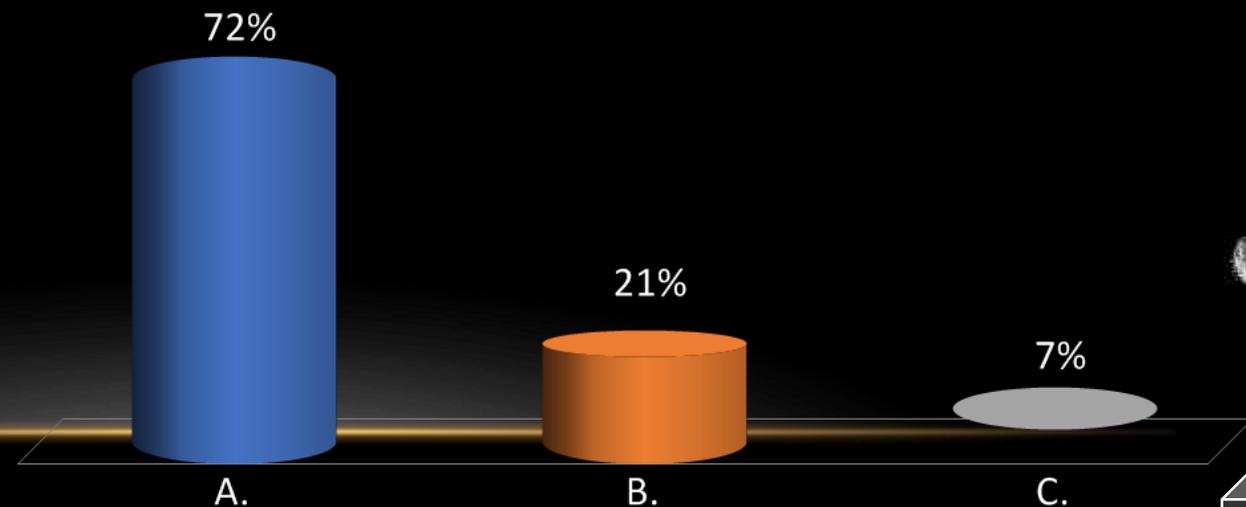
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 18**
- **Limited evidence suggesting that PJI must be included in the differential diagnosis of all symptomatic modular femoral neck THA using recently established criteria.**



Recommendation: Modular femoral neck implants are associated with increased revision rates due to hardware failure, metal corrosion, and adverse local tissue reaction (ALTR). In patients with failed THA as a result of use of a modular femoral neck, a higher incidence of subsequent SSI/PJI is expected.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 6: Can implant factors (i.e. type of bearing) influence the thresholds for serum and synovial markers in acute and chronic PJI?

RESEARCHED BY:



Kevin Perry MD, USA



Andrew A Freiburg MD, USA



AliSina Shahi MD, USA



Literature:

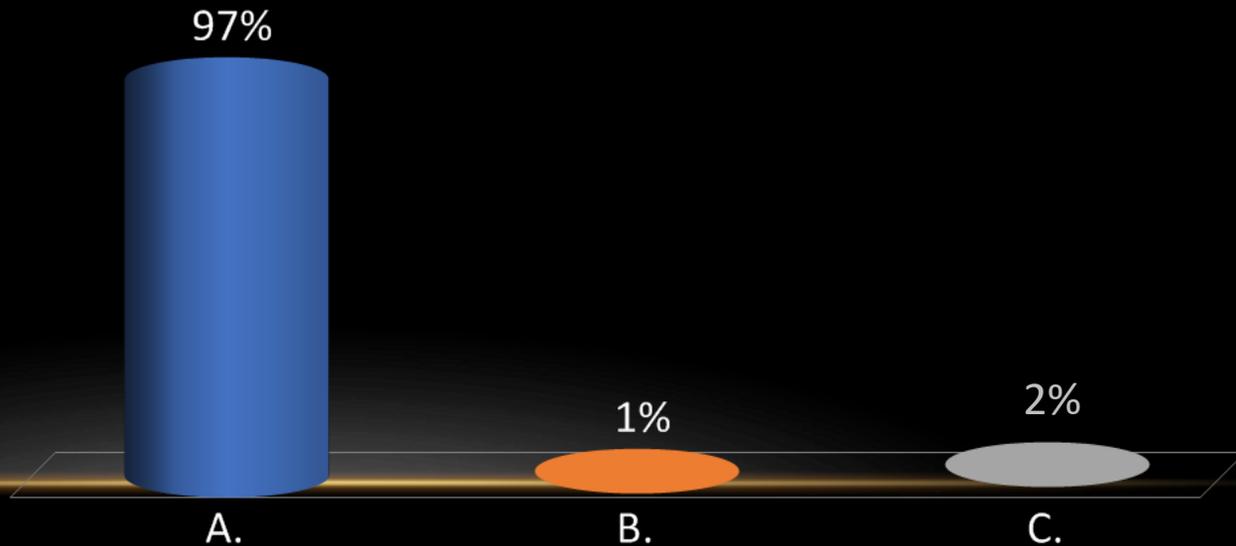
- Automated synovial cell counts and differentials in the setting of a failed metal-on-metal THA have been reported to be inaccurate (Wyles et al, Yi et al, Parvizi et al).
 - Manual cell count and differential preferred in this setting (Alijanipour et al)
- Yi et al. studied PJI in patients with failed MoM bearing surfaces and recommended a synovial WBC cutoff of 4,350 WBC/uL with
 - 100% sensitivity and 95% specificity
 - But low PPV of 43% and 39% for ESR and CRP, respectively, with MoM bearings.
- Kwon et al. reported that ESR and CRP have limited value PJI diagnostic value in dual taper modular implants with evidence of corrosion, but acknowledged the utility of ESR and CRP in excluding PJI.
 - Synovial WBC and differential sensitivity and specificity of 86% and 80%, respectively, when utilizing a synovial WBC cutoff of 730 cells/microliter.
 - Synovial PMN% cutoff >65% yielded a 100% sensitivity and 70% sensitivity.
- Okroj et al. evaluated alpha-defensin to diagnose PJI in the setting of ALTRs.
 - 26 patients reviewed with 1/26 (3.8%) meeting the MSIS criteria. The one PJI had a metal-on-polyethylene bearing surface with head-neck taper corrosion.
 - Of note, there were 8 falsely positive alpha-defensin tests. Authors concluded that in the setting on ALTRs, alpha-defensin testing can lead to a high rate of false positives



Recommendation: Yes. Different bearing surfaces such as metal-on-metal, metal-on-polyethylene, and dual taper modular stems in the setting of taper corrosion can influence the serum and synovial markers. Metal debris may interfere with automated cell counts. Manual cell counts are preferred when evaluating patients for periprosthetic joint infection (PJI) who have elevated synovial fluid metal levels. Optimal thresholds for serum and synovial markers for diagnosing PJI in these settings still need to be established.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 7: What can be done with a prosthesis that has been dropped on the floor or allowed to come into contact with a non-sterile portion of the operating room?

RESEARCHED BY:



Julio César Palacio Villegas



Peter Kay



Hamidreza Yazdi



Literature:

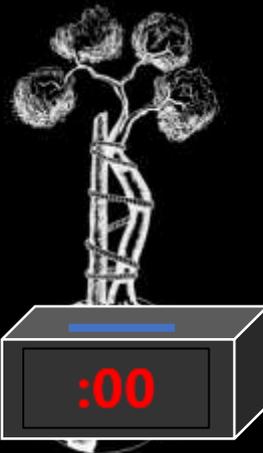
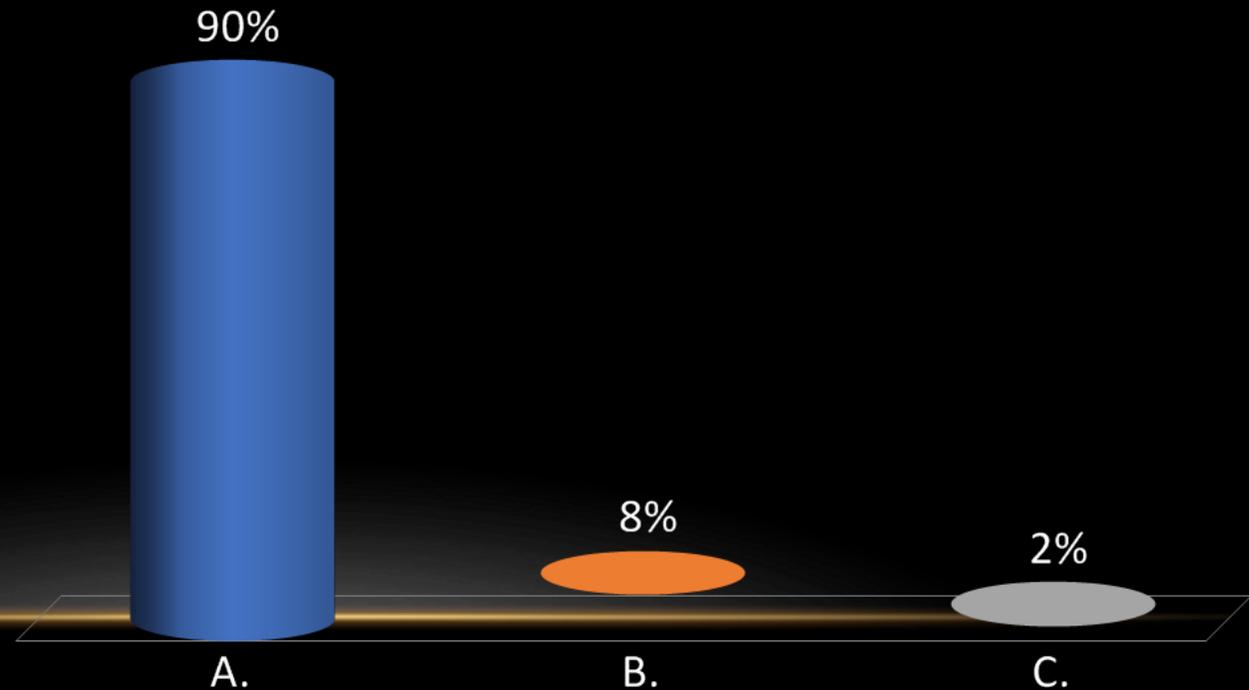
- **Meta-Analysis 0, Prospective/Randomized 0, Retrospective 11**
- Jung Hwa Park et al. evaluated the effect of cleaning and sterilization on titanium implant surface properties and cellular response.
 - The study indicated that re-cleaning and re-sterilized Ti implant resulted in surface alterations that could potentially affect the osseointegration of the surface and other biological behavior of the biomaterial in vivo
- A study by Martin et al. in 1996 demonstrated that Ti implant surfaces are unaffected by cleaning and re-sterilization. This suggests the possibility that implants, in the same patient, could be safely reused.



Recommendation: Cleaning, re-sterilization and reuse of dropped prostheses or implants is not permitted in most hospitals and should not be done. Only in extremely rare circumstances, such as the use of a custom implant, a dropped prosthesis may be decontaminated and used.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



1.8 - Prevention: Postoperative Issues



Question 1: Should patients with cellulitis following total joint arthroplasty be treated with antibiotic therapy?

RESEARCHED BY:



Adolph Yates,



Timothy Tan



Literature:

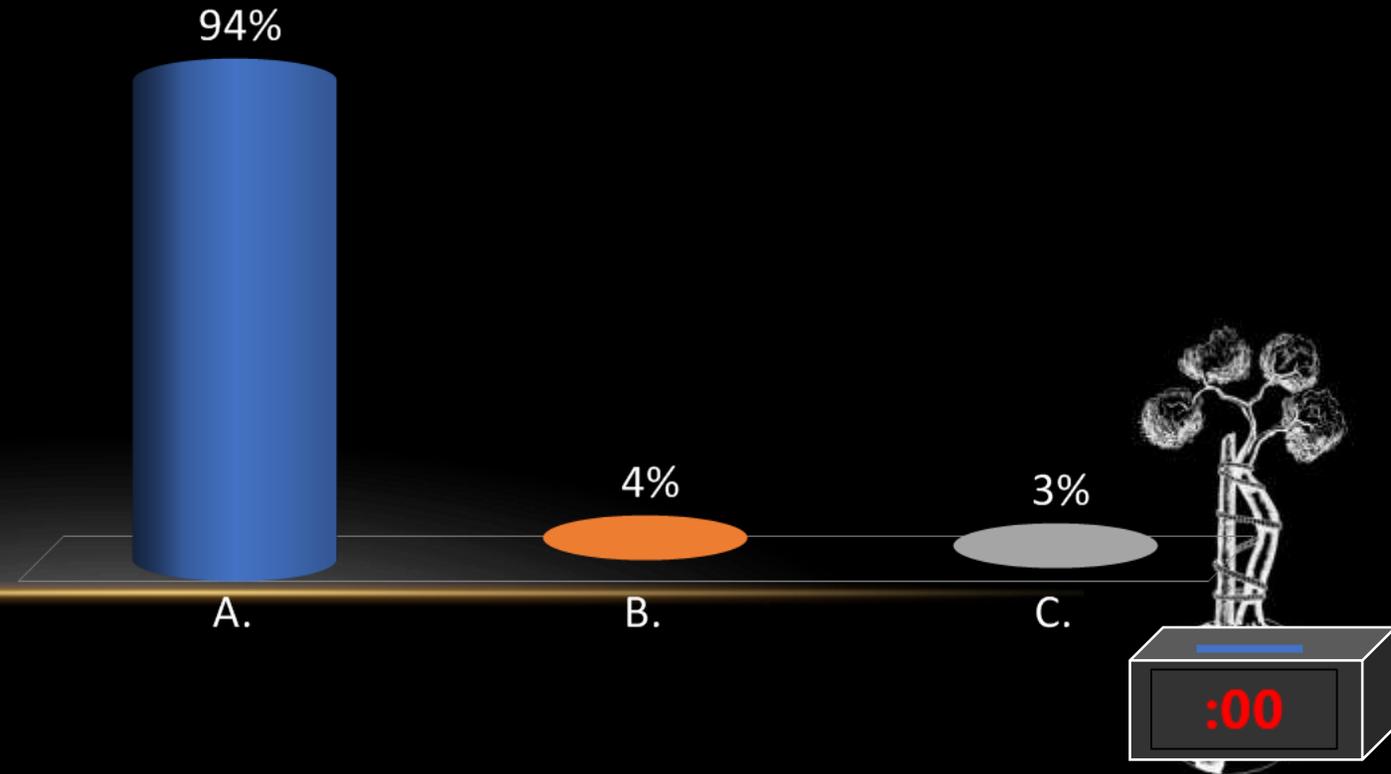
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 6
- One study reports their series of 45 cases of SSI in 3,000 joints with 6 years follow-up, without any evidence of recurrence of infection or progression to deeper periprosthetic infection, 13.3% of these patients required surgical treatment in addition to antibiotic therapy.
- Another case series found 18/1790 (1%) of patients developed MRSA SSI following THA. 6/18 were defined as superficial infections, 5 successfully treated with antibiotics, with one progression to deep infection.



Recommendation: Yes. When periprosthetic joint infection has been ruled out, it is reasonable to treat patients presenting with cellulitis with empiric antibiotics.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Is undergoing a colonoscopy or upper GI endoscopy after total joint arthroplasty associated with an increased risk of SSI/PJI? If yes, does antibiotic prophylaxis prior to a colonoscopy or upper GI endoscopy after total joint arthroplasty reduce the risk?

RESEARCHED BY:



Nicolaas Budhiparama, MD



Tricia Bravo, MD



Literature:

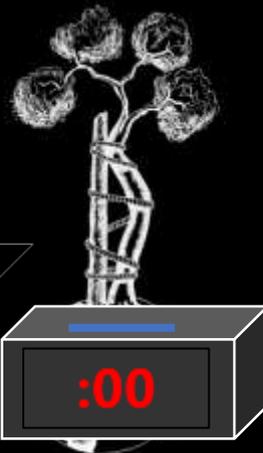
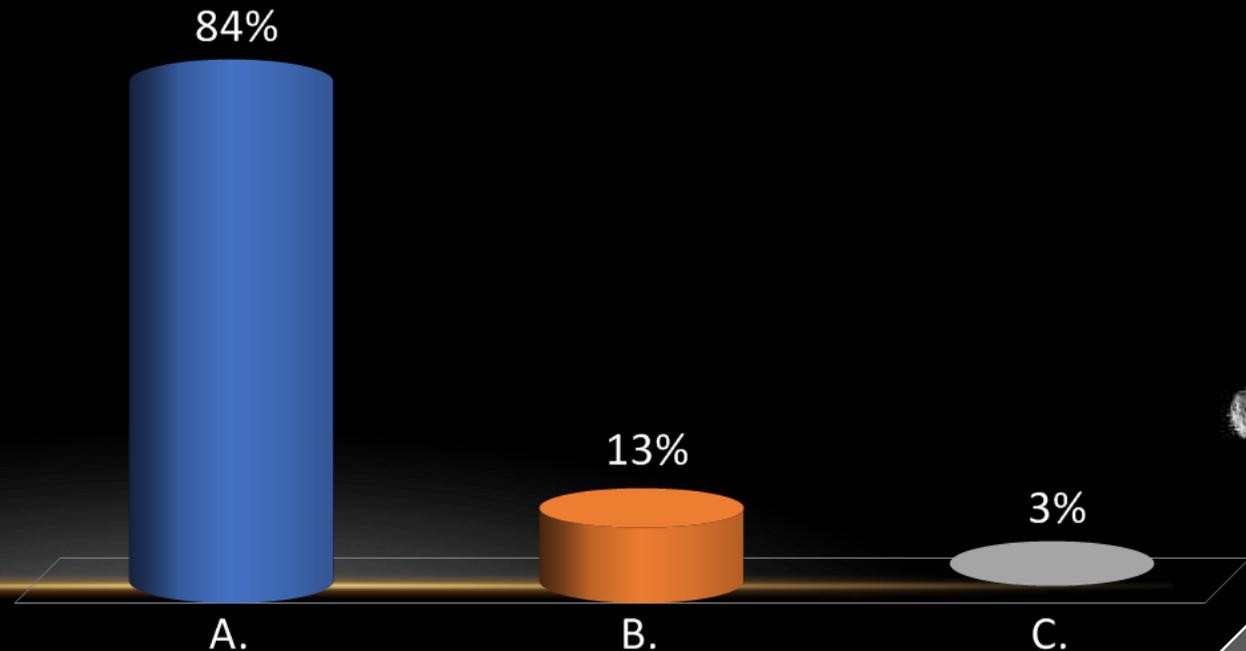
- Meta-analysis , Prospective/Randomized 3, Retrospective 8
- EGD is known to cause transient bacteremia but only four case reports exists of patients developing PJI within 2 weeks of an endoscopic procedure
- No evidence exists demonstrating a reduction in PJI rates with administration of antibiotic prophylaxis prior to endoscopic procedure



Recommendation: Colonoscopy and upper GI endoscopy have the potential to cause transient bacteremia, though the evidence is limited to support an associated risk of SSI/PJI. There is no evidence that administration of antibiotics prior to GI procedures decreases the risk of SSI/PJI and this practice should be avoided. Further research is needed to see if this practice may be beneficial in selected or high risk patients.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Section 2: Diagnosis

- 2.1 - Definitions
- 2.2 - Algorithm
- 2.3 – Laboratory Tests
- 2.4 – Pathogen Isolation, Culture Related
- 2.5 - Reimplantation



2.1 - Diagnosis: Definitions



Question 1: 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
Barry Brauser MD
Nicolaas Budhiparma MD
Antonia Chen MD
Craig Della Valle MD
Lorenzo Drago MD
Thorsten Gehrke MD
Luiz S Marcelino Gomes MD
Fares Haddad MD
Seung Beom Han MD
Yutaka Inaba MD

Jean-Yves Jenny MD
Per Kjaersgaard-Andersen,MD
Mel Lee MD
Adolfo Lina MD
Alex McLaren MD
Konstantinos Malizos MD
Rhidian Morgan Jones MD
Javad Parvizi MD
Patricia Peel MD
Salvador Rivero-Boschert MD
Carlo Romano MD
John Segreti MD
Alex Soriano MD

Ricardo Sousa MD
Mark Spanghel MD
Bryan Springer MD
Aaron Tande 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 α 2M, have high sensitivity and specificity in diagnosing the presence of PJI.



Recommendation: This is the proposed 2018 ICM criteria for 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	

Minor Criteria	Threshold		Score	Decision
	Acute [€]	Chronic		
Serum CRP (mg/L) <i>or</i> 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) <i>or</i> Leukocyte Esterase	10,000 ++	3,000 ++	3	
<i>or</i> Positive Alpha-defensin (signal/cutoff)	1.0	1.0		
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.

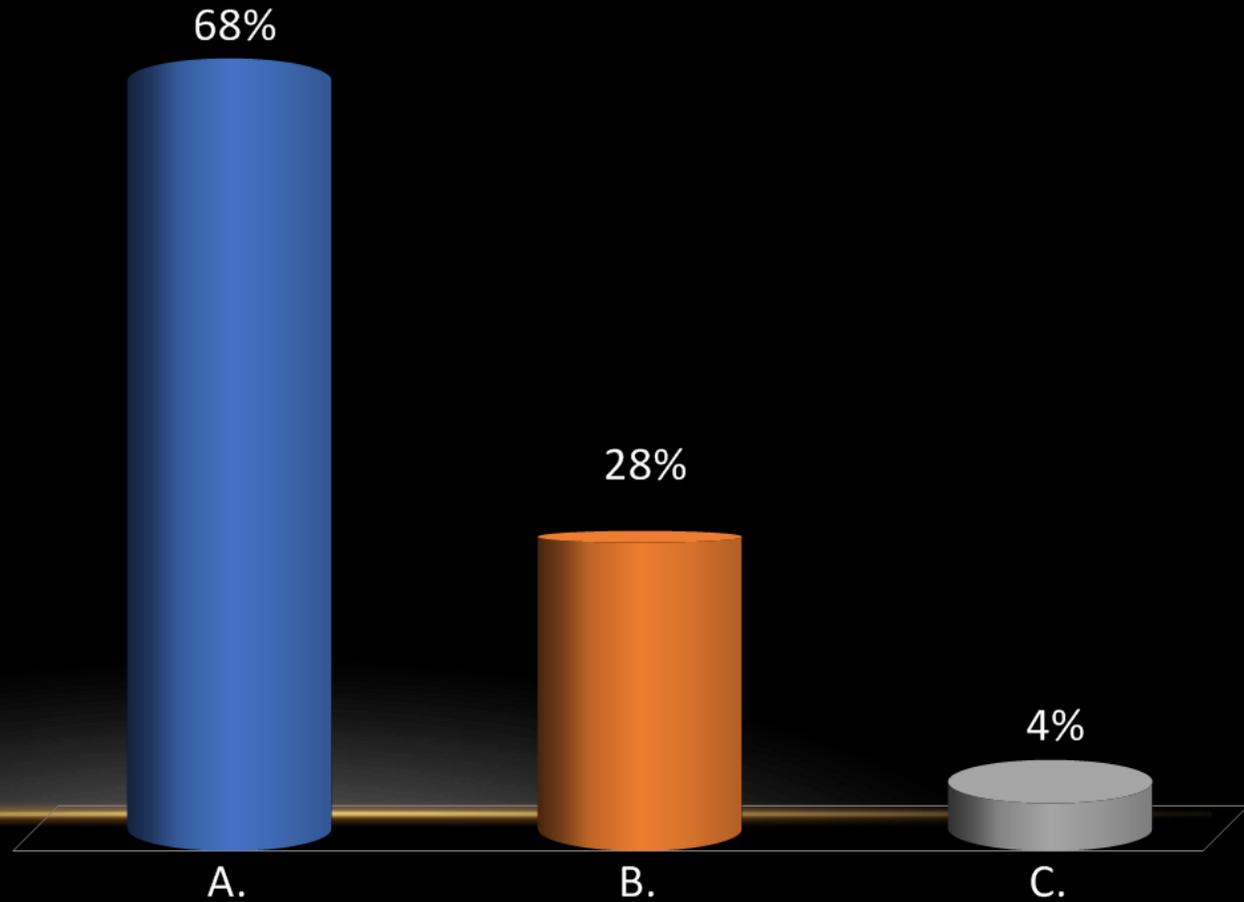
Level of Evidence: Moderate



Recommendation: This is the proposed 2018 ICM criteria for PJI:

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: What is the definition of septic arthritis in a native knee?

RESEARCHED BY:

Douglas Dennis MD

Ali Parsa MD

Jose Ricardo Pecora MD



Literature:

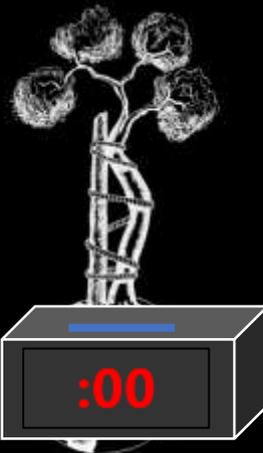
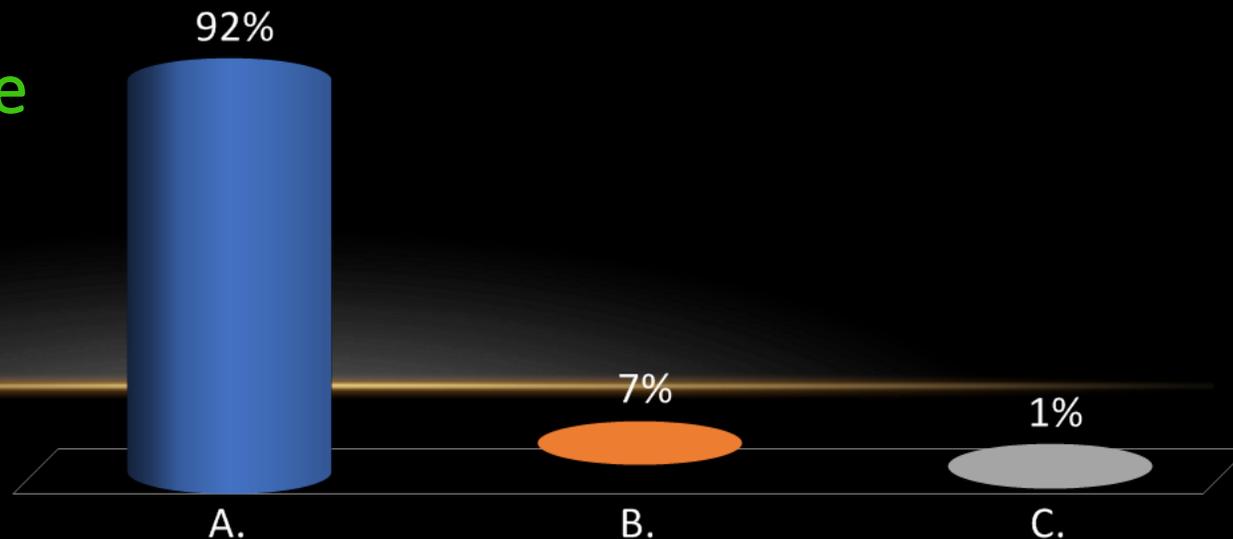
- **Meta-Analysis 1, Prospective/Randomized 2, Retrospective 19**
- A meta-analysis performed by Margaretten et al. in 2007 looking at clinical features of septic arthritis found that synovial fluid white blood cell (WBC) count and the percentage of Polymorphonuclear cells from arthrocentesis were the most powerful predictors for septic arthritis.
- Jennings et al. published a prospective study in 2017 that demonstrated that, in 166 aspirations of native knees, the false-positive rate for septic arthritis was 0%.



Recommendation: Native septic arthritis of the knee is a clinical diagnosis supplemented by relevant laboratory data. Signs of septic arthritis include painful effusion, limited range of motion and warmth. Elevated serum inflammatory markers, particularly C-reactive protein (CRP), synovial white blood cell (WBC) counts (50,000 cells/mm³), polymorphonuclear (PMN) cell count percentages (> 90%) and purulent appearance of the synovial fluid indicate a high likelihood of septic arthritis.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: How can superficial SSIs be differentiated from deep SSIs (i.e. PJI)?

RESEARCHED BY:



Konstantinos Malizos
MD, Greece



Gergios Komnos MD,
Greece



Literature:

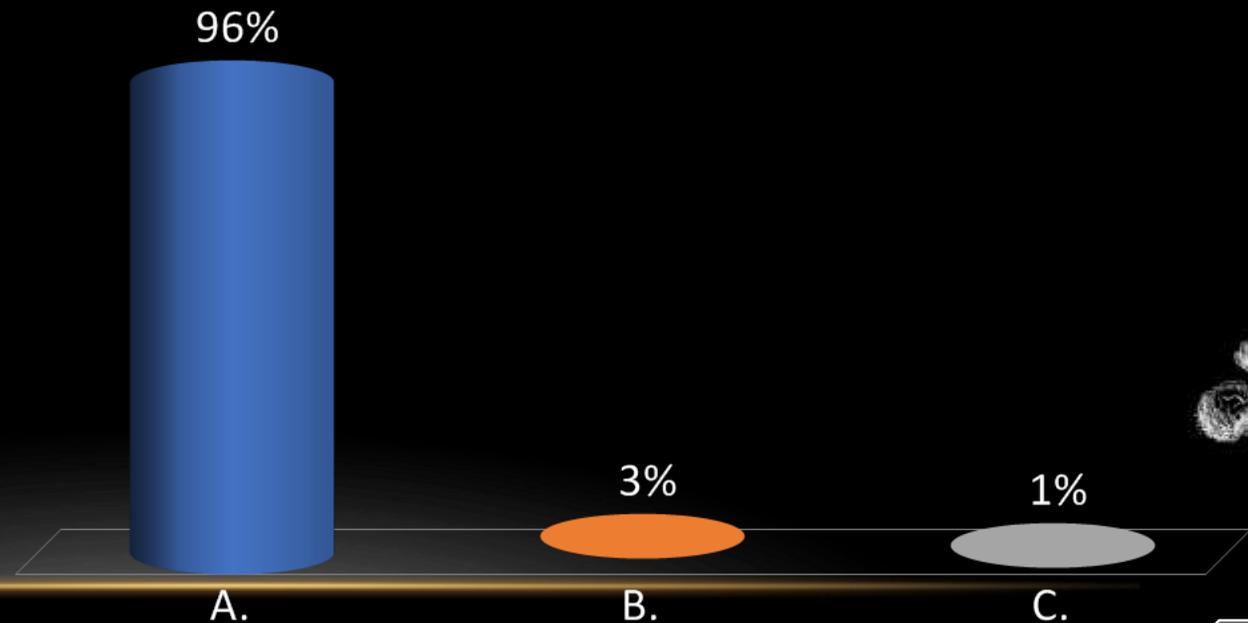
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 18**
- **CDC definition-** There is no clinical, laboratory, or imaging procedure to reliably allow differentiation between SSI and PJI or even between the three different subtypes of SSI. Furthermore, diagnostic criteria for superficial SSI, such as tenderness, redness, localized swelling, and local heat, have low inter-observer reliability (Allami, JBJS 2005). In the CDC definition, fever above 38⁰ Celsius is considered a clinical sign of deep incisional SSI. Nevertheless, it is difficult to differentiate the two without inspecting intra-articular.



Recommendation: There is no single objective clinical test or imaging approach established for differentiation between the superficial SSI, deep SSI, and PJI. We recommend that clinical evaluation, workup for infection, and early joint aspiration should guide the decision.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: How can hip septic arthritis be differentiated from toxic synovitis?

RESEARCHED BY:



Alexander Shope MD,
USA



Aresh Hashemi-Nejad
MD, UK



Literature:

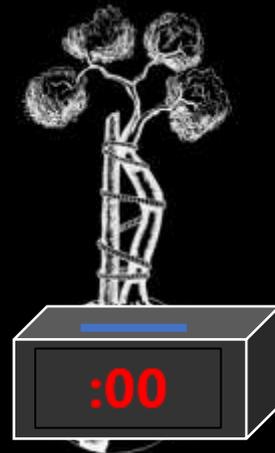
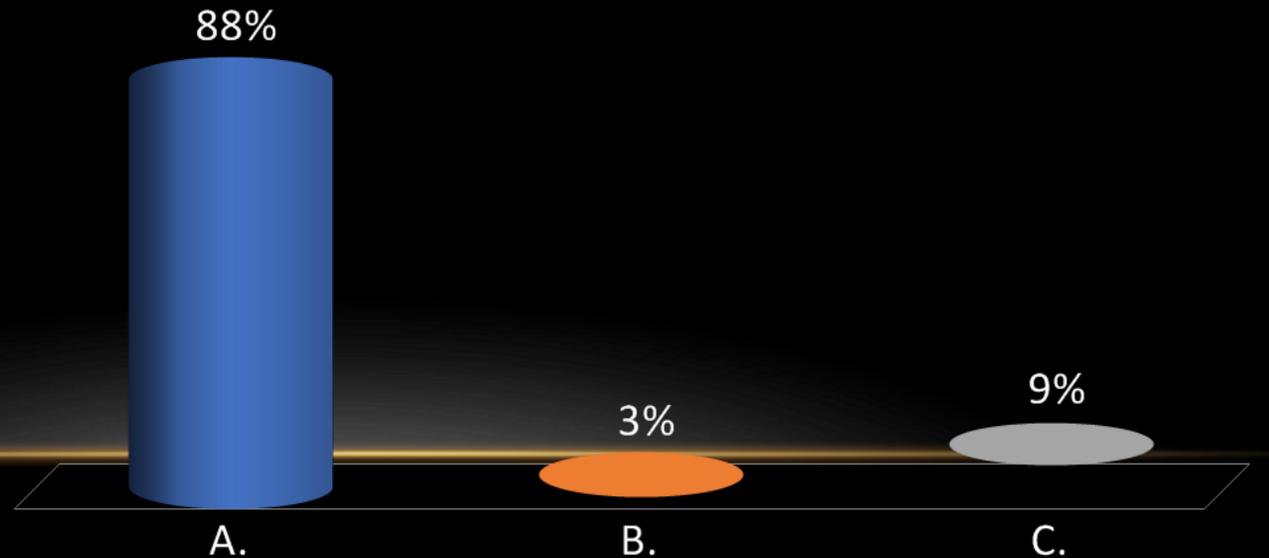
- **Meta-analysis 0, Prospective/Randomized 2, Retrospective 8**
- **Retrospective study followed by a prospective study to validate the algorithm (Kocher et al.)**
 - 4 predictive values
 1. inability or refusal to bear weight
 2. history of a fever (defined as an oral temperature $>38.5^{\circ}\text{C}$)
 3. a serum white blood cell count greater than 12,000 cells per cubic millimeter (cells/mm³)
 4. erythrocyte sedimentation rate (ESR) greater than 40 millimeters per hour (mm/hr)



Recommendation: Currently there is no single diagnostic test or step that can be performed in order to distinguish a patient with a septic hip from one with toxic synovitis non-invasively. Although algorithms have been created to aid in clinical decision making, there is not enough evidence to support their generalization across all populations, therefore more research still needs to be conducted before they can be fully validated. Clinical reasoning, evaluation and judgment should still be the standard for which physicians make the distinction between these pathologies as they care for their patients.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: What clinical findings (e.g. fever, erythema, reduced ROM) are most sensitive and specific for the diagnosis of PJI?

RESEARCHED BY:



Noam Shohat MD



Luiz S Marcelino Gomes MD

Literature:

- **Meta-Analysis 1, Prospective/Randomized 4, Retrospective 34**
- **Table 1.** Diagnostic accuracy of different clinical findings in periprosthetic joint infection (PJI)

Clinical Findings (References)	# PJI / Controls (# THA/ TKA/ Other)	Study design (Level of Evidence)	Sensitivity (95% CI)	Specificity (95% CI)
Pain ((Petti 2015), (Jenny 2016))	95 / 237 (77/ 18/ 0)	(Petti 2015), (Jenny 2016) Retrospective cohort (III)	57.9 (47.3 – 67.9)	28.3 (22.6 – 34.5)
Fever ((Teller 2000), (Jenny 2016))	65 / 205 (62/ 3/ 0)	(Teller 2000) Retrospective cohort (III)	13.8 (6.5 – 24.7)	96.1 (92.5 – 98.3)
Periarticular Inflammation ^a ((Berbari 1998), (Teller 2000), Petti 2015)	536 / 700 (316/ 220/ 0)	(Berbari 1998) Matched 1:1 Case- control (III)	14.9 (11.9 – 18.4)	94.7 (92.8 – 96.2)
Superficial disturbances ^b ((Surin 1983), (Berbari 1998), Petti 2015, (Jenny 2016), (Berbari 2000))	930 / 1807 (538/392/ 0)	(Surin 1983) Retrospective cohort (III) (Berbari 2000) Case control (III)	23.6 (21.3 – 26.1)	88.6 (87.0 – 90.0)
Deep involvement ^c ((Portillo 2012))	24 / 62 (4/ 17/ 3)	(Portillo 2012) Prospective cohort (II)	43.7 (29.5 – 58.8)	100.0 (97.0 – 100.0)

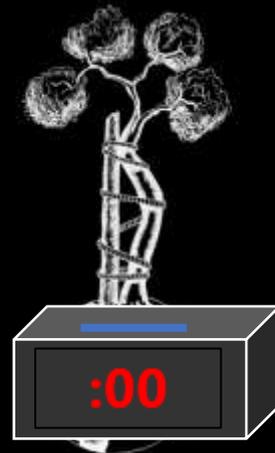
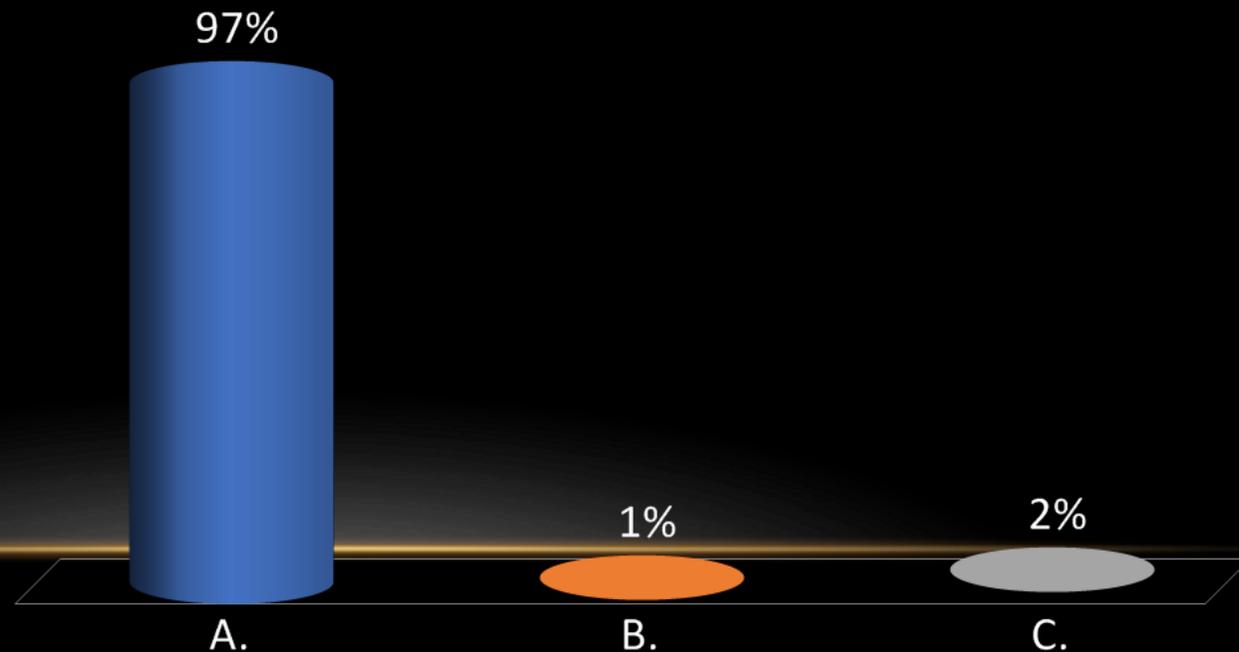
^a Including effusion/swelling, warmth, and/or erythema, ^b Including delayed healing, non-purulent wound drainage, and/or superficial dehiscence, ^c Including sinus tract, suppuration, purulent drainage, abscess, and/or extensive necrosis.



Recommendation: A painful prosthetic joint is the most sensitive but least specific clinical finding in PJI. Signs of deep tissue involvement (sinus tract, purulence, abscess and extensive necrosis) are the most specific signs. It is important to note that clinical findings differ notably based on the type of joint involved (hip or knee) as well as to the timing and presentation of PJI (early postoperative, acute hematogenous and chronic).

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 6: Should intraoperative purulence be considered as a definitive sign of PJI?

RESEARCHED BY:



Javad Mortazavi, MD



Erik Hansen, MD



Literature:

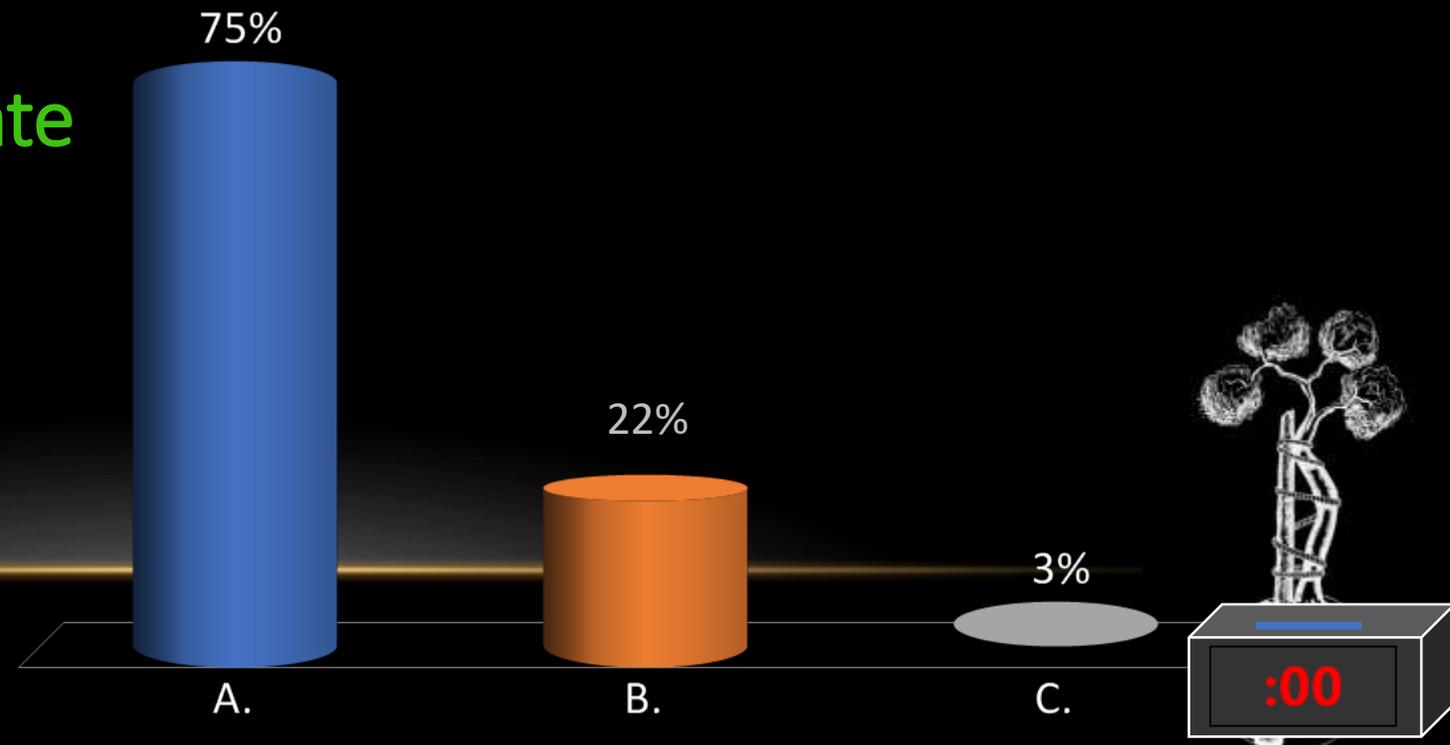
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 19
- Purulence is a subjective measure which can be present in aseptic conditions
- Purulence has acceptable sensitivity and PPV but low specificity and NPV in diagnosing PJI



Recommendation: Intraoperative purulence should NOT be considered a definitive sign of PJI. The definition of purulence is subjective and is neither a sensitive, nor specific diagnostic marker of PJI. A validated, objective definition for purulence due to infection is required to set purulence as a diagnostic criterion for PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 7: Is aseptic loosening associated with an undiagnosed PJI?

RESEARCHED BY:

Juan C Martinez Pastor MD, Spain

Derek Amanatullah MD, USA

Stuart Goodman MD, USA



Literature:

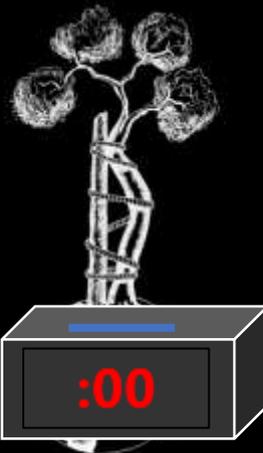
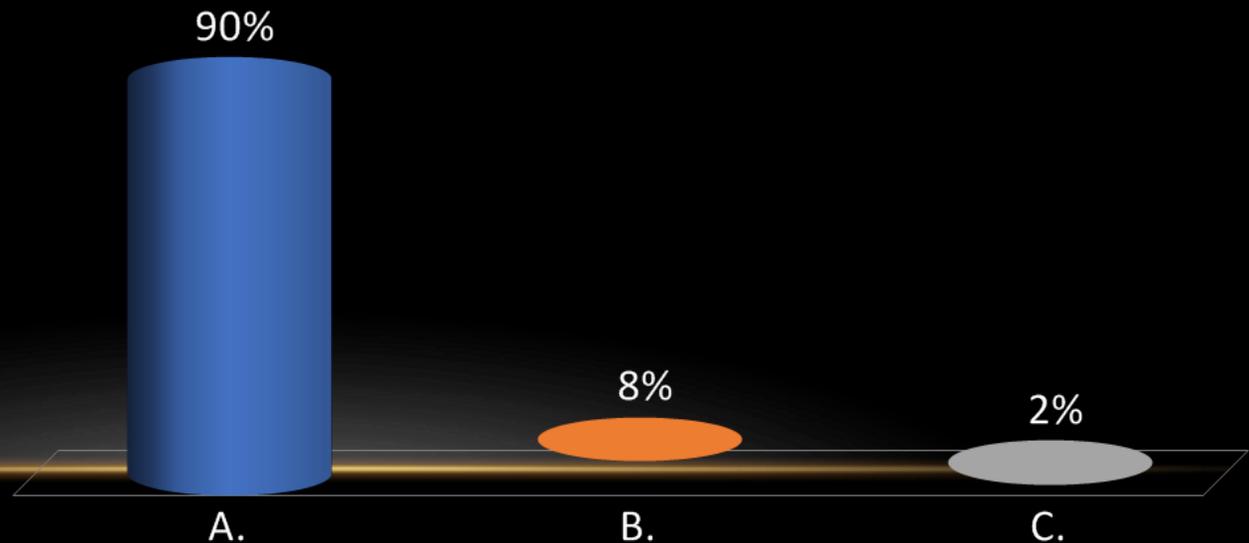
- **Reported prevalence of unexpected positive cultures in presumed aseptic revision ranges from 5.9%-23.9%**
 - There is the possibility that microorganisms live on implants without any signs of infection
- **Some authors have related early aseptic loosening to hidden prosthetic joint infection**
- **It is likely that a periprosthetic joint infection is present in a greater number of cases with implant loosening than previously suspected**
 - More detailed studies are required to determine the true incidence of loosening due to infection



Recommendation: Some percentage of aseptic loosening are due to culture negative infection, since up to 10% of culture negative cases contain bacteria when screened by molecular methods. Whether this correlates to undiagnosed infection causing aseptic loosening remains unclear. Understanding this issue is limited by the ability of bacterial culture to function as an effective gold standard for detecting infection. The role of molecular techniques such as next generation sequencing in this setting needs to be explored.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 8: Can PJI be assigned a high or low grade? If so, what is the definition of each grade?

RESEARCHED BY:



Geert Meermans MD,
Netherlands



Brian Hamlin MD,
USA



Ed McPherson MD, USA



Literature:

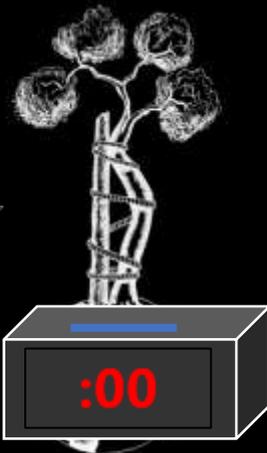
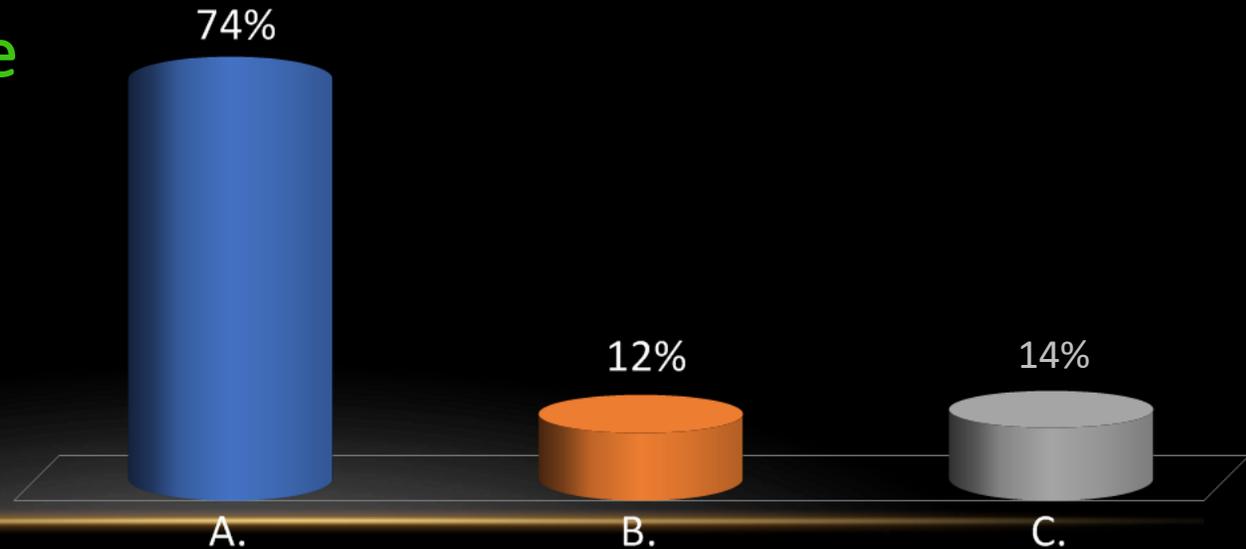
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 11**
- Numerous comorbidities, medications, and treatments can suppress immune system function and alter the course of a PJI
- Use of the McPherson schema is recommended as a starting point for grading PJI, as this system demonstrates outcomes correlating with worsening host *and* limb scores.



Recommendation: Yes, Periprosthetic joint infection (PJI) can be scored and assigned an “infection grade.” At this juncture, we recommend using the McPherson schema as a starting point for grading PJI, as this system demonstrates outcomes correlating with worsening host and limb scores. We suggest this schema (or a modified version) as a starting point until an international workgroup establishes a codified staging system.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



2.2 - Diagnosis: Algorithm



Question 1: Do you agree with the American Academy of Orthopaedic Surgeons' algorithm for diagnosis of Periprosthetic Joint Infection?

RESEARCHED BY:



Timothy L. Tan MD, USA



Javad Parvizi MD, USA



Craig Della Valle MD, USA

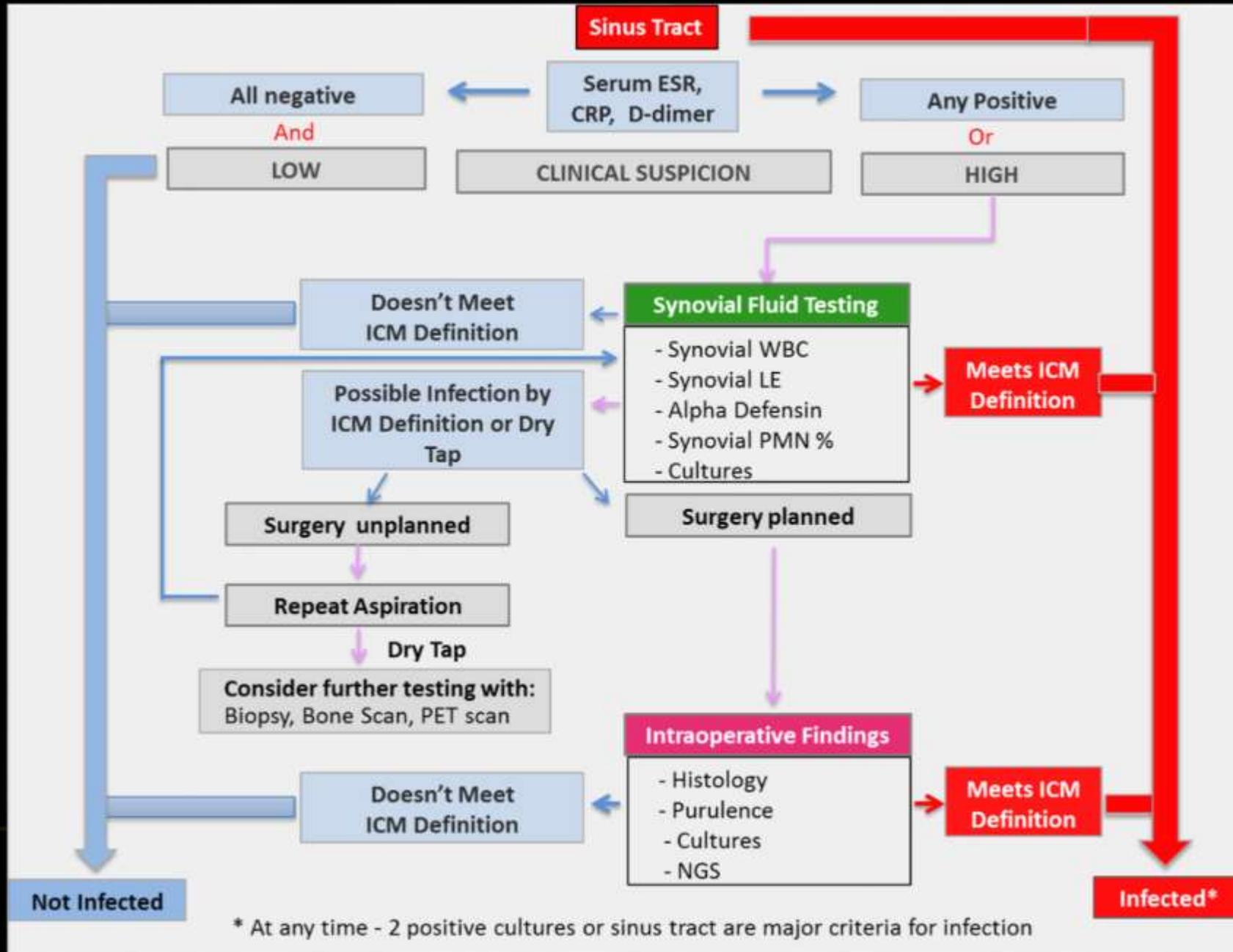


Literature:

- 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:



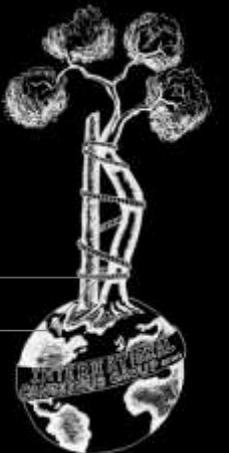
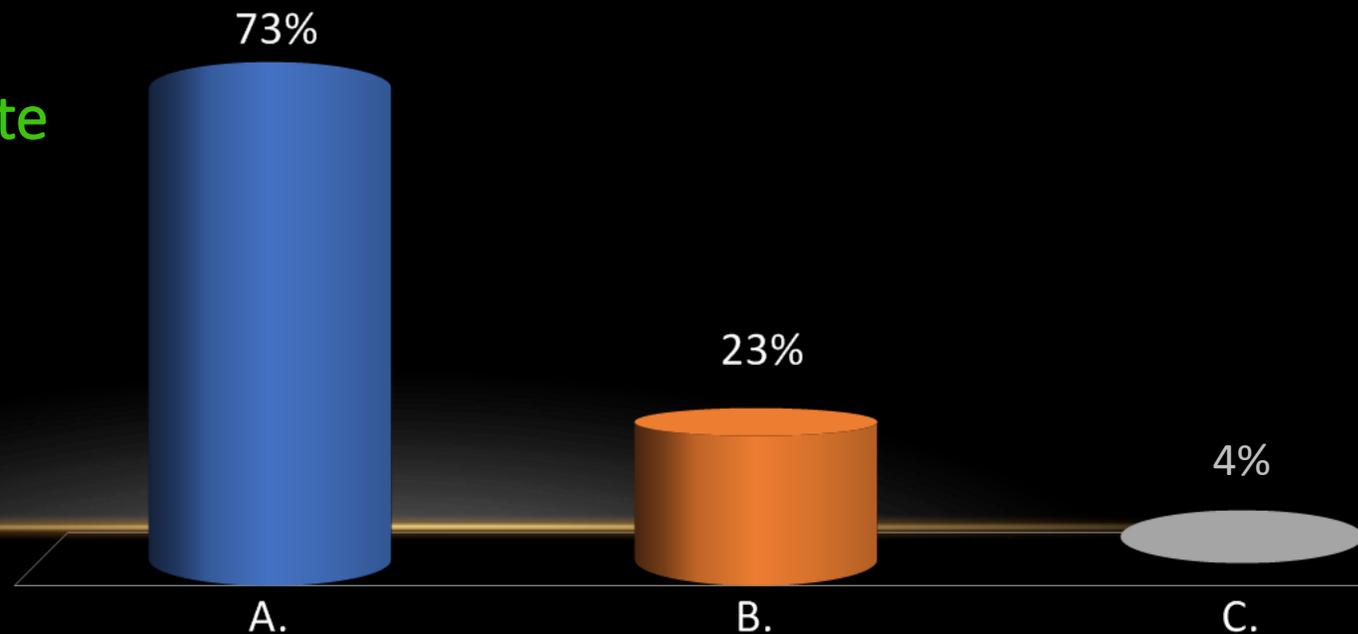
Recommendation: Yes. However, since the introduction of the AOS algorithm for diagnosis of PJI numerous new tests and diagnostic modalities have become available. The proposed evidence-based and validated algorithm includes the guidelines from AOS and the 2013 International Consensus Meeting on PJI.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

Level of Evidence: Moderate

A. Agree

B. Disagree

C. Abstain



Question 2: Are there any contraindications to knee or hip aspiration prior to revision surgery?

RESEARCHED BY:



Mahmoud Abdel Karim MD,
Egypt



Derek Ward MD, USA



Jonathan Danoff MD, USA



Literature:

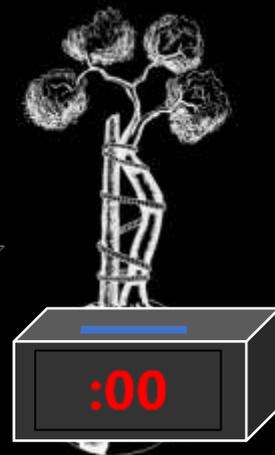
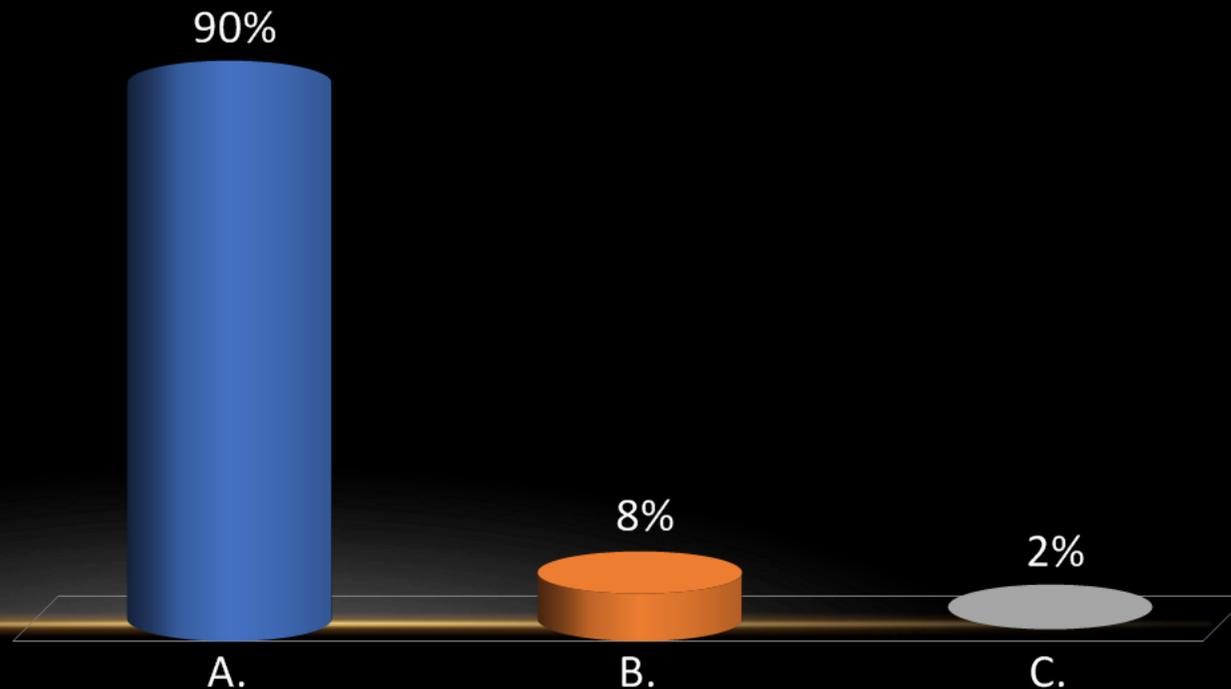
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 6**
- **No publications specifically address contraindications to aspiration**
- **Clinical situations in which surgeons may consider avoiding aspiration include:**
 - Cellulitis or skin lesions overlying site of aspiration
 - Anticoagulation (minimal evidence for increase in complications)



Recommendation: There are no clearly identified contraindications to aspiration of the knee or hip joint performed as part of the patient work-up for infection.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain

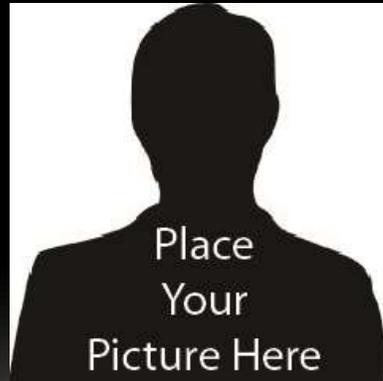


Question 3: In the setting of a dry tap, should lavage with a fluid be performed?

RESEARCHED BY:



Faiz Shivji MD,
UK



Riccardo Compagnoni
MD, Italy



Ernest Guerra
MD, Spain



Literature:

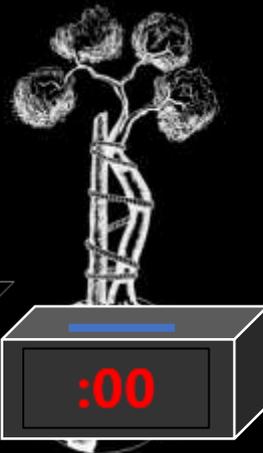
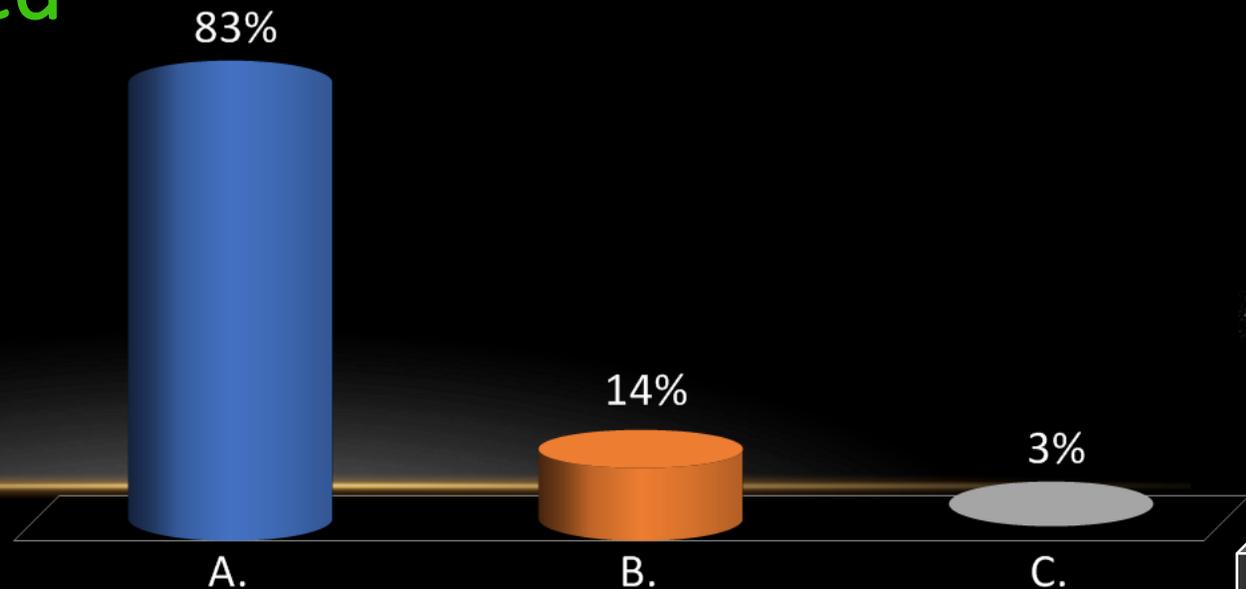
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 16**
- **Retrospective review (Newman et al.) in infected and non-infected hips comparing aspiration with or without saline lavage**
 - Aspirations performed without lavage yielded positive culture in 84% [95% confidence interval (CI), 81%–90%]; but in the saline lavage group, positive culture were found in 76% [95% CI, 76%–86%].
 - no difference in the WBC count or PMN percentage in infected versus non-infected hips when using saline lavage
 - saline lavage was not recommended for diagnosis of persistent infection
- **Retrospective review (Somme et al.) use of lavage to aid in the diagnosis of PJI**
 - 109 patients for hip revision
 - Of the 109 aspirates, 23 were gained using lavage, and 10 of these patients were correctly diagnosed with infection, with the remaining 13 patients found to not have an infection



Recommendation: We recommend against injection of normal saline or other fluids into a joint that did not yield any synovial fluid (dry tap) and is being investigated for periprosthetic joint infection; except in certain circumstances (a dedicated radiologist performing aspirate in a sterile fashion)

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: In patients with multiple arthroplasties in place who have developed PJI of one joint, should other joints be investigated for PJI also?

RESEARCHED BY:



Georgios Komnos
MD, Greece



Akos Zahar MD,
Germany



Thorsten Gehrke
MD, German



Literature:

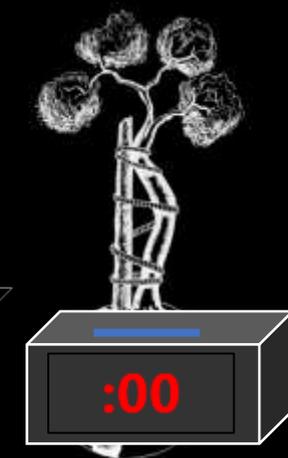
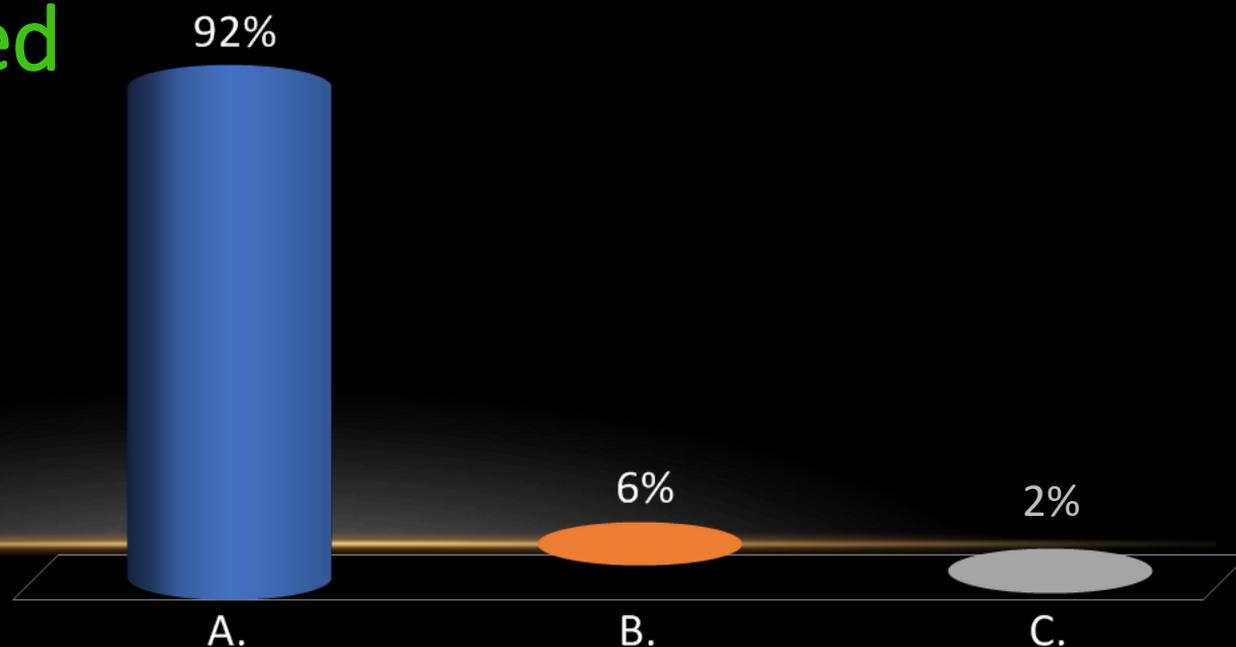
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 18**
- Retrospective review (Luessenhop et al.)
 - 19% of different joint infection among 145 patients with more than one joint in place at initial PJI
 - Also identified rheumatoid arthritis as a risk factor among these patients
- Retrospective review (Haverstock et al.)
 - 6.3% risk of a subsequent PJI of a total 206 patients
 - They identified the same microbe of the subsequent PJI in only 2.9%.



Recommendation: We recommend that when a patient develops a PJI in one joint, the other total joint arthroplasties should be examined clinically and if suspicion for PJI remains, or the patient is immunocompromised, they should be aspirated.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Are point-of-care/rapid tests for diagnosing PJI useful?

RESEARCHED BY:



Akos Zahar MD,
Germany

Jeroen Neyt MD,
Belgium

Cesar H Rocha MD,
Colombia

Thorsten Gehrke
MD, Germany



Literature:

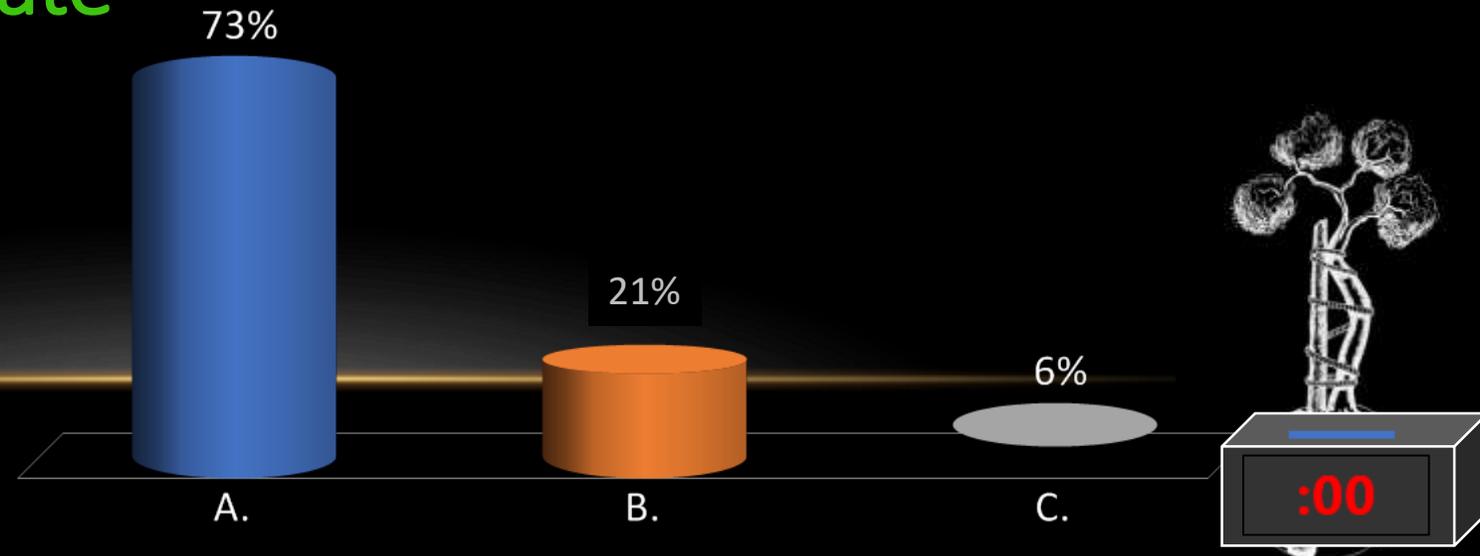
- **Meta-analysis 3, Prospective/Randomized 0, Retrospective 24**
- **Systematic review of Leucocyte esterase literature**
 - Extracted data from 11 original papers and 4 review articles
 - Pooled data (n=2,061 patients) revealed a sensitivity of 85.7%; specificity of 94.4% ; PPV of 84.3%; and NPV of 94.0%
- **Systematic review of Alpha-defensin laboratory test literature**
 - Extracted data from 6 original papers and 1 review article
 - Pooled data (n=486 patients) revealed a sensitivity of 78.5%; specificity of 93.3% ; PPV of 87.2%; and NPV of 90.2%
- **Meta-analysis of Alpha-defensin lateral flow test (Suen et al.)**
 - Pooled sensitivity 77.4% and specificity 91.3%



Recommendation: Yes, there are several useful point-of-care tests which can be added to the diagnostic workup of PJI. A number of studies support the usefulness and reliability of the leukocyte esterase (LE) test strip and alpha-defensin lateral flow test kit. Diagnostic criteria for PJI should be updated and consider including these tests.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 6: What is the prevalence of culture-negative infections and what are the diagnostic protocols for further investigating these cases?

RESEARCHED BY:



Karan Goswami MD,
United Kingdom



Marie-Jacque Reisener MD,
Germany

Pedro Foguet MD, United
Kingdom



Literature:

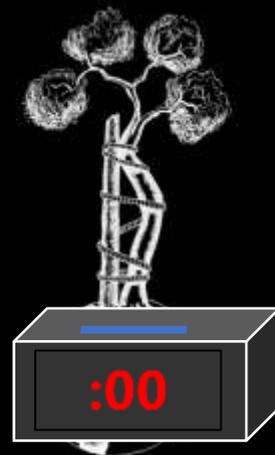
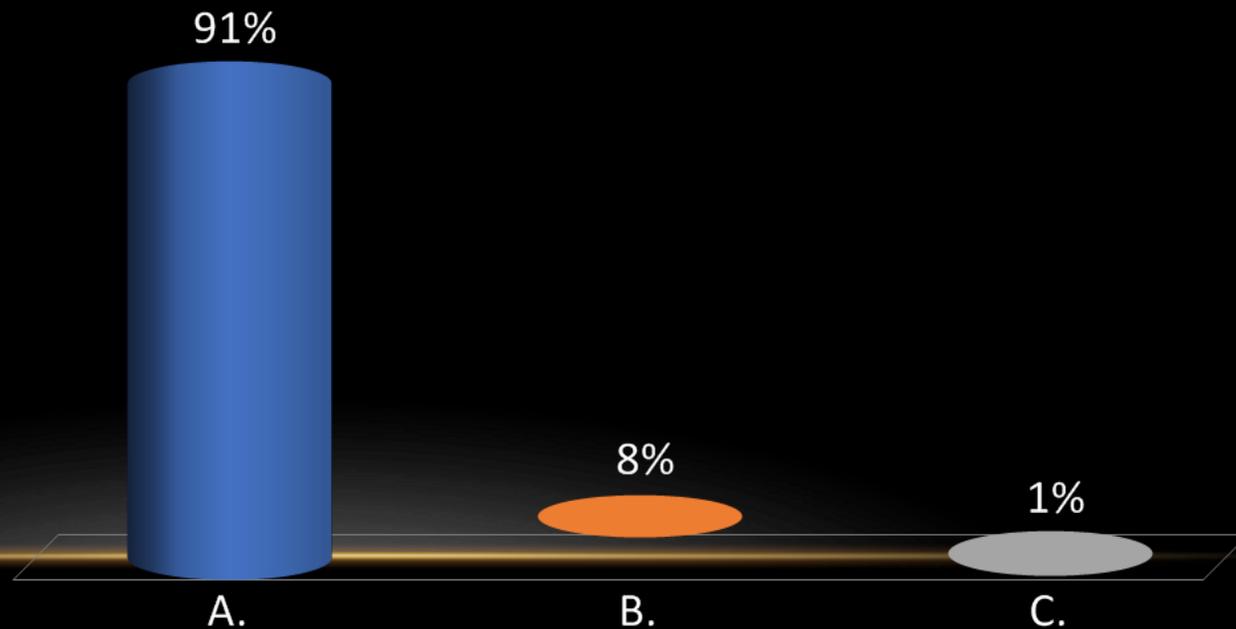
- **Meta-analysis 1, Prospective/Randomized 1, Retrospective 6**
- **A meta-analysis and comparative studies indicate that CN PJI's are associated with older age, smoking, referral from outside institutions, pre-op antibiotic tx, and post-operative wound drainage**
- **A meta-analysis of the current literature reports that 46% of CN PJI were caused by fungi, 43% by mycobacteria and 11% by other bacteria such as *Listeria monocytogens*, *Propionibacterium acnes*, Brucella, Coxiella burnetii and others**
- **PCR is a promising molecular technique being used to identify CN organisms**
 - The extreme sensitivity of PCR makes it easy to amplify contaminated samples so caution must be taken to keep the preparation process sterile, and PCR is not currently a first line diagnostic tool



Recommendation: The reported prevalence of CN-PJIs in the hip or knee has ranged from 5-42%. Diagnostic protocols for further investigating these cases include repeat sampling, longer incubation of culture samples, sonication of implants, the use of dithiothreitol (DTT) technology, polymerase chain reaction (PCR) and next generation sequencing (NGS).

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 7: Do patients with adverse local tissue reaction (ALTR) have a higher incidence of PJI?

RESEARCHED BY:



Benjamin A McArthur MD, USA



Michael Cross MD, USA



Literature:

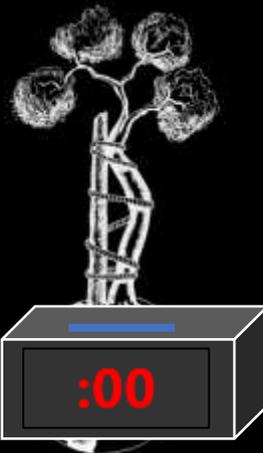
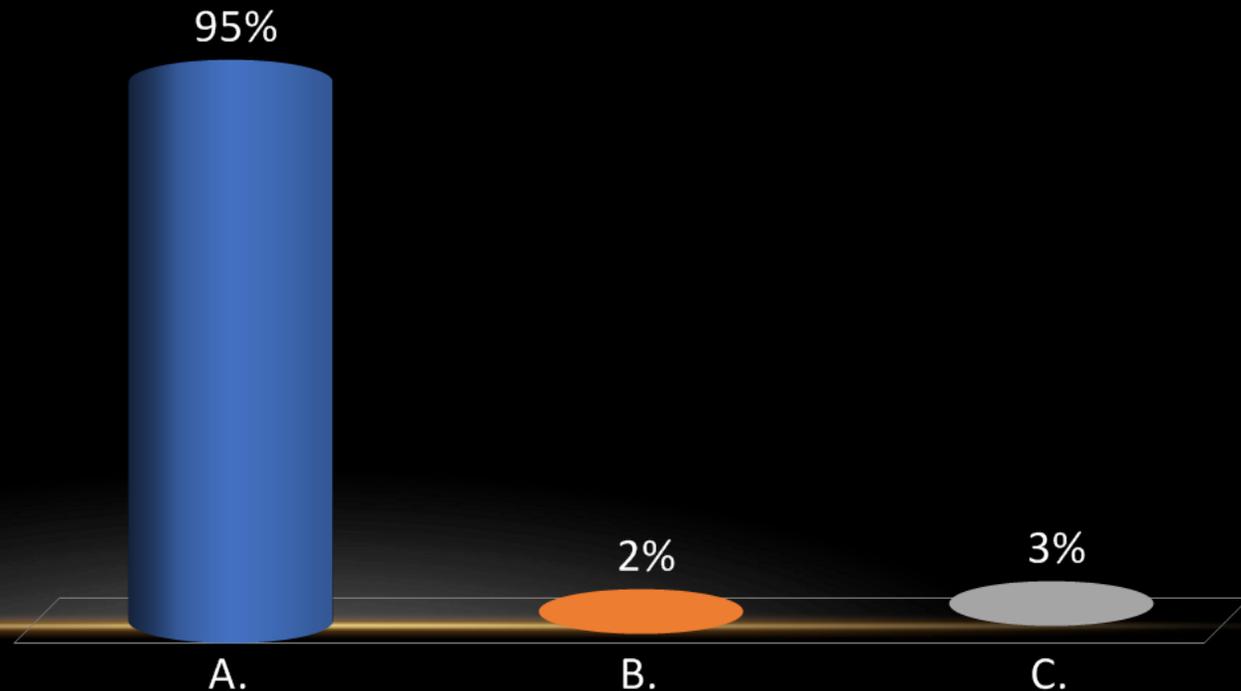
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 18**
- A growing body of both *in vitro* and clinical evidence suggests that ALTR may foster periprosthetic soft tissue changes that predispose to the development of PJI
- Multiple studies suggest that metal-on-metal wear and corrosion particles may alter the periprosthetic environment, and influence the risk of infection by
 1. impeding the immune system,
 2. preventing or accelerating bacterial growth,
 3. altering antibiotic resistance and metal resistance mechanisms,
 4. providing an ideal milieu for pathogens to proliferate in the necrotic tissues around the joint
- Registry data from the Mayo Clinic reveals an increased risk of PJI among patients who underwent a primary metal on metal total hip (MoM THA) ⁵.
- Prieto et al. reported a 5.6% rate of revision for PJI in 124 patients who had undergone MoM THA ⁵, which considerably exceeds the historical incidence of 1.3%
- Donell et al. reported a high rate of early failures in 652 MoM THA with 90 (13.8%) hips revised over 9 years ¹. In their revision cohort, 9 patients (10%) were noted to have deep infection.
- Grammatopolous et al. identified 7 cases of PJI (6.7%) in a series of 104 MoM THA revisions ¹⁹.
- In contrast, a few studies refute the possible link between ALTR and higher incidence of PJI. Dimitriou et al., Liow et al. and Matharu et al. each reported PJI rates of 2% or less in their cohorts of 178, 102, and 64 ALTR revisions, respectively
- However due to small sample sizes, significant heterogeneity in study design, and lack of consistent use of strictly defined diagnostic criteria, the quality of the evidence is currently limited



Recommendation: Yes. Patients with adverse local tissue reaction appear to have a higher incidence of PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 8: Should we routinely assess for serum/blood metal levels (cobalt and chromium) when working up a patient with a painful total joint arthroplasty?

RESEARCHED BY:



Paul Lachiewicz MD

Brett Levine MD

Daniel Schweitzer MD



Literature:

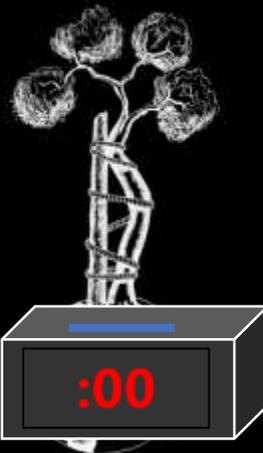
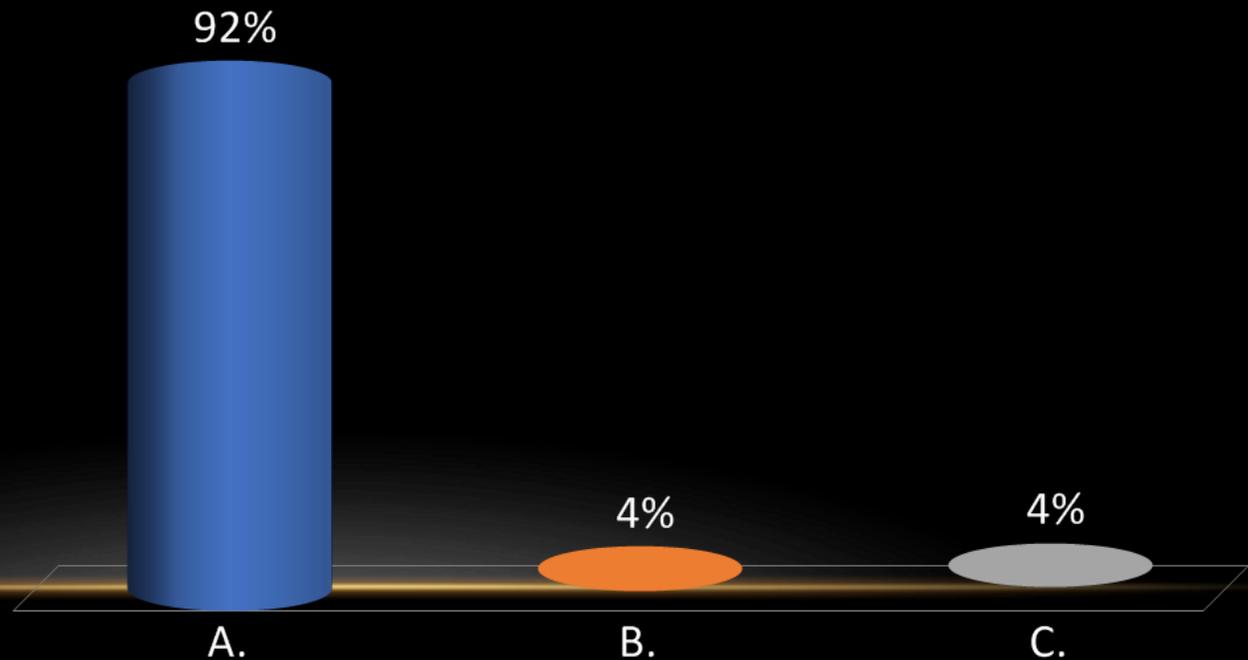
- **Meta-analysis 1, Prospective/Randomized 0, Retrospective 14**
- Plummer et al. reviewed 27 patients undergoing revision for adverse local tissue reactions (ALTR) 2/2 corrosion at head-neck junction with metal-on-polyethylene (MoP) bearings. They noted elevated mean serum chromium and cobalt levels in all cases
- Fillingham et al. noted that 44/64 (69%) of THA patients in their study with MoP bearings were positive for ALTR, and that a serum cobalt threshold value of ≥ 1.0 ng/mL had sensitivity of 100% and Specificity of 90% in detecting the presence of ALTR.



Recommendation: There is no data to suggest routine assessment of serum/blood metal ion levels (cobalt and chromium) in all patients with painful joint replacement. There may be rationale for second-line assessment of metal levels in painful metal-on-metal (MOM) total hip arthroplasty (THA), hip resurfacing, modular neck femoral components, and in certain metal-on-polyethylene (MOP) THA in which trunnion corrosion is suspected.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 9: How is PJI diagnosed in the presence of adverse local tissue reaction?

RESEARCHED BY:



Carlos Bracho MD,
Ecuador

Rafael Sierra MD, USA

Rene Mihalic MD,
Slovenia

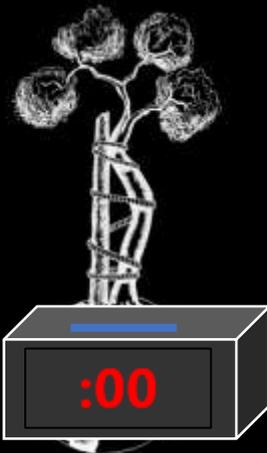
Craig Della Valle
MD, USA

Literature:

- **Meta-analysis 3, Prospective/Randomized 1, Retrospective 22**
- **Largest retrospective study focusing on diagnosis of PJI in hip revision due to ATR (Yi et al.)**
 - 150 consecutive failed THAs were reviewed
 - Examined preoperative ESR, CRP, synovial WBC, and differential
 - 19 of the patients met MSIS criteria for PJI
 - 141 attempted synovial WBC counts, 33% of samples had a synovial fluid WBC count that was inaccurate or unreliable due to presence of gross debris, clots, or some other abnormality in the specimen.
 - Concluded that automated synovial fluid WBC count was prone to false-positive results and should only be relied on if a manual cell count was performed



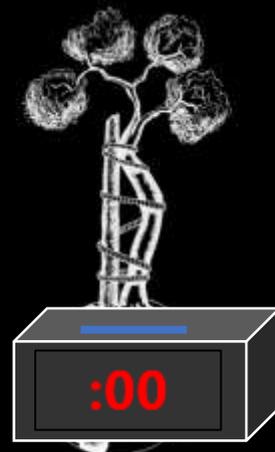
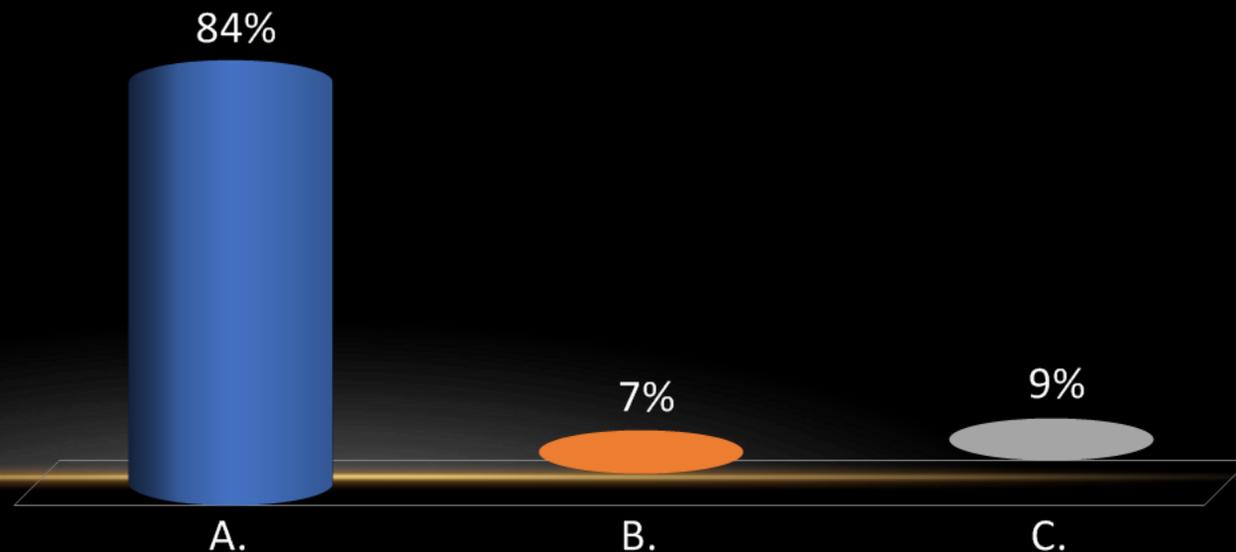
Recommendation: The diagnosis of periprosthetic joint infection in the presence of an adverse local tissue reaction (ALTR) is challenging as many of the commonly used tests for diagnosis (including the appearance of the surgical site) can be falsely positive. An aggressive approach to preoperative evaluation including an aspiration of the hip joint (sending the fluid for a manual synovial fluid white blood cell count, differential, and culture) is recommended. Testing the synovial fluid for leukocyte esterase test appears as a feasible, inexpensive, and reliable test for diagnosis of PJI in ALTR. There is no supporting evidence for other synovial fluid biomarkers in the diagnosis of PJI in presence of ATLRs.



Level of Evidence: See Table

Test	Strength
Clinical and radiological findings	Consensus. There is no supporting evidence for PJI diagnosis in ALTR.
Serum markers (ESR and CRP)	Strong
Synovial fluid WBC count, manual and PMNs	Strong
Leukocyte esterase in synovial fluid	Moderate
CRP in synovial fluid	Limited
Other fluid biomarkers (i.e., α -defensin, IL-6, and IL-8)	Consensus. There is no supporting evidence for PJI diagnosis in ALTR.

- A. Agree
- B. Disagree
- C. Abstain



2.3 - Diagnosis: Laboratory Tests



Question 1: What is an acceptable sensitivity, specificity, negative predictive value, and positive predictive value for a diagnostic tool for PJI?

RESEARCHED BY:



Noam Shohat MD



Susan Odum MD



Literature:

- **Meta-Analysis 2, Prospective/Randomized 0, Retrospective 13**
- Deirmengian et al. (2014) conducted a prospective study looking at the levels of five synovial fluid biomarkers in suspected PJI. These biomarkers correctly predicted the diagnosis of PJI (as outlined in the MSIS criteria) with 100% sensitivity and specificity.
- Sigmund et al. (2016) studied the sensitivity and specificity of a novel α -defensin test called Synovasure to predict the presence of PJI. They found that Synovasure achieved a sensitivity of 69% and specificity of 94%.



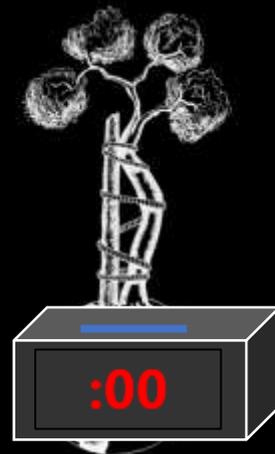
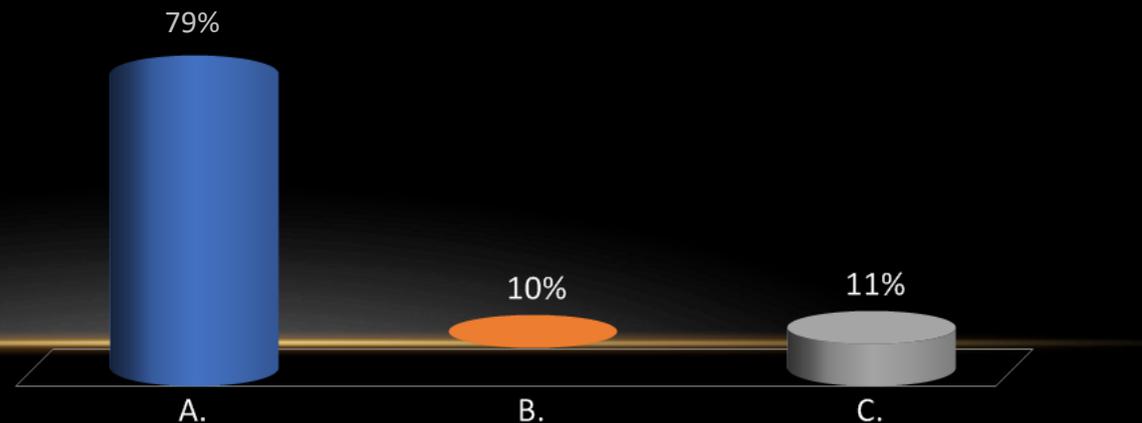
Recommendation: The validity of a diagnostic tool is traditionally measured by sensitivity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV). A perfect diagnostic tool would be able to correctly classify 100% of patients with PJI as infected and 100% of aseptic patients as non-infected. Without a perfect test available, we are left to balance between sensitivity and specificity; increasing one would reduce the other. To reduce the rates of false positives and negatives it is extremely important to take into account the pretest probability for infection, derived from patient's risk factors, clinical exams and any other exams available at the point of assessment.

Variable	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
Serum testing	98.5%* (96.2-99.6)	100% (97.6-100)	100% (100-100)	97.5% (93.7-99.1)
Synovial fluid testing	100%* (98.3-100)	100% (85.2-100)	100% (100-100)	100% (100-100)
Intraoperative Findings	92.9% (80.5-98.5)	95.8% (78.8-99.9)	97.5% (85.1- 99.6)	88.5% (72.0-95.8)
Overall	96.9% (93.8-98.8)	99.5% (97.2-100)	100% (99.7-100)	96.7% (93.3-98.4)

*Sensitivity for being diagnosed as infected or for moving forward for additional workup.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does the presence of both an ESR and CRP below the PJI thresholds rule out the diagnosis of PJI?

RESEARCHED BY:



Montri D Wongworawat MD, USA

Jay Shah MD, India



Literature:

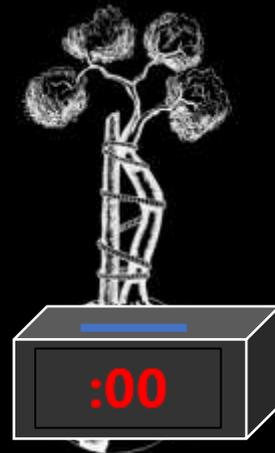
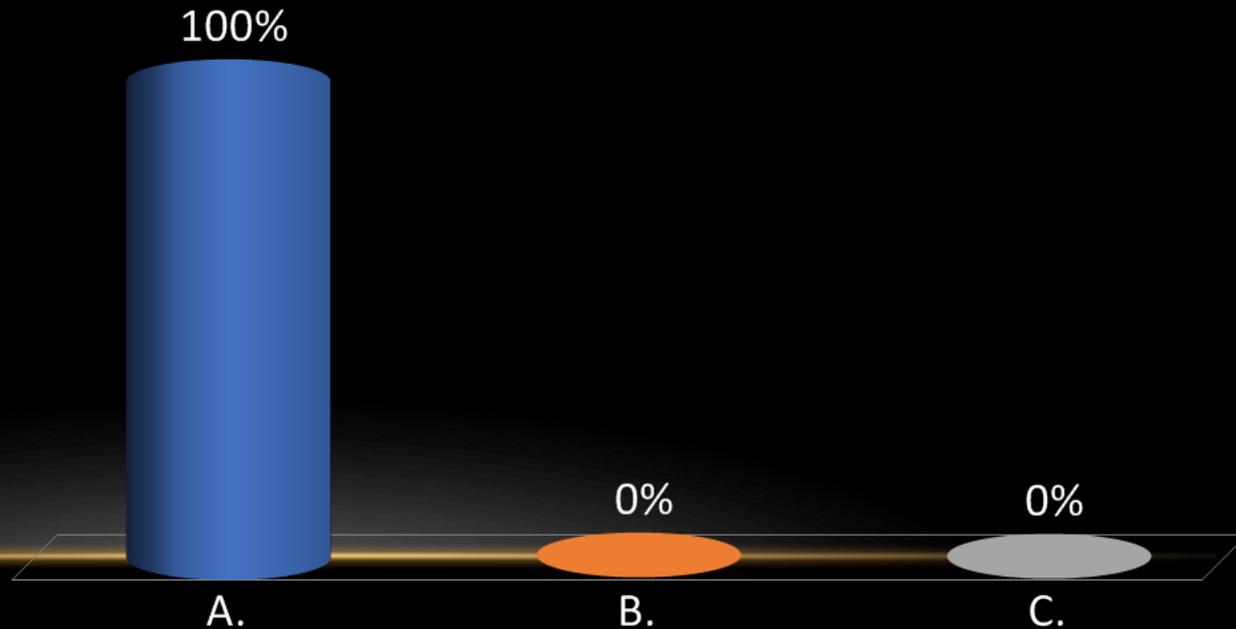
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 14**
 - One study reports a 4% risk of PJI following normal CRP/ESR
 - Antibiotic treatment prior to diagnosis may result in falsely-negative ESR/CRP
 - *P. acnes* PJI has been isolated in a number of studies as having below-threshold values for CRP and ESR
 - Combined ESR and CRP increases specificity at a cost to sensitivity
 - Higher threshold values for ESR & CRP should be used in the acute post-operative period



Recommendation: Serum erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels below the threshold (as determined by the MSIS and ICM) does not exclude the diagnosis of periprosthetic joint infection (PJI). Serum levels of ESR and CRP can be normal in some cases of PJI caused by slow growing organisms.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: What is the diagnostic accuracy and threshold of D-dimer in the diagnosis of PJI?

RESEARCHED BY:



Majd Tarabichi MD

AliSina Shahi MD



Literature:

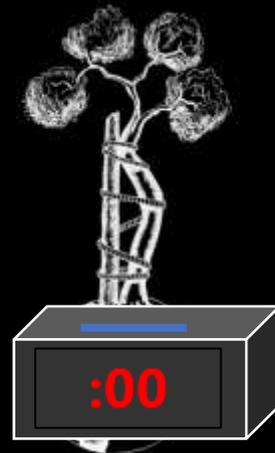
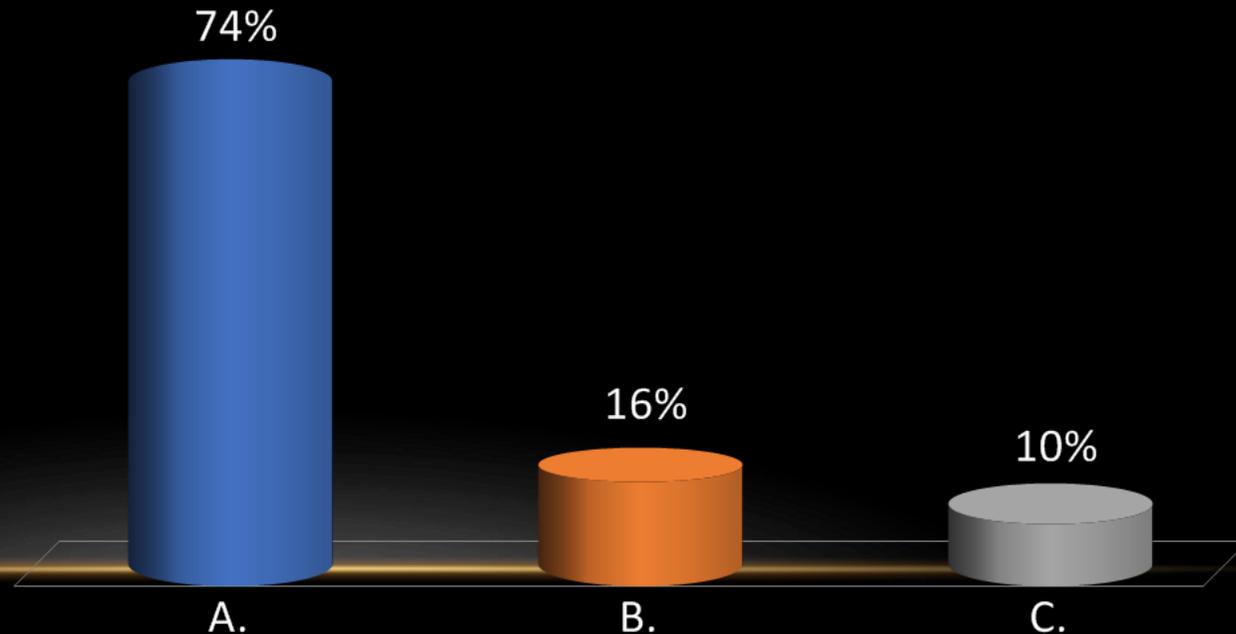
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 13**
- 850 ng/mL = Optimum serum D-dimer threshold for PJI (Youden index)
- Shahi et al. (2017), prospectively studied D-Dimer in 143 revision arthroplasties undergoing surgery for both septic and aseptic failure.
 - Median D-dimer level was significantly higher ($p < 0.0001$) in patients w/PJI (1,110 ng/mL [range, 243 to 8,487 ng/mL]) than for patients w/aseptic failure (299 ng/mL [range, 106 to 2,571 ng/mL])
 - D-dimer sensitivity and specificity = 89% and 93%
 - ESR and CRP sensitivities were 73% and 79%, and specificities of 78% and 80%, respectively.



Recommendation: Recent literature supports the use of D-dimer as a serological marker for the diagnosis of PJI. D-dimer has been shown to best perform at a threshold of 850 ng/ml. However, this threshold was determined internally from a cohort in a single institution study. Further studies are needed in order to validate this threshold or establish a more rigorous threshold.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: How does the level of leukocyte count and neutrophil percentage in the synovial fluid change with time following total joint arthroplasty?

RESEARCHED BY:



Jess Lonner MD,
USA



Yale Fillingham MD,
USA



Hany Bedair MD,
USA



Literature:

- Meta-analysis 0, Prospective/Randomized 0, Retrospective 7

	Acute Hip PJI ³	Chronic Hip PJI ⁴	Acute Knee PJI ⁵	Chronic Knee PJI ⁶
Cut-off Values WBC count (cells/ μ L); %PMNs	>12,800; >89%	>3,966; >80%	>10,700; >89%	>3000; >80%
Sensitivity (WBC count; %PMNs)	89%; 81%	89.5%; 92.1%	95%; 84%	80.6%; 83.9%
Specificity (WBC count; %PMNs)	100%; 90%	91.2%; 85.8%	91%; 69%	91.2%; 94.9%
Positive Predictive Value (WBC count; %PMNs)	100%; 91%	76.4%; 59.3%	62%; 29%	67.5%; 78.8%
Negative Predictive Value (WBC count; %PMNs)	88%; 79%	97.5%; 98.0%	99%; 97%	95.4%; 96.3%

3 = Yi et al. CORR, 2014

4 = Higuera et al. JBJS, 2017

5 = Bedair et al. CORR, 2011

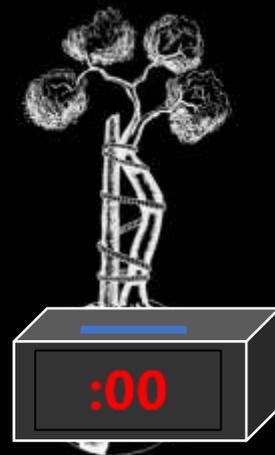
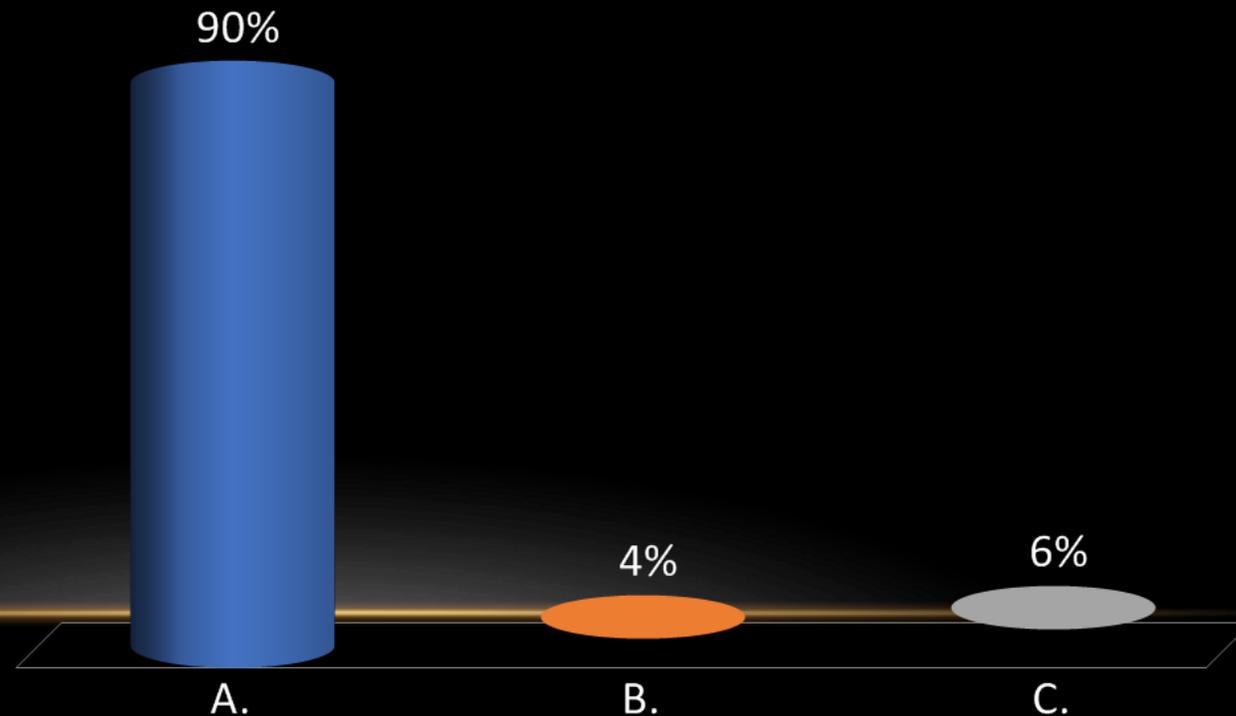
6 = Balato et al. AOTS, 2018



Recommendation: The levels of leukocyte count and neutrophil percentage in the synovial fluid drop as one moves further away from the index arthroplasty. The latter is the rationale behind using different thresholds for these parameters in diagnosis of acute versus chronic periprosthetic joint infection.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: What is the role of alpha-defensin in the diagnosis of PJI?

RESEARCHED BY:



Stergios Lazarinis MD,
Sweden



Carl Deirmengian MD, United
States of America



Literature:

- The alpha defensin laboratory assay has been studied at numerous institutions. Both the sensitivity and specificity of the alpha-defensin laboratory test exceed 95% when using the MSIS consensus criteria for PJI as a gold standard.

Institution	N	Gold Standard	Sensitivity	Specificity
Rothman Institute	149	MSIS Criteria	97% (36/37)	96% (107/112)
Mayo Arizona	61	MSIS Criteria	100% (33/33)	95% (83/87)
Cleveland Clinic	111	MSIS Criteria	100% (24/24)	98% (53/54)
ENDO Klinik	156	MSIS Criteria	97% (28/29)	97% (123/127)
Cleveland Florida	70	MSIS Criteria	97% (34/35)	97% (34/35)
Combined	547		98.1% (95%CI: 95-100%)	96.4% (95%CI:94-98%)

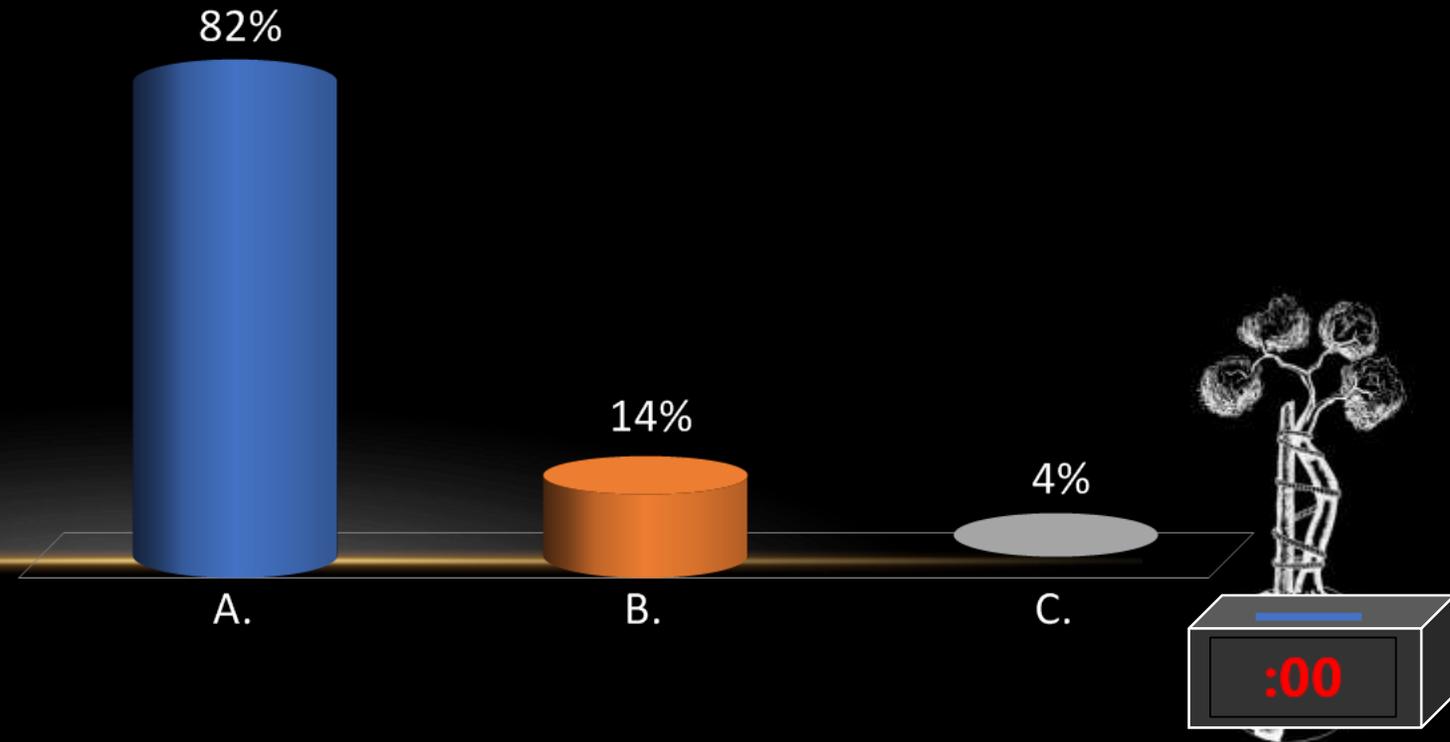
- Appropriate use of the alpha-defensin test should be exercised as there are limitations. However, the alpha-defensin laboratory test appears to be the most sensitive and specific single test for PJI, and therefore appears suitable to be included in the armamentarium of tests routinely used.
- Recent recent pooled analyses (incorporating the lateral flow point of care test) suggest



Recommendation: Measurement of alpha-defensin in synovial fluid is a complement to existing diagnostic tests for PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 6: What is the diagnostic accuracy of histologic tests and thresholds used in the diagnosis of PJI?

RESEARCHED BY:

Thomas W Bauer MD

Lars Lidgren MD

Annette W-Dahl MD



Literature:

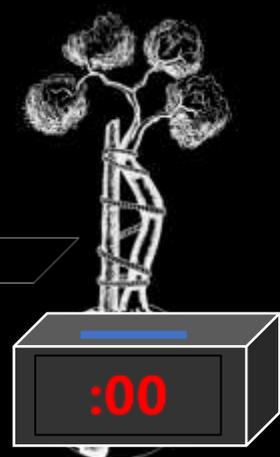
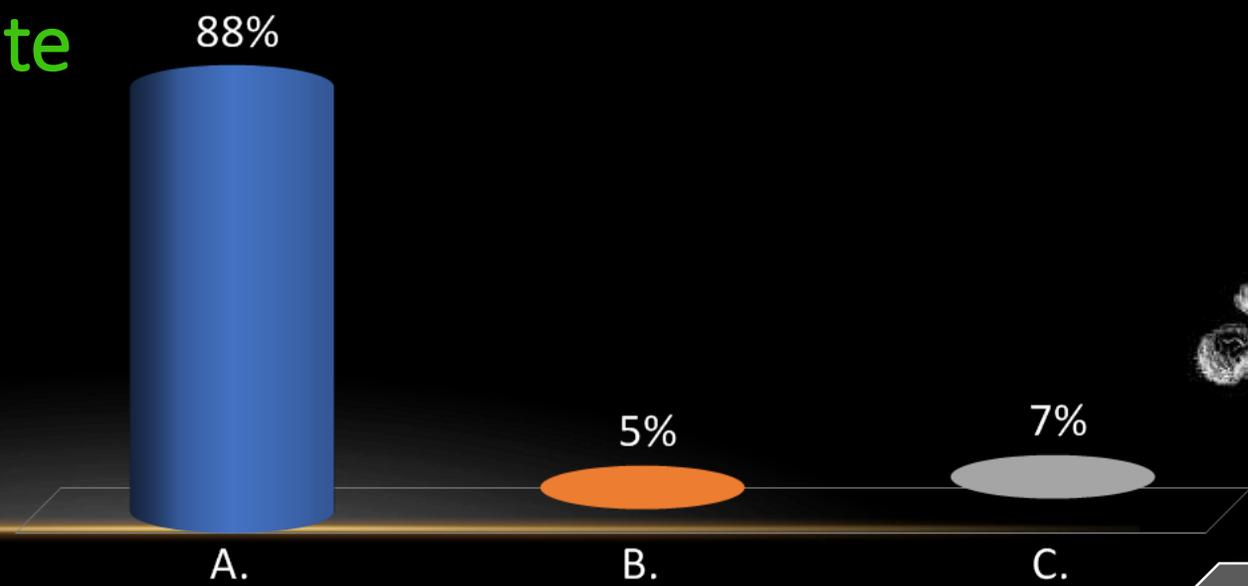
- **Meta-analysis 2, Prospective/Randomized 0, Retrospective 21**
- Zhao et al. (2013) conducted a 12-study meta-analysis involving 1,011 patients undergoing hip arthroplasty of which 194 (19.2%) had a PJI.
 - In 7 studies the threshold 5 PMNs per HPF was used, in 2 studies the threshold of 10 PMNs per high-power field while 3 studies included both thresholds.
 - The diagnostic odds ratio was 23.5 (95% CI 10.5 – 52.7) when 5 PMNs per HPF was used and 35 (95% CI 7.7– 159.3) when 10 PMNs per HPF was used.
 - No statistically significant difference between the two thresholds.
 - Conclusion: Although both thresholds are stable and effective, a threshold of 10 PMNs per HPF is better for diagnosing PJI.
- Kashima et al. analyzed frozen and paraffin sections of peri-prosthetic tissues in 76 cases of failed hip and knee arthroplasties, stained with chloroacetate esterase (CAE).
 - All cases of aseptic loosening contained fewer than <2 neutrophil polymorphs/HPF
 - Some cases of septic loosening had <5 neutrophil polymorphs/HPF
 - The histological criterion of >2 neutrophil polymorphs/HPF showed increased sensitivity and accuracy for the diagnosis of septic loosening.
 - Conclusion: the MSIS histological criterion of >5 neutrophil polymorphs/HPF is too high an index figure for PJI Dx.



Recommendation: There is a variability of the histologic examination of intraoperative per frozen sections as well as the thresholds used for the presence of neutrophils. The preparation and interpretation of frozen sections can be highly operator dependent.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 7: What is the role of Specific Granulocyte Counting Methods and New Immunohistologic Staining Techniques in diagnosing PJI?

RESEARCHED BY:

Thomas W. Bauer MD, France

Veit Krenn MD, Germany

Noreen Hickok MD, United States of America



Literature:

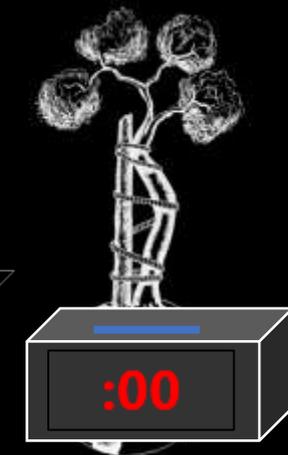
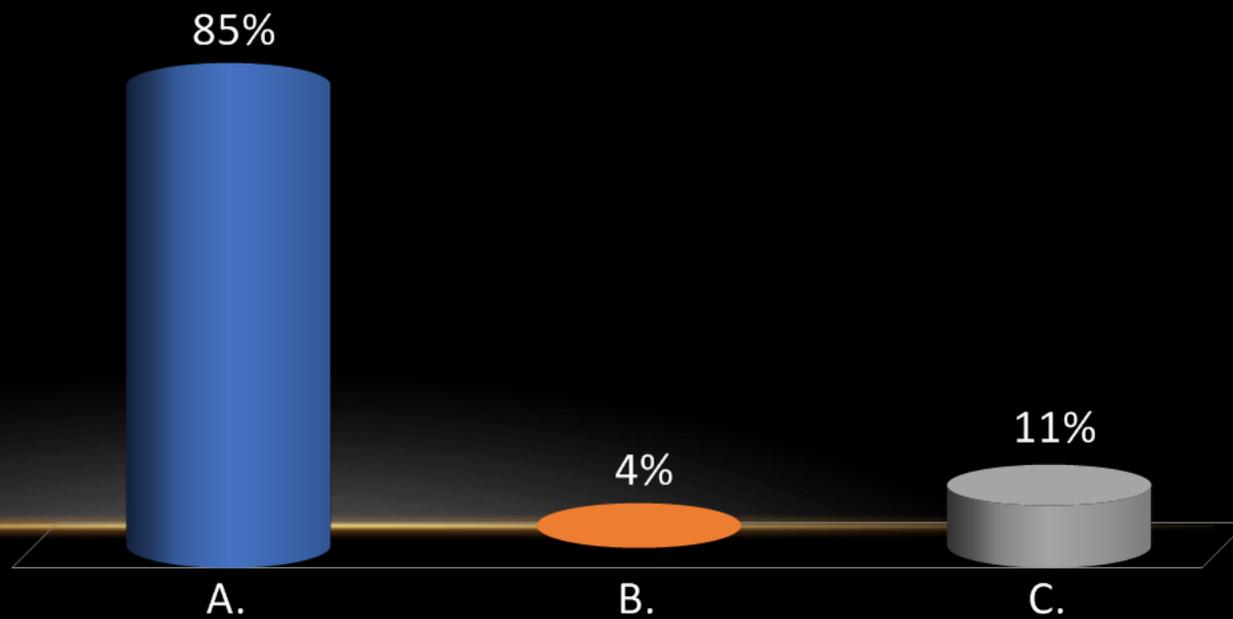
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 3**
- Based on studies by Kashima et al., Krenn et al., and Munemoto et al. it is recommended that neutrophil counting methods be included when diagnosis is uncertain.
 - In general, 5 or more PMN's per field in each of 5, high power (40 X objective) magnification fields can be used as the threshold to support the diagnosis of infection.
- Additional studies are needed to determine the optimum use of special stains.



Recommendation: The role of Specific Granulocyte Counting Methods and New Immunohistologic Staining Techniques is to support the diagnosis of infection when diagnosis is uncertain. The recommended threshold is 5 or more PMN's per field in each of 5, high power (40 X objective) magnification fields. The stains reported to date can only be performed on sections of formalin-fixed, paraffin embedded tissue. Therefore, they are not available for use on frozen sections obtained during an operation.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



2.4 - Diagnosis: Pathogen Isolation, Culture



Question 1: Should intra-operative cultures be taken during every revision total joint arthroplasty? If so, how many?

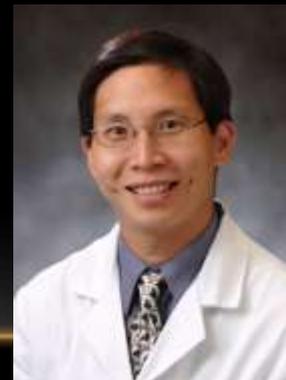
RESEARCHED BY:



Felix Ogedegbe, MD



Elie Ghanem, MD



Gwo-Chin Lee, MD



Literature:

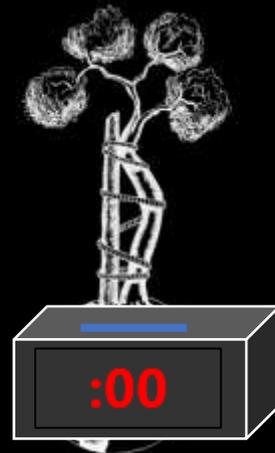
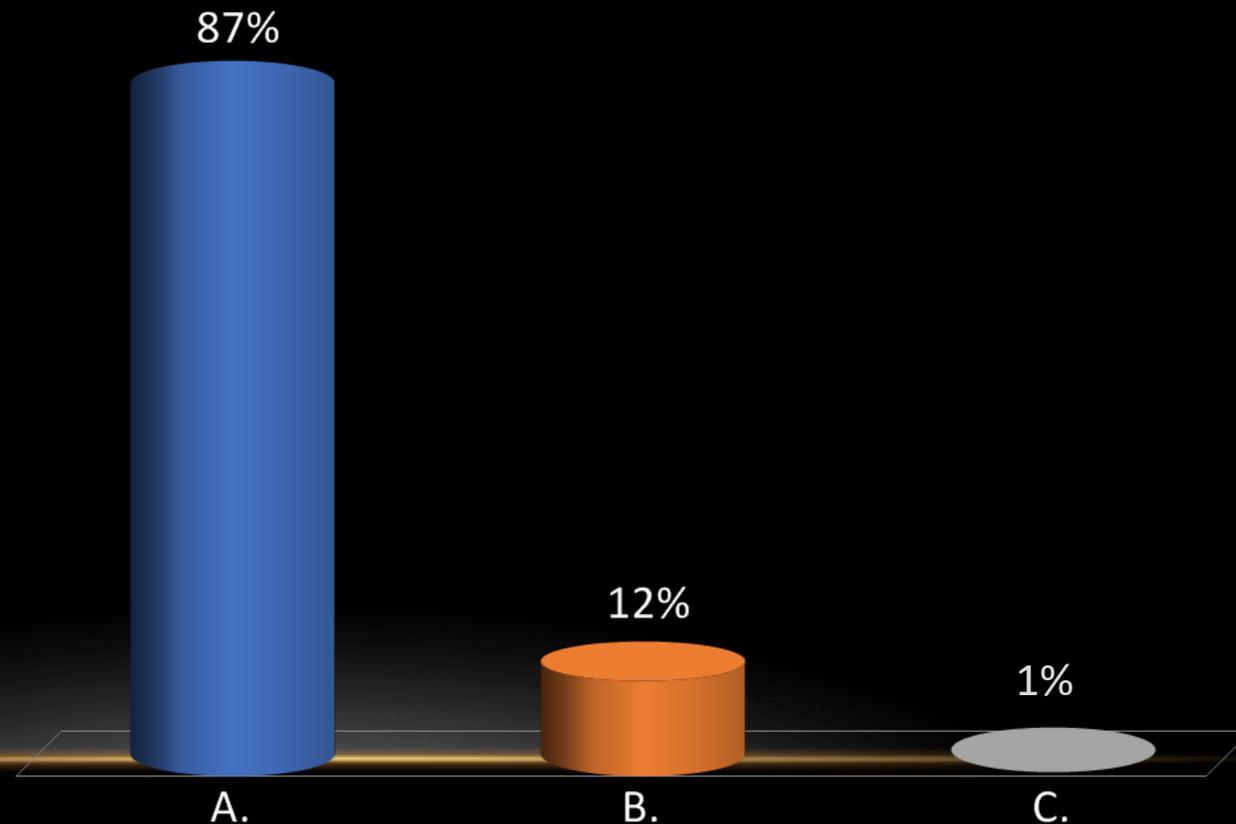
- Meta-analysis 0, Prospective/Randomized 3, Retrospective 12
- 3 or more samples yielded higher NPV without decreased PPV across all studies
- No RCTs regarding optimal number of tissue samples



Recommendation: Yes, routine cultures should be taken during every revision total joint arthroplasty. At least three intra-operative culture samples should be obtained.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Are there significant differences in the yield of culture between pre-operative aspiration and intra-operative culture samples? If so, which result should be utilized?

RESEARCHED BY:



Tobias Winkler MD, Austria



Carl Deirmengian MD, USA



Literature:

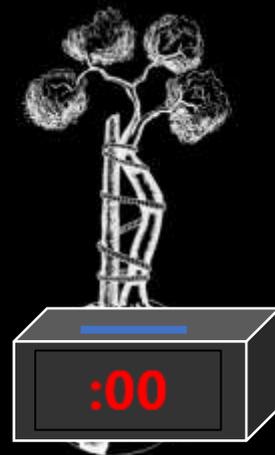
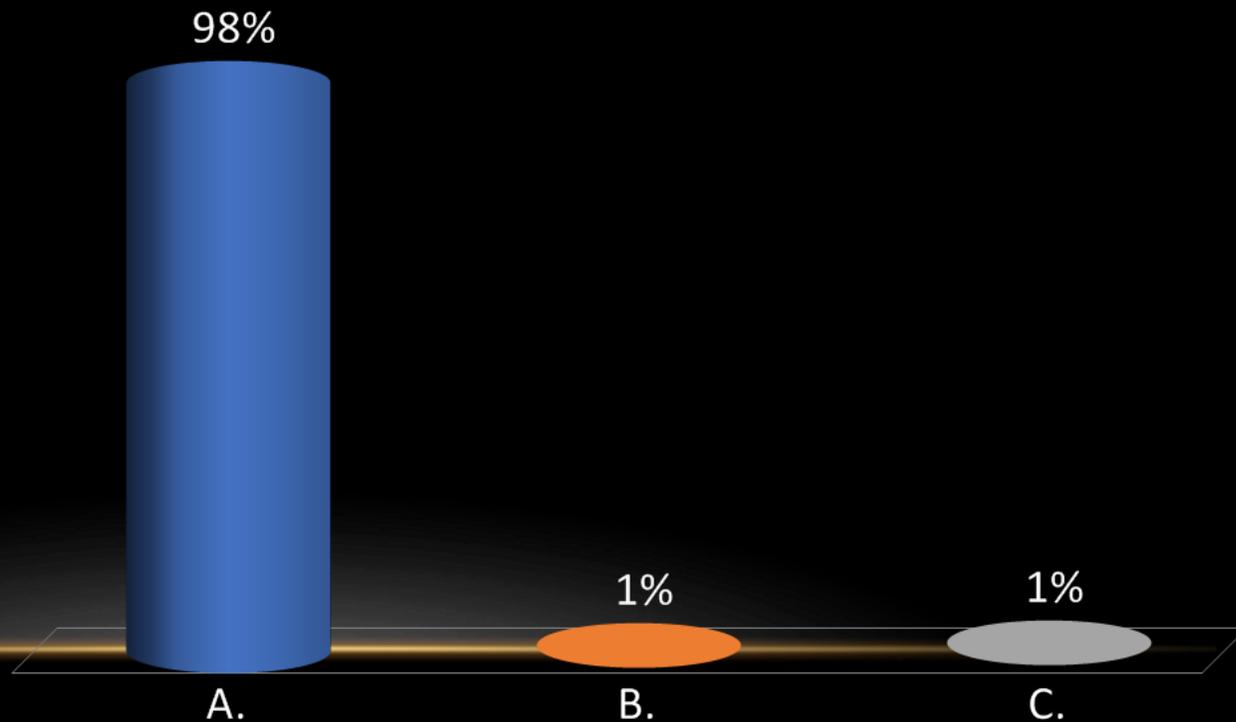
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 18**
- Limited data comparing synovial fluid versus tissue culture yield, with the majority of studies having fewer than n=10 patients
- Concordance between synovial aspiration and intraoperative tissue culture results ranges from 57-95% in the literature.
- Shanmugasundaram et al. showed no association of microbial virulence on organism isolation with timing of sampling (preop aspiration versus intraop culture)
- Collection of multiple intraoperative tissue samples is considered by to provide the highest yield in isolating organisms from a joint.



Recommendation: There may be differences in the yield of culture between pre-operative aspiration and intra-operative culture samples, particularly in the case of polymicrobial infections or low-virulence organisms. The collection of multiple intraoperative tissue samples is considered by many experts to provide the highest yield in isolating organisms from a joint.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Do bone cultures provide additional diagnostic accuracy in the diagnosis of PJI?

RESEARCHED BY:



Richard de Steiger MD, Australia

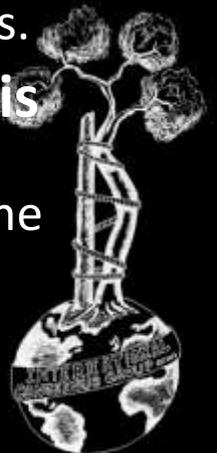


Brian Hamlin MD, USA



Literature:

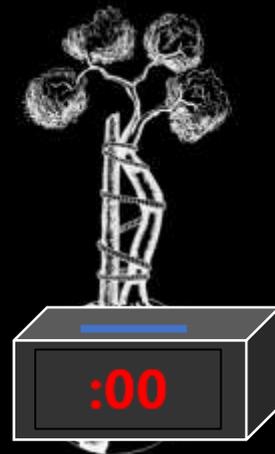
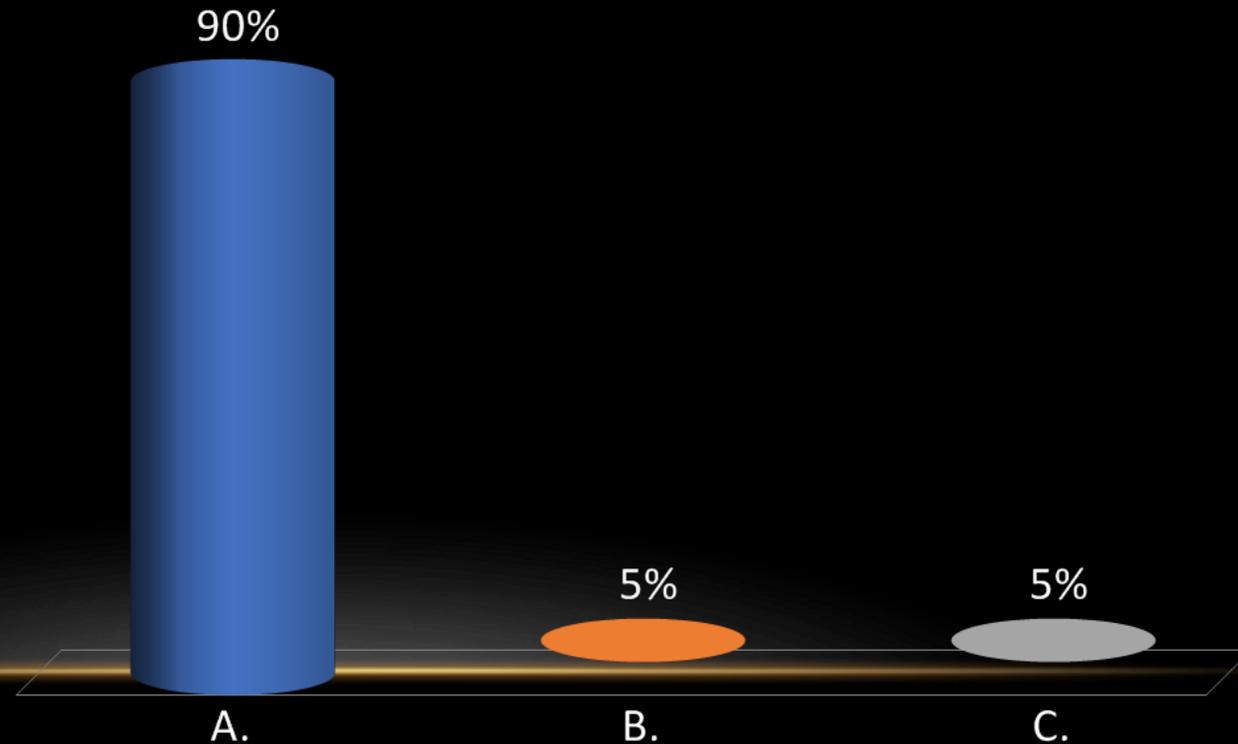
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 10**
- **While data supports obtaining at least 3 distinct intraoperative samples for culture, the site of specimen retrieval may include synovium as well as tissue from femur/tibia in the knee or femur/ acetabulum in the hip.**
- **Only one study addresses the role of utilizing bone biopsy in the detection of infection in TJA.**
 - Larsen et al. assessed the contribution of different specimen types in detecting PJI in a prospective cohort study. Bone biopsy did not confer any additional information and did not contribute independently to the diagnosis of infection.
 - Only 28% (9/32) bone biopsy samples resulted in a positive culture after 6 days
 - This was less yield than soft tissue biopsies which resulted in 88% (37/42) positive cultures.
- **Other studies have assessed the role of bone biopsy in detecting osteomyelitis and septic arthritis (Akinyoola et al and Chadayammuri et al)**
 - Bone biopsy in osteomyelitis showed improved sensitivity and specificity in determining the organism when compared to sinus tract biopsy and soft-tissue and deep wound biopsy



Recommendation: Inconclusive. We cannot recommend for or against bone biopsy to provide additional diagnostic accuracy in the diagnosis of periprosthetic joint infection (PJI).

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



MISSING QUESTION 4

- QUESTION: “Is there a role for obtaining cultures before, and at the time of, insertion prosthesis during second stage (reimplantation) of a two-stage exchange arthroplasty?”
- Recommendation: Preoperative aspiration of a joint should be determined based on the index of suspicion for persistent infection. During reimplantation, however, multiple fluid and tissue samples should be sent for culture. There is a direct correlation between the outcome of two-stage exchange arthroplasty and culture results during reimplantation
- LOE: Moderate
- Delegate Vote: Agree 95%, Disagree 4%, Abstain 1% (Unanimous, Strong Consensus)



Question 5: Should routine cultures be taken in patients undergoing total joint arthroplasty who had a previous open reduction and internal fixation of the same joint (e.g. prior acetabular fracture)?

RESEARCHED BY:



Alencar, Paulo

Borens, Olivier

Cabral, Rui
Manuel Vicente

Manrique, Jorge



Literature:

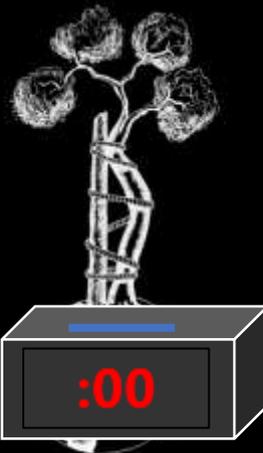
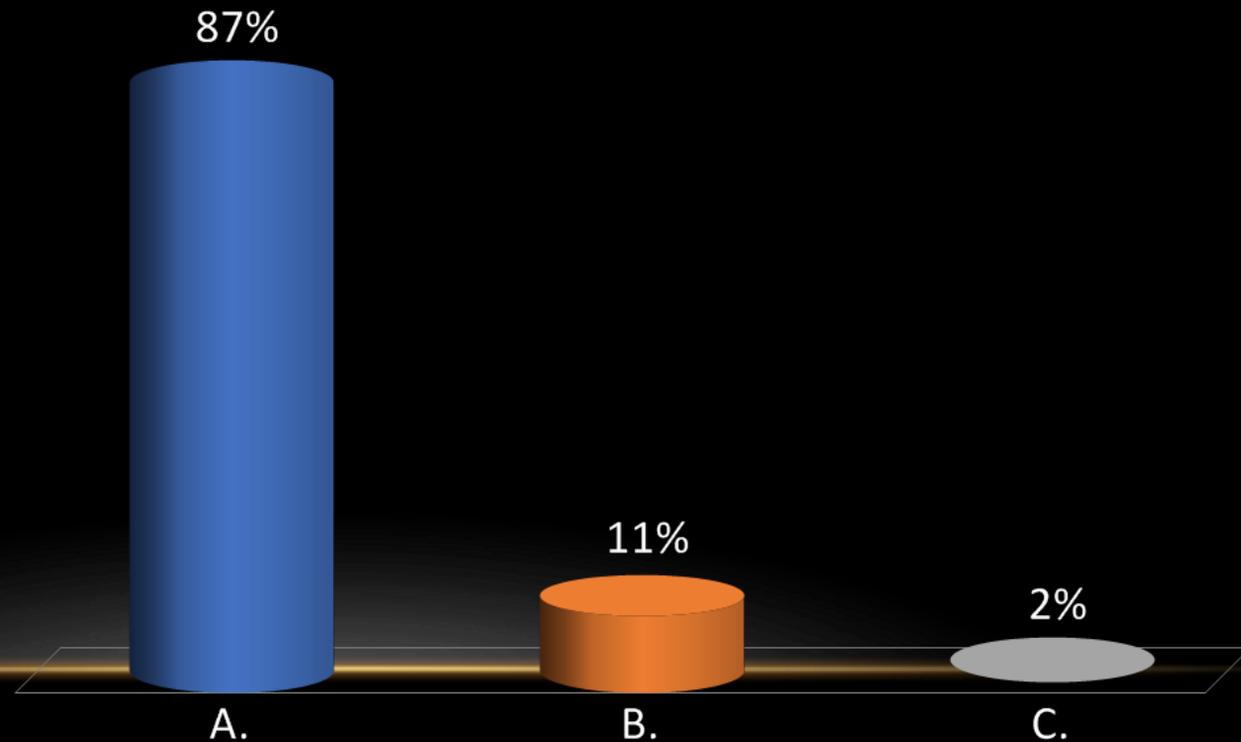
- Meta-analysis 0, Prospective/Randomized 1, Retrospective 12
- Studies have identified that any prior surgery to the joint is a risk factor for PJI, both in knees and in hips.
- Underlying infection has a reported incidence of 11-18% and a pre-op workup should be performed to minimise the risk of subsequent SSI/PJI
- Literature is consistent in showing that TJA patients have an increased risk of subsequent PJI following prior surgery of the same joint, therefore, routine cultures should be included in the workup for possible infection prior to TJA.



Recommendation: Intraoperative cultures should be taken in patients undergoing total joint arthroplasty who had a prior open reduction and internal fixation of the same joint.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 6: Is there a role for sonication of implants retrieved during explantation?

RESEARCHED BY:



Matthew Abdel, MD



Brian Klatt, MD



Shaoqi Tian , MD



Literature:

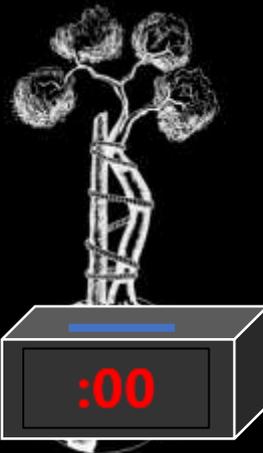
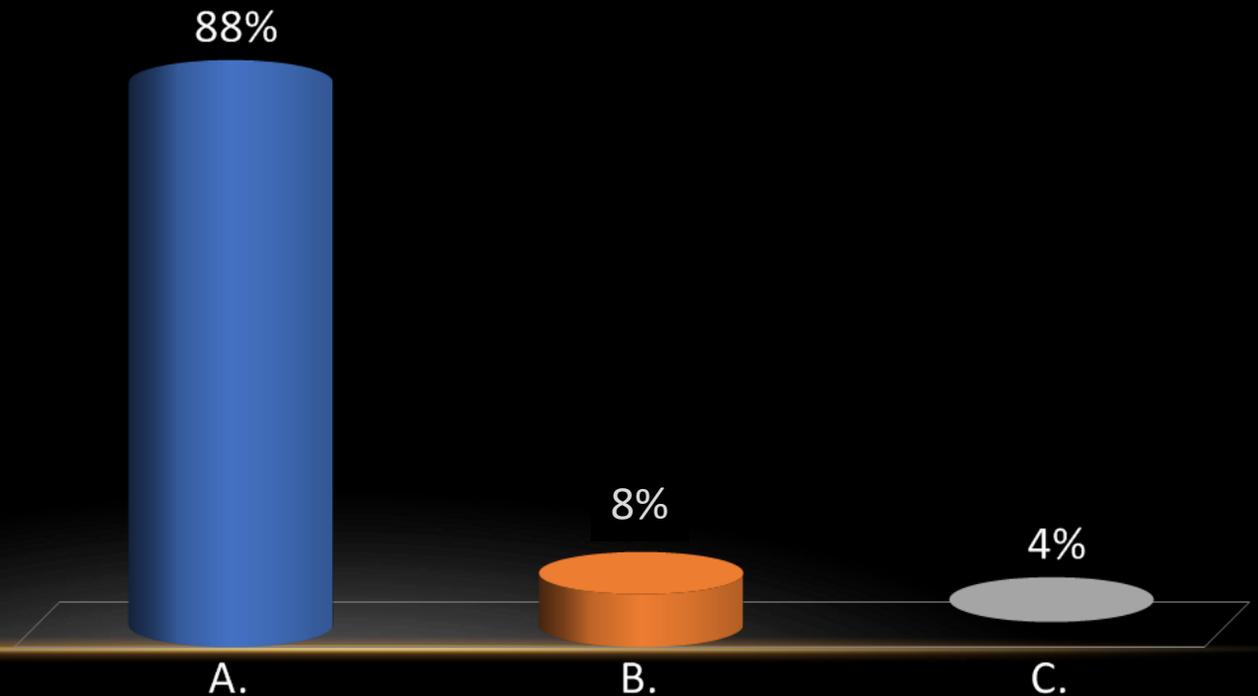
- Meta-analysis 0 , Prospective/Randomized 19, Retrospective 0
- Literature shows sonication fluid culture to be superior in sensitivity of identification of organisms with no decrease in specificity compared to standard synovial fluid culture or tissue culture
- Sonication not shown to be superior in early PJI



Recommendation: Several studies have demonstrated that sonication of explanted orthopedic prostheses is a viable method for detecting pathogens, particularly in the setting of culture negative infections.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



2.5 - Diagnosis: Reimplantation



Question 1: Are the MSIS/ICM criteria valid for decision-making before reimplantation?

RESEARCHED BY:



Carlos A Higuera MD, USA



AliSina Shahi MD, USA



Literature:

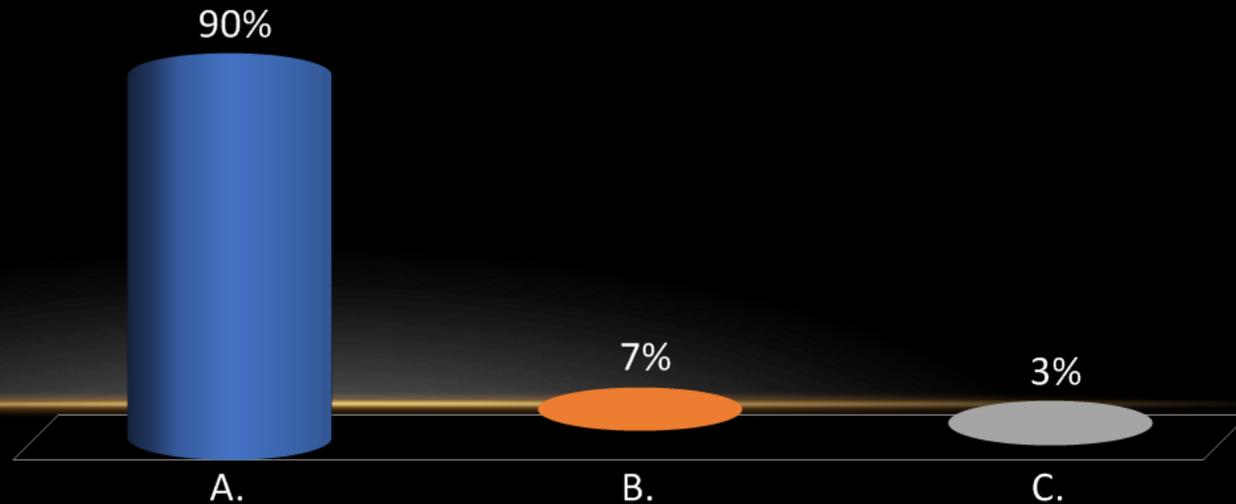
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 18**
- George et al. studied 79 patients undergoing reimplantation and found that MSIS criteria had a high specificity (96%) in predicting persistent infection, though the sensitivity was low (26%).
- Kheir et al. also investigated the MSIS criteria in patient who were undergoing two-stage exchange for PJI and reported a sensitivity of 25% and a specificity of 87% for detecting persistent infection



Recommendation: The validity of the Musculoskeletal Infection Society (MSIS) and International Consensus Meeting (ICM) criteria for determination of the reimplantation timing is unclear. Components of MSIS criteria such as cultures, histology, synovial white blood cell (WBC) count, synovial polymorphonuclear neutrophil percentage (PMN%), and leukocyte esterase (LE) strip test have been found to be useful and are recommended for decision making before reimplantation. However, serum markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have limited utility at their current thresholds.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 2: What metrics should be considered to determine the timing of reimplantation after two-stage exchange arthroplasty of the hip and knee?

RESEARCHED BY:

Arash Aalirezaie MD, Iran

Dirk-Jan Moojen MD, Netherlands

Job Diego Velázquez Moreno MD, Mexico



Literature:

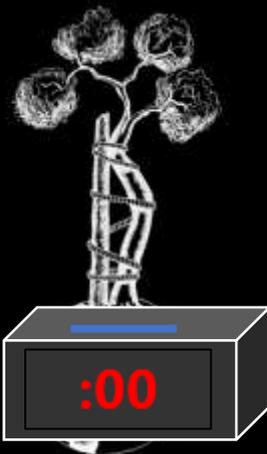
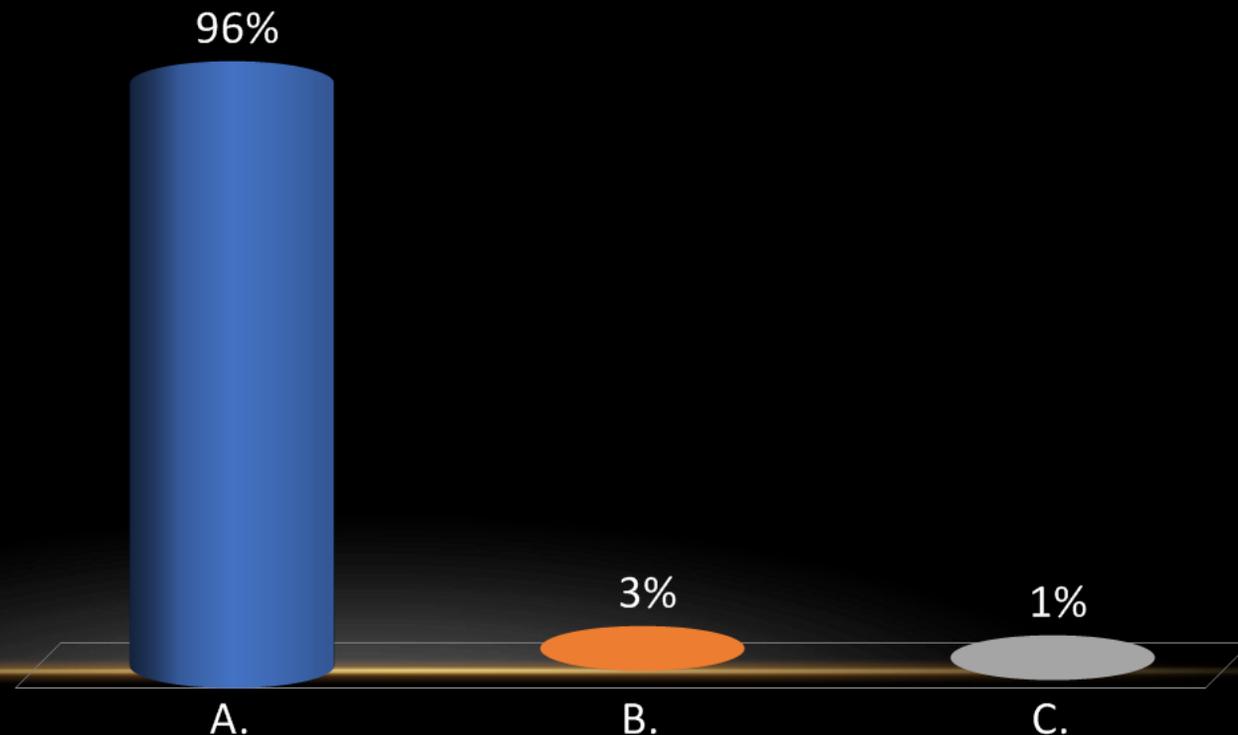
- **Meta-analysis 1, Prospective/Randomized 0, Retrospective 23**
- There is no gold standard that can guide surgeons to determine the optimal time of reimplantation
- Various serum and synovial markers have been studied to identify the most accurate test for screening for persistent PJI.
 - A common finding of most of the studies is a high specificity, but low sensitivity
- A decreasing trend is seen in CRP and ESR during the interval period; however, these numbers can be misleading.
- D-dimer is an inexpensive and widely available test that can aid in identifying the timing of reimplantation – ongoing research is currently investigating its utility.
 - In a recent study D-dimer outperformed CRP and ESR for determining time for reimplantation.



Recommendation: There are no definitive metrics to allow determination of optimal timing of reimplantation. Thus, timing of reimplantation should rely of resolution of clinical signs of infection, down-trend in the serological markers, and reliance on synovial analysis, if aspiration is performed.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Is normalization of serological markers necessary prior to reimplantation arthroplasty performed as part of a two-stage exchange?

RESEARCHED BY:



Scott Sporer MD, USA



Marco Teloken MD, Brazil

Literature:

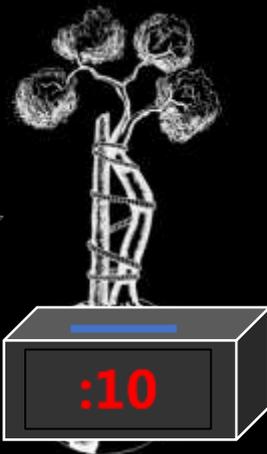
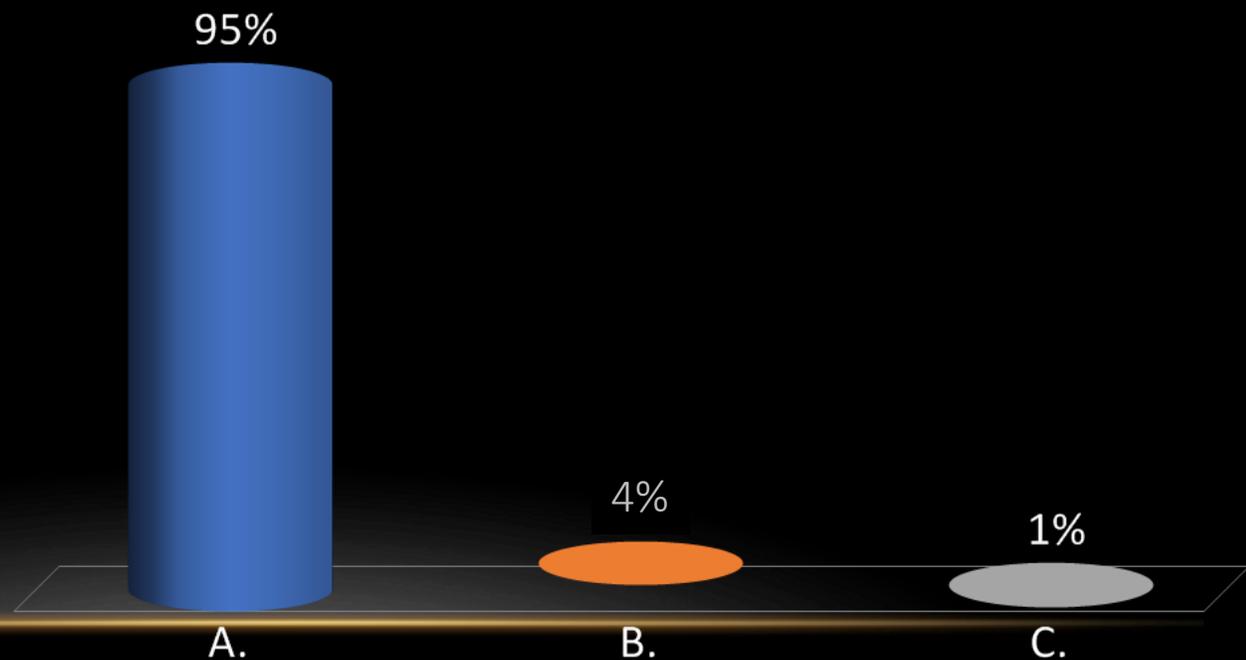
- **Meta-analysis/Systematic Review 0, Prospective 2, Retrospective 27**
- ESR and CRP levels can remain elevated for weeks after surgery
- Kubista et al. found no statistically significant differences in mean values for CRP or ESR before resection or reimplantation when comparing the treatment failure group to the control group
- Many authors rely on a downward trend in inflammatory markers before reimplantation.



Recommendation: No. A trend and decline in C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) is expected, but we still recognize that there are certain cases in which reimplantation may be performed despite abnormal levels of ESR and CRP. Surgeons should not wait for complete normalization of the inflammatory markers as this may not occur in some patients and/or take a long period of time.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4: What is the importance of two-week drug holiday prior to reimplantation?

RESEARCHED BY:



Hangama Fayaz MD

Carlos A Higuera MD

Igor Shubnyakov MD

Literature:

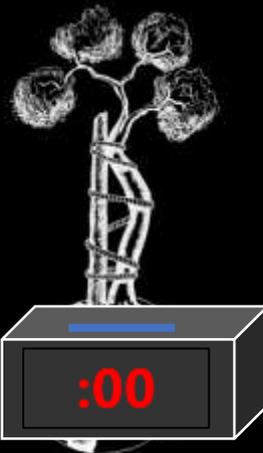
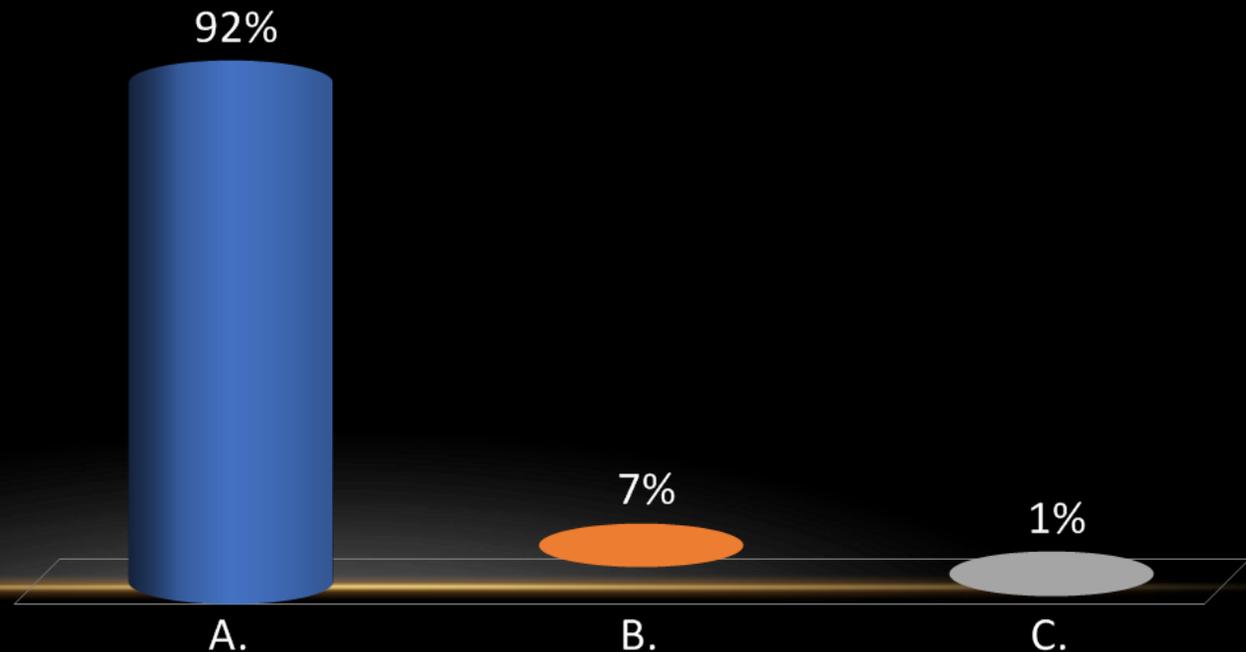
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 9**
- Limited data exists on the utility of an antibiotic-free period prior to reimplantation
- Bejon et al. conducted a retrospective study of 152 cases of PJI managed with 2-stage revision and an antibiotic-free period.
 - Most unplanned debridements following the first stage were carried out before antibiotics were stopped.
 - Conclusion: They did not identify evidence supporting use of antibiotic-free periods prior to re-implantation



Recommendation: Unknown. There is no conclusive evidence to support the need or the ideal length of a drug holiday prior to reimplantation.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: What is the diagnostic accuracy of joint aspiration of a cement spacer in conjunction with clinical evaluation, imaging, serologic tests, and biopsies? Should it routinely be performed prior to reimplantation?

RESEARCHED BY:



Hangama Fayaz MD

Carlos A Higuera MD

Igor Shubnyakov MD

Literature:

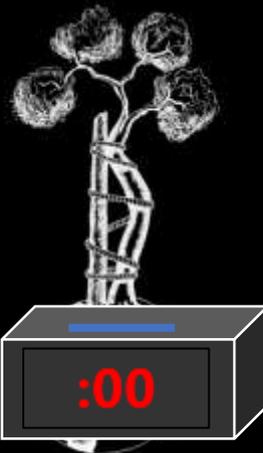
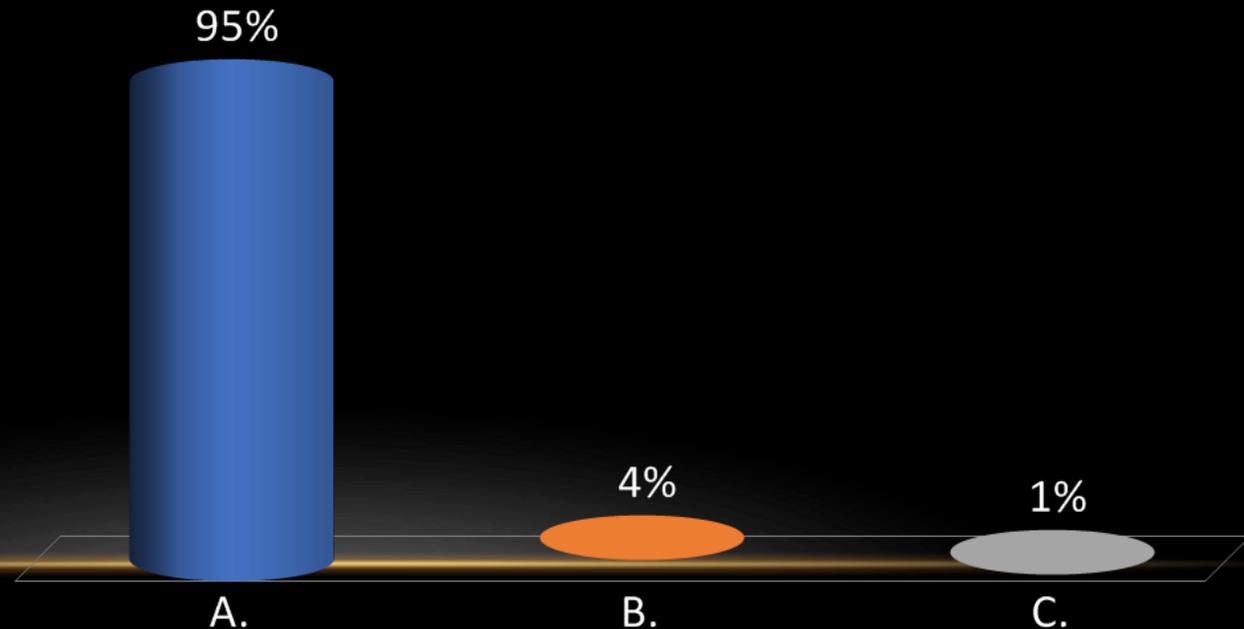
- **Meta-analysis 0, Prospective/Randomized 3, Retrospective 18**
- Meermans and Haddad prospectively followed 120 patients with assumed infection of TJAs.
 - Sensitivity was 83% for aspiration, 79% for biopsy, and 90% for the combination of both the techniques.
 - Specificity was 100% for aspiration, biopsy, and the combination
 - Overall accuracies were 84%, 81%, and 90%, respectively.
 - Conclusion: Routine aspiration should be followed by a biopsy in the work up of septic joints.
- Spangehl et al. prospectively analyzed perioperative + intraoperative investigations used for PJI diagnosis in 178 patients.
 - Conclusion: ESR/CRP is reliable for predicting the absence of infection.
 - Aspiration should be used if ESR/CRP elevated or if high clinical suspicion of infection



Recommendation: The diagnostic accuracy of joint aspiration prior to reimplantation is not known. None of the parameters being used to diagnose PJI, and their respective thresholds, have been determined for aspiration. The decision to perform aspiration should be made based on the index of suspicion for persistent infection and individualized.

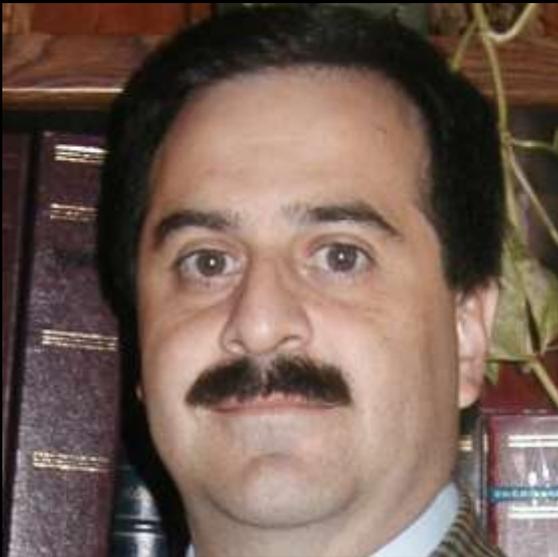
Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 6: What intra-operative metrics can be utilized at the time of intended reimplantation to help decision-making and reduce the risk of subsequent recurrence?

RESEARCHED BY:



Camilo Restrepo MD

William Griffin MD



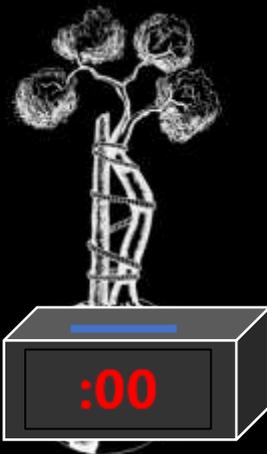
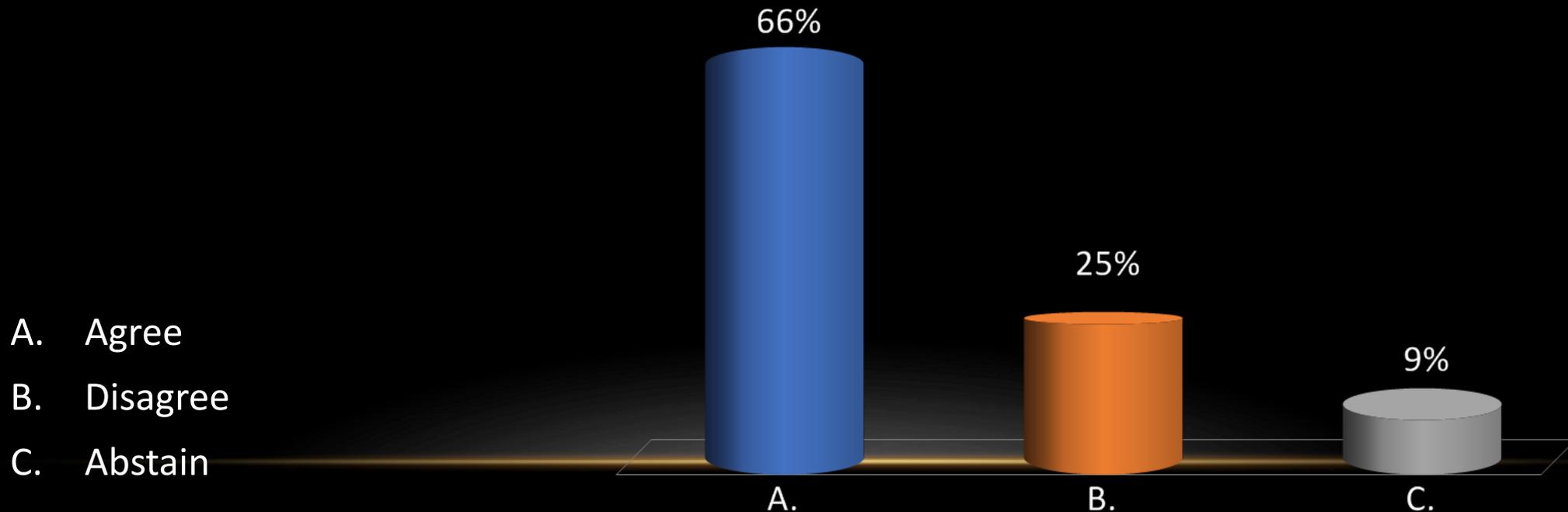
Literature:

- **Meta-Analysis 4, Prospective/randomized 0, Retrospective 29**
- Several recently published studies and a meta-analysis have shown that the Leukocyte Esterase (LE) strip test has the advantages of being fast, accurate and reliable in diagnosing PJI. (Parvizi et al. 2011, Wetters et al. 2012, Tischler et al. 2014, Lee et al. 2017)
- Della Valle et al. (1999) published a retrospective study looking at the sensitivity of frozen section in diagnosing PJI in the intraoperative setting. They found that intraoperative analysis of frozen sections had a sensitivity of 25 percent, a specificity of 98 percent, a positive predictive value of 50 percent and a negative predictive value of 95 percent.



Recommendation: Intra-operatively, frozen section and Leukocyte Esterase (LE) strip test can be used as decision-making metrics for reimplantation.

Level of Evidence: Limited



Question 7: What is the diagnostic accuracy of a frozen section during reimplantation surgery? What thresholds should be used in this context?

RESEARCHED BY:

Thomas W Bauer MD

Veit Krenn MD



Literature:

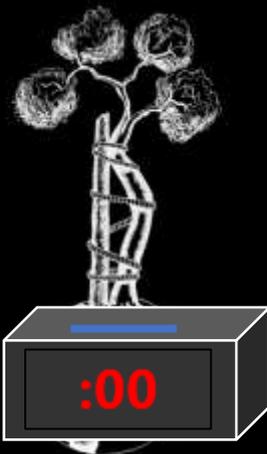
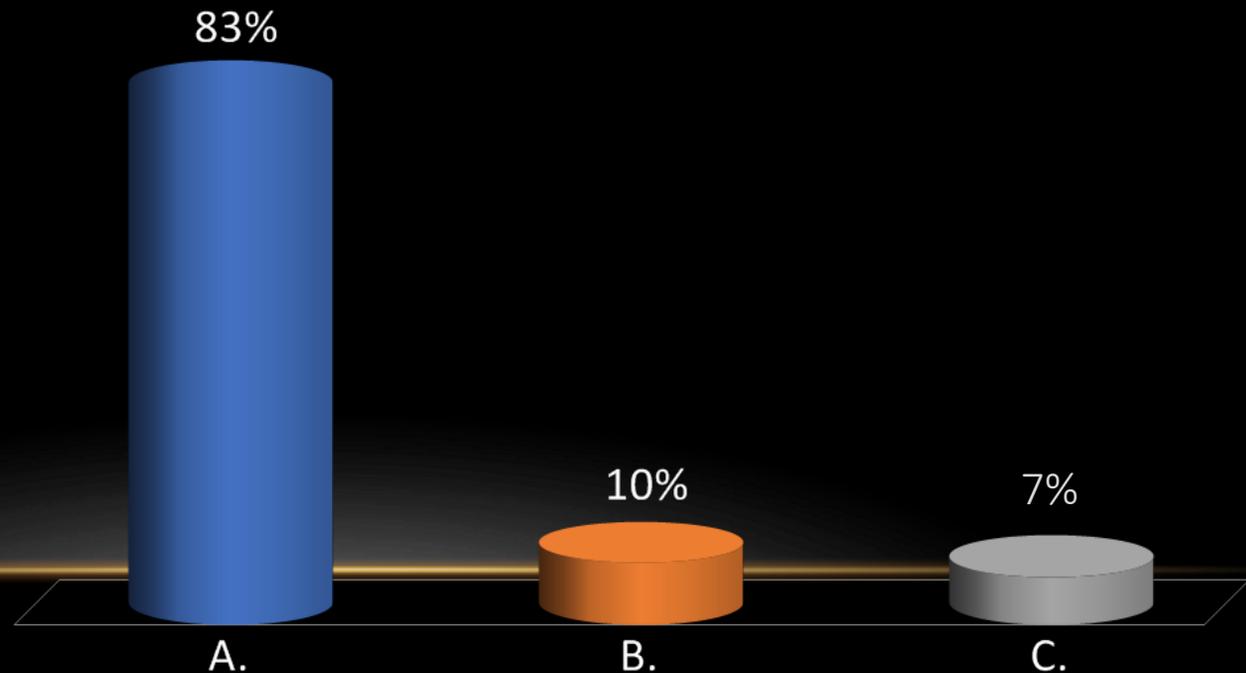
- **Meta-Analysis 2, Prospective/Randomized 0, Retrospective 16**
- Tsaras et al. conducted a meta-analysis of 26 studies on the utility of intraoperative frozen section histopathology in the diagnosis of PJI. They concluded that intraoperative frozen sections are valuable in the diagnostic work-up of PJI.
- Zhao et al. concluded in their meta analysis that a threshold of 10 PMN/hpf had the same sensitivity but higher specificity than 5 PMN/hpf for the diagnosis of PJI



Recommendation: Adequate peer-reviewed literature exists to support either of two diagnostic thresholds for supporting the diagnosis of periprosthetic infections of the hip and knee: 5 neutrophils (PMNs) in each of at least 5 high power (400X) microscopic fields (HPF), or 10 PMNs in each of at least 5 HPFs.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 8: Should patients with PJI caused by *Mycobacterium tuberculosis* undergo the typical two-week drug holiday prior to reimplantation?

RESEARCHED BY:

Tanavalee, Aree

Molano, Miguel



Literature:

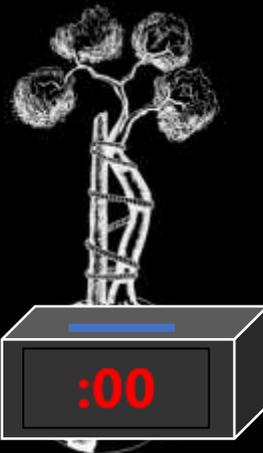
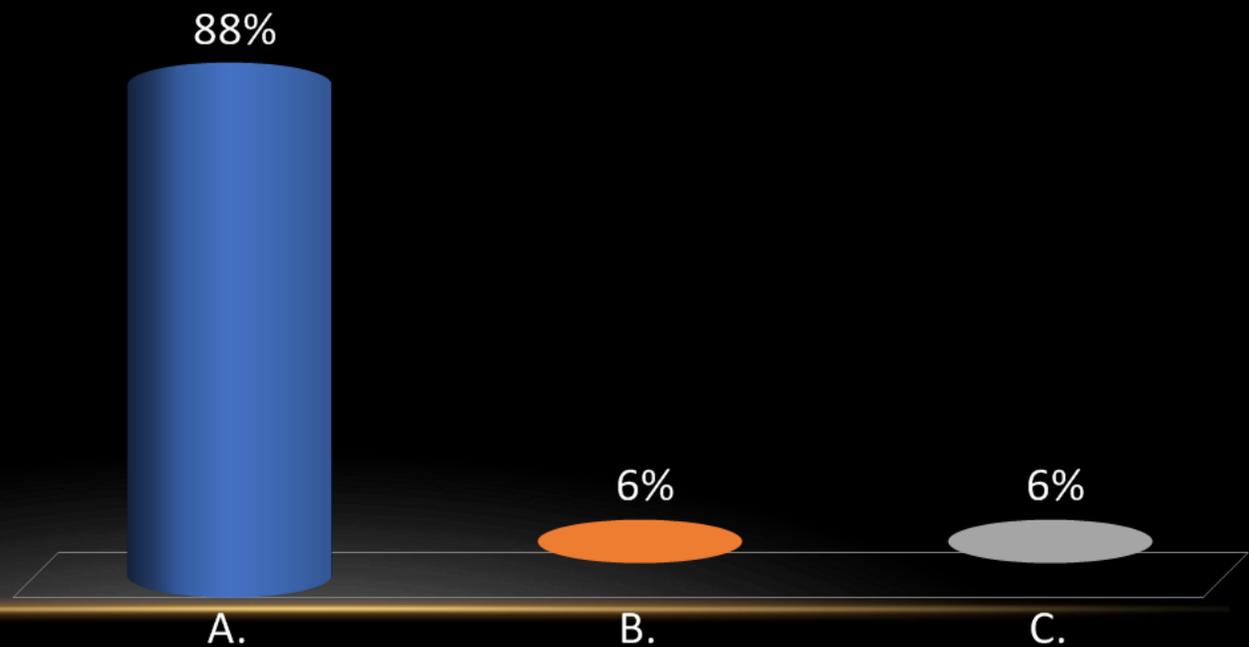
- Meta-analysis 1, Prospective/Randomized 0, Retrospective 13
- In a systematic review of 15 patients, 33% underwent a DAIR, while 20% underwent a staged revision arthroplasty, for which the anti-TB chemotherapy was continued at the time to reimplantation.
- A second study reported varying durations of anti-TB chemotherapy from between 4-39 months, with 56% of patients received at least 12-month treatment. Surgical treatment ranged from debridement 17%, debridement & polyethylene exchange 8%, two-stage exchange 23% and revision to arthrodesis 33%.



Recommendation: There is no evidence supporting the two-week drug holiday before reimplantation. Patients with PJI caused by *Mycobacterium tuberculosis* do not need to have the two-week drug holiday.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Section 3: Pathogen Factors



Question 1: Does the virulence (low or high) of the infecting organism affect the treatment of acute hematogenous or chronic PJI?

RESEARCHED BY:



Henk Scheper MD,
Netherlands



Marjan Wouthuyzen-
Bakker MD, Netherlands



Juliana Matos MD,
Brazil



Literature:

- Meta-analysis 2, Prospective/Randomized 3, Retrospective 51

Late acute / hematogenous PJI treated with DAIR			
Article, yr	n	Success rate	Comments
Wouthuyzen-Bakker 2018 [19]	340	55%	Unpublished data
Lora-Tamayo, 2017 [20]	242	59%	Only streptococci
Akgün, 2017 [21]	16	69%	Only streptococci
Tande, 2016 [22]	35	74%	Only S aureus bacteremia, 2y survival 62%
He, 2016 [23]	11	82%	
Koh, 2015 [24]	20	55%	
Holmberg 2015 [25]	12	75%	
Puhto, 2015 [26]	35	46%	
Koningsberg 2014 [27]	42	76%	
Geurts, 2013 [28]	6	83%	
Lora-Tamayo, 2013 [29]	52	35%	Only staphylococci
Kuiper 2013 [30]	32	59%	
Rodriguez, 2010 [31]	50	48%	
Byren, 2009 [32]	12	83%	Only hips
Giulieri, 2004 [33]	27	78%	
Everts, 2004 [34]	16	94%	Only streptococci, only 1pt had formal microbiological cure
TOTAL	948	56%	

Literature:

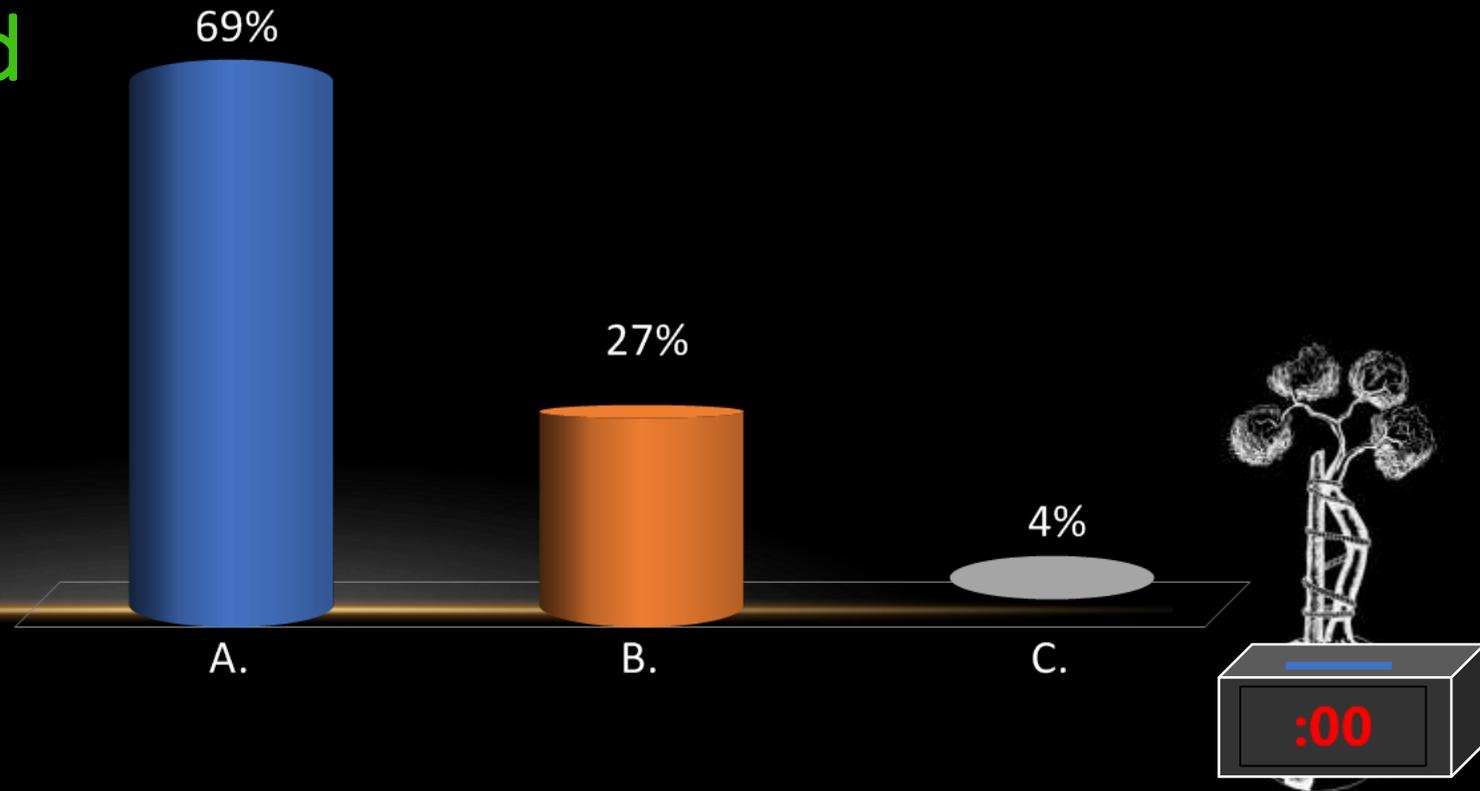
Chronic PJI treated with 1-stage or 2-stage exchange

Article, yr	n	Success rate	Comments
Beswick 2014 [35]	4197	90%	Meta-analysis comprising 62 studies with 1-or 2-stage exchange. Subanalysis of 11 studies with 1225 patients and only 1-stage: success 91.4%
Singer 2012 [36]	63	95%	Only 1st. exchange for TKA
Jenny 2013 [37]	47	87%	Only 1st. exchange for TKA
Haddad 2015 [38]	28	100%	Only 1st. exchange for TKA
Tibrewal 2014 [39]	50	98%	Only 1st. exchange for TKA
Zahar 2016 [40]	70	93%	Only 1st. exchange for TKA
Gooding 2011 [41]	115	88%	2-step exchange for TKA

Recommendation: There is currently no evidence showing that the virulence of an infecting organism affects the treatment of acute hematogenous or chronic PJI.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Is there a difference in the treatment outcome for PJI caused by a single organism and polymicrobial PJI?

RESEARCHED BY:



Timothy Tan MD, USA

Igor Shubnyakov MD, Russia



Literature:

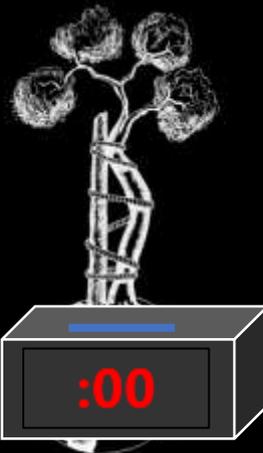
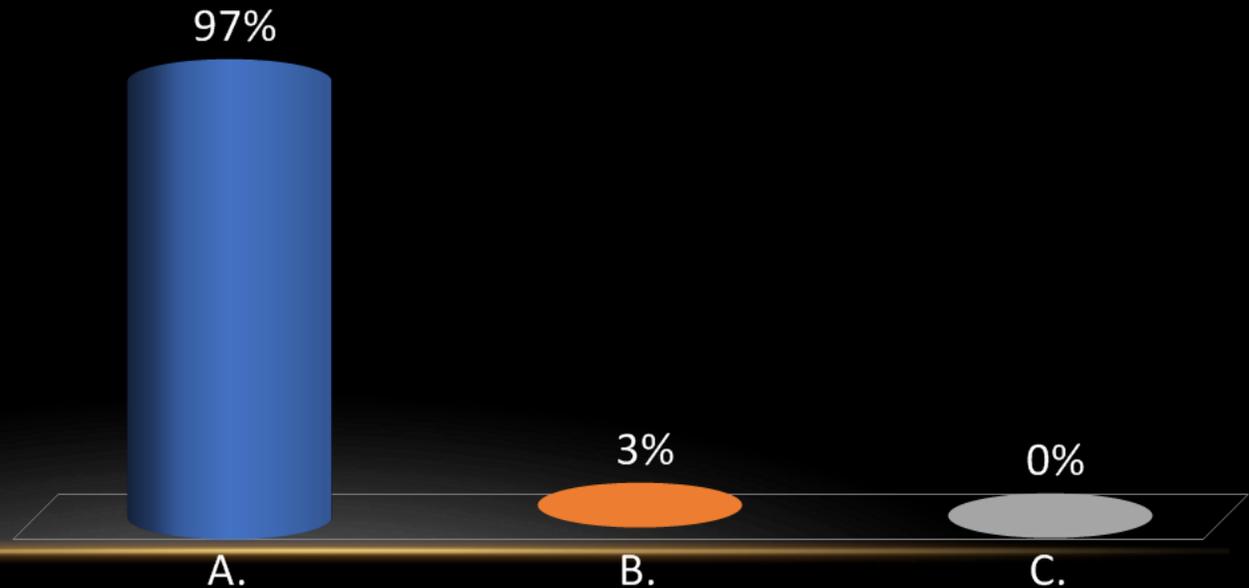
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 13**
- Patients with polymicrobial PJI have higher failure rates (50.5%) than monomicrobial PJI patients (31.5%)
 - These results are corroborated by a number of other studies
- Several reasons for increased failure in polymicrobial PJI have been demonstrated, including an association with organisms that are difficult to treat



Recommendation: Polymicrobial periprosthetic joint infection (PJI) demonstrates inferior treatment outcomes when compared to monomicrobial PJI. This finding is true for both patients treated with irrigation and debridement and two-stage exchange arthroplasty.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Is there a difference in the type of pathogens that can cause SSI/PJI between hip and knee arthroplasty?

RESEARCHED BY:



Karan Goswami, MD



Hannah Groff



Literature:

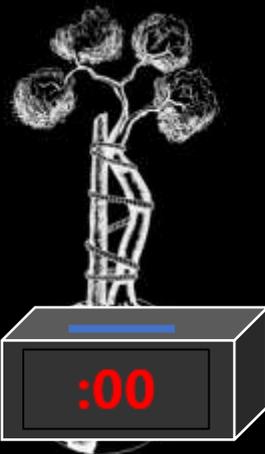
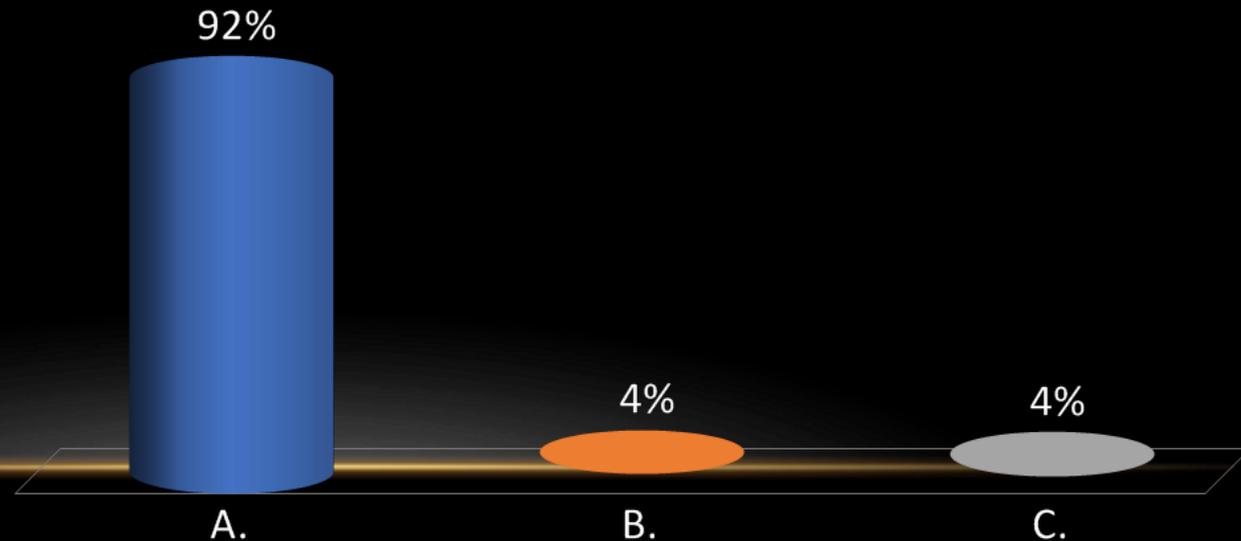
- Meta-analysis 0, Prospective/Randomized 3, Retrospective 9
- No definitive evidence to suggest significant difference in pathogen profile between hip and knee arthroplasty
- A few studies show increased prevalence of Streptococcal species in the knee and Staphylococcal, Enterococcal and Pseudomonal species in the hip



Recommendation: There is limited evidence to support a difference in the organism profile causing surgical site infection (SSI) and periprosthetic joint infection (PJI) between hip and knee arthroplasty. Isolated studies have reported an increased prevalence of Streptococcal and culture-negative PJI around the knee, whereas Staphylococcal, Enterococcal, Pseudomonas PJI may be more prevalent around the hip. Further work regarding the different flora in these respective body regions is needed, as it may determine antibiotic selection.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Is there a difference in the organism profile that causes PJI in different countries?

RESEARCHED BY:



Paul M Courtney MD, USA

Nemandra A Sandiford MD, UK

Daniel Kendoff MD, Germany



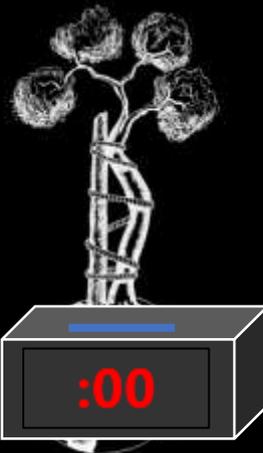
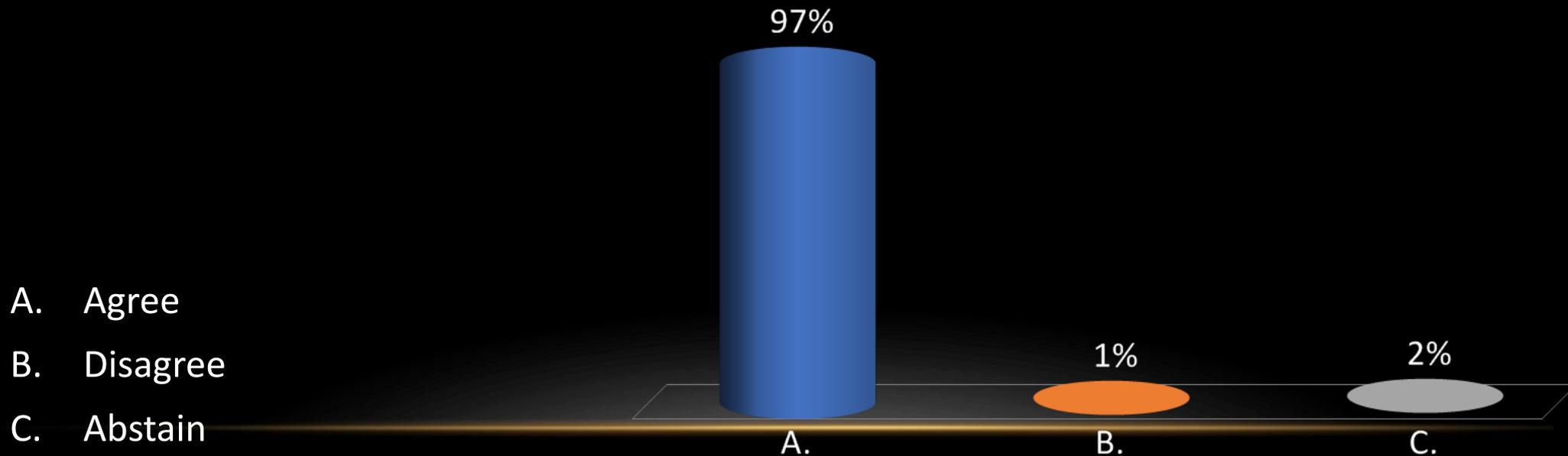
Literature:

- **Meta-analysis 0, Prospective/Randomized 2, Retrospective 10**
- Two studies, one prospective, found a higher incidence of coagulase-negative *Staphylococcus* (CoNS) and *Streptococcus* pathogens compared with *S. aureus* within various European registries
- Other studies have demonstrated a significantly higher percentage of MRSA pathogens in the USA than in Europe



Recommendation: Yes, there is a difference in the organism profile causing periprosthetic joint infection (PJI) in different countries and regions of this world. There seems to be a higher incidence of PJI caused by Methicillin-resistant *Staphylococcus aureus* (MRSA) in the United States and Australia compared to Europe.

Level of Evidence: Moderate



Section 4: Fungal PJI

- 4.1 Diagnosis and Treatment



4.1 - Fungal PJI: Diagnosis and Treatment



Question 1: What is the optimal method to diagnose fungal PJI?

RESEARCHED BY:

Feng Chih Kuo MD, Taiwan

Majd Tarabichi MD, United States of America



Literature:

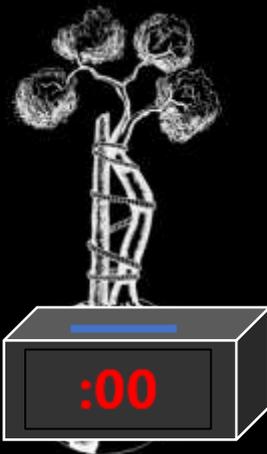
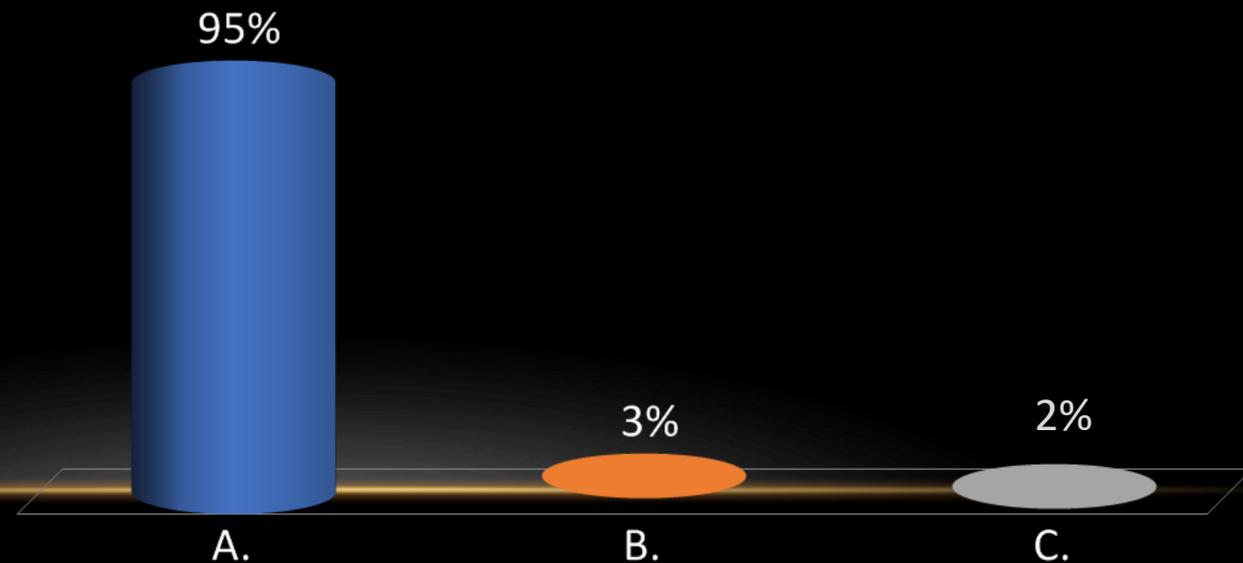
- **Meta-analysis 1, Prospective/Randomized 0, Retrospective 21**
- Based on available retrospective data, perioperative cultures such as aspirated synovial fluid, intraoperative tissue and swab samples have been considered diagnostic standards for fungal PJI.
 - Despite this standard, culture has been shown to have sensitivity as low as 50%
- Sequencing of the Internal Transcribed Spacer segment, (fungal sequence analogous to the 16S segment) was demonstrated to have a sensitivity of approximately 90%, with a turnaround time of a week
 - This would potentially be a massive improvement over culture diagnosis



Recommendation: Diagnosis of fungal PJI is established by incubating joint aspirations or tissue samples collected intraoperatively on to specialized culture media. Furthermore, isolation of fungal species may take up to four weeks. However, given the shortcomings associated with the use of culture, alternative techniques capable of detecting fungi such as molecular techniques may be used as an adjunct.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Should patients with PJI caused by a fungus undergo the typical two-week drug holiday prior to reimplantation?

RESEARCHED BY:

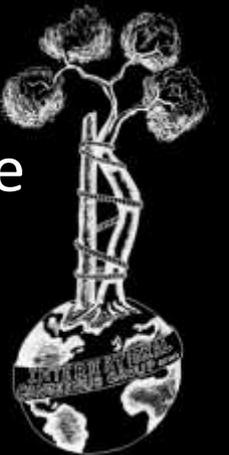
Kuo, Feng Chih

Riccio, Giovanni



Literature:

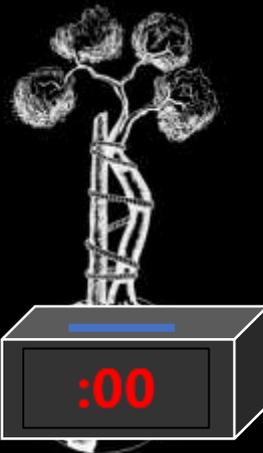
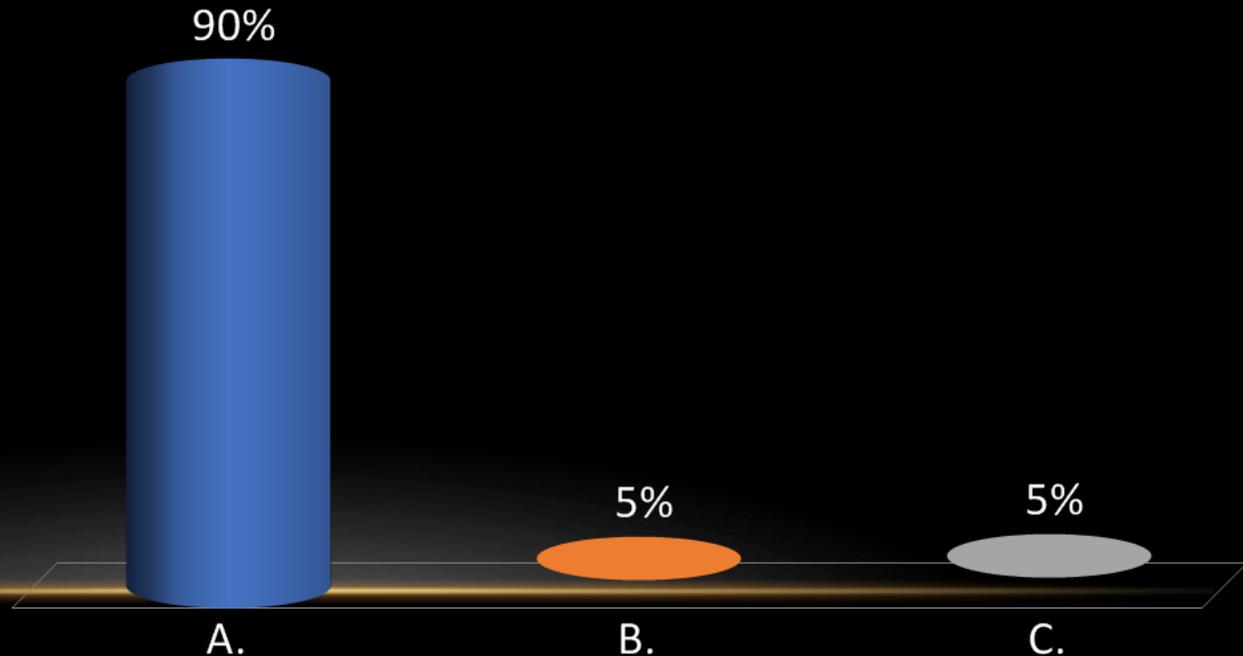
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 18
- Only level IV and V evidence exists. Most patients appear to have at least 6 weeks of systemic antifungal treatment after first operation, in agreement with the 2013 Consensus conclusions.
- Following reimplantation, antifungal agents (fluconazole) were continued for between 2 weeks to 6 months.
- Most authors seem to prefer a drug-holiday of two or more weeks before second surgical stage.



Recommendation: There is no conclusive evidence to support the use of a drug holiday period prior to reimplantation in case of fungal PJI treated with staged revision.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Can debridement, antibiotics, and implant retention be used to treat acute fungal PJI?

RESEARCHED BY:



Li Cao MD, China

Feng Chih Kuo MD, Taiwan



Literature:

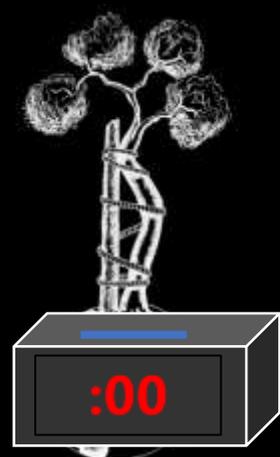
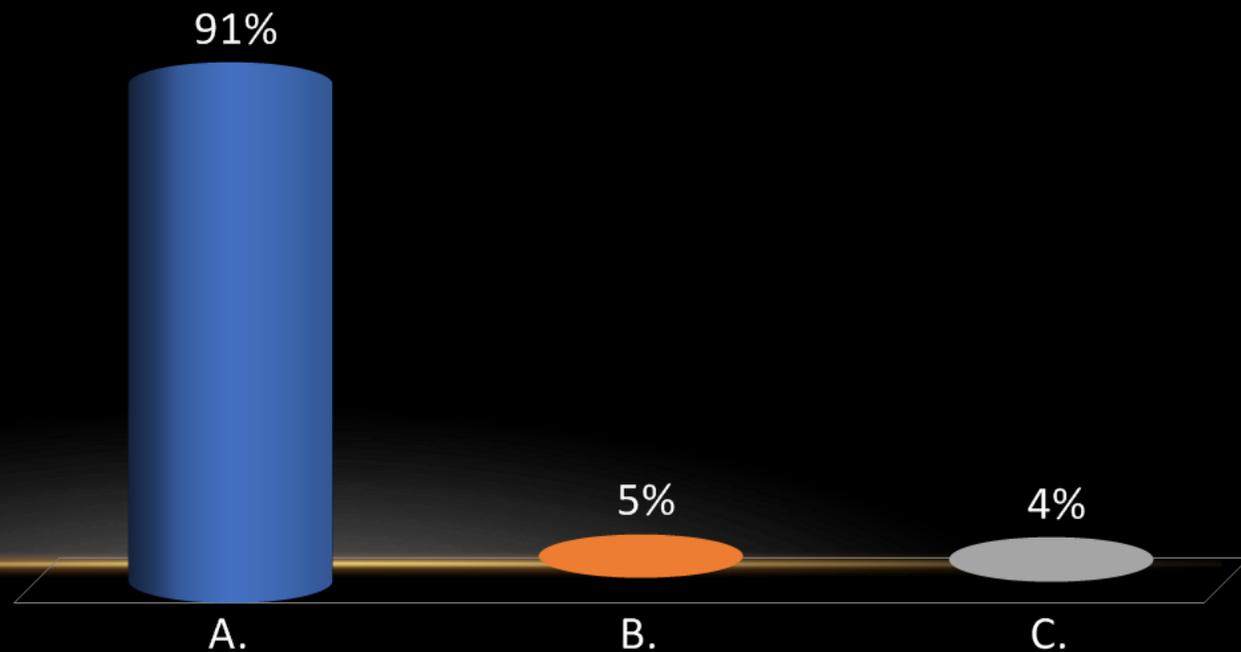
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 12**
- Systematic review of literature (1979 to 2018) identified 22 fungal PJI undergoing DAIR
 - Overall failure rate was 82% (18/22)
 - Azzam et al reported 100% failure case of fungal PJI undergoing DAIR (n=7)
 - Isolated case reports demonstrate successful results at 2-year follow up, but all required 6-months to 1-year of antifungal treatment after I&D



Recommendation: Debridement, antibiotics, and implant retention (DAIR) has a relatively high failure rate in fungal periprosthetic joint infection (PJI), especially for immunocompromised patients. DAIR should be reserved for patients with truly acute PJI after an index arthroplasty and in healthy patients (Type A). If DAIR is performed for fungal PJI, consideration should be given to anti-fungal suppression therapy.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4: What antifungals, route of administration, and duration of treatment should be utilized to treat fungal PJI?

RESEARCHED BY:

Katherine Belden MD

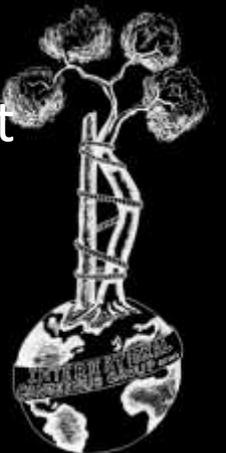
Jiying Chen MD

Feng-Chih Kuo MD



Literature:

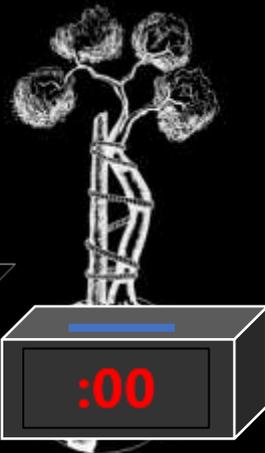
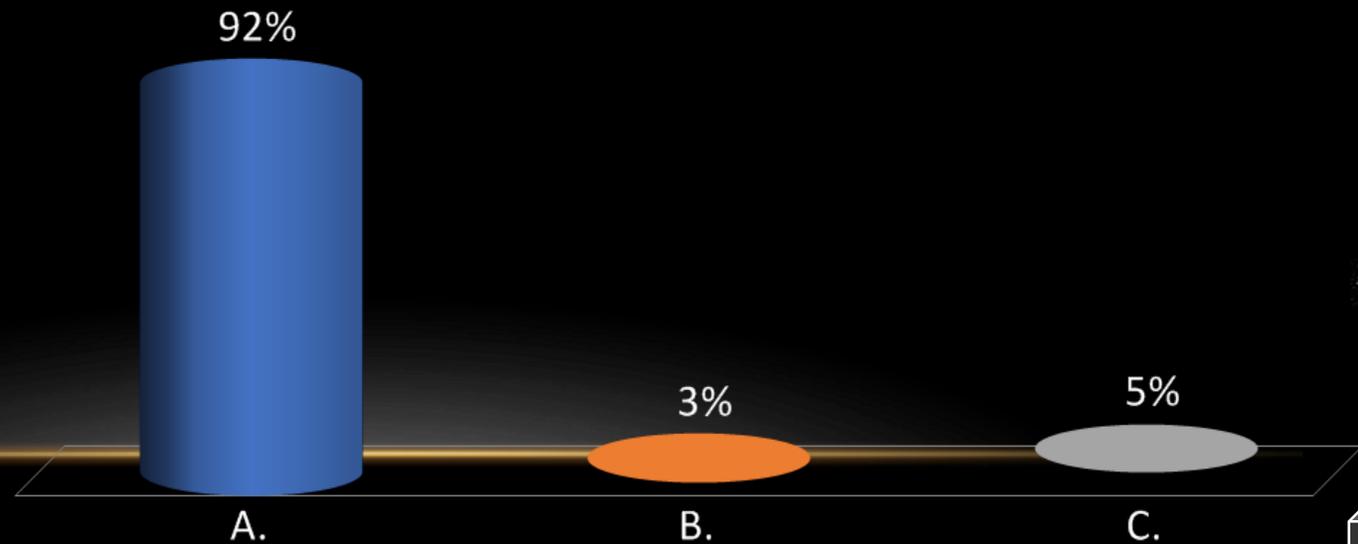
- **Meta-Analysis 2, Prospective/Randomized 0, Retrospective 21**
- Jakobs et al. (2015) conducted meta-analysis on 36 studies reporting TKA complicated by fungal PJI.
 - Candida spp = 80% of cases
 - >80% of cases received either Amphotericin B or Fluconazole
 - Resection arthroplasty was the surgical tx of choice
- A review of 8 cases of fungal PJI by Geng et al. (2016) showed an average systemic antifungal agent administration of 1.5 months.
 - 2-stage revision with implantation of antimicrobial-impregnated spacer performed 8 times in 7 cases.
- Wu et al. (2010) described a case of candida PJI following revision TKA. Patient received IV fluconazole for 6 weeks followed by amphotericin B-loaded cement spacer and continuous PO fluconazole for 9 weeks. Revision surgery was successful



Recommendation: Fluconazole, by both oral and intravenous routes, is currently the treatment of choice for prosthetic joint infections (PJI) due to susceptible fungi including *Candida* species, which are responsible for the majority of fungal PJI cases. Amphotericin B lipid formulations or echinocandins given intravenously are secondary considerations but may be less well tolerated. Culture data including antifungal susceptibilities should be used to guide therapy. Two-stage revision is currently the standard of care. Antifungal treatment should be administered during the spacer interval with a minimum treatment duration of 6 weeks. Following revision, treatment with oral fluconazole 400mg daily should be continued for 3-6 months, if tolerated.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Section 5: Treatment

- 5.1 – Algorithm
- 5.2 – Debridement and Retention of Implant
- 5.3 – One-State Exchange
- 5.4 – Two-Stage Exchange, Spacer Related
- 5.5 – Two-State Exchange
- 5.6 – Surgical Technique
- 5.7 – Prosthesis Factors
- 5.8 – Salvage
- 5.9 – Antimicrobials
- 5.10 – Antimicrobials (Two-Stage)
- 5.11 – Antimicrobial Suppression



5.1 - Treatment: Algorithm



Question 1: Should early postoperative infection and acute hematogenous infection be treated and managed differently?

RESEARCHED BY:



Marc Nijhof



Rudolf Poolman

Feng-Chih Kuo



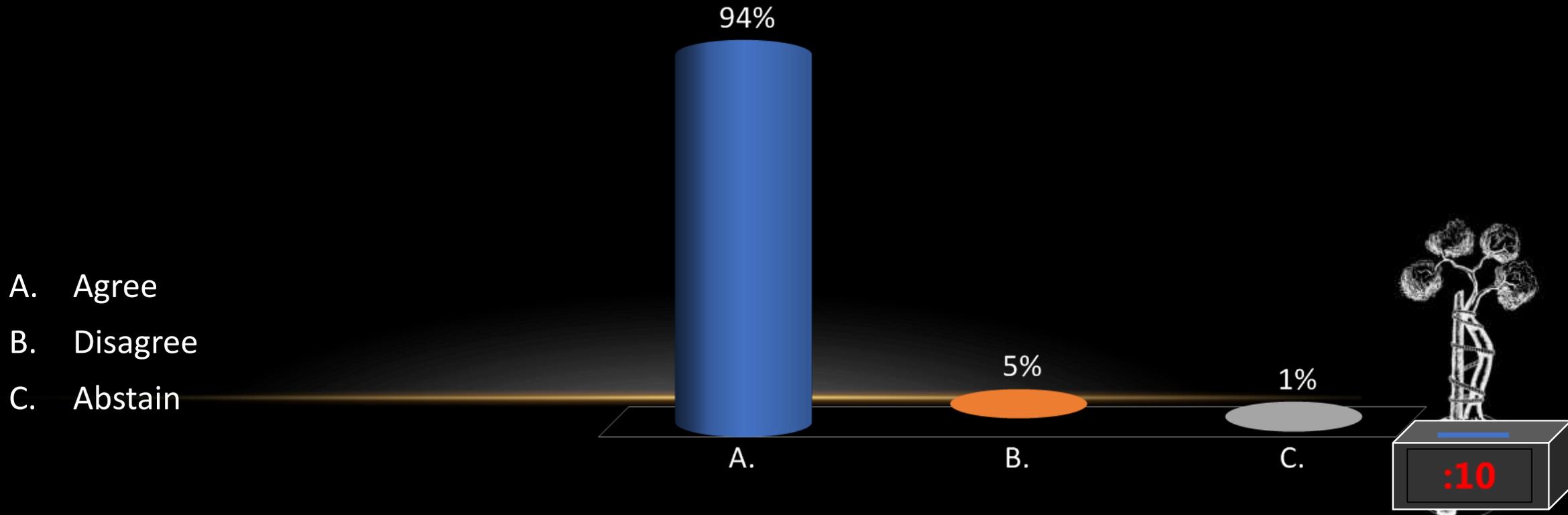
Literature:

- **Meta-Analysis 4, Prospective/Randomized 1, Retrospective 11**
- There is lacking evidence to support different treatment and management strategies between acute postoperative infections and acute hematogenous infections.
- The Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) notes that patients who have a well-fixed, functioning prosthesis without a sinus tract, infection occurring within 30 days of index arthroplasty or an antimicrobial-susceptible organism should be candidates for debridement and implant retention (DAIR)



Recommendation: There is no evidence to support the notion that early postoperative infection and acute hematogenous infection should be treated differently as long as the onset of symptoms is <4 weeks (favorable <7 days), Implants are well-fixed, no sinus tract exists, and the isolated infecting organism is sensitive to an antimicrobial agent

Level of Evidence: Moderate

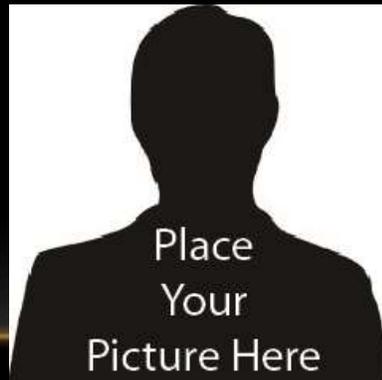


Question 2: Should operative treatment differ in patients with systemic sepsis in the setting of PJI?

RESEARCHED BY:



Antony Rapisarda, MD



Tae-Kyun Kim, MD



Salvador Rivero-Boschert, MD



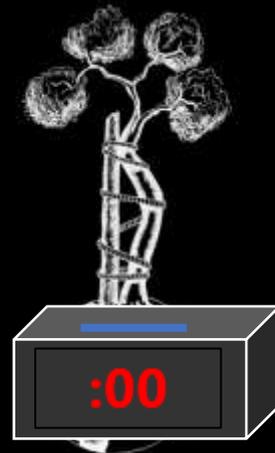
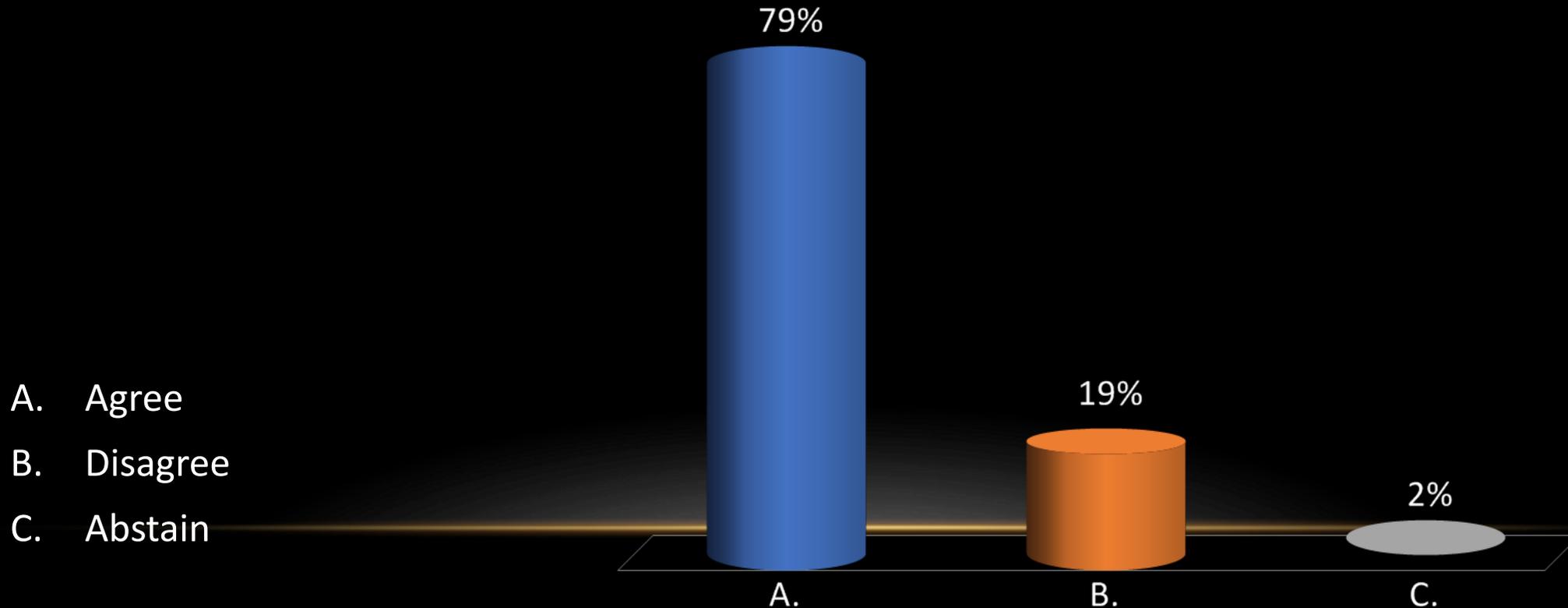
Literature:

- Meta-analysis 0, Prospective/Randomized 0, Retrospective 13
- All studies recommend 2-stage revision
- No studies that directly evaluate whether operative treatment should differ in patients with systemic sepsis in setting of PJI



Recommendation: Yes. Patients with systemic sepsis in the setting of PJI should have resection of the components and bioburden reduction along with concurrent antimicrobial therapy. Reimplantation should be delayed until sepsis is resolved.

Level of Evidence: Limited



Question 3: What should be done for patients with persistent wound drainage after total joint arthroplasty? What are the indications for surgical intervention?

RESEARCHED BY:



James Purtill MD,
United States of America



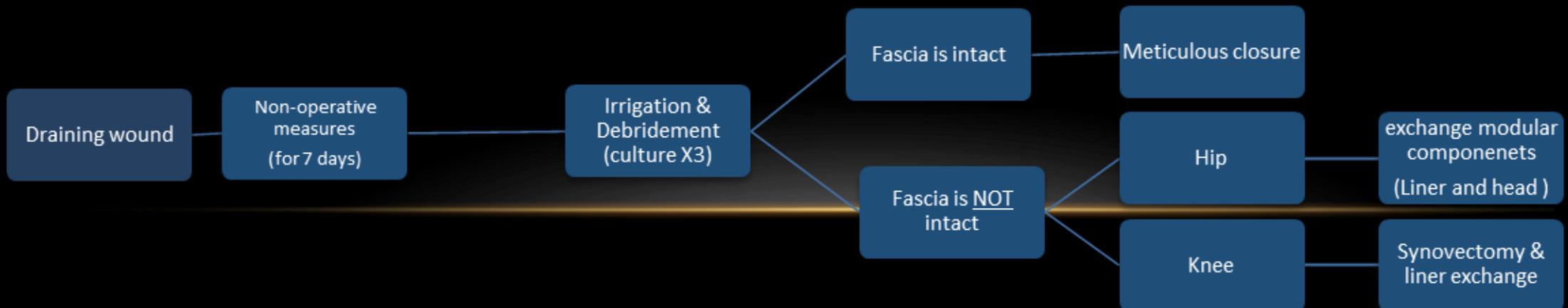
Brianna Fram MD,
United States of America



Ali Oliashirazi MD, United
States of America

Literature:

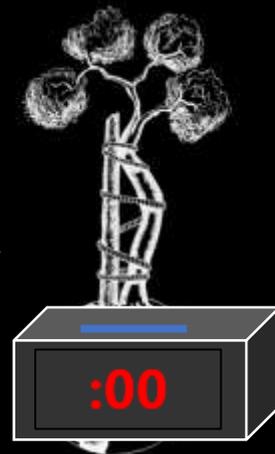
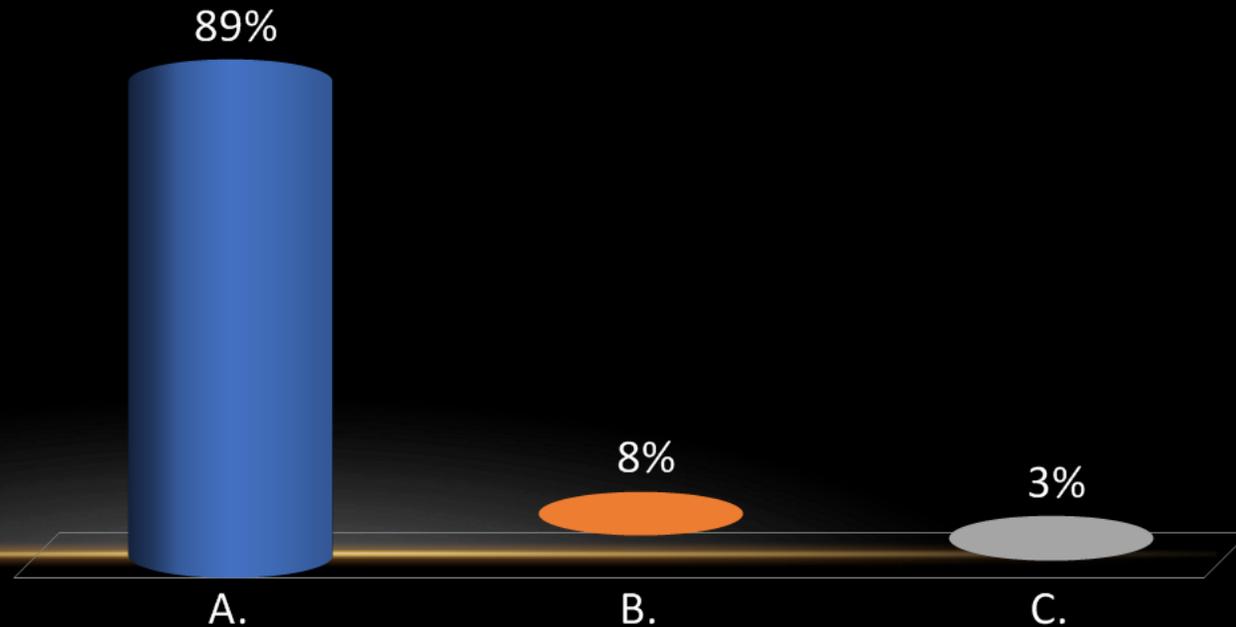
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 12**
- One of the first steps in patients with PWD is to cease the anticoagulation medications, followed by negative pressure wound therapy
- Surgical intervention for drainage should be considered after 5 to 7 days of PWD (Patel et al., Jaber et al.).



Recommendation: Management of draining wounds after total hip or knee arthroplasty consists of two main steps; non-operative and operative. The non-operative measures include: modification of VTE prophylaxis, nutritional supplementation, dressing measures (such as negative pressure wound therapy), and restriction of range of motion. If draining continues for more than 7 days after implementing the nonoperative measures, operative interventions may be indicated – including irrigation and debridement, synovectomy and single-stage exchange. In certain situations, superficial wound washout may be indicated.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: How should infected bilateral hip or knee arthroplasties be managed?

RESEARCHED BY:



Paul M. Courtney

Thanainit Chotanaphuti



Sébastien Lustig



Literature:

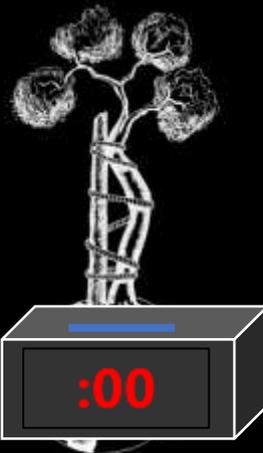
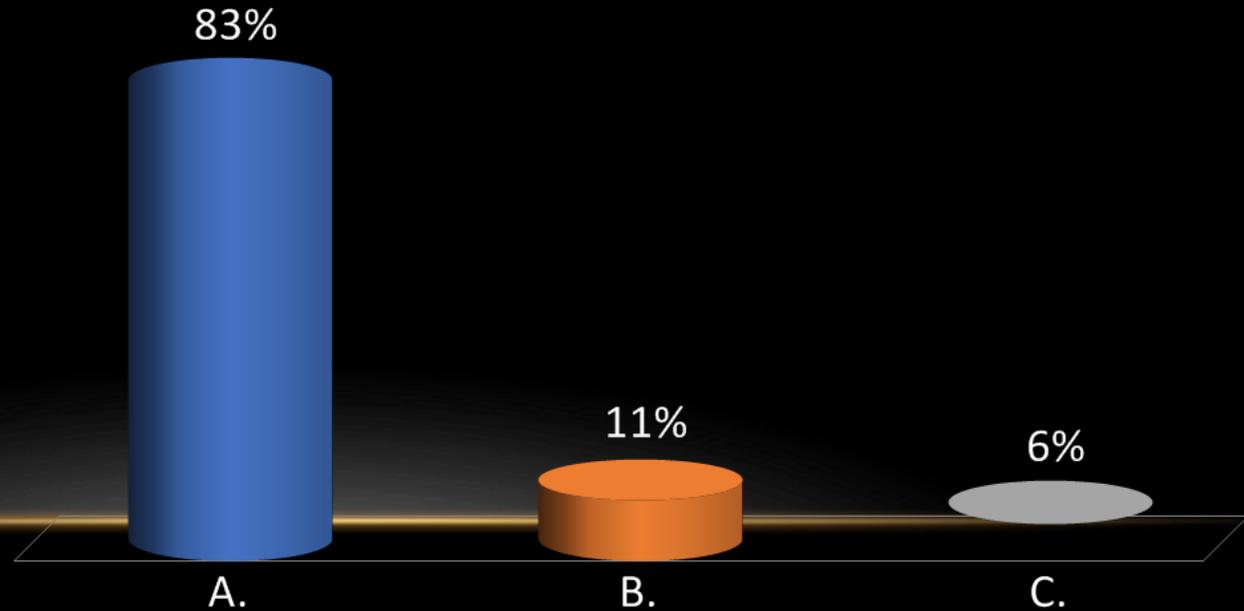
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 18
- The literature on this topic is limited, with only 2 small case series and at least nine case reports describing multiple simultaneous periprosthetic joint infections (PJI).



Recommendation: The optimal surgical treatment for infected bilateral hip or knee arthroplasties is unknown. While revising the components likely provides improved outcomes over limited debridement with component retention, data does not preferentially support either a single-stage or two-stage exchange revision arthroplasty

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



5.2 – Treatment: Debridement and Retention of Implant



Question 1: What are the indications and contraindications of using debridement, antibiotics, and implant retention with exchange of modular components for the management of PJI?

RESEARCHED BY:



Marjan Wouthuyzen-
Bakker MD

Choe Hyonmin MD

Ayman Ebied MD

Noam Shohat MD



Literature:

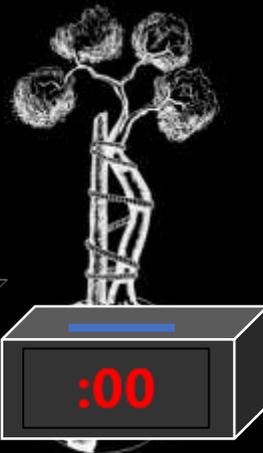
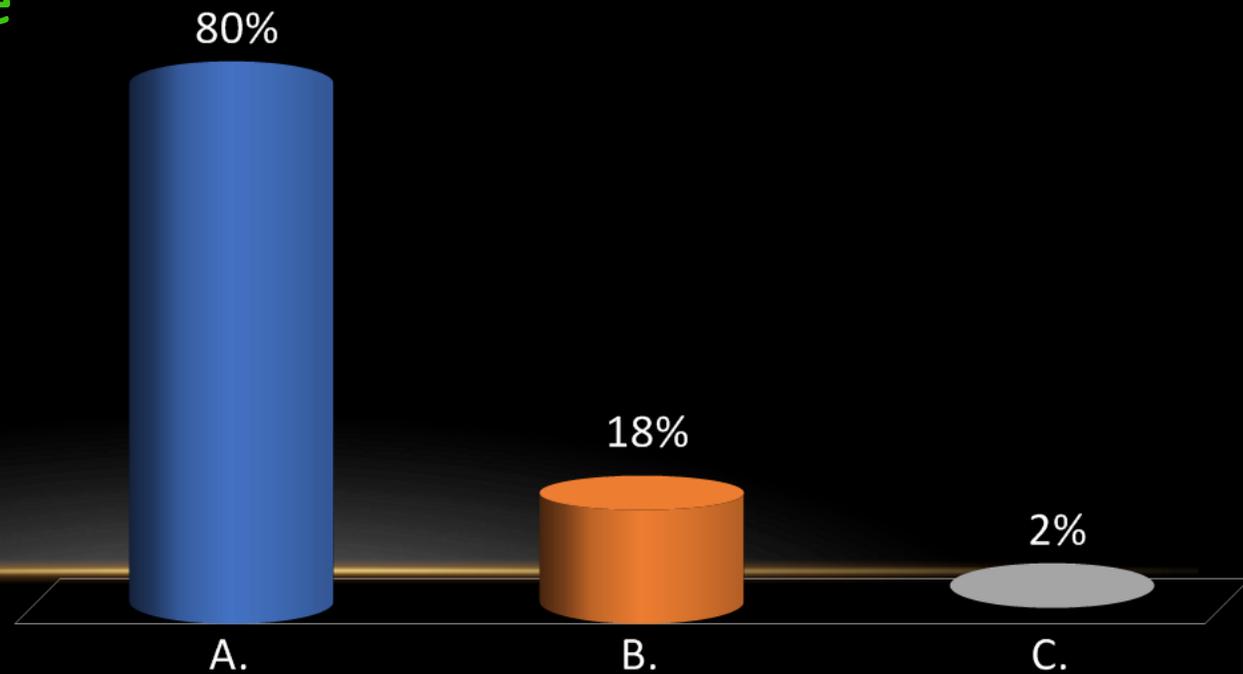
- **Meta-Analysis 1, Prospective/Randomized 1, Retrospective 43**
- A meta-analysis by Tsang et al., in 2017 shows the following
 - Improved success with early debridement (< 7 days; 75.7%) and exchange of modular components (77.5%).
 - No significant improvement following treatment if debridement was performed within four weeks of the initial procedure (73.0%).
- Barberan et al. demonstrated in 60 elderly patients with a staphylococci infection who underwent DAIR.
 - Shorter duration of symptoms ($P = 0.001$) and time to diagnosis ($P = 0.01$) were found in patients who were cured.
 - Global failure was 35% and ranged from 16.6% to 69.2% ($P = .0045$) in patients with symptoms that lasted from less than 1 month to more than 6 months.



Recommendation: The best advantage in performing DAIR of the prosthesis is seen in early postoperative PJI and acute hematogenous PJI, defined as symptoms existing for no longer than four weeks, and if the implant is stable. The KLIC and CRIME80 scores

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Is debridement, antibiotics, and implant retention (DAIR) an emergency procedure for patients with acute PJI or should patient optimization be implemented prior to surgery to enhance the success of this procedure?

RESEARCHED BY:

Anna Stefánsdóttir MD, Sweden

Georgios Komnos MD, Greece



Literature:

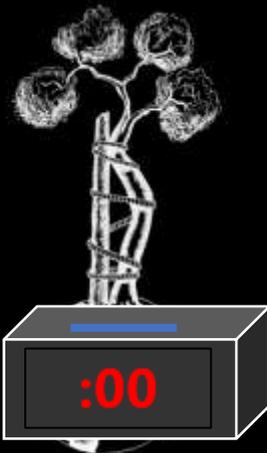
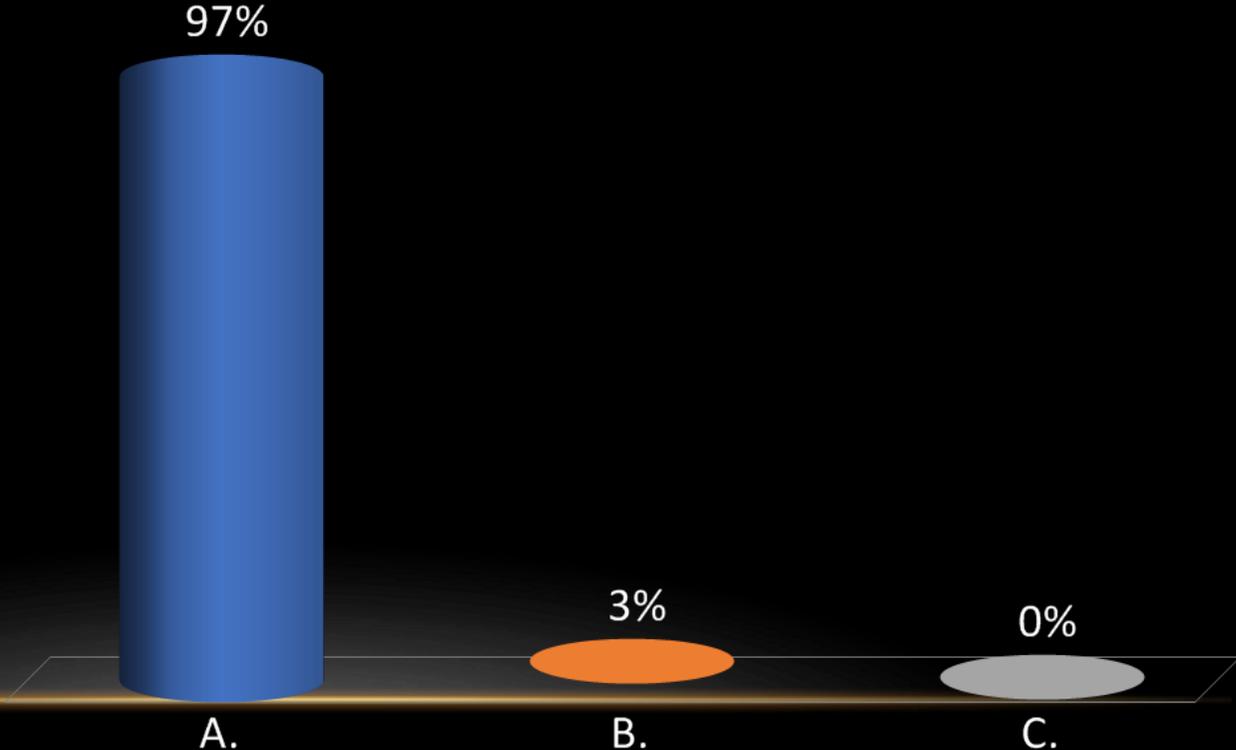
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 24, Literature Review 1**
- **No studies have focused on the urgency of DAIR as a procedure**
- **DAIR should be an urgent but not emergent procedure in patients with acute PJI**
 - **Duration of <1 week and implant age <15 days have been correlated with higher success rate**
- **Patients should be evaluated on an urgent basis and surgery performed when patient is optimized from a medical and surgical perspective**



Recommendation: Debridement, antibiotics, and implant retention (DAIR) is not an emergency procedure but should be performed on an urgent basis when the patient with acute PJI is medically and surgically optimized.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Does identification of the pathogen prior to performing debridement, antibiotics and implant retention (DAIR) help guide the surgeon's decision making? If so, should you wait in a clinically stable patient until the pathogen has been identified?

RESEARCHED BY:



Jaime Lora-Tamayo MD, Spain



Benjamin Zmistowski MD, USA



Literature:

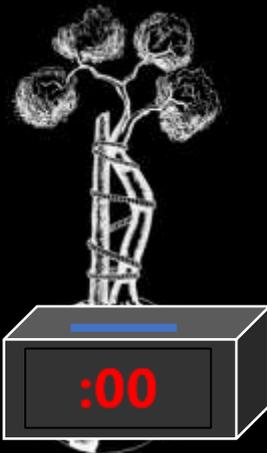
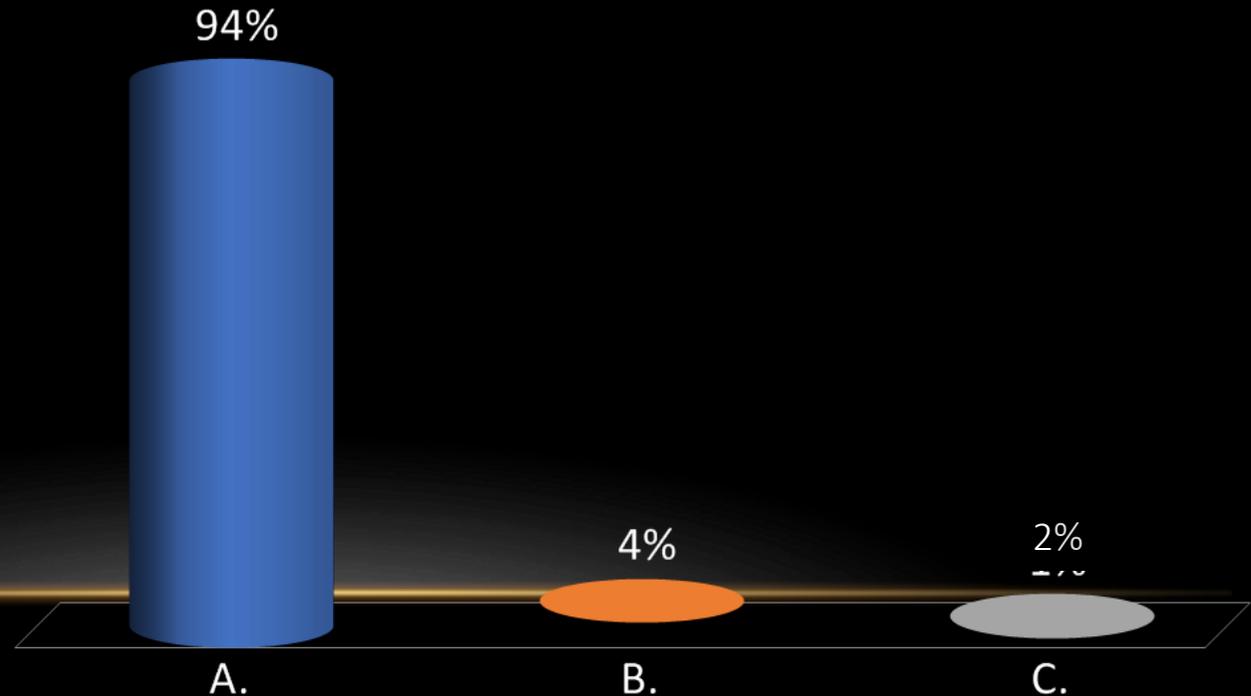
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 26**
- Limited evidence suggests that while determining type of infecting pathogen can be valuable information in the treatment algorithm for patients and surgeons considering DAIR, prompt surgery is also of utmost importance.
- That said, variable clinical success rates have been reported for common pathogens when managed by DAIR: 13-90% for *Staphylococcus aureus*; 27-94% for Gram-negative bacilli; and 40% to 94% for *Streptococci*.



Recommendation: The identification of the responsible microorganism before DAIR is desirable. However, it should not prevent timely surgical intervention if delay in surgery is believed to promote further establishment of biofilm formation and compromise the outcome of surgical intervention.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Does exchange of all modular components during debridement and implant retention (DAIR) reduce the rate of SSI/PJI recurrence?

RESEARCHED BY:



In Jun Koh MD,
South Korea



Adrian Taylor MD,
United Kingdom



Tae-Kyun Kim MD,
South Korea



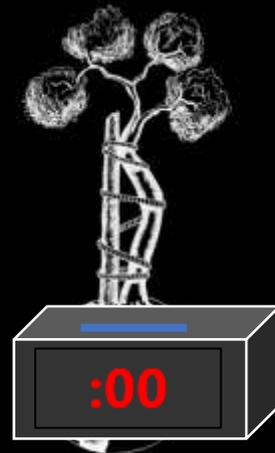
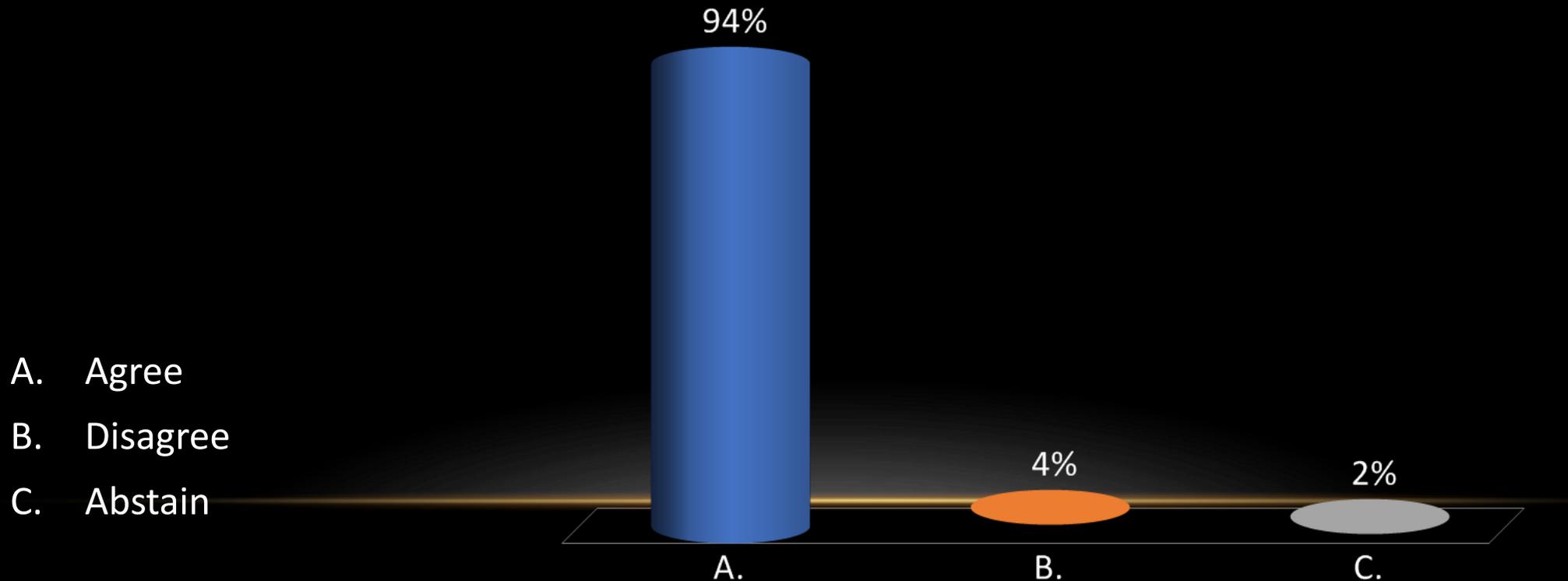
Literature:

- **Meta-analysis 1, Prospective/Randomized 1, Retrospective 49**
- Several studies (1 meta-analysis; 39 retrospective) support the exchange of modular components to reduce the rate of PJI
- A recent systematic review of DAIR performed for THA showed that mean % success in studies where modular components were exchanged was significantly higher (73.9%) vs. studies in which components were not exchanged (60.7%).
- A multicenter review of 349 patients with *Staphylococcus aureus* PJI of both THA and TKA reported that modular exchange reduced the risk of failure by 33% (Lora-Tamayo et al)



Recommendation: Yes. Exchange of all the modular components during debridement and implant retention (DAIR) reduces the risk of PJI recurrence.

Level of Evidence: Moderate



Question 5: What is the minimum necessary volume of irrigation solution to use in debridement, antibiotics, and implant retention treatment of acute PJI?

RESEARCHED BY:



Wayne G. Paprosky MD,
United States of America

Evan Schwechter MD, United
States of America



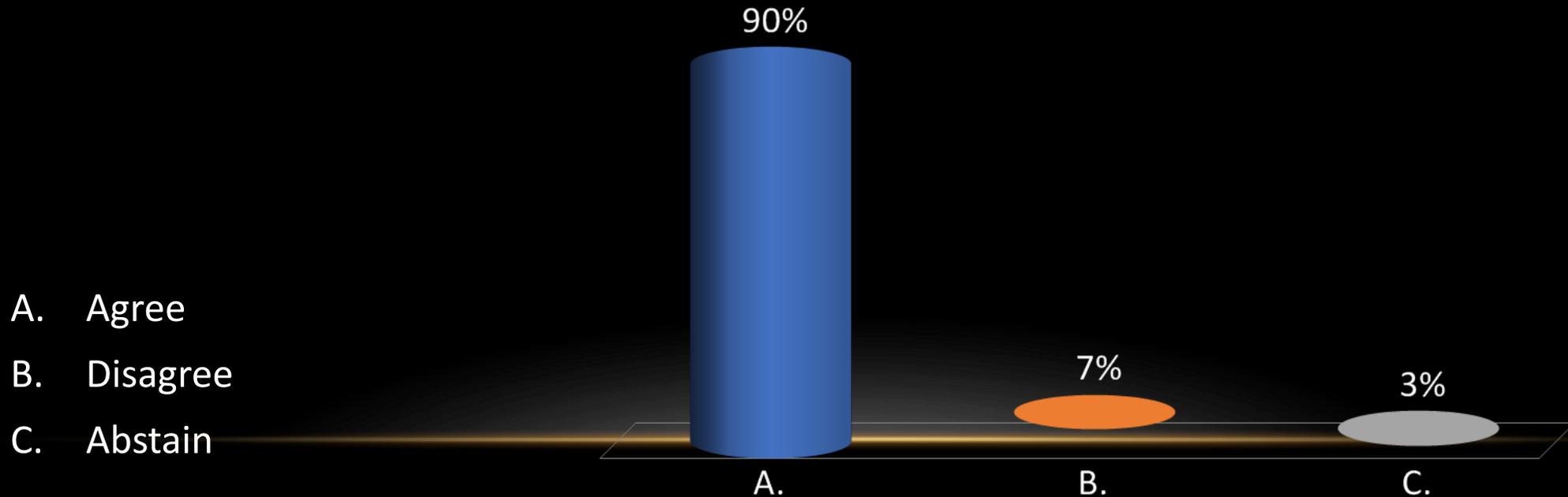
Literature:

- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 11**
- There are a small number of studies providing limited secondary data regarding the ideal volume of irrigation to be used during TJA
 - These studies either did not take biofilms into account or did not examine volume of irrigation solution as an endpoint
- Limited evidence available indicates the presence of staphylococcal infection, elevated ASA score, or purulence are more likely to determine failure than volume of irrigation.
- Delegates performed a comprehensive systematic review of the literature relating to open DAIR treatment of acute postoperative and hematogenous hip and/or knee PJI.
 - Typically 6 to 9L of solution were used during a single DAIR treatment, with twelve of the fourteen studies utilizing up to 9L or more of irrigation solution
- No studies currently exist directly linking the necessary volume of irrigation to use in debridement, antibiotics, and implant retention in acute PJI



Recommendation: We recommend that 6-9L of irrigation solution, including saline or antiseptic solution such as sterile dilute povidoneiodine, is used during DAIR treatment of acute PJI.

Level of Evidence: Consensus



Question 6: Is there a role for direct intra-articular antibiotic infusion following irrigation and debridement for PJI?

RESEARCHED BY:

Leo Whiteside MD, USA

Brian de Beaubien MD, USA



Literature:

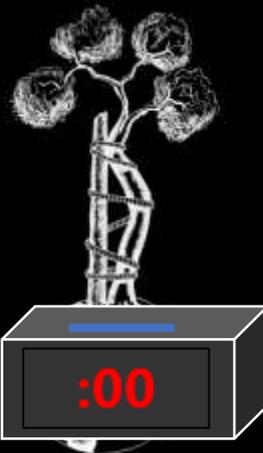
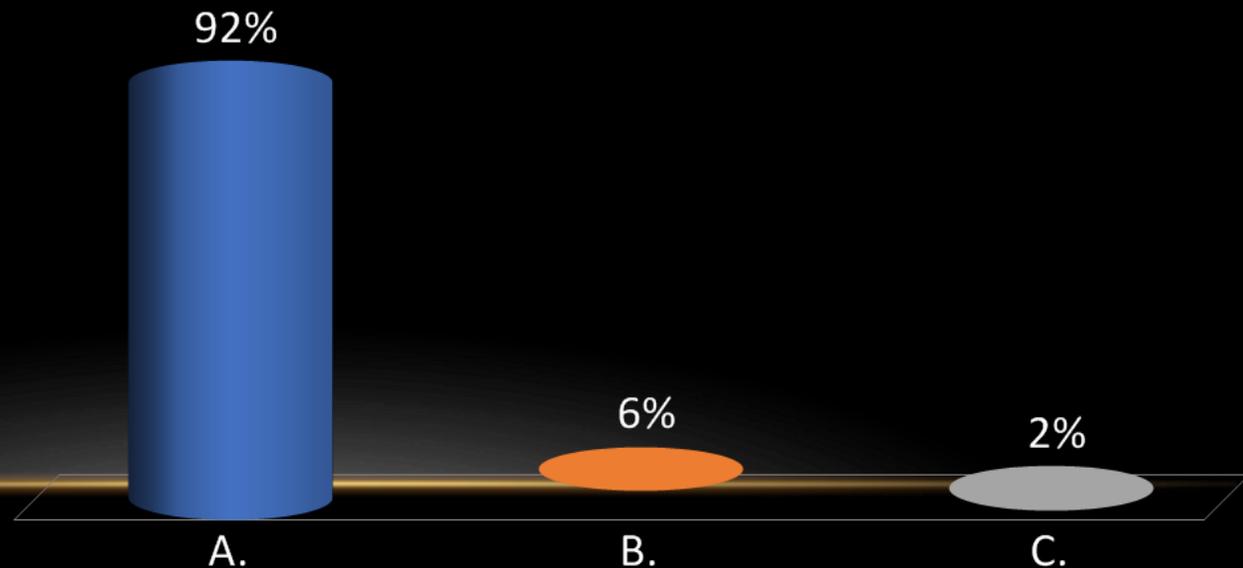
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 17**
- A study of 16 knees treated for PJI with I&D and polyethylene exchange followed by intra-articular and systemic antibiotic use reported: all patients infection free at a mean of 46.7months
 - However, 4 patients did develop recurrent infections at a mean of 28 months
- In one study intra-articular antibiotic infusion using a Hickman catheter was performed as an adjunct to meticulous debridement
 - One out of eighteen patients had a recurrent infection
- These findings are promising but do not rise to the desired level of evidence



Recommendation: The concept of achieving a minimum biofilm eradication concentration (MBEC) of antibiotics at the site of the infection is compelling. Despite the presence of retrospective studies reporting favorable outcome, because of heterogeneity in terms of adjunctive antibiotics, absence of a control group, and small cohort size the routine administration of intra-articular antibiotics in treatment of PJI is not justified. Prospective, randomized controlled trials are needed to support the routine use of intra-articular antibiotics as a stand-alone or adjunct treatment of PJI.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 7: Can debridement, antibiotics, and implant retention (DAIR) be utilized in patients with an acute or chronic infection of a unicompartmental knee arthroplasty (UKA)?

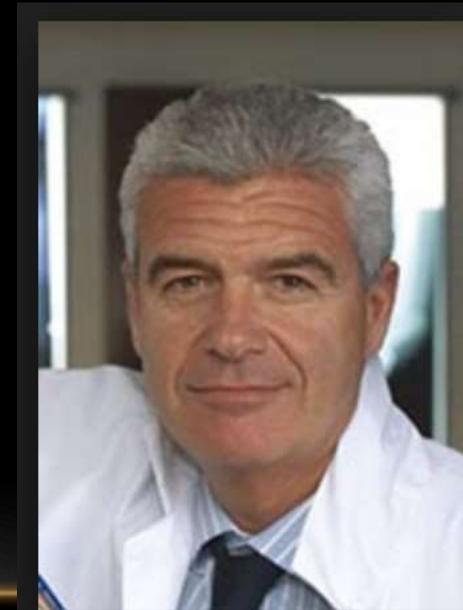
RESEARCHED BY:



Rafael J Sierra MD,
USA



George Babis MD, Greece



Jean Noël Argenson
MD, France



Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 6**
- In acute infection following UKA, early DAIR can be a proper treatment option (Kim et al., 2016).
- However, if chronic infection is present, the implanted prosthesis should be removed and a one-stage or two-stage revision surgery should be considered

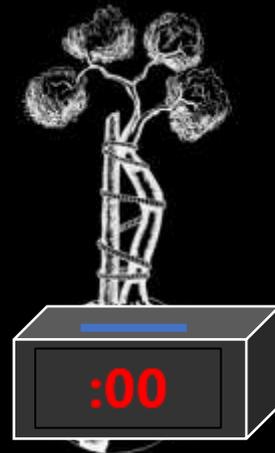
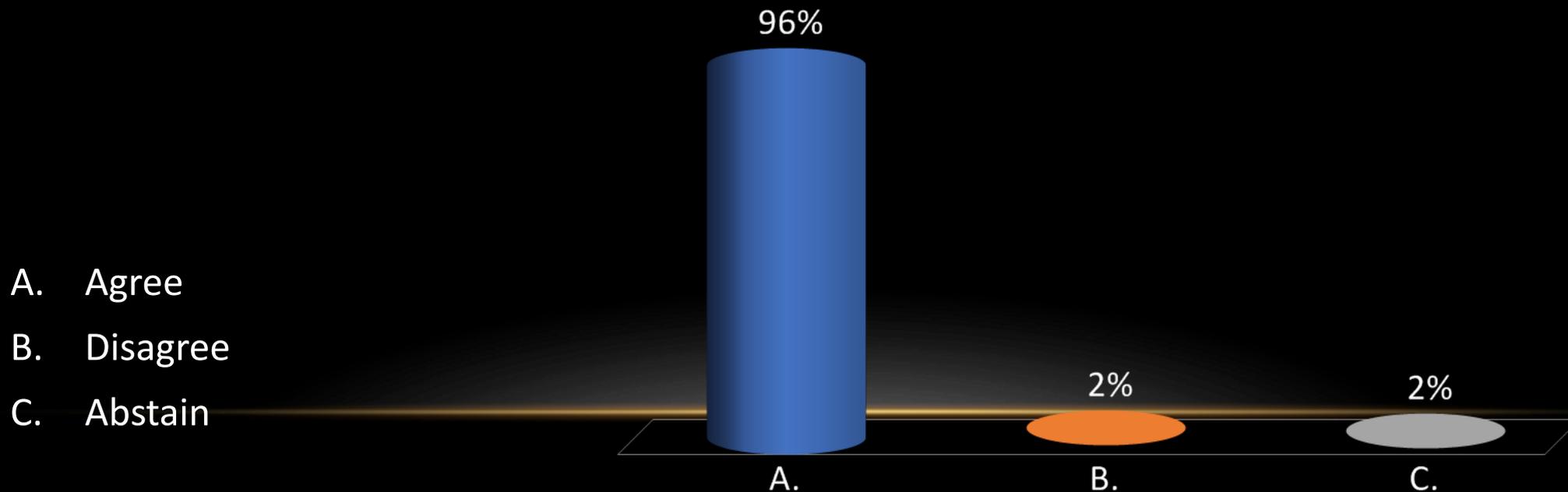
Table 1: Summary of Infected UKA Cases in the Literature

Author/Year	N (infected UKA cases)	Failed DAIR	Treatment	Failures	Follow-up
<u>Labruyere</u> 2015[1]	9	5	1-stage conversion to TKA (9)	0	Median 60 months
Bohm 2000[4]	2 (0.7% infection rate)	?	1-stage (1) 2-stage (1)	1 (AKA)	Mean 4 years
<u>Saragaglia</u> 2013[5]	8 (2% of failed UKAs)	?	?	?	?
Kim 2016[3]	5 (0.3% infection rate)	?	2-stage (5)	?	?



Recommendation: In the event of acute infection following UKA, early DAIR can be considered. However, if initial treatment effort results in failure or chronic infection is present, the implanted prosthesis should be removed and a one-stage or two-stage conversion to total knee arthroplasty (TKA) should be performed in combination with antibiotic therapy.

Level of Evidence: Limited



Question 8: Can debridement, antibiotics, and implant retention (DAIR) be utilized in the treatment of acute PJI with a megaprosthesis?

RESEARCHED BY:



Dwikora Novembri Utomo MD,
Indonesia



Nicolaas Budhiparama
MD, Indonesia



Andrew Battenberg
MD, USA



Literature:

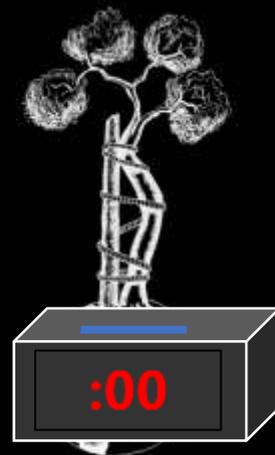
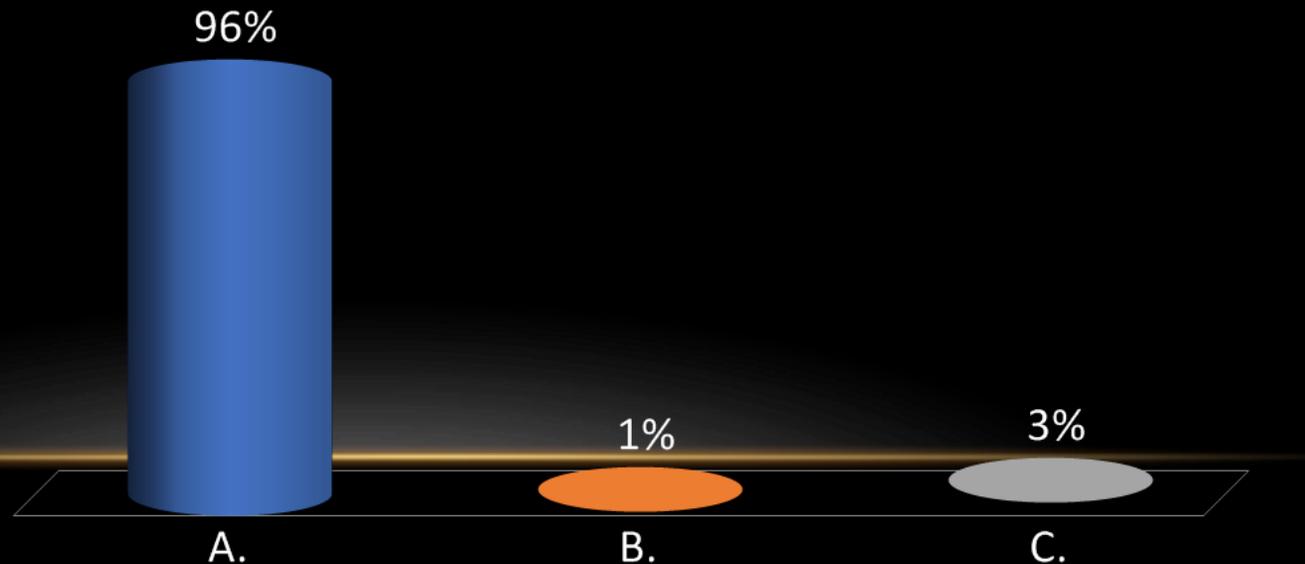
- Limited evidence regarding DAIR utility for acute PJI in the setting of a mega-prosthesis
- DAIR may be appropriate for acute PJI in the absence of complicating factors (Singh et al.), such as:
 - Extensive and pervasive infection
 - Highly virulent, polymicrobial or resistant organism
 - Presence of sinus tract
 - Immunosuppressed host
 - Multiple prior debridements



Recommendation: Debridement, antibiotics, and implant retention (DAIR) is a viable treatment option in acute PJI of a megaprosthesis. The effectiveness of DAIR is still unclear due to lack of comparative data among the treatment options and limited evidence to suggest superiority of any one treatment. The treatment decision must be made on a case-by-case basis and account for underlying medical conditions, infection history, organism characteristics, and surgical history. DAIR is most appropriate for acute PJI without complicating factors, such as extensive and pervasive infection by a high virulence or resistant organism.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 9: What factors are associated with the successful treatment of acute PJI using debridement, antibiotics, and implant retention?

RESEARCHED BY:

Marjan Wouthuyzen-Bakker MD

Alex Soriano MD



Literature:

- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 45**
- **Retrospective studies show that intraoperative exchange of modular components leads to increased rates of treatment success.**
- **Performing DAIR within one week of symptom onset was associated with increased treatment success**
 - Urish et al. demonstrated that the chance of failure increased when DAIR was postponed to two weeks after onset of symptoms (HR 1.68), and further increased after four weeks of symptoms (HR 2.34) (p=0.002)
- **An RCT and retrospective studies have demonstrated that adding Rifampin and fluoroquinolones to the antibiotic regimen is associated with lower rates of Gram positive and Gram negative infections, respectively.**
- **Large cohort studies have found that underlying chronic medical conditions, such as Rheumatoid Arthritis, is an independent predictor of treatment failure in DAIR.**
- **Fracture as an indication for the prosthesis has been shown to be associated with DAIR failure in 3 studies of early acute PJIs**
- **It has been demonstrated in several studies that an infection caused by *S. aureus* is associated with an increased risk of failure**



Recommendation: The following factors have been shown to be associated with treatment success in acute PJIs treated with DAIR:

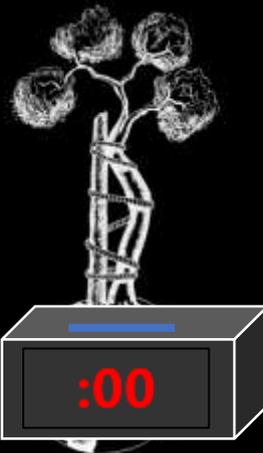
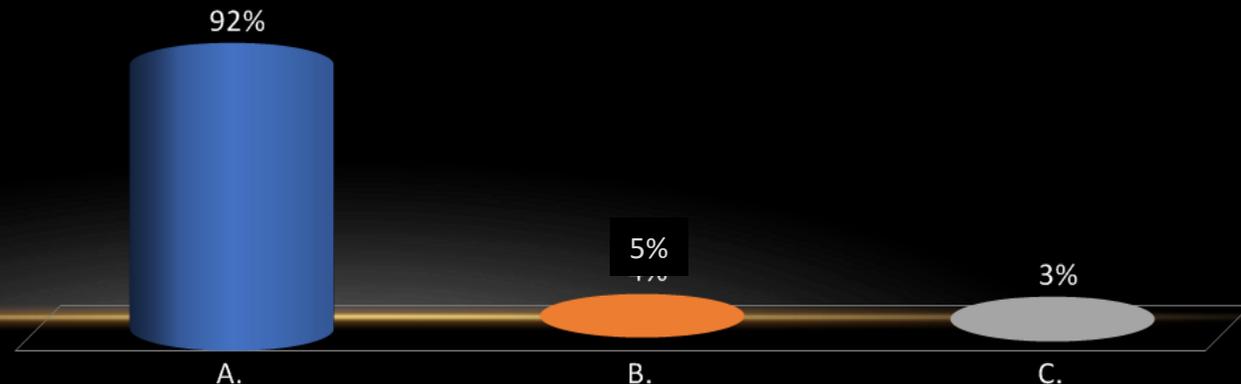
- Exchanging the modular components during debridement
- Performing a debridement within at least 7 days, but preferably as soon as possible, after the onset of symptoms
- Adding rifampin to the antibiotic regimen, particularly when combined with a fluoroquinolone, in cases of susceptible staphylococci
- Treatment with fluoroquinolones in cases of susceptible Gram-negative bacilli

The following factors have been shown to be associated with treatment failure in acute PJIs treated with DAIR:

- Host related factors: rheumatoid arthritis, old age, male sex, chronic renal failure, liver cirrhosis and chronic obstructive pulmonary disease
- Prosthesis indication: fracture as indication for the prosthesis, cemented prostheses, and revised prostheses
- Clinical presentation representing the severity of the infection: a high C-reactive protein, a high bacterial inoculum, and the presence of bacteremia
- Causative microorganisms: *S. aureus* and Enterococci

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 10: Does performing a debridement, antibiotics, and implant retention affect the outcome of a subsequent two-stage exchange arthroplasty?

RESEARCHED BY:



Erik Hansen MD, USA

Jay Shah MD, India



Literature:

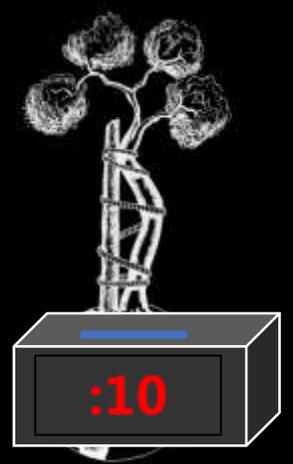
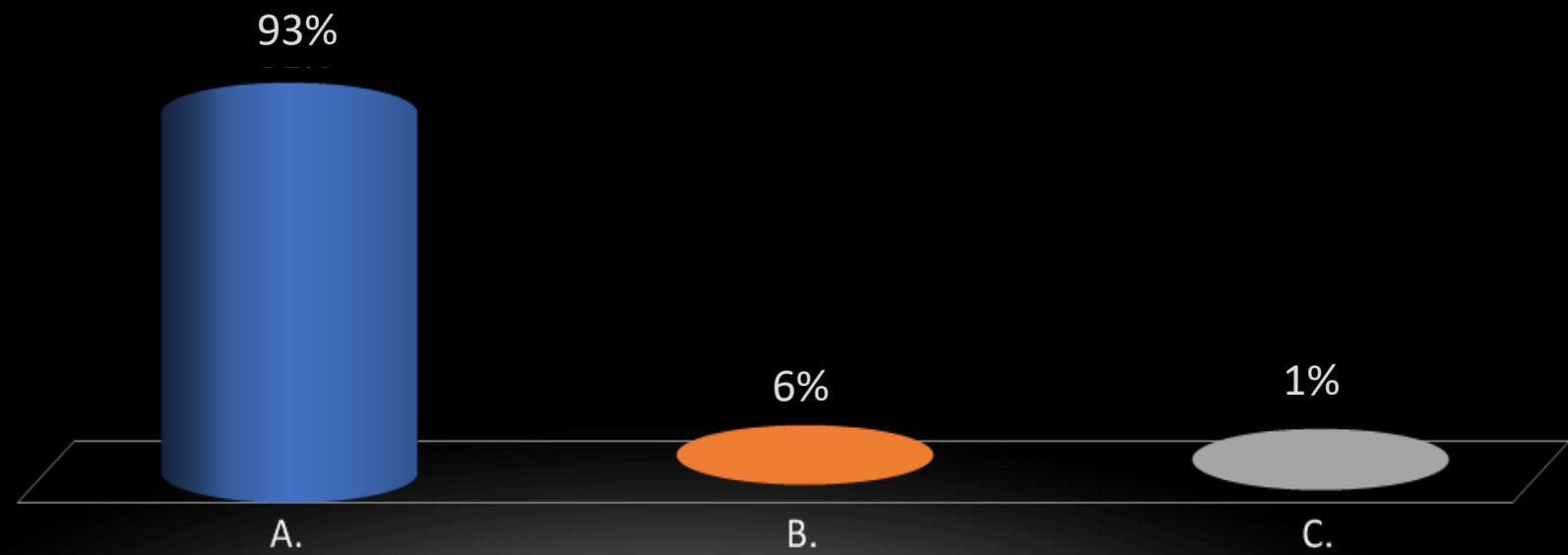
- Sherell et al (34% failure), Gardner et al (42% failure), Rajgopal et al (24% failure) all indicate that failure of an initial I&D and modular component exchange leads to a higher than expected failure rates of subsequent two-stage exchange arthroplasty.
- Two more recent studies (Brimmo et al. and Nodzo et al) on this topic report the opposite findings, namely that I&D before a two stage exchange does not increase the risk of failure.
- Data remains limited – all articles reviewed, whether single institution, multicenter, or database-derived included small numbers of patients who actually had a 2-stage exchange arthroplasty after a failed I&D (N's=83, 25, 88, 57, 45)



Recommendation: Unknown. Based on the available evidence, it is not known if prior DAIR adversely affects the outcome of a subsequent two-stage exchange arthroplasty.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 11: How many debridement, antibiotics, and implant retention procedure(s) (DAIR) are acceptable in management of patients with acute periprosthetic joint infection before resection arthroplasty needs to be performed?

RESEARCHED BY:



Fabio Catani MD,
Ecuador



Lazaros Poultides
MD, USA



Henry Flores MD,
Slovenia



Literature:

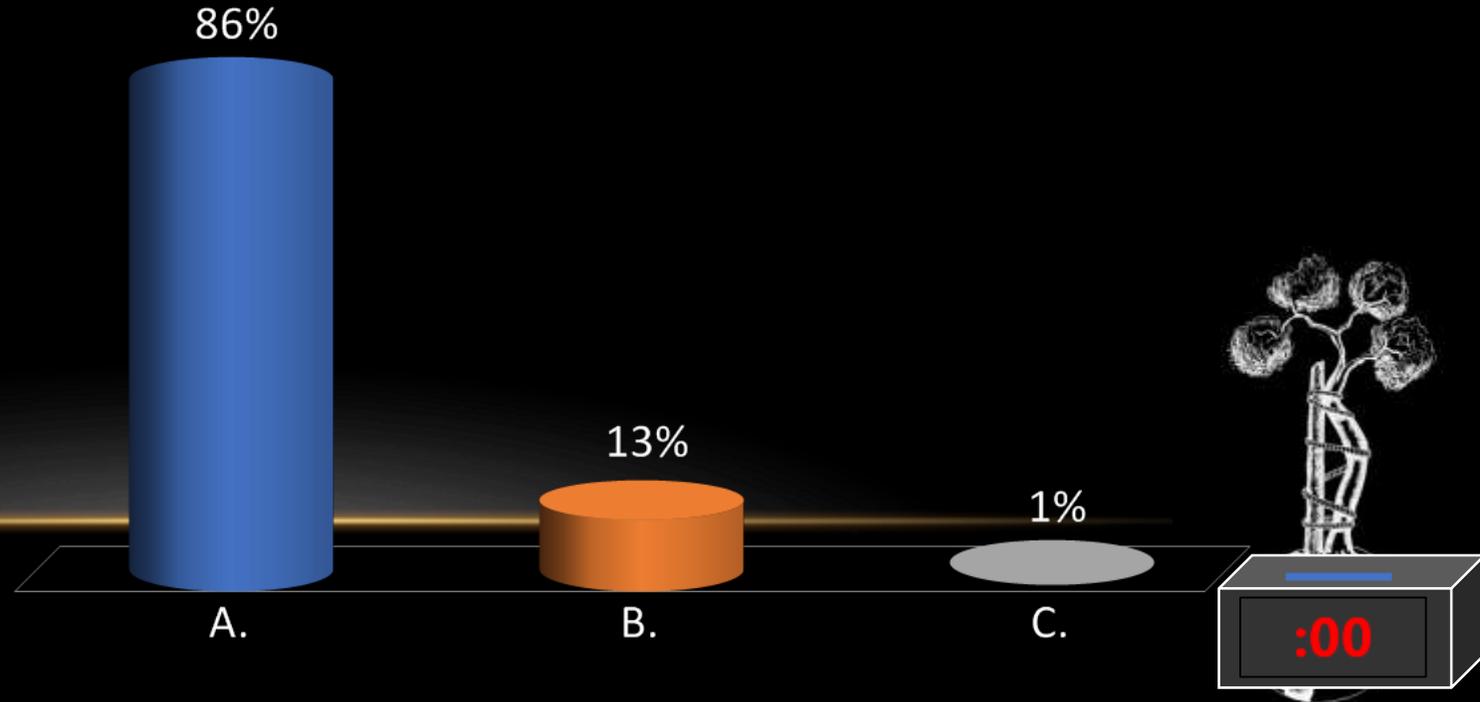
- **Meta-analysis 3, Prospective/Randomized 0, Retrospective 6**
- **A multicenter retrospective analysis demonstrated 109 out of 216 patients who underwent DAIR after TKA required an additional procedure. Of the 109 failures, 59 underwent repeat DAIR (Urish et al.)**
- **Retrospective review (Triantafyllopoulos et al.)**
 - **Attempted to address # of DAIR for treatment of deep PJI after primary or revision TKA and THS.**
 - **19 patients underwent multiple DAIR procedures**
 - **Of the 19, 10 (52.6%) achieved implant retention with infection control**
 - **Of the 122 patients who underwent a single DAIR, 78 (63.9%) achieved implant retention with infection control**
 - **Difference however, was not statistically different**



Recommendation: After one failed debridement, antibiotics and implant retention (DAIR) procedure, strong consideration should be given to resection arthroplasty.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 12: What is the optimal length of antibiotic treatment following debridement, antibiotics, and implant retention (DAIR) for acute PJI?

RESEARCHED BY:

Jaime Lora-Tamayo MD, Spain

David Warren MD, United States of America



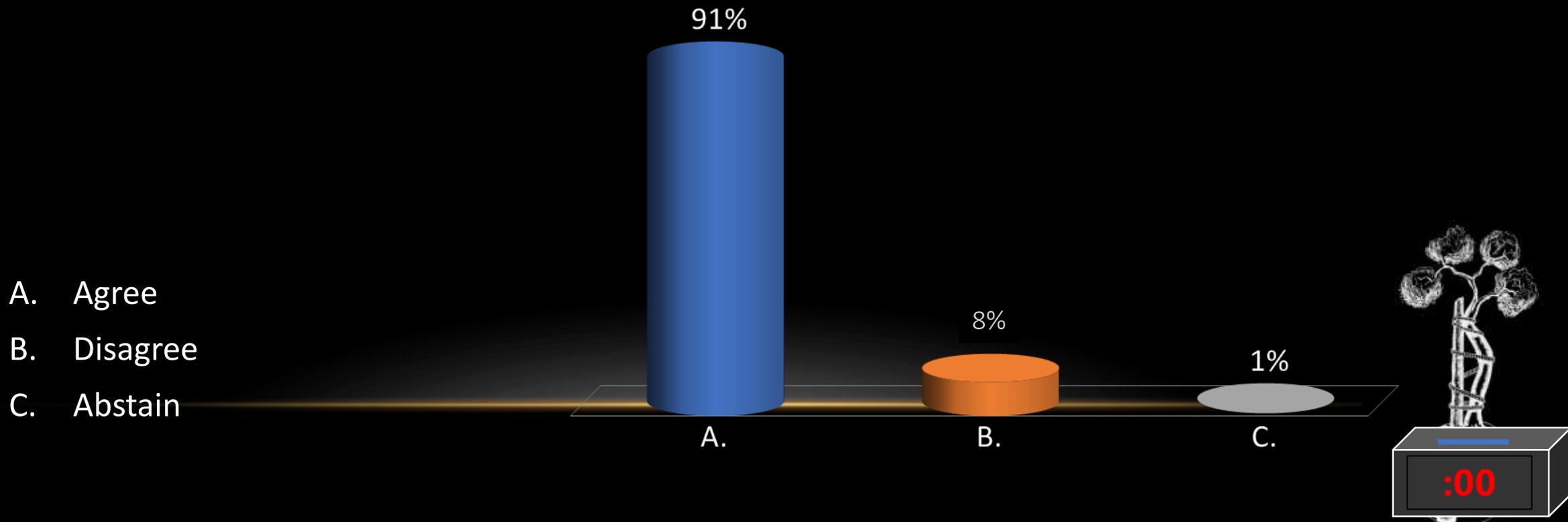
Literature:

- Meta-analysis 0, Prospective/Randomized 2, Retrospective 21
- The majority of the studies reporting the outcome of DAIR (3) (5-7)(13-18) used an antibiotic treatment regimen of 7-14 days of intravenous antibiotics, followed by 3-6 months of oral antibiotics with activity against bacteria in biofilm (e.g., ciprofloxacin, adjunct therapy with rifampin) (based on Zimmerli et. al)
- There is conflicting evidence regarding whether the length of antimicrobial treatment matters
 - The majority of studies that advocate the use of a 6- to 8-weeks course of antibiotic therapy, state that intravenous antibiotics for two weeks followed by 4-6 weeks of oral antibiotics is optimal
- One randomized multicenter study compared an 8-week course of levofloxacin plus rifampin vs a long course, 3 of oral therapy for hip PJI and 6 months of therapy for knee PJI in the setting of Staphylococcal PJI managed by DAIR
 - Non-inferiority hypothesis of the 8-week course was proven in the intention-to-treat analysis and a trend towards non-inferiority was observed in the per-protocol analysis



Recommendation: The optimal length of antibiotic treatment following DAIR remains relatively unknown as there is considerable heterogeneity regarding the length, dose, and administration of treatment. Four to six weeks of antibiotic therapy seems to be sufficient in most cases of PJI managed by DAIR.

Level of Evidence: Moderate



Question 13: What is the most effective combination of antibiotics in the treatment of acute PJI caused by methicillin resistant staphylococcus aureus (MRSA) that has undergone surgical management with debridement, antibiotics and implant retention (DAIR)?

RESEARCHED BY:

Camelia Marculescu MD, United States of America

Silvano Esposito MD, Italy



Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 5**
- An ideal combination of antimicrobial therapy has not been established.
- Rifampin-based combination therapy regimens have been shown to be effective in eradication of staphylococcal organisms and cure PJI
 - However, rifampin alone should never be used due to the rapid development of resistance
- The duration of antimicrobial therapy for PJI managed with debridement and retention has not been well established
 - Based on currently available literature delegates recommend recommend 2-6 weeks of parenteral antimicrobial therapy in combination with rifampin 300-450 mg orally twice a day, followed by rifampin plus a susceptible companion oral drug
- Current IDSA guidelines recommend Vancomycin as the primary parenteral agent for treatment of MRSA infections, but its utility has been questioned due to increasing reports of heterogeneous resistance, treatment failure, and nephrotoxicity

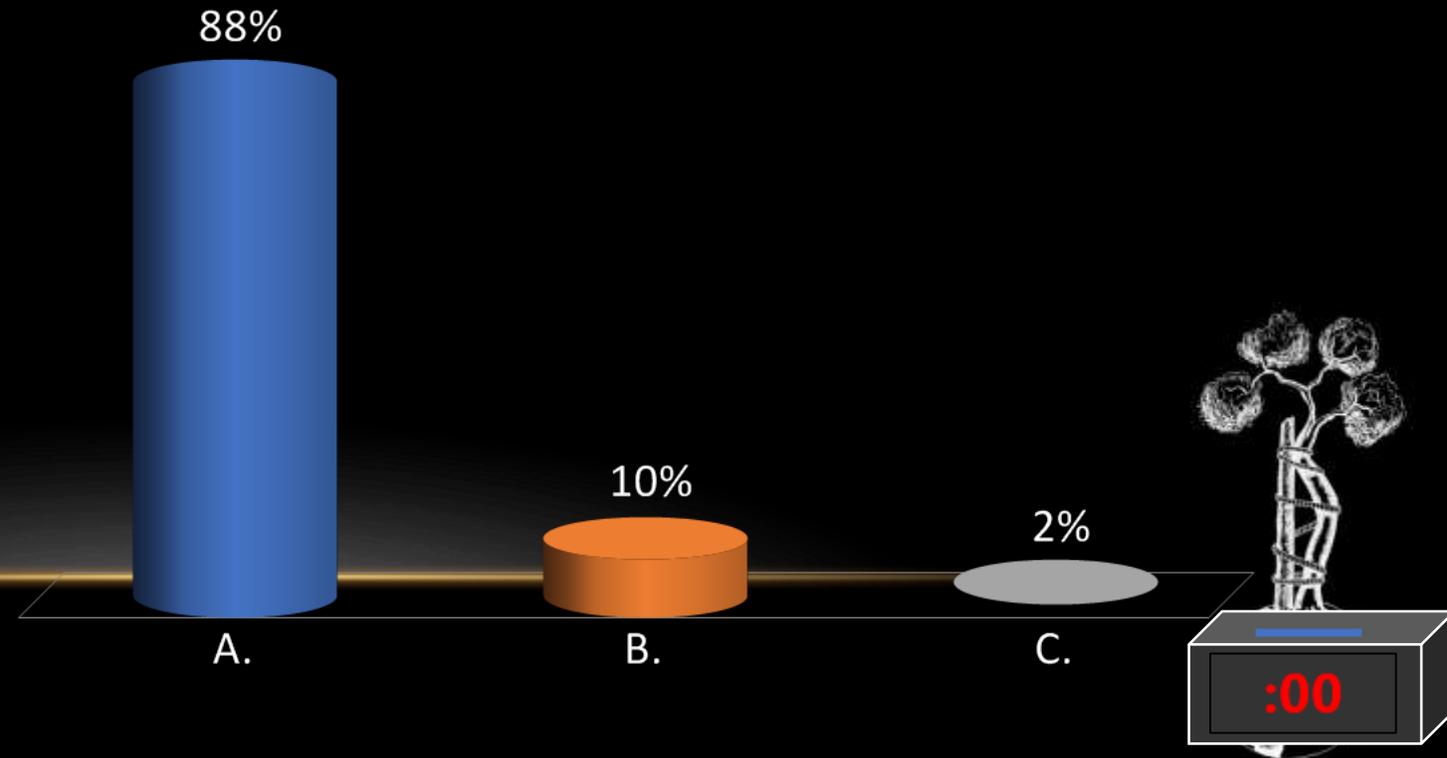


Recommendation: We recommend a combination of a parenteral antibiotic plus oral rifampin for one to six weeks, followed by rifampin and a companion highly bioavailable oral drug for additional 3 months, depending on the susceptibility profile of MRSA, patient tolerability, and side effect profile.

When small colony variants (SCVs) of MRSA are suspected, β -lactam combinations with daptomycin may offer a new option for treatment. Chronic oral suppression may be considered in selected patients.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 14: What antibiotic therapy (agent, route, dose, and duration) is recommended for Gram-negative acute PJI being treated with debridement, antibiotics, and implant retention?

RESEARCHED BY:

Jean Yombi MD

Marjan Wouthjuyzen-Bakker MD



Literature:

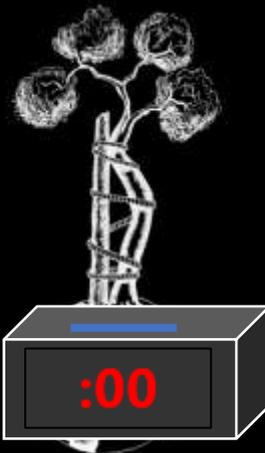
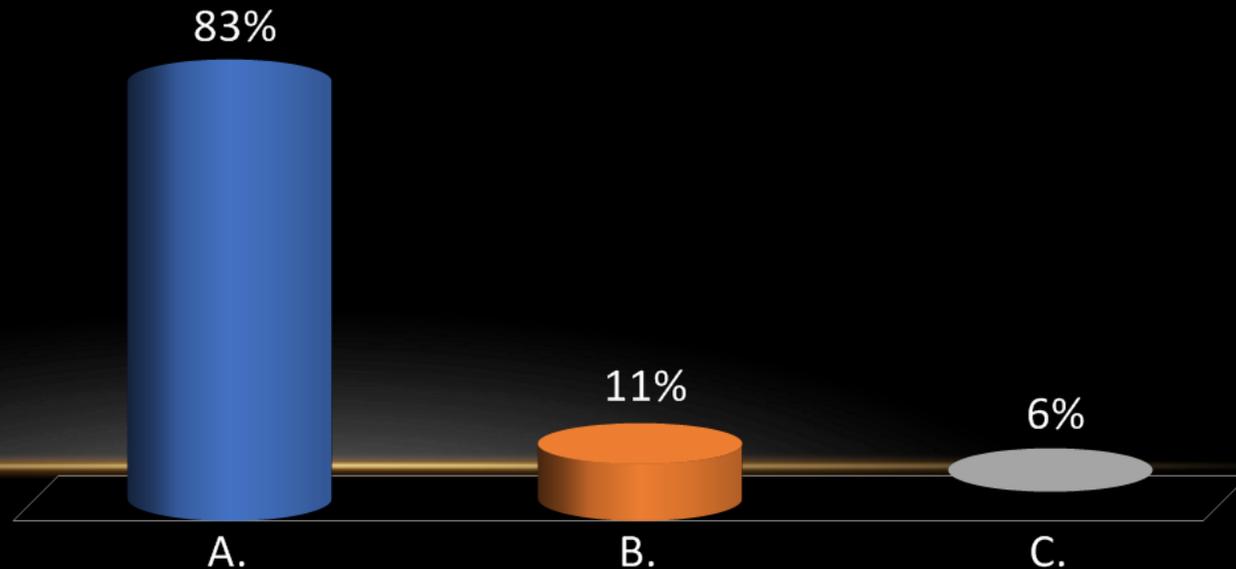
- **Meta-analysis 0, Prospective/Randomized 4, Retrospective 11**
- Puhto et al. concluded in a retrospective study that if the patient completes the antibiotic therapy, treatment duration of 3 months in TKA PJs and 2 months in THA PJs is as good as longer antibiotic treatment of 6 months or 3 months, respectively, in patients treated with DAIR.
- Perez-Jorge et al. recommended individualized antibiotic therapies based on microbe susceptibilities, etiology, and pathogenesis of infection in the treatment of PJs.



Recommendation: Following surgical intervention (DAIR), gram-negative acute PJI patients should also receive antibiotic treatment for 6 to 12 weeks based on the type of organism. In fluoroquinolone-susceptible cases, the recommended antibiotic agent is a fluoroquinolone.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



5.3 – Treatment: One-Stage Exchange



Question 1: What are the potential advantages of one-stage exchange arthroplasty?

RESEARCHED BY:



Robert Molloy MD,



Karan Goswami MD

Navin Fernando MD,

Ariel Saldana MD,



Literature:

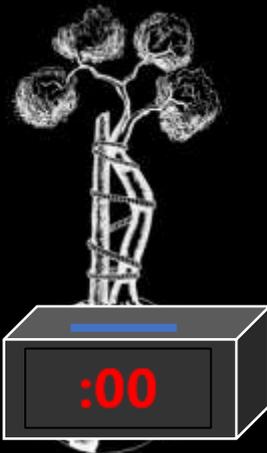
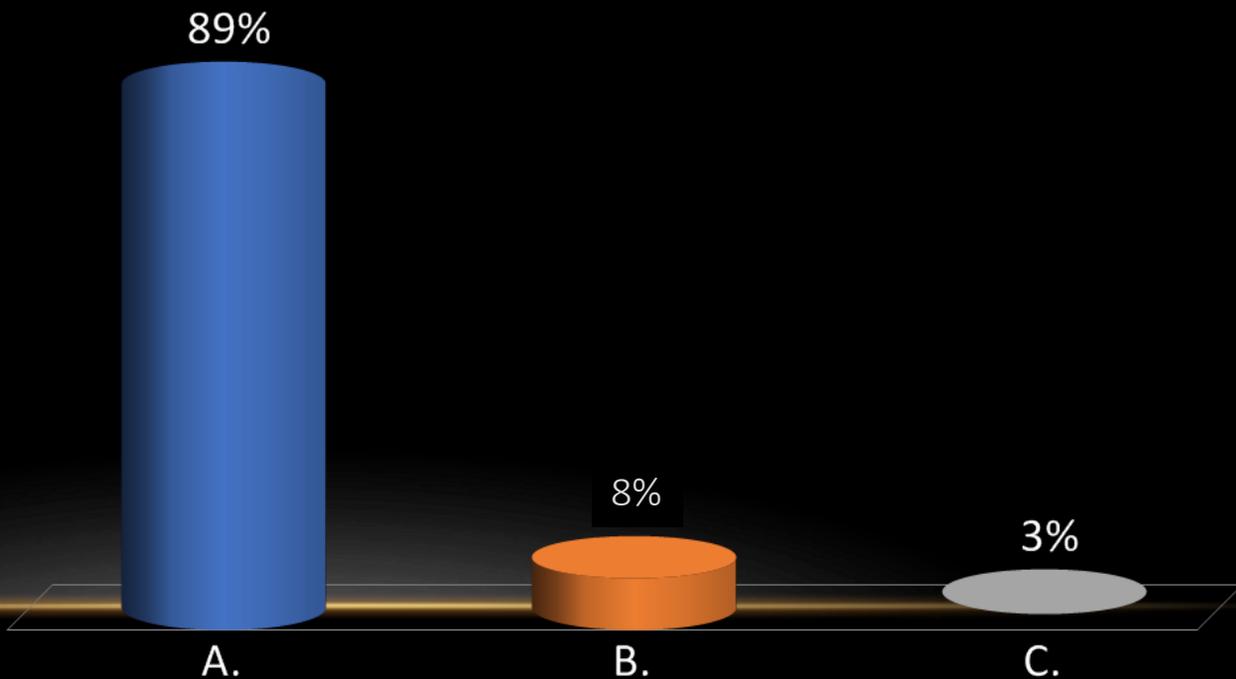
- **Meta-Analysis 2, Prospective/randomized 1, Retrospective 21**
- Kunustor et al. (2015) performed a meta-analysis comparing re-infection rates between one-stage and two-stage revision hip arthroplasties for PJI.
 - One-stage (8.2%, [95%CI 6.0-10.8]) and two-stage (7.9% [6.2-9.7]) surgery had similar reinfection rates.
- Kunustor et al. published another meta-analysis comparing re-infection rates following one- and two-stage revision knee arthroplasties (2016).
 - One-stage (7.6% [3.4-13.1]) and two-stage (8.8% [7.2-10.6]) knee revisions also had similar reinfection rates.
- These findings were limited by the quality of the studies included in the meta-analyses, as well as a relative paucity of studies evaluating one-stage protocols in comparison to two-stage exchange



Recommendation: The potential advantages of a one-stage exchange arthroplasty are multiple, including a decrease in surgical morbidity and mortality, earlier functional return, decrease in healthcare and global economic costs as well as an increase in health-related quality adjusted life years.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: What are the indications and contraindications for a one-stage exchange arthroplasty for the treatment of chronic PJI's?

RESEARCHED BY:

Shengjie Guo MD

Fares Haddad MD

Peter Keogh MD

Lars Lidgren MD

Akos Zahar MD



Literature:

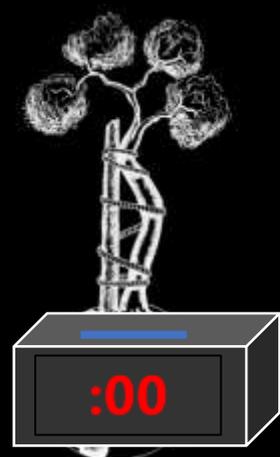
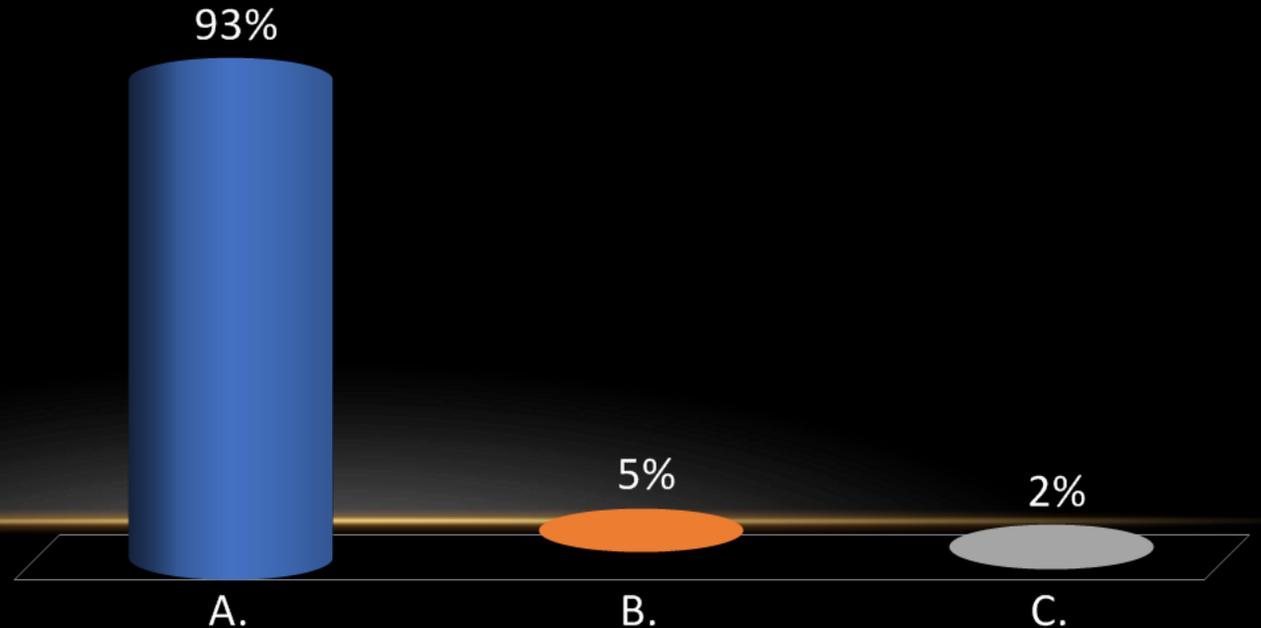
- **Meta-Analysis 2, Prospective/randomized 0, Retrospective 18**
- **A meta-analysis performed by Nagra et al. in 2016 on five cohort studies compared one-stage and two-stage exchange arthroplasty in 231 patients.**
 - No significant differences in risk of reinfection following one- or two-stage exchange arthroplasty (OR -0.06, 95 % confidence interval -0.13, 0.01).
 - In studies published since 2000, one-stage procedures have significantly lower reinfection rate.
 - Conclusion: One-stage exchange arthroplasty can lead to better clinical and functional outcomes, but patient selection criteria needs to be defined.
- A study by Goksan et al. in 1992 on a small cohort of 18 cases reported a 94% success rate with knees (success = eradication of infection).
 - Of the 2 reported cases of failure, both patients were noted to have severe immunosuppression



Recommendation: One-stage exchange arthroplasty remains a viable option for the management of chronic prosthetic joint infections (PJIs). In patients with signs of systemic sepsis, extensive co-morbidities, infection with resistant organisms, culture-negative infections, and poor soft tissue coverage, one-stage exchange arthroplasty may not be a good option.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Is there a role for single-stage exchange arthroplasty in acute PJI of cementless THA?

RESEARCHED BY:



Rhidian Morgan-Jones MD,
Wales

Fares Haddad MD, UK

Erik Hansen MD, USA

Literature:

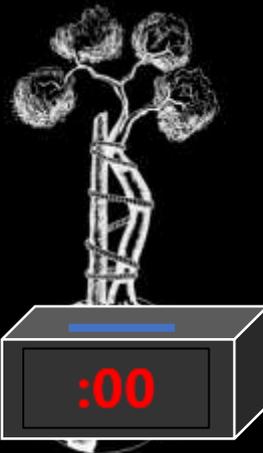
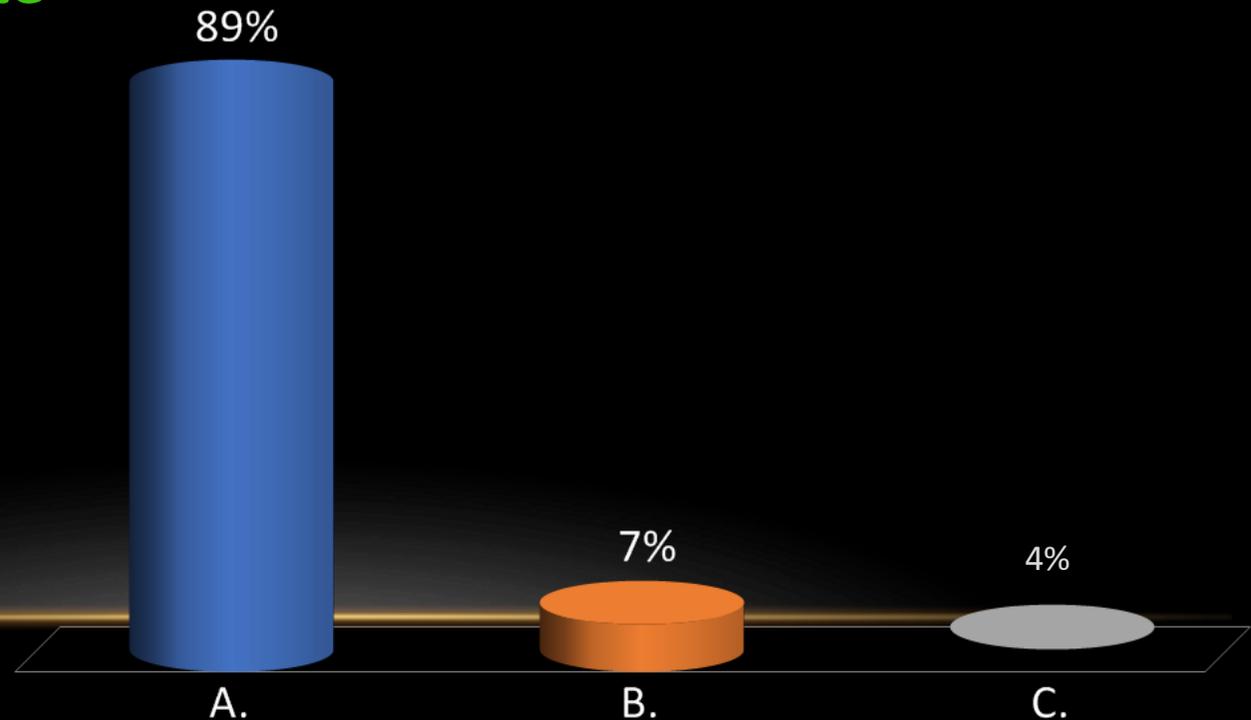
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 11**
- With shorter total hospital stay, less risk of perioperative complications and lower overall costs, single-stage revision has been considered an attractive treatment option for the devastating complication of PJI
- Literature is quite heterogeneous with control of infection being reported in 56%, 75%, and 100% in 3 studies respectively
 - These studies varied in their inclusion criteria, follow-up time, and other factors
- Single stage revision does limit postoperative morbidity, surgical complexity, and healthcare costs compared to two stage arthroplasty



Recommendation: Yes. Single-stage exchange arthroplasty can be employed to treat patients with acute periprosthetic joint infection of cementless total hip arthroplasty.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Does the morbidity and mortality differ between single-stage and two-stage exchange arthroplasty?

RESEARCHED BY:



Laszlo Bucsi MD,
Hungary



Andrew Toms MD,
United Kingdom

Jerzy Bialecki MD,
Poland

Stephen Jones MD,
United Kingdom



Literature:

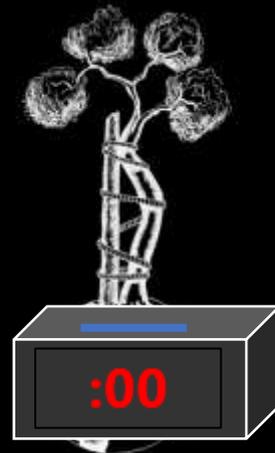
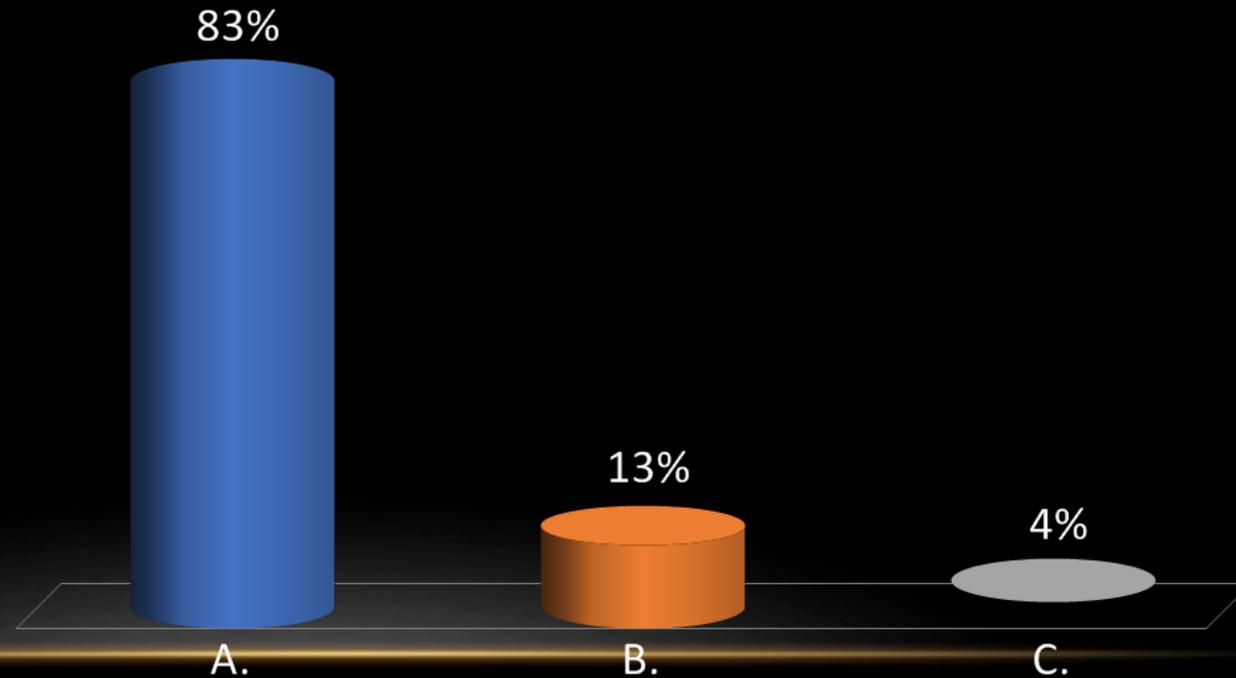
- **Meta-analysis 5, Prospective/Randomized 8, Retrospective 24**
- **Systematic review of literature reviewing morbidity**
 - Majority of studies found no significant differences between one and two stage
 - One prospective study did note significantly improved HHS, VAS & patient satisfaction with one-stage exchange at 5-years
- **Systematic review of literature reviewing mortality**
 - One review included 18 papers and found an improved mortality rate following single stage exchange (0.52% vs 2.5%)
 - Direct comparisons are difficult to be drawn



Recommendation: Putting aside the effect on successful treatment of periprosthetic joint infection (PJI), it is logical that a single surgical procedure puts patients at lower risk of both mortality and morbidity compared to a two-stage exchange arthroplasty that involves two separate operations.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



5.4 – Treatment: Two-Stage Exchange, Spacer Related



Question 1: What are the indications for the use of non-articulating (vs articulating) spacers during resection arthroplasty of the hip or knee?

RESEARCHED BY:



DO Kendoff MD

Matthew Adbel MD

Amir N. Sandiford MD



Literature:

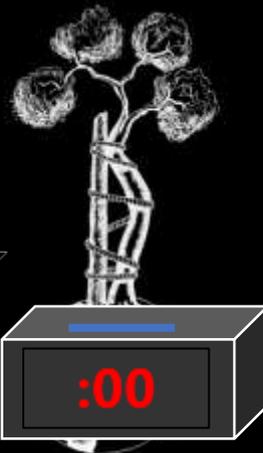
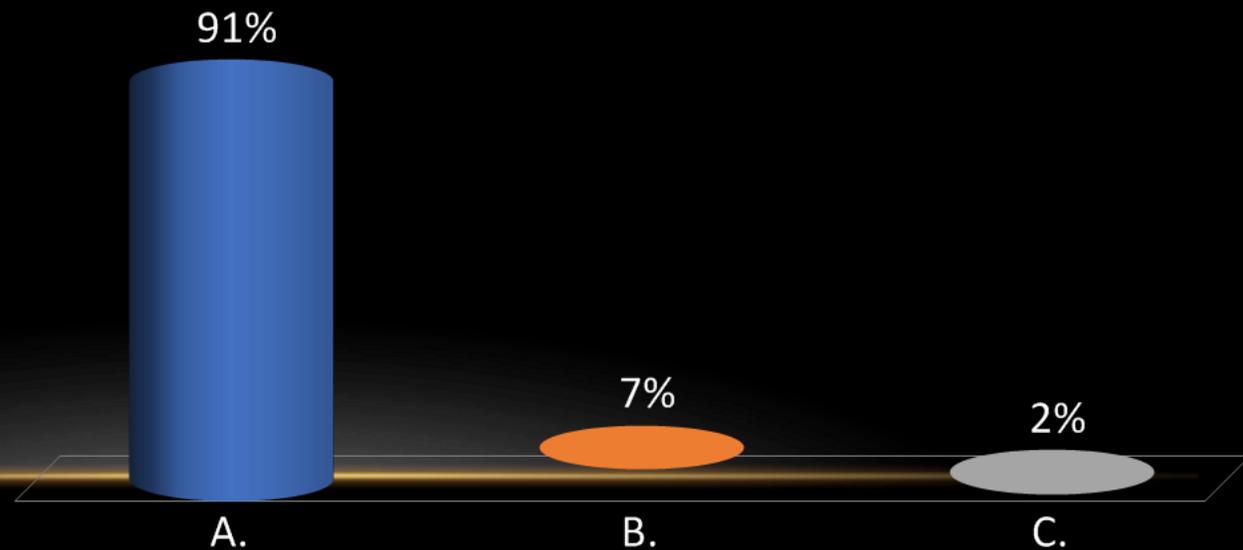
- **Meta-Analysis 2, Prospective/Randomized 1, Retrospective 15**
- Della Valle et al. demonstrated in a multicenter randomized controlled trial (AAHKS abstract) that articulating spacers for hip are associated with reduced length of hospital stay after both the first and second stage.
 - The articulating spacer group also had improved range of motion in the knee at 1 year (113 vs 100 degrees ($p=0.033$) and a more significant improvement from preoperative and postoperative range of motion (18 vs 3 degrees ($p=0.045$)).
- Lichstein et al. (2016) demonstrated in a prospective study that static spacers had comparable flexion and infection eradication as articulating spacers when compared with contemporary studies.



Recommendation: Articulating spacers appear to provide better range of motion and less functional limitations to the patients undergoing resection arthroplasty and should be used whenever possible. The indications for the use of non-articulating spacers during resection arthroplasty include patients with significant bone loss, lack of ligamentous integrity (knee) or abductor mechanism (hip) that places these patients at elevated risk for dislocation or periprosthetic fracture, and patients with significant soft tissue defects in whom motion is protected to allow better wound healing.

Level of Evidence: Strong

- A. Agree
- B. Disagree
- C. Abstain



Question 2: What are the indications for interim cement spacer exchange or repeat irrigation and debridement instead of reimplantation?

RESEARCHED BY:



Igor Shubnyakov MD



Karan Goswami MD



Jorge Manrique MD

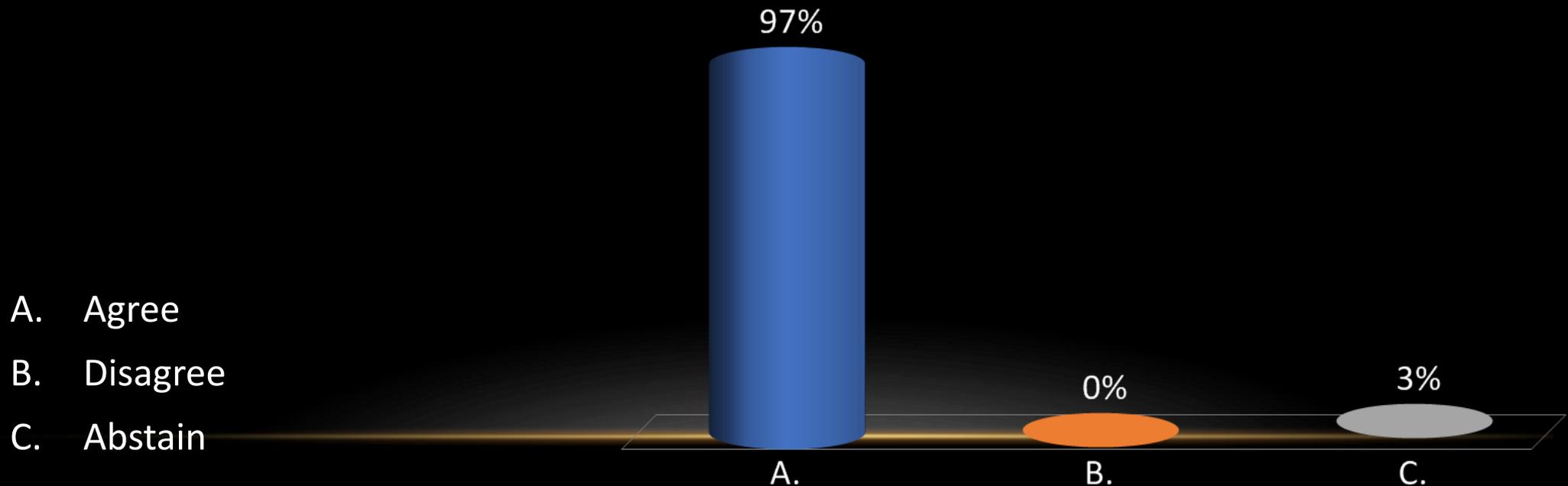
Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 16**
- **Limited data exists on this subject**
- **A retrospective study done by Gomez et al. in 2015 showed that of 87 cases that underwent spacer implantation without reimplantation, 72 (82.8%) underwent spacer retention.**
- **George et al. presented a series of 416 two-stage exchanges for PJI, of which 59 (17%) had an interim spacer exchange performed.**
 - 2-year and 5-year success rates were 77% and 66% in the exchange group, versus 86% and 77% in the non-exchange group.
 - The spacer exchange group had a lower infection-free survival (adjusted HR 10.69, 95% CI 1.02-2.81; p=0.039).

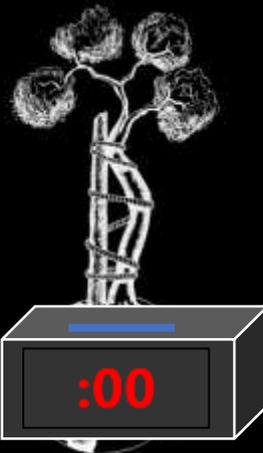


Recommendation: Interim cement spacer exchange and/or repeat irrigation and debridement may be performed, instead of reimplantation, in the presence of persistent infection and/or mechanical complications.

Level of Evidence: Limited



- A. Agree
- B. Disagree
- C. Abstain



Question 3: Should the antibiotics placed in a cement spacer be tailored to the sensitivity of the infective organism?

RESEARCHED BY:



Zahar, Akos

Porteous, Andrew

Janz, Viktor



Literature:

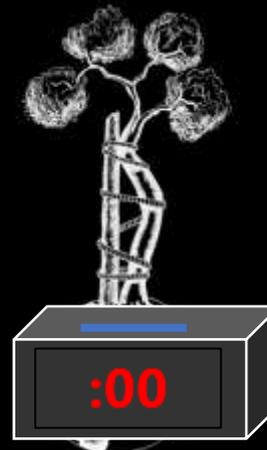
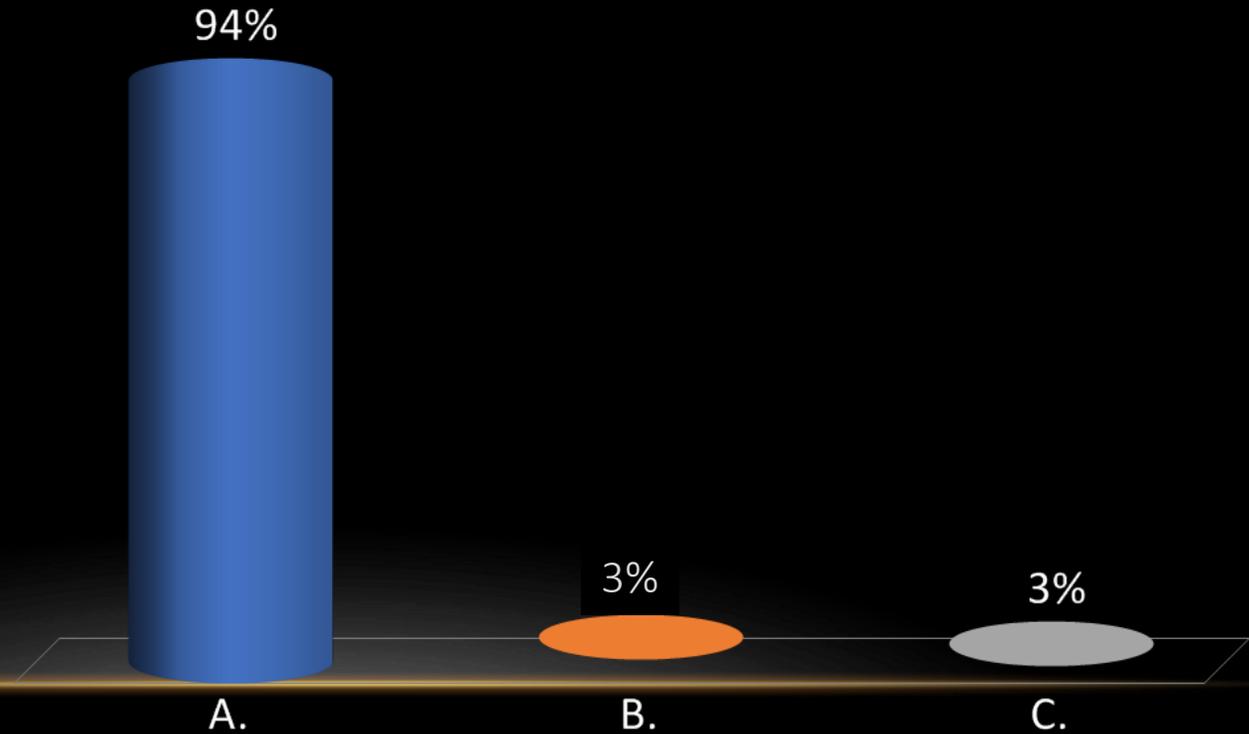
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 24
- One review found no clear evidence, but supported the concept of tailored antibiotics when pathogen and its susceptibilities was known
- Antibiotics should be be safe, thermostable, hypoallergenic, water soluble, adequate bacterial spectrum and available as sterile powder



Recommendation: Antibiotics added to cement spacer during resection arthroplasty should be tailored towards the causative organism and its susceptibility. In case of culture negative PJI consideration should be given to addition of a broad-spectrum antibiotic to cement spacer to cover most potential pathogens causing PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Which antibiotic(s) should be added to a cement spacer in patients with PJI caused by multiresistant organisms?

RESEARCHED BY:

Valeriy Murylev MD, Russia

Lars Frommelt MD, Germany

Matthew W Squire MD, United States of America



Literature:

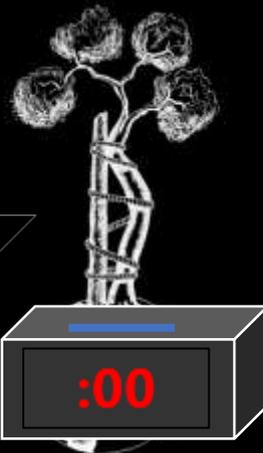
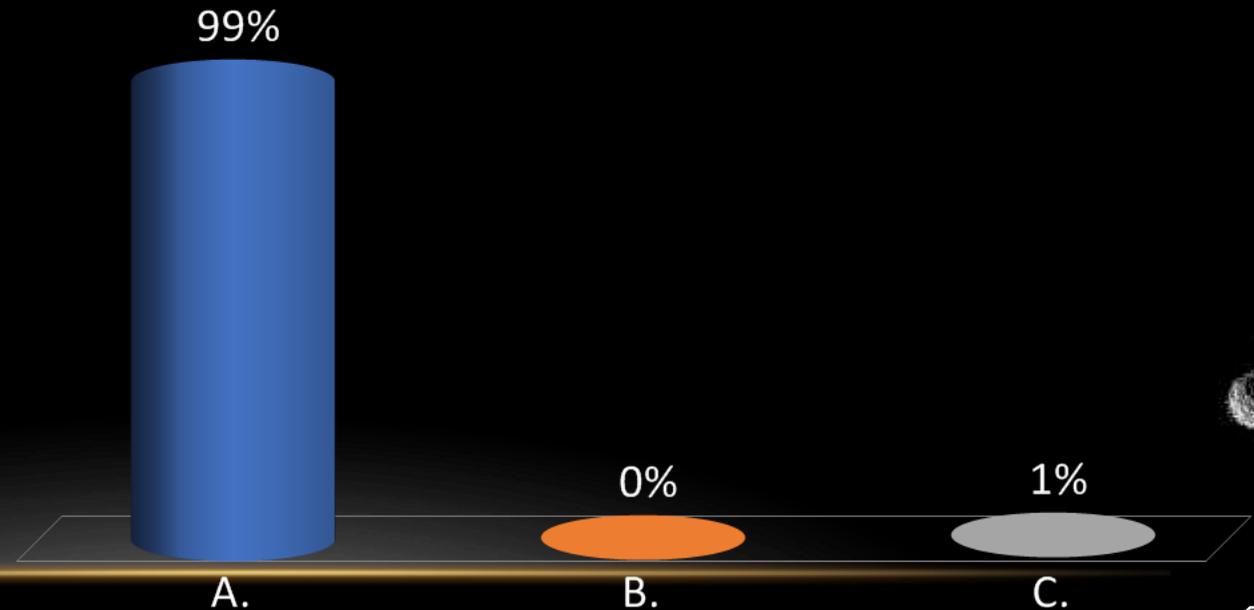
- **Meta-analysis 1, Prospective/Randomized 0, Retrospective 22**
- For the treatment of PJI caused by MRSA, vancomycin is usually used for antibiotic therapy and commonly incorporated into bone cement as well as intravenous treatment
 - Most PJI are caused by Gram-positive cocci, including Staphylococcus species (Davis et al.) and in some reports Methicillin-resistant organisms account for up to 74% of PJI
- The optimal combination of antibiotics in polymethylmethacrylate cement is not known. Most surgeons prefer to add between 2-4g of Vancomycin and a similar dose of an aminoglycoside, such as gentamycin or tobramycin, to the cement
- For susceptible gram-negative bacteria, third-generation cephalosporins, carbapenems, and monobactam antibiotics have strong activity



Recommendation: In case of PJI caused by MRSA/MRSE, vancomycin should be added to the bone cement spacer. In Vancomycin resistant strains, such as VRE or in multi-resistant Gram-negative PJI cases, individual decision making is mandatory based on the known susceptibility. Consultation with a microbiologist/infectious disease specialist is strongly recommended.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 5: What are the contraindications to using antibiotics in a cement spacer

RESEARCHED BY:



Scott Sporer MD



Thomas Turgeon MD

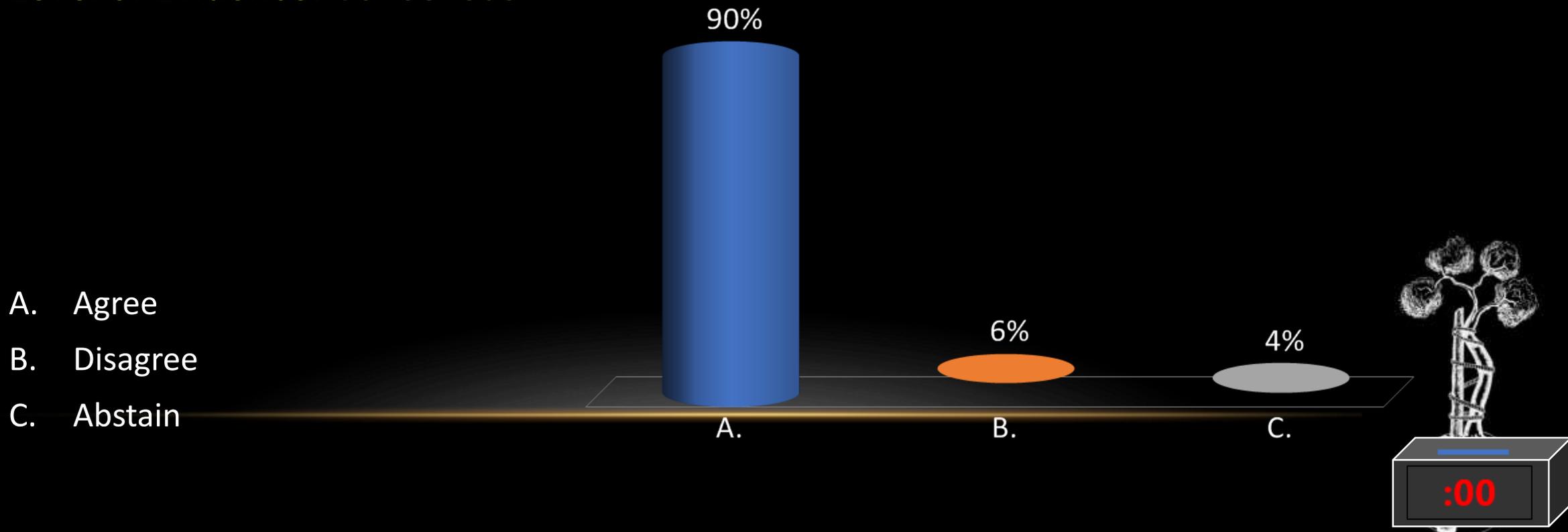
Literature:

- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 14**
- **No prospective studies directly comparing use of cement spacer to abx.**
- A small RCT by Cabrita, et al. (2007) compared 30 patients with PJI of the hip treated with a Vancomycin-loaded spacer versus 38 treated with no spacer.
 - Compared to the control group, the spacer group had significantly higher improvement in Harris hip score (19.3 to 69.0 vs. 19.7 to 75.2, $P < 0.05$) and higher rates of infection control following revision surgery (66.7% vs 89.1%, $P < 0.05$).
- A retrospective assessment by Wimmer et al. in 2011 of 120 joints treated with two-stage exchange found difference in infection eradication with the use of an antibiotic-loaded spacer. However, they also noted no adverse effects from their use.



Recommendation: With the exception of a scenario in which a patient has a history of severe adverse reaction to each of the thermally-stable antibiotics intended for use in cement spacers in the treatment of prosthetic joint arthroplasty, there are no definite contraindications to using antibiotics in a cement spacer.

Level of Evidence: Consensus



Question 6: Does the use of surgical drains reduce the effectiveness of antibiotic-impregnated cement spacers?

RESEARCHED BY:



Ian Stockley MD,
United Kingdom



John O'Bryne MD,
Ireland



Kier Blevins MD,
USA



Literature:

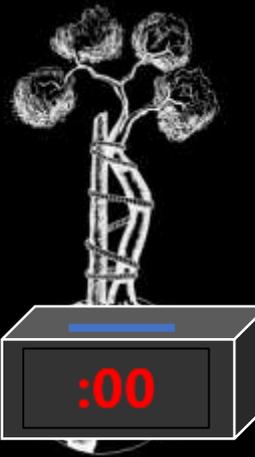
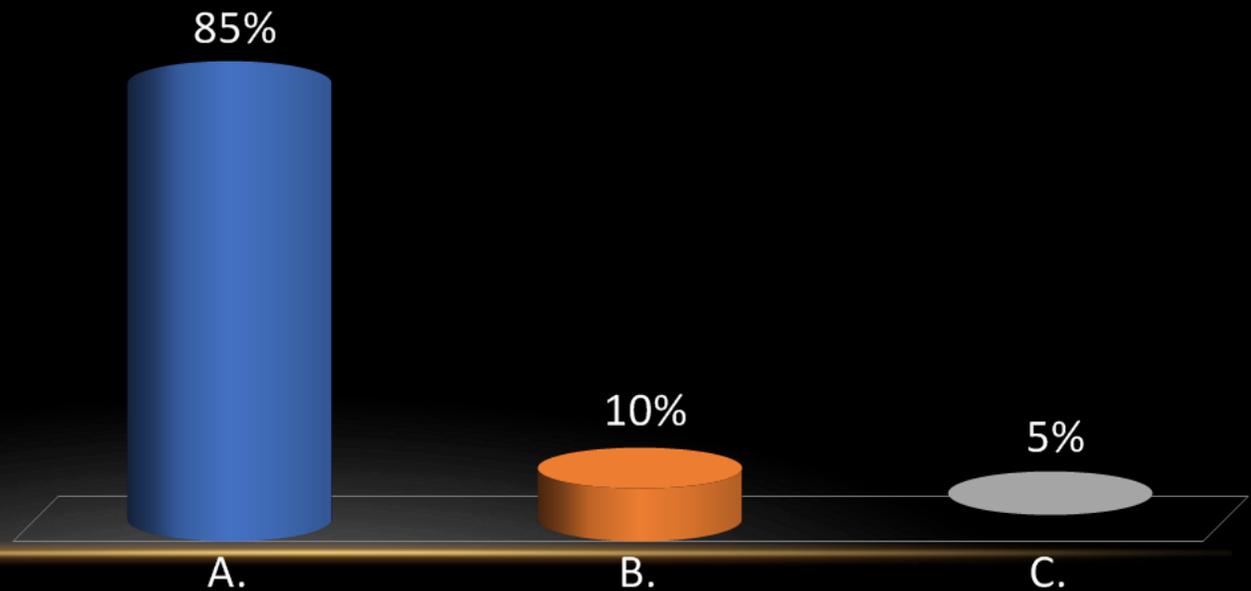
- **Meta-analysis 0, Prospective/Randomized 4, Retrospective 12**
- **Moderate evidence suggesting that suction drains will remove joint fluid and therefore remove antibiotic from the joint, this is probably only a proportion of the total eluted antibiotic.**
- **Once the drains have been removed altogether, elution should continue locally at effective levels as justified by the aforementioned studies.**



Recommendation: The current literature indicates that the use of surgical drains does not reduce the overall effectiveness of antibiotic impregnated cement spacers.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 7: Is there a role for intraoperative autoclaving and re-use of an infected prosthesis as a spacer during resection arthroplasty?

RESEARCHED BY:



Samuel Wellman MD,
USA

Biagio Moretti MD,
Italy

Lluís Font-Vizcarra MD,
Spain

Andrew Battenberg MD,
USA

Literature:

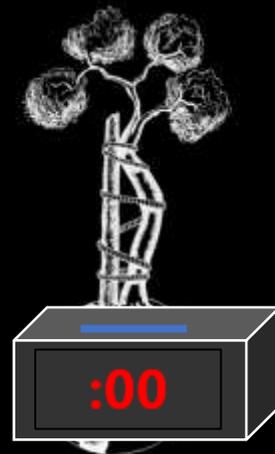
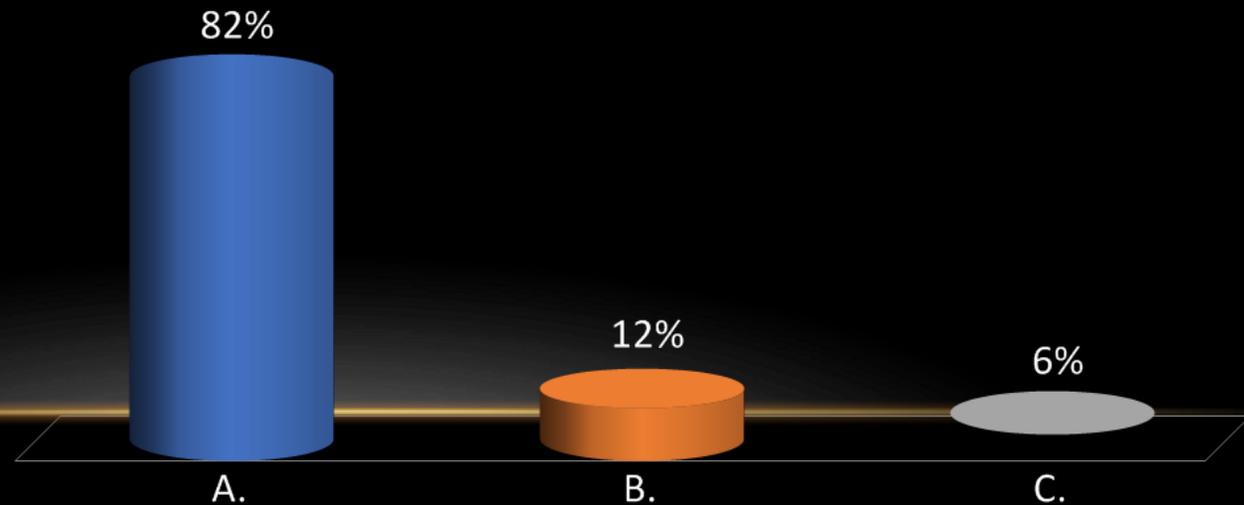
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 16**
- Hofmann et al. reported 44/50 patients (88%) with an autoclaved femoral component as a spacer had successful reimplantation and were infection free at latest follow-up
 - Lee et al reported 19/20 patients successfully treated in a similar study
- Only one study discussed the use of autoclaved hip components, and while they reported excellent results in 31/32 patients, information on autoclave protocol and other details were lacking



Recommendation: Multiple studies have demonstrated that the re-use of autoclaved prosthetic components, during knee resection arthroplasty, did not compromise the eradication of an established infection. Though a viable option, there are potential legal implications associated with the re-use of autoclaved components and a proper standard for autoclaving of these components is also not known. Re-use of autoclaved components in resection arthroplasty, particularly for the knee, may be suitable in scenarios when proper dynamic spacer components are not available or for economic considerations.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 8: Is it necessary to revise or reduce dislocated articulating antibiotic spacers?

RESEARCHED BY:



Daniel Berry MD, USA



Pedro Barreira MD, Portugal

Literature:

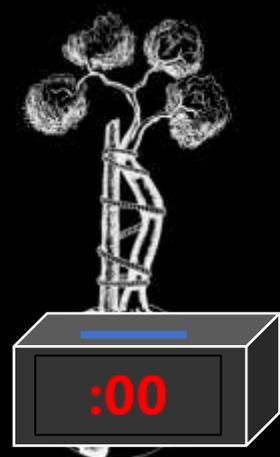
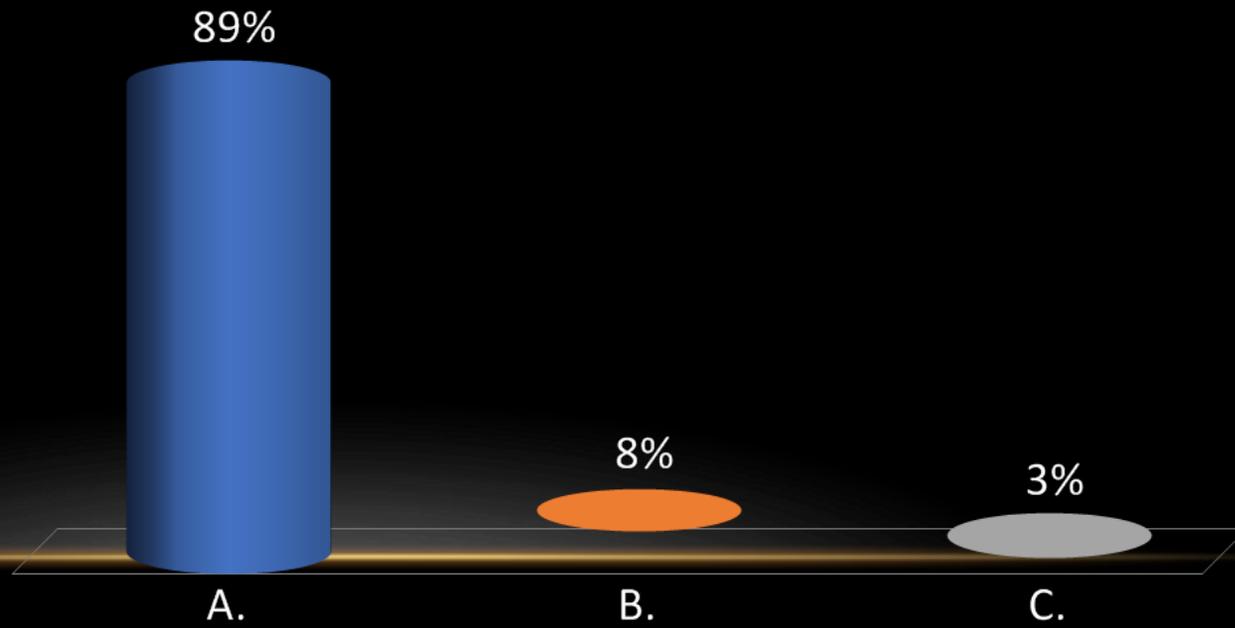
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 5**
- Struelens et al: 57% of knee patients experienced issues with spacers
 - 45% were minor (ex. tilting, medio-lateral translation)
 - 12% were major (ex. dislocation, fracture)
- Closed reduction and stable retention was possible in only four of 12 dislocations of hip spacers



Recommendation: Unless the spacer is pressing against the skin with imminent necrosis/ulceration, resulting in severe, progressive loss of essential soft tissue or bone, neurovascular compromise, or notable pain and disability for the patient, a dislocated or fractured antibiotic impregnated cement spacer is safe to leave in place until definitive second stage surgery.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



5.5 – Treatment: Two-Stage Exchange



Question 1: What is the optimal timing for reimplantation of a two-stage exchange arthroplasty of the hip and knee?

RESEARCHED BY:

Arash Aalirezaie MD, Iran

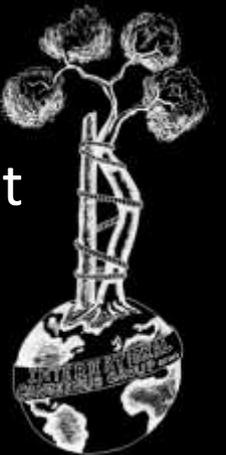
Dirk-Jan Moojen MD, Netherlands

Job Diego Velázquez Moreno MD, Mexico



Literature:

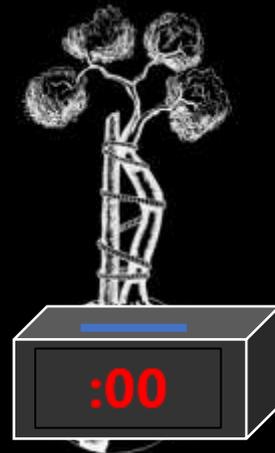
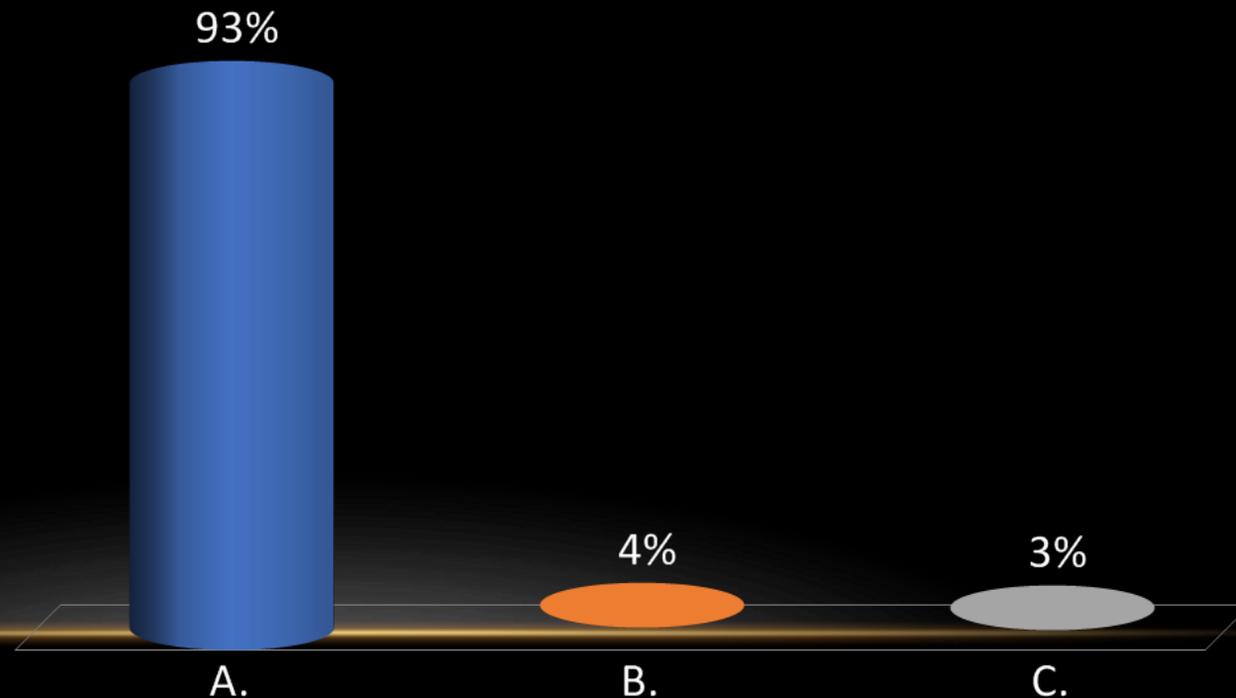
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 11**
- Numerous definitions have been used for two-stage PJI treatment success and this heterogeneity makes determining optimal timing for reimplantation very difficult/impossible
- There is conflicting evidence regarding the best interval between stages
- A recent, large retrospective cohort study evaluating patients with two-stage exchange arthroplasty did not detect a clear association between time to reimplantation and treatment failure.
 - Delaying the time to reimplantation Did not significantly improve treatment success of two-stage exchange arthroplasty



Recommendation: The optimal timing for reimplantation of a two-stage exchange arthroplasty of the hip or knee has not been established. Reimplantation may be performed when the treating medical team feels that the infection is under control.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Is it safe to retain a stable cement mantle, for later use, in patients undergoing resection arthroplasty for PJI?

RESEARCHED BY:

Douglas Dennis MD, USA

Thiago Busato MD, Brazil

Michael Kelly MD, USA



Literature:

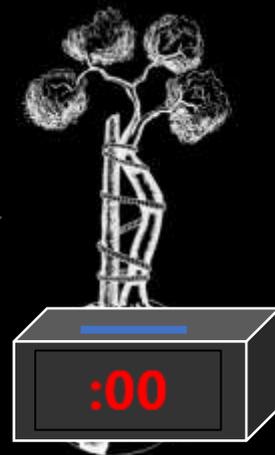
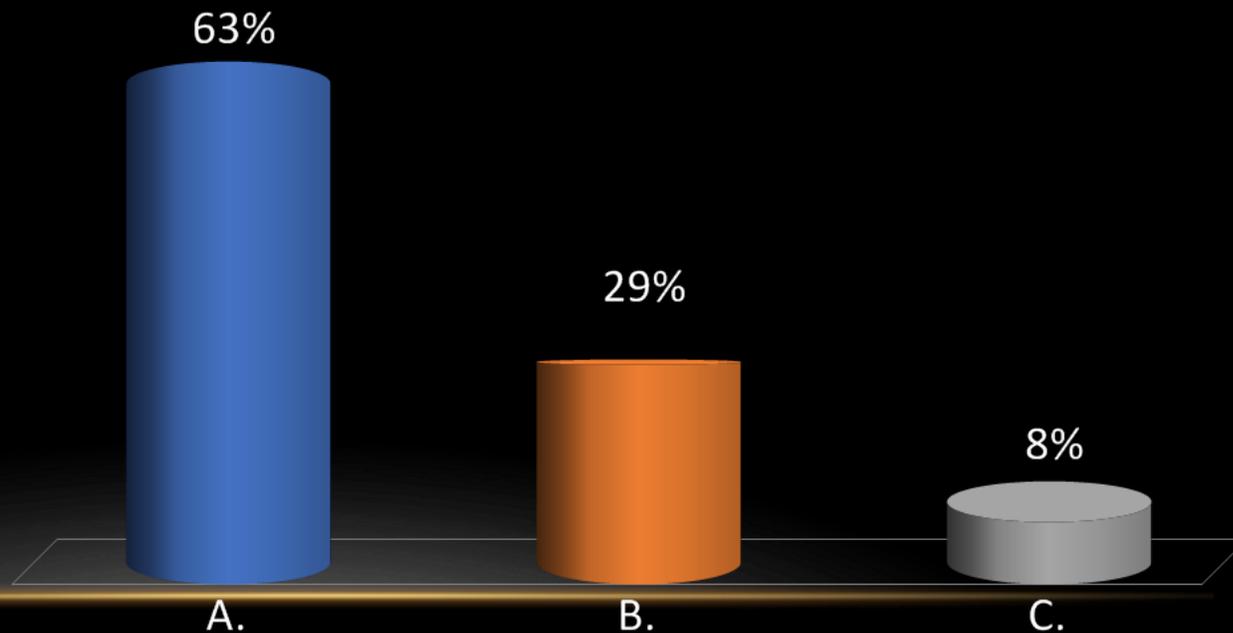
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 19**
- Cement removal is technically demanding and increases patient morbidity according to numerous studies
- Studies show conflicting success in cement retention cases
 - 14/15 successful – Morley et al
 - 2/10 successful – Leijtens et al
- One level IV study shows good results with retained stable cement



Recommendation: Meticulous debridement and removal of all foreign material, including cement, should be part of resection arthroplasty in management of periprosthetic joint infection (PJI). Limited data suggests that under strict conditions and following a meticulous surgical technique, a stable cement mantle in the femur may be left in place for later use in order to minimize damage to the femoral bone stock.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Should surgeons make effort to remove cement that has extruded into pelvis or difficult anatomical position in patients with PJI?

RESEARCHED BY:

Schreurs, Berend Willem

Poolman, Rudolf



Literature:

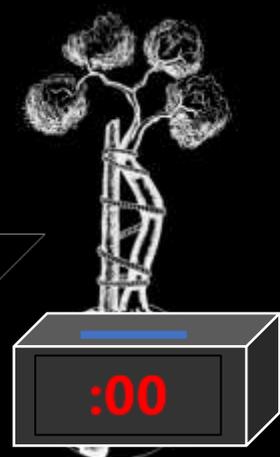
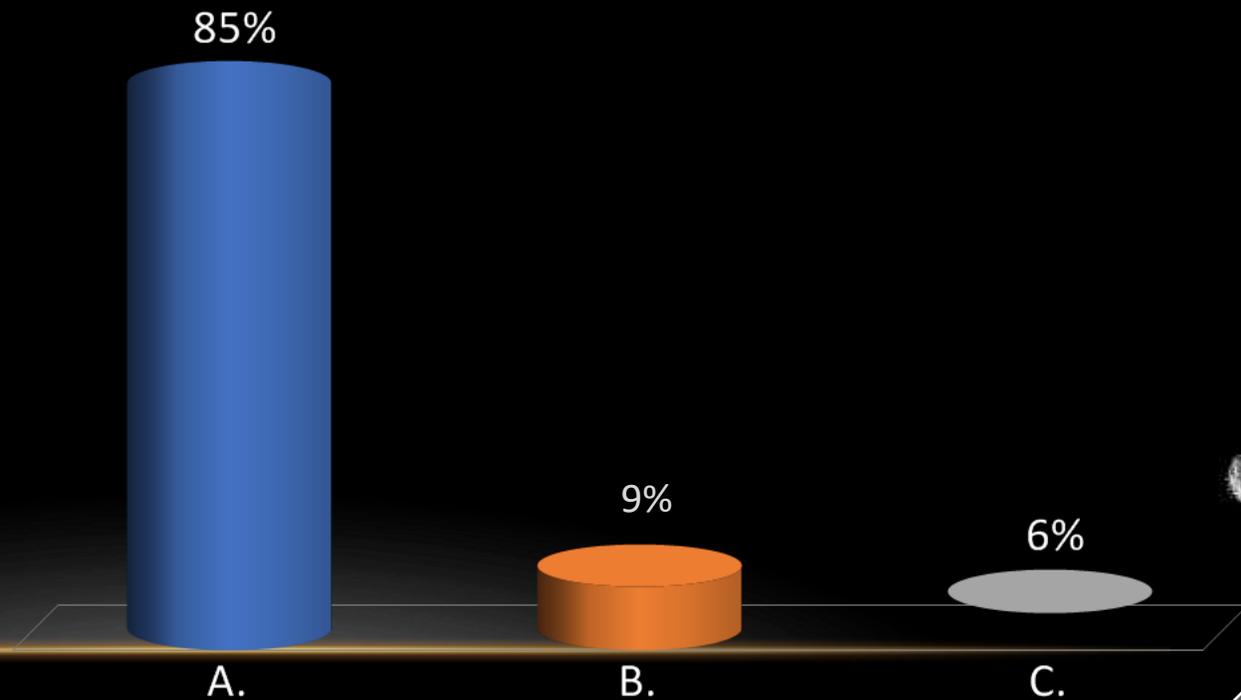
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 8
- When cement is extruded into the pelvis or difficult anatomic position during primary arthroplasty there is a risk of neurological, vascular or urological complication
- This risk may be even greater during attempted extraction



Recommendation: The orthopaedic surgeon should carefully consider whether the potential benefits of cement extraction from the pelvis or difficult anatomical positions outweigh the potential risk of persistence of infection.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Does the use of non-antibiotic impregnated allograft for bone defects during reimplantation increase the risk of recurrence of SSI/PJI?

RESEARCHED BY:



Mohammad Ghazavi
MD, Iran



Jeffrey Lange MD,
USA



Mansour Abolghasemian
MD, Iran



Literature:

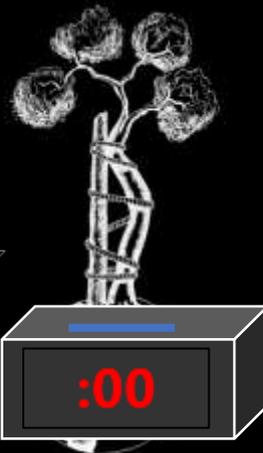
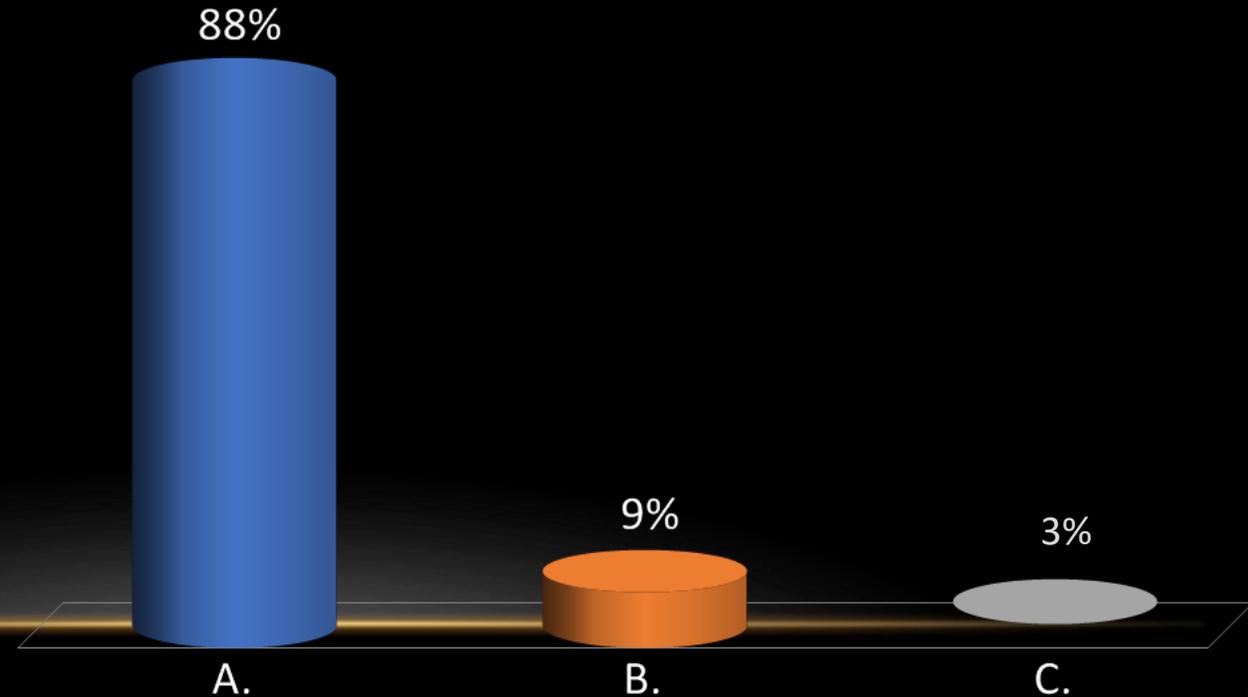
- **Meta-analysis 2, Prospective/Randomized 2, Retrospective 37**
- **Meta-analysis on bulk allograft for second stage implantation**
 - Reinfection rate of 4 out of 43 (9.3%)
 - Comparable to infection rate reported for 2-stage without using allograft
- **Retrospective review (Alexeef et al.)**
 - No recurrence of infection in 11 septic failures of THA that underwent 2-stage using massive structural allografts
- **Retrospective review (Stockley et al.)**
 - 32 deep-frozen irradiated allografts used for reconstruction of bone defects in 20 knees.
 - 3 knees developed infection (9.3%) and 1 required revision for infection.



Recommendation: There is no evidence to demonstrate that using non-antibiotic impregnated allograft for management of bone defects during reimplantation (following PJI) increases the risk of recurrence of SSI/PJI.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



5.6 – Treatment: Surgical Technique



Question 1: Does arthroscopic surgery have any role in the treatment of acute or chronic PJI of the knee or the hip?

RESEARCHED BY:



Alejo Erice MD,
Spain



Michael A Mont MD,
USA

Katsufumi Uchiyama MD,
Japan



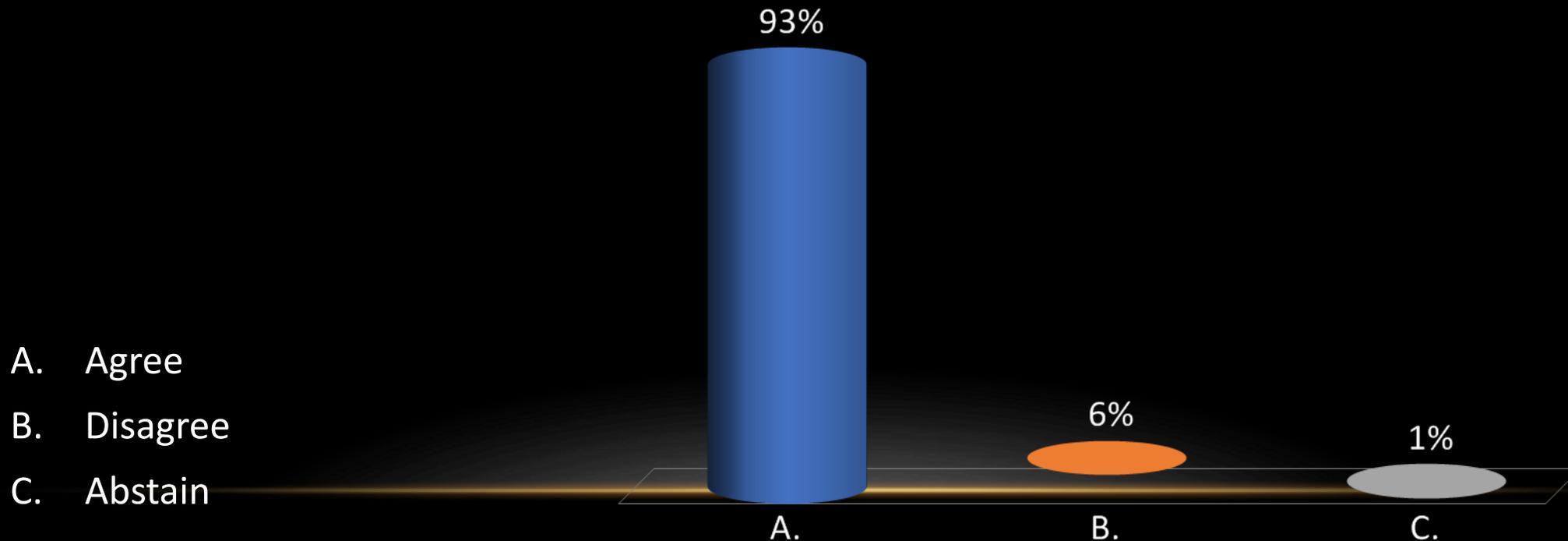
Literature:

- **Meta-analysis XX, Prospective/Randomized XX, Retrospective XX**
- Pooled analysis of available literature suggests that the success from acute/late infection is approximately 60%
- The only comparative series available, concluded that arthroscopic debridement has a significantly lower success rate to open debridement
 - Byren et al compared arthroscopic with open debridement in a retrospective review of 112 cases (51 hips and 52 knees), to assess outcomes of patients treated for PJI. They found that the 15 patients with PJI treated with arthroscopic washout had significantly lower success (47%) than the 97 treated with open debridement (88%) (HR = 4.2, 95% CI 1.5–12.5, $P = 0.008$).
- Current literature recommends against the routine use of arthroscopic surgery for management of PJI.

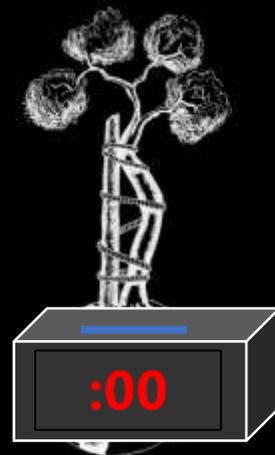


Recommendation: Arthroscopic surgery has no role in the treatment of acute or chronic PJI of the knee or the hip

Level of Evidence: Moderate



- A. Agree
- B. Disagree
- C. Abstain



Question 2: Do all metallic implants need to be removed to eradicate PJI? Does this apply to other metal hardware present (e.g. hook plates, cables) too?

RESEARCHED BY:



Matthew Dietz MD, USA



Andrew Battenberg MD, USA



Literature:

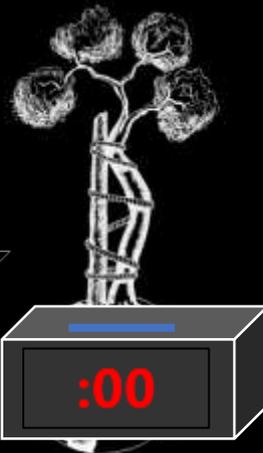
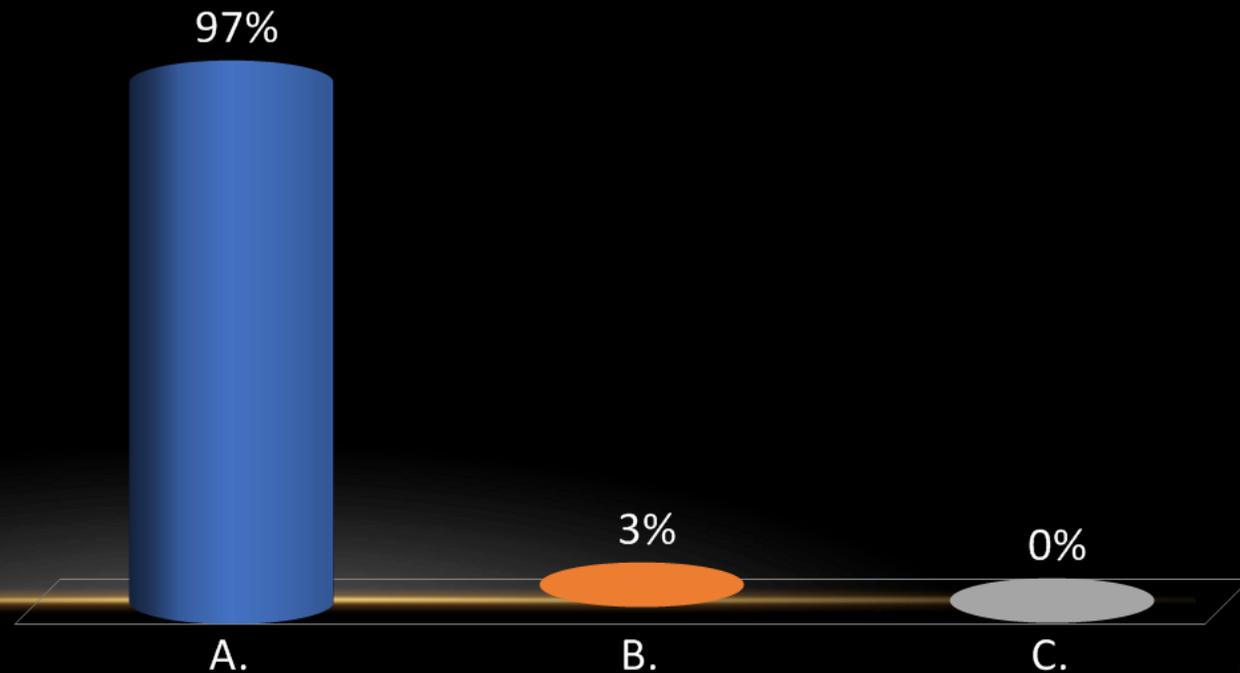
- Ideally, all foreign material, including bone cement and hardware, should be removed to better reduce microbial bioburden and eliminate biofilm
- However, the removal of these materials must be balanced with the morbidity of their removal, and considered carefully in surgical planning.
- Suzuki et al. reported on 2022 TKA, of which 17 cases were infected TKA with a prior history of ORIF – and suggested presence of retained internal fixation material was correlated with postoperative infection.
- Manrique et al. demonstrated a trend toward increasing rates of PJI with partial or complete retention of hardware, but there was no statistical significance when compared to controls



Recommendation: Complete debridement of the hip or knee joint and removal of all hardware is ideal during surgical treatment of periprosthetic joint infection (PJI). This principle should be followed whenever possible. However, there may be rare cases of PJI when removal of all hardware may lead to significant morbidity and preclude future reconstruction. In the latter situation some hardware may be retained.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Should all knee compartments be resected during resection of an infected unicompartmental knee arthroplasty (UKA)?

RESEARCHED BY:



Jeffrey Granger, MD



Tae-Kyun Kim, MD



Rafael J Sierra, MD



Literature:

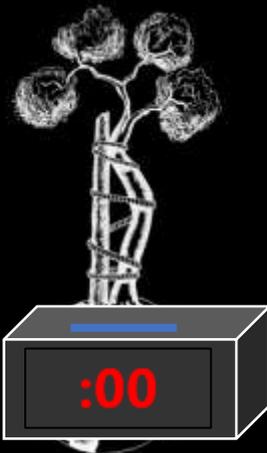
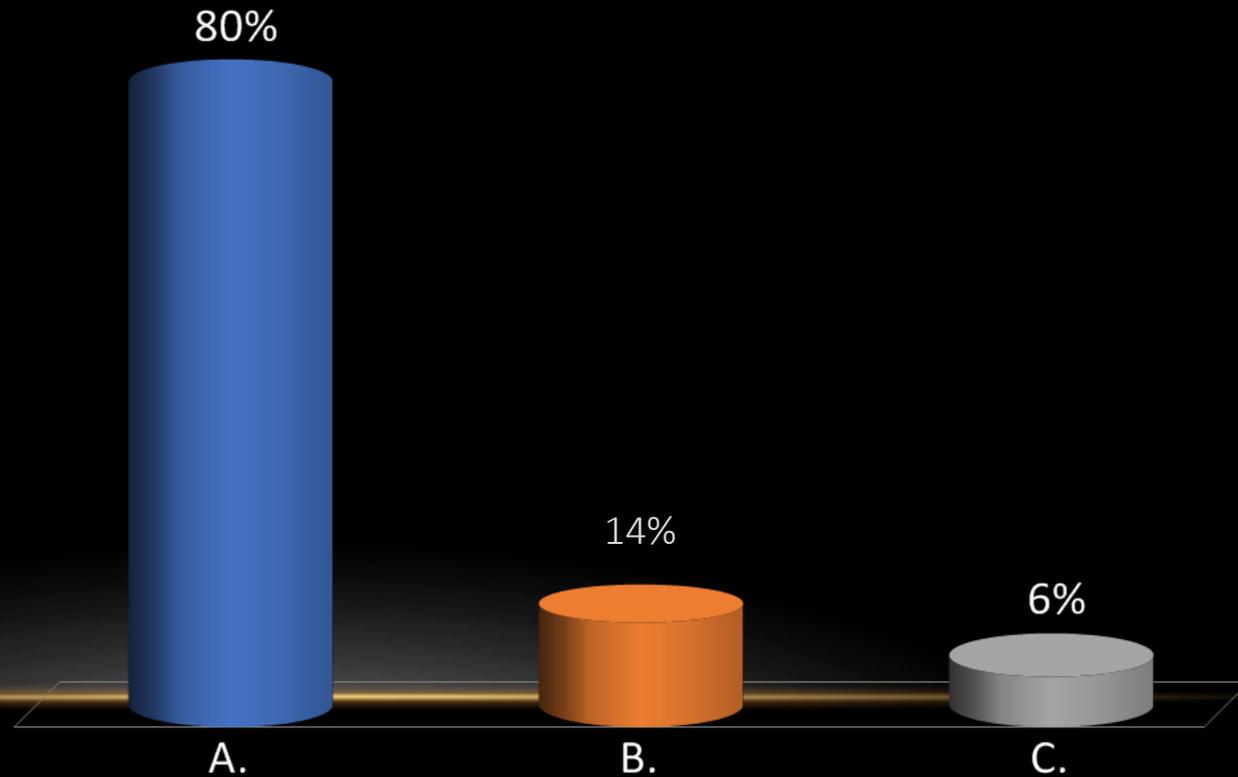
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 11
- Relatively few studies evaluating treatment and outcomes of PJI and UKA
- More high-quality studies needed



Recommendation: Yes, during resection of an infected unicompartmental knee arthroplasty (UKA) other compartments of the knee, including the fat pad, should also be resected.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Can sub-radical resection arthroplasty (leaving parts of implants in place) be considered during management of patients with chronic PJI?

RESEARCHED BY:



Kyung-Hoi Koo MD,
South Korea



Jorge Manrique MD,
Colombia



Adolf Lombardi MD,
USA



Literature:

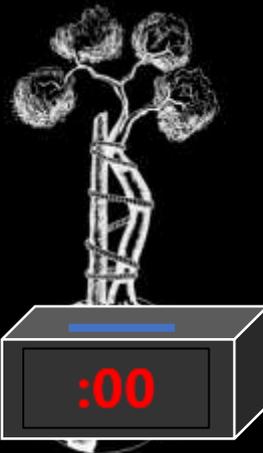
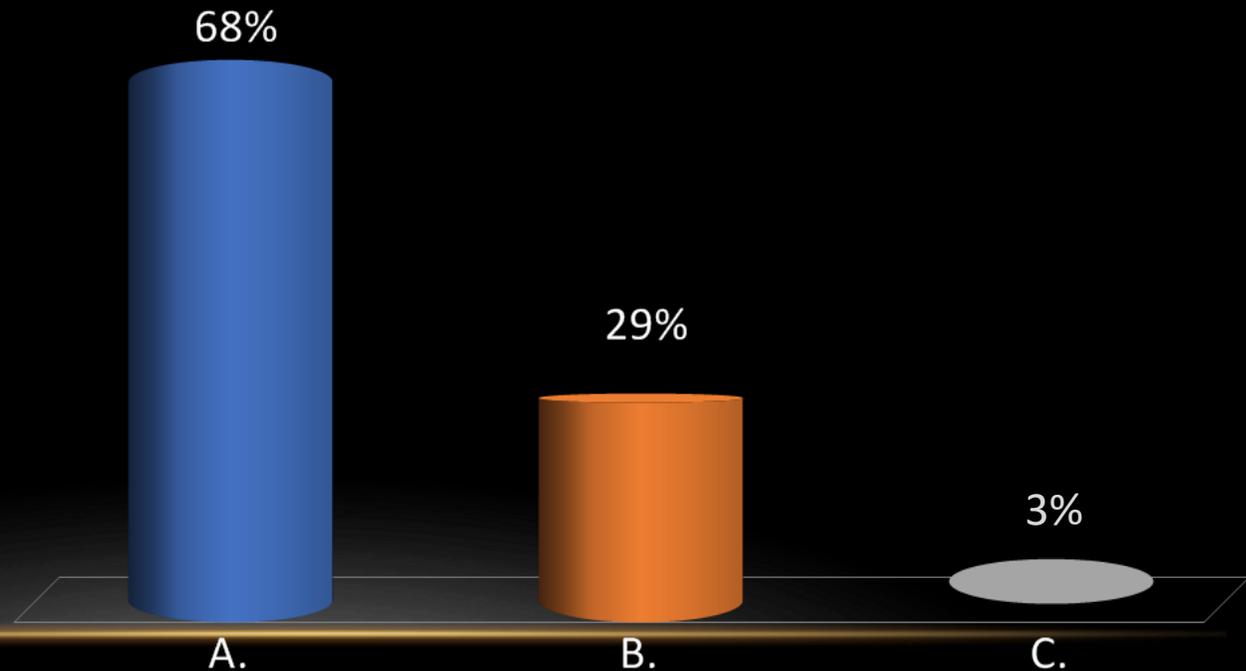
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 12**
- While two-stage revision with removal of all prostheses is considered gold standard, removal of a well-fixed stem may necessitate additional procedures (e.g. ETO) or result in compromise of the proximal femur and future fixation at reimplantation.
- Retaining a well-fixed stem, or acetabular component may be an option to avoid this in the setting of PJI treatment
- Results of sub-radical resection arthroplasty have shown acceptable success rates ranging from 87 to 89% (Lee et al, Ekpo et al, Lombardi et al, El-Husseiny et al, Ji et al)
- However data are limited to retrospective observational studies of limited sample size (range 17-31 patients).



Recommendation: Sub-radical resection arthroplasty (leaving parts of implants in place) may be considered during management of patients with chronic PJI when a component is proven to be well-fixed, and its removal precludes opportunity for future reconstruction.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Is it possible to have an isolated infection of only a portion of the joint (for example the femur and not the acetabulum or tibia and not the femur)?

RESEARCHED BY:

Derek Ward MD, USA

Yona Kosashvili MD, Israel



Literature:

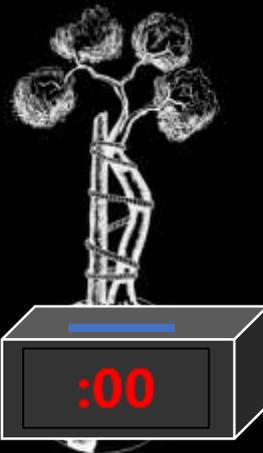
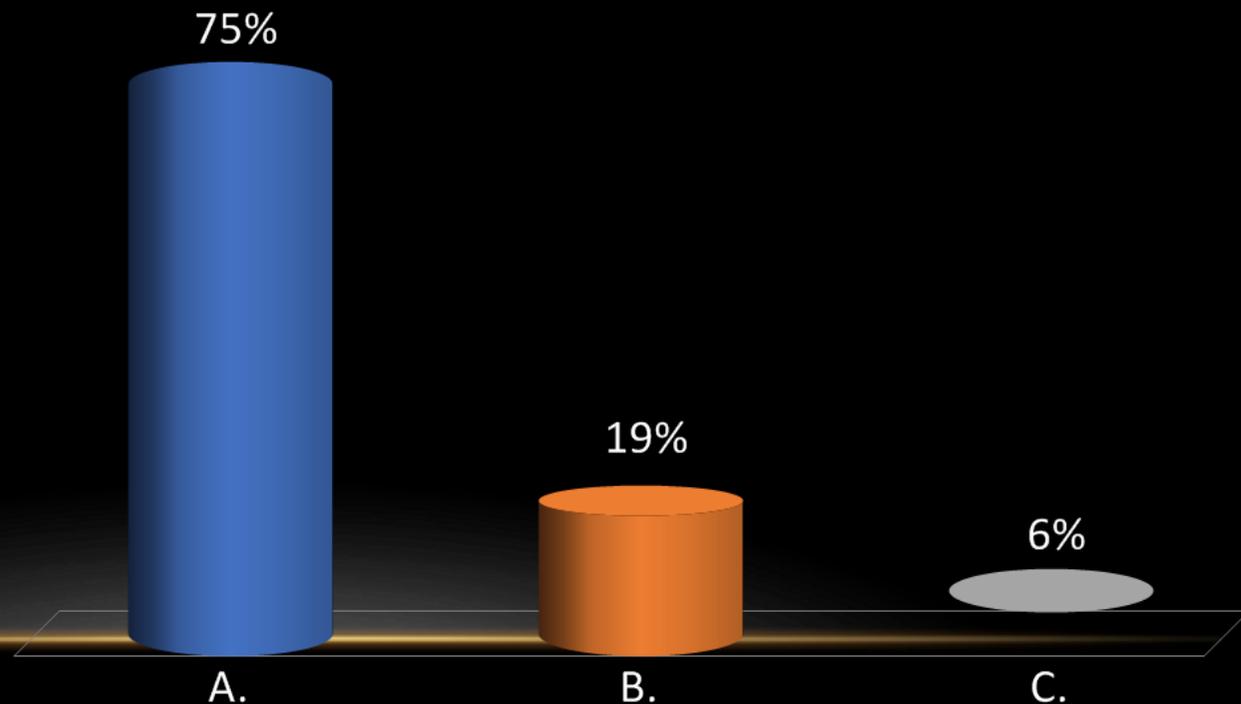
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 9**
- 9 relevant articles accounting for 130 revisions were reviewed
- In THA/TKA the surfaces of prosthetic material are in contact with bone, and knowing the fact that infective organisms are capable of attaching to foreign material surfaces and forming biofilms, the authors are inclined to believe that partial infection of a prosthesis does not exist



Recommendation: Unknown. Infection of a prosthetic joint is likely to involve biofilm formation on surfaces of all foreign material. However, there may be rare circumstances when infective organisms may not be able to reach the surface of a well-fixed implant and form a biofilm.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 6: Should heterotopic ossification (HO) be removed during resection arthroplasty of an infected prosthetic joint?

RESEARCHED BY:



Konstantinos Malizos, MD

Andrew Freiberg, MD

Per Kjaersgaard-Anderson, MD

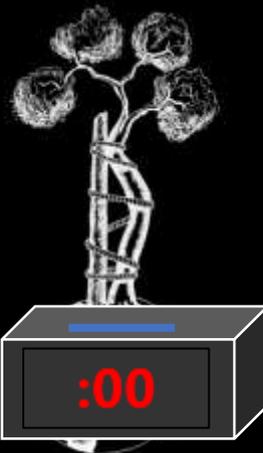
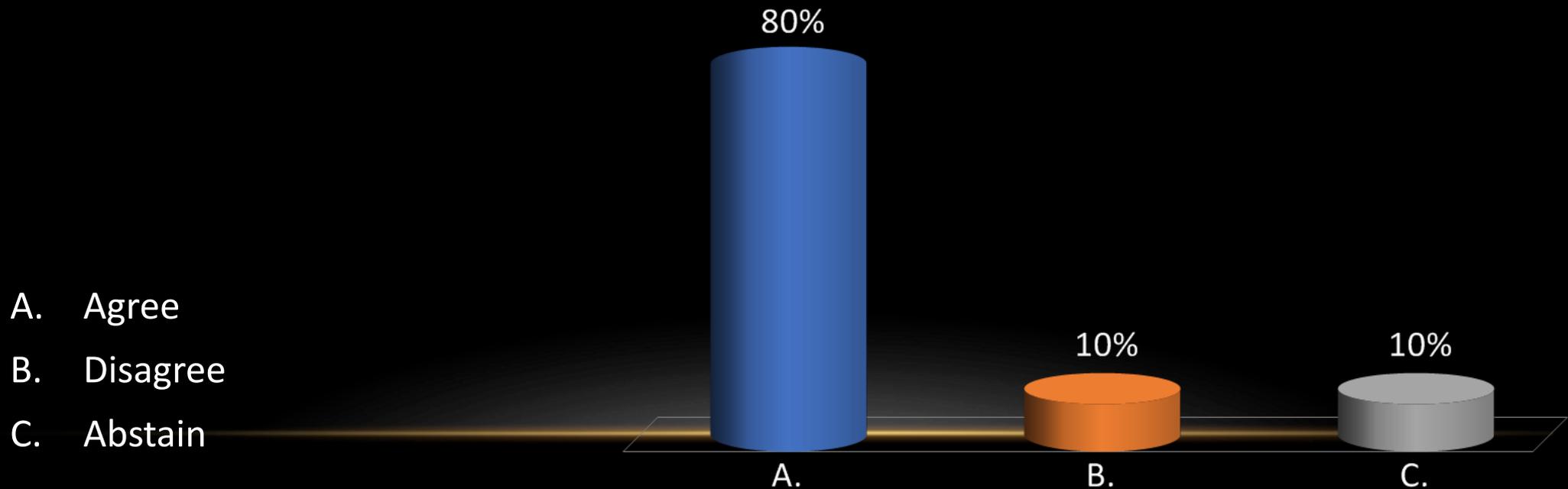
Literature:

- Meta-analysis 0, Prospective/Randomized 0, Retrospective 0
- No studies evaluating HO excision during resection arthroplasty



Recommendation: We recommend that surgeons give a strong consideration to removal of accessible heterotopic ossification (HO) in an infected prosthetic joint that will not compromise future reconstruction.

Level of Evidence: Consensus



Question 7: When soft tissue coverage requires a reconstructive flap, can it be performed at the time of explant or should it be deferred until reimplantation?

RESEARCHED BY:

David Backstein MD, Canada

Maik Stiehler MD, Germany



Literature:

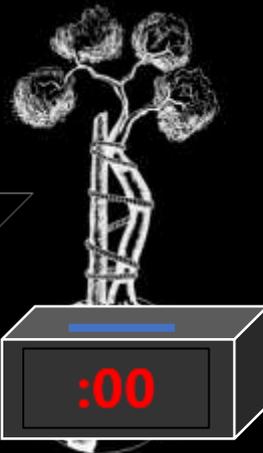
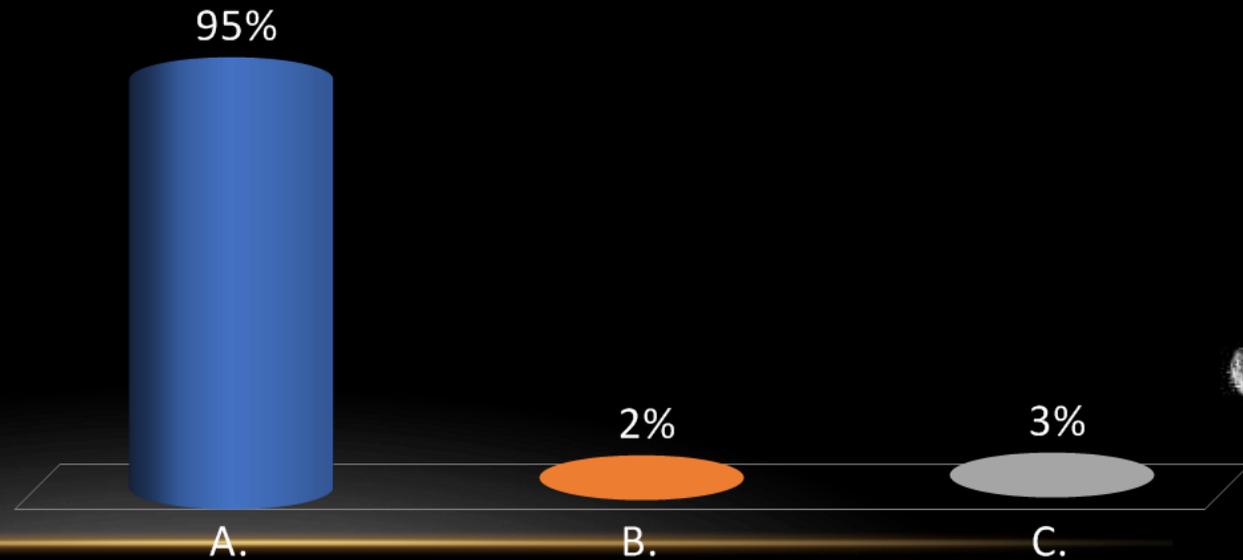
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 7**
- The only study identified which evaluated patients based on the timing of flap coverage showed a non-significant trend toward higher failure rates when the flap was performed with spacer implantation (first or repeat) compared to with definitive implants (re-implantation or retention with liner exchange) (Tetrault et al.)
 - Overall reinfection rate among all groups was 52% at four years
- Based on the published reports, there is limited evidence to support soft tissue flap reconstruction at the time of implant removal and antibiotic cement spacer insertion



Recommendation: When a soft tissue defect requires a reconstructive flap, it is safe to perform flap coverage at the time of explant or at the time of re-implantation. Early flap coverage at the time of explant improves soft tissue biology for eradication of infection and allows for earlier mobilization following re-implantation given greater flap maturity.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



5.7 – Treatment: Prosthesis Factors



Question 1: Does the use of cemented or cementless components at the time of reimplantation affect the success of treating chronic PJI? If yes, what is the optimal antibiotic(s), dosage, and cement to maximize antibiotic delivery and mechanical properties of the cement?

RESEARCHED BY:



Guillem Bori MD,
Spain

Laurens Manning MD,
Australia



Literature:

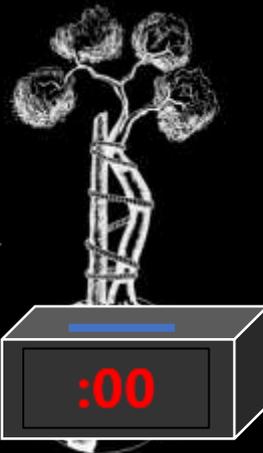
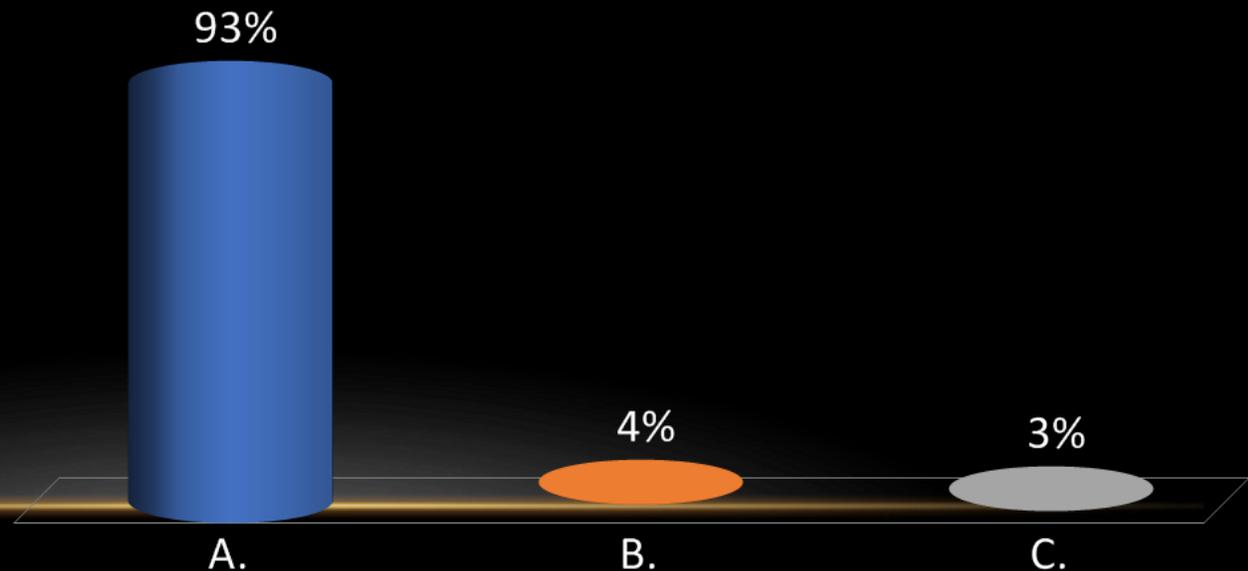
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 38**
- **Limited evidence as it is not yet clear that antibiotic impregnated cement is required at the time of reimplantation to increase infection cure rate.**
- **Further research is required.**



Recommendation: There is no evidence to suggest that the use of cemented or cementless components at the time of reimplantation affects the success rate of infection treatment. However, the mode of fixation may affect implant survivorship. The bone mass and the quality should dictate the choice of implant and the mode of fixation during reimplantation. If cemented prostheses are used, consideration should be given to the addition of antibiotics, directed towards the infective organisms, at the time of reimplantation.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does the use of tantalum augments during a single-stage revision for PJI influence the rate of subsequent SSI/PJI?

RESEARCHED BY:



Rafael Llopis MD, Spain



Nemandra Sandiford
MD, UK



Daniel Kendoff MD,
Germany



Literature:

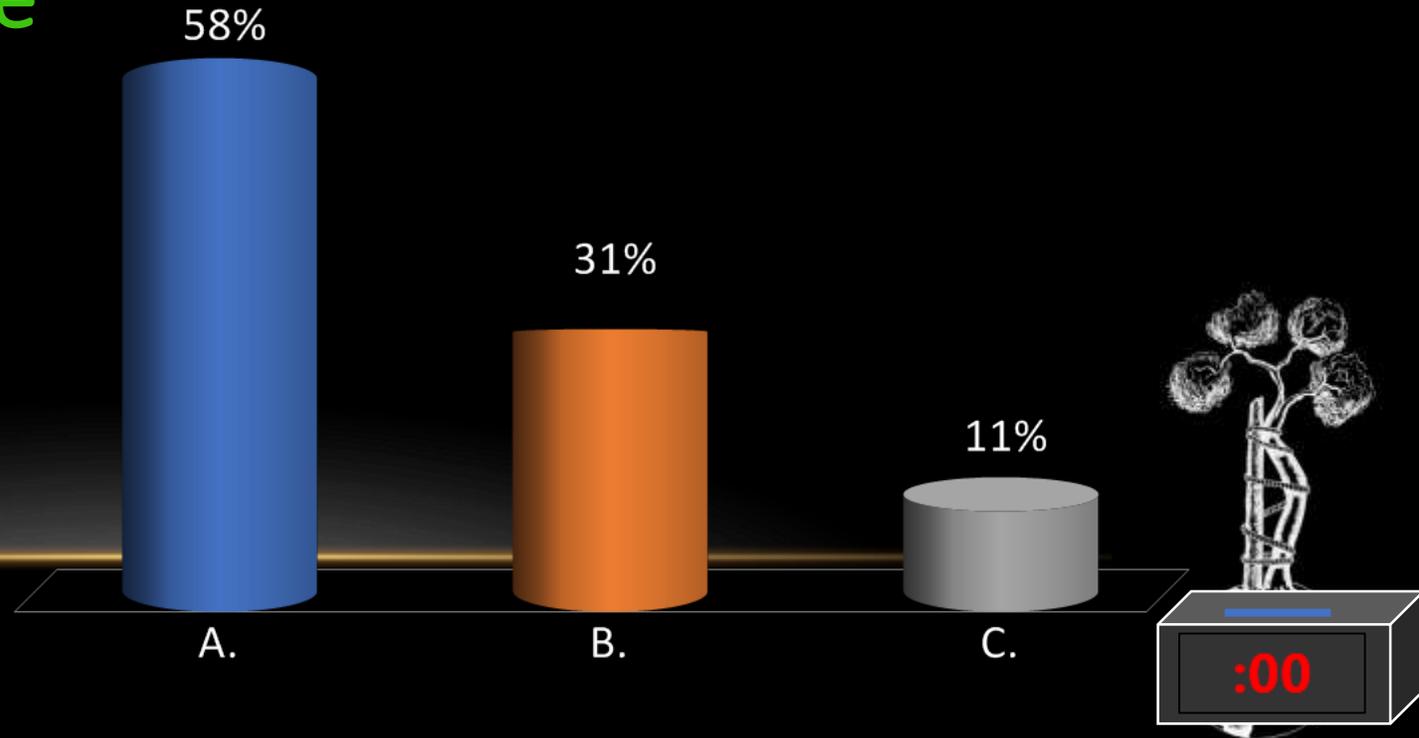
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 11**
- **Retrospective study of revision hip arthroplasty using tantalum or titanium implants (Tokarski et al.)**
 - 144 hips for which revision had been performed because of infection
 - Failure due to a subsequent infection was 3.1% (2/64) in the tantalum group and 17.5% (14/80) for the titanium group ($p = 0.006$)
- **Retrospective study of evaluating tantalum on infection rates for 1-stage revisions (Klatte et al.)**
 - **Cohorts were well matched and infection diagnosed on standardized criteria**
 - There was no difference observed in the re-infection rates in either group (two cases in each group)



Recommendation: Findings of retrospective studies suggest that tantalum augments might have a protective effect against subsequent infection following single-stage revision THA and TKA in the context of PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Is the use of highly porous tantalum associated with a reduced risk of SSI/PJI recurrence in revision total joint arthroplasty?

RESEARCHED BY:



Ian Stockley MD, UK

Michael Kelly MD, USA

Javad Parvizi MD, USA

Literature:

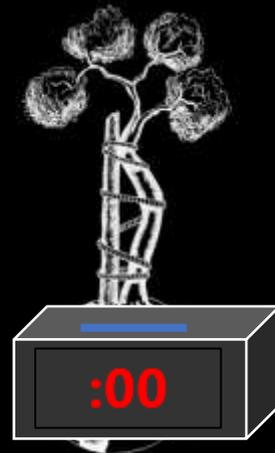
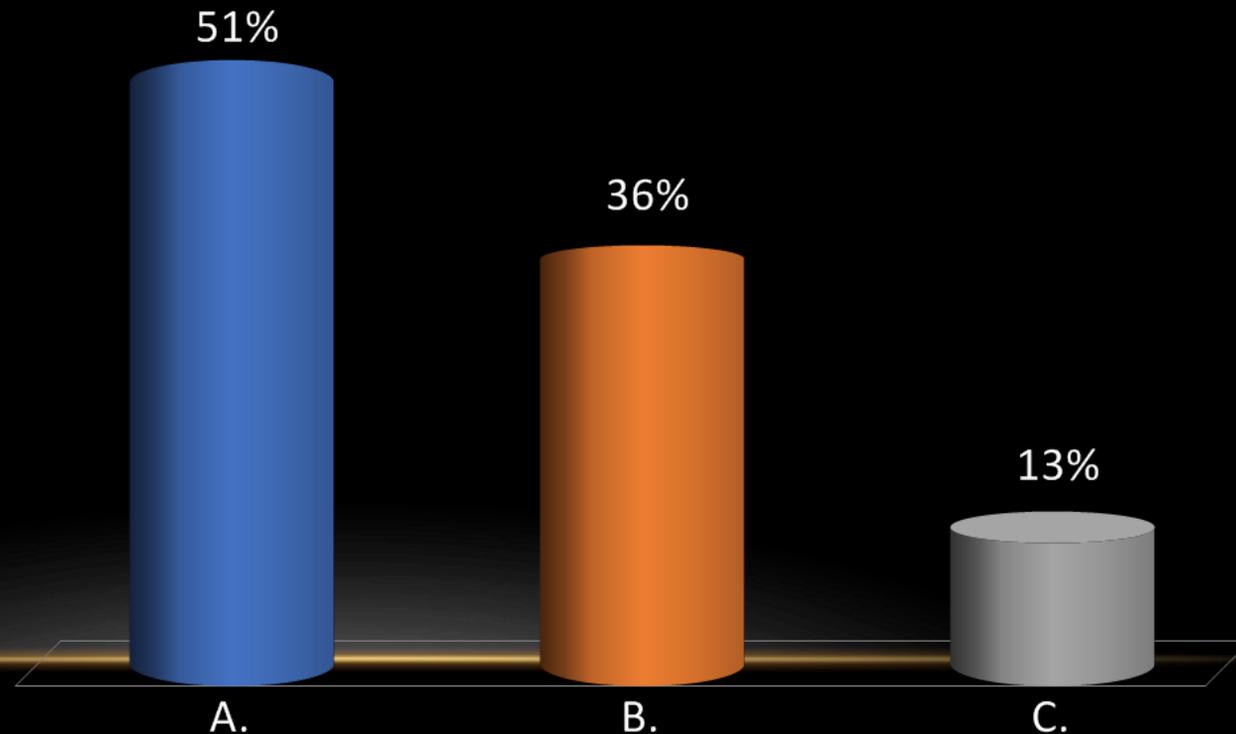
- **Meta-analysis 0, Prospective/ Randomized 1, Retrospective 16**
- Literature has reported that reconstruction with Ta implants demonstrates superior outcomes vs other cementless components
- A collaborative study reviewing 2 national registries found no benefit in survival in Ta implants compared to other cementless implants
- The existing data for Ta implants is promising but limited



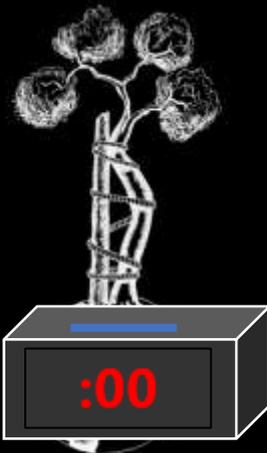
Recommendation: There is some evidence to suggest that the use of highly porous tantalum is associated with a reduced risk of SSI/PJI recurrence in patients undergoing revision total joint arthroplasty, particularly for treatment of PJI.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



5.8 – Treatment: Salvage



Question 1: Are there differences in outcomes and survivorship between knee arthrodesis and above-knee amputations for chronic knee PJI?

RESEARCHED BY:

Mohammad Ghazavi MD, Iran

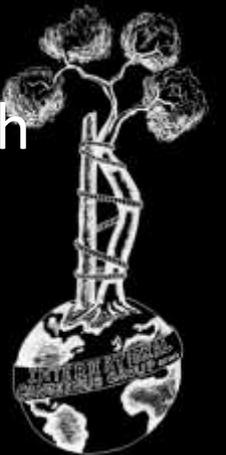
Hamidreza Yazdi MD, Iran

Hamidreza Yazdi MD, Iran



Literature:

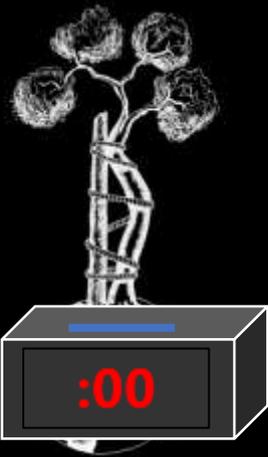
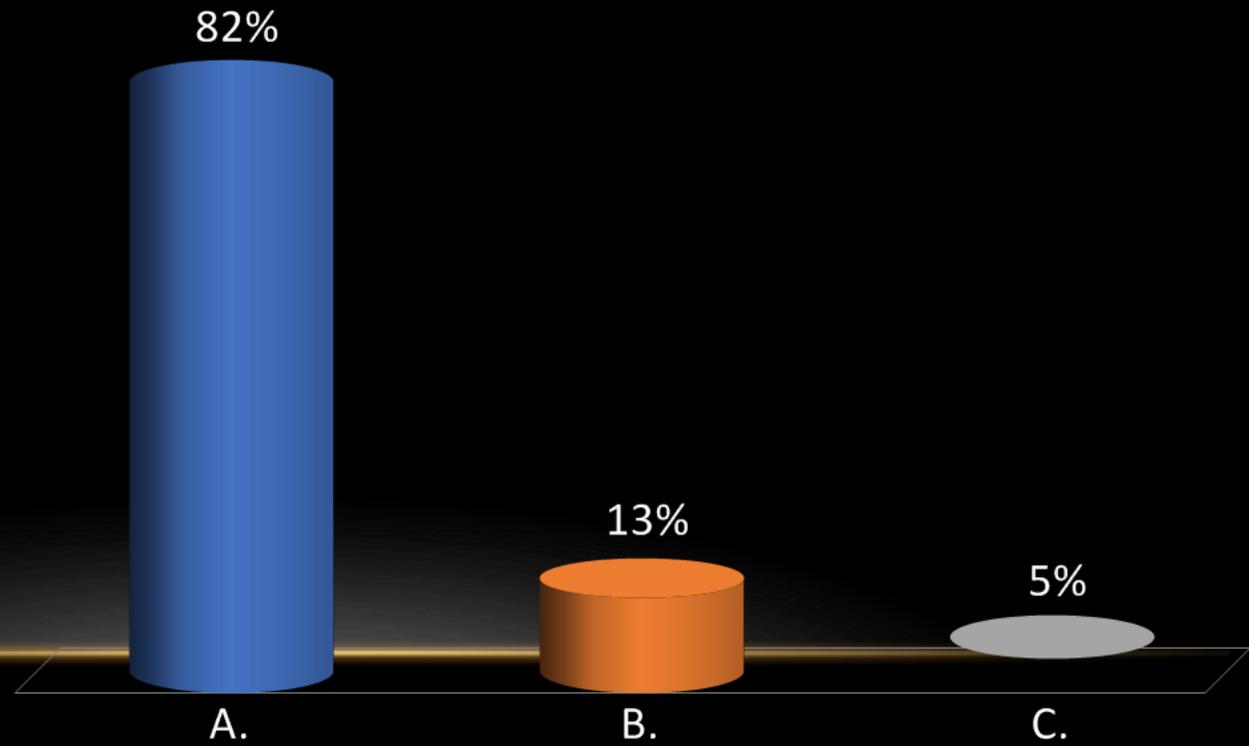
- **Meta-analysis/systematic review 1, Prospective/ 0, Retrospective 16**
- A review of 69 revision cases had a 5.8% infection rate
 - Two infected cases who underwent KA demonstrated comparable Oxford scores with patients who were treated with a two-stage revision
- A retrospective review of 35 patients who underwent AKA after an infected TKA showed:
 - after a mean follow up of 39 months, fifteen of the patients receiving AKA had died
 - eleven patients needed repeated surgery
- Authors of a systematic review concluded that KA should be strongly considered as it provides higher quality of life when patients present with failed two-stage revision for infected TKA



Recommendation: Yes, above the knee amputation (AKA) for the treatment of chronic periprosthetic joint infection (PJI) in total knee arthroplasty (TKA) has a lower functional outcome and higher mortality rate than knee arthrodesis (KA).

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: How many exchange arthroplasties are reasonable before a salvage operation (such as amputation or arthodesis) should be considered?

RESEARCHED BY:



Timothy Tan MD,
USA



Javad Mortazavi MD,
Iran



Literature:

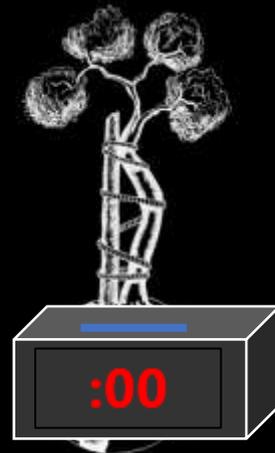
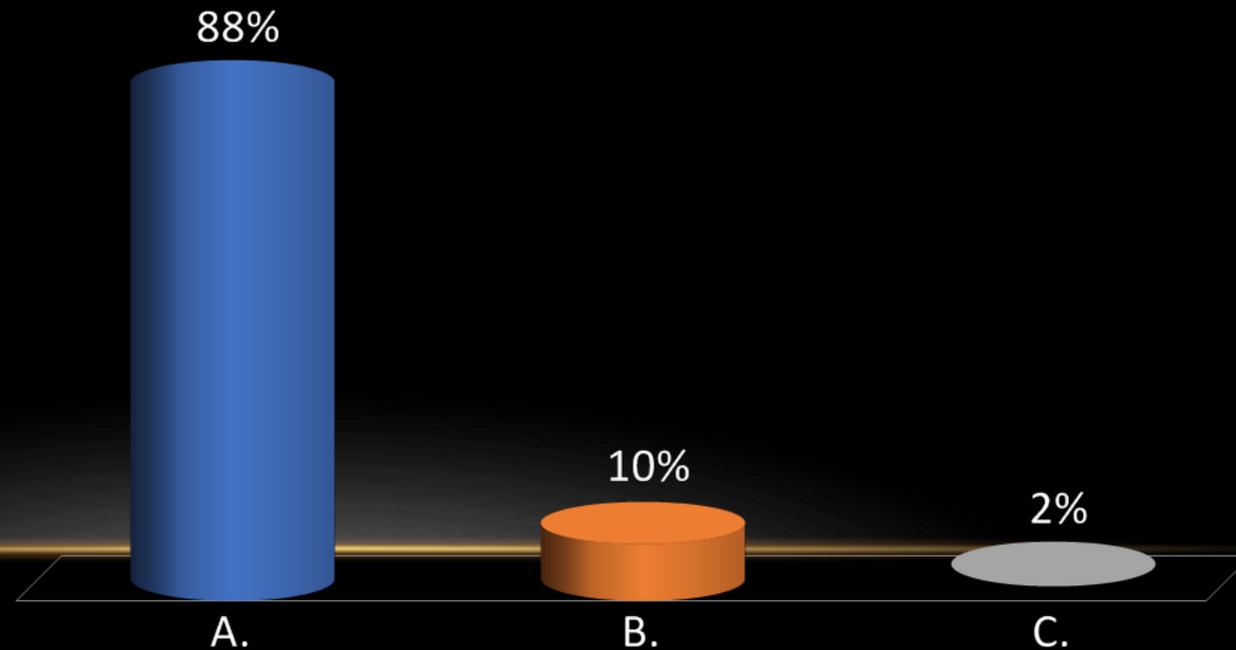
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 6**
- Retrospective review (Azzam et al.)
 - Demonstrated that recurrent or persistent infection after a failed two-stage exchange was found in 4 out of 18 patients (22.2%). In this series, two patients underwent a third two-stage exchange arthroplasty and both were infection free at two years.
- Retrospective review (Kheir et al.)
 - Patients undergoing a second two-stage exchange arthroplasty, reimplantation occurred in only 65% of cases, and successful outcomes occurred in only 61.6%
 - Furthermore, of the 14 cases that were not re-implanted, there was a high rate of retained spacers (n=6), amputations (n=5), PJI-related mortalities (n=2), and arthrodesis (n=1)



Recommendation: Patients with a failed two-stage exchange arthroplasty that undergo a repeat two-stage exchange arthroplasty demonstrate poor outcomes. Failure of the repeat two-stage exchange arthroplasty appears to be dependent on the host grade and status of the extremity. Surgeons thus should consider the patient's comorbidities and expectations when deciding whether to subject the patient to repeat two-stage exchange arthroplasties. The outcome of a third or fourth two-stage exchange arthroplasty are dismal.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 3: What are surgical alternatives to hip disarticulation in patients with persistent joint infection?

RESEARCHED BY:

Michael Patzakis MD

Eoin Sheehan MD



Literature:

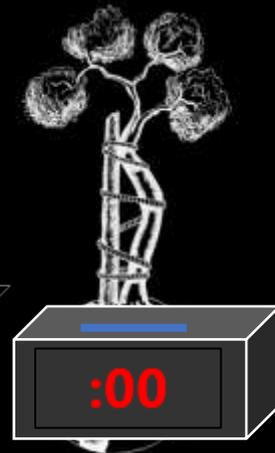
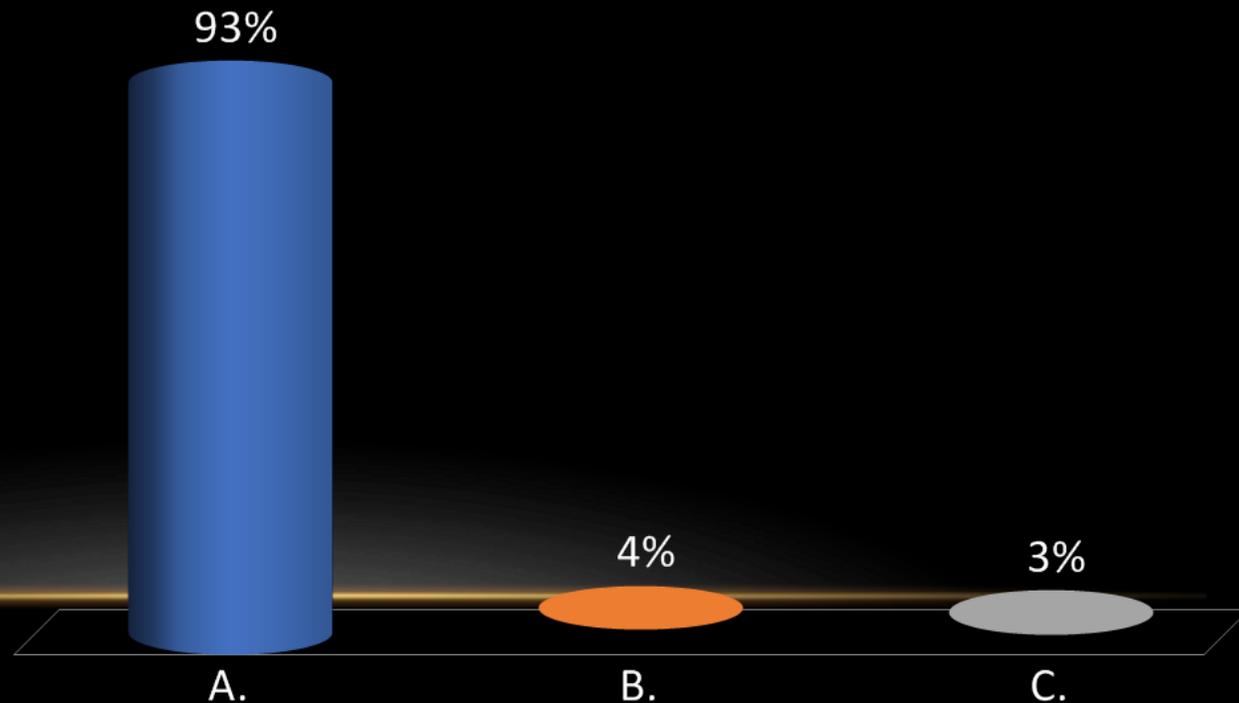
- **Meta-Analysis 1, Prospective/Randomized 0, Retrospective 14**
- Limited, low-level evidence found for surgical alternatives for hip disarticulation.
- Fountain et al (2007) identified 14 patients over a 25-year period who had a total femoral arthroplasty (TFA) as a limb salvage procedure after complications following revision arthroplasty surgery.
 - There was an overall improvement in function in all patients with 4/14 patients achieving a 75% improvement.
- Parvizi et al. (2007) conducted a retrospective review of 48 patients who underwent implantation of proximal femoral replacement.
 - Proximal femoral replacement had good to excellent functional outcomes in 22/43 hips.
 - Significant improvement ($P < 0.05$) in Harris hip score at time of follow-up (mean = 36.5 MO)
 - 10 patients required reoperation or revision due to at least one complication.



Recommendation: Surgical alternatives to hip disarticulation include resection arthroplasty when reconstruction of the joint with the use of megaprosthesis is not possible. Hip disarticulation should be reserved for patients with systemic sepsis and/or extreme soft tissue infection of the extremity in whom the surgery is performed as part of a life-saving procedure.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



5.9 – Treatment: Antimicrobials



Question 1: What is the recommended duration of antibiotics after a single-stage exchange for PJI?

RESEARCHED BY:

Sujith Konan MD, United Kingdom

Lars Frommelt MD, Germany

Christian Lausmann MD, Germany

Thorsten Gehrke MD, Germany



Literature:

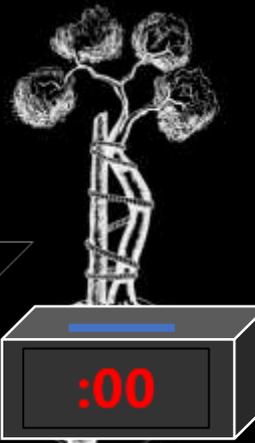
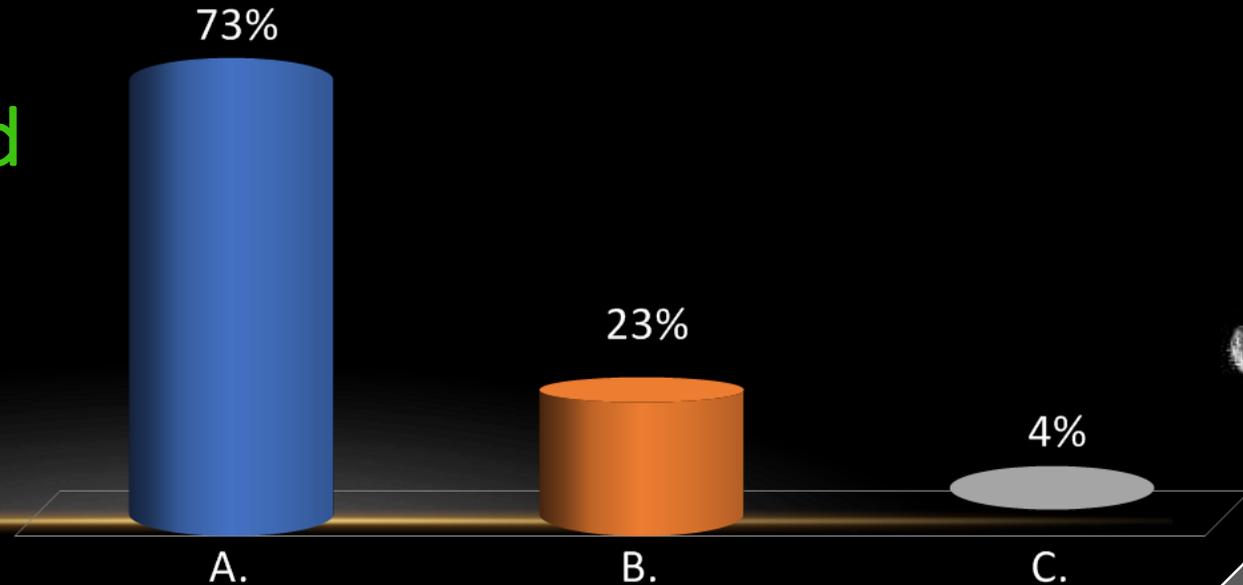
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 15**
- Most studies related to one-stage exchange arthroplasty highlight the importance of preoperative identification of the infective organism.
 - This is important for several reasons including incorporating the appropriate antibiotic into the cement
- The antibiotic therapy following single-stage revision surgery usually starts with an intravenous agent, based on antibiogram of the infective agent.
 - The intravenous antibiotic is usually administered for a few days and then replaced by an oral agent and continued 4-6 weeks (Yoo et al., Haddad et al. Hansen et al.)
- Two retrospective studies advocate for the importance of using antibiotics in cement (Hansen et al., Wolf et al.) for infection control



Recommendation: In the setting of single-stage exchange arthroplasty, intravenous application of antibiotics should be applied for 10 to 14 days followed by oral antibiotics. Generally, the overall duration of antibiotics of 4-6 weeks is sufficient.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Are there any tests that can guide antimicrobial treatment in patients with PJI and allow stopping these agents?

RESEARCHED BY:



Angela Hewlett MD, USA

Isabel Ramirez MD, Colombia



Literature:

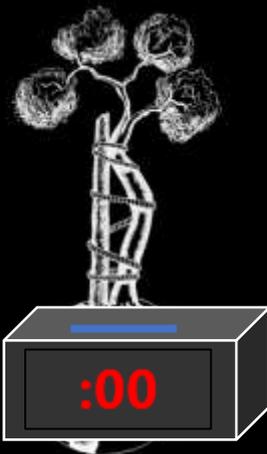
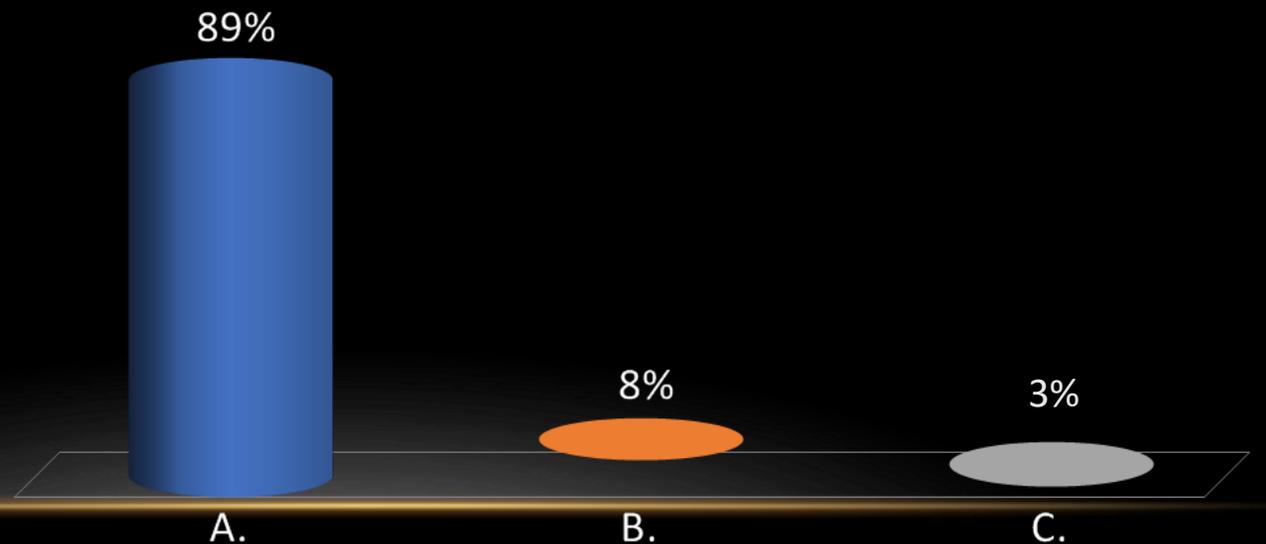
- **Meta-analysis 0, Prospective/Randomized 9, Retrospective 2**
- Serum ESR and CRP are poor predictors of persistent infection and they are frequently abnormal even when the infection has been controlled.
- New markers such as the cytokines in synovial fluid, leukocyte esterase, and serum D-dimer tend to normalize at the time of reimplantation.
- Further studies are required to show their trends with antimicrobial treatments.



Recommendation: No. There are no tests that can be used to guide therapy and monitor response to treatment in patients with periprosthetic joint infection (PJI). Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are considered useful for monitoring response to treatment, however, sustained elevation after treatment does not predict persistent infection. Emerging biomarkers, such as D-dimer and presepsin, have shown promising results. Nevertheless, more studies are required to assess their role in monitoring response to treatment in patients with PJI.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: Does the International Consensus Group (ICG) agree with the IDSA guidelines regarding the recommended duration of antibiotic therapy in orthopedic infection?

RESEARCHED BY:



Jean Yombi MD,
Belgium



Camelia Marculescu MD,
USA



Literature:

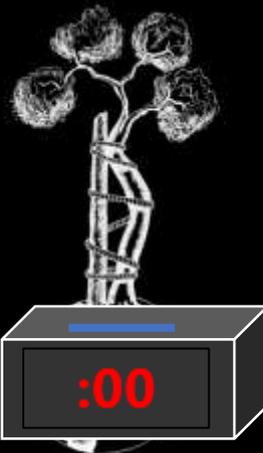
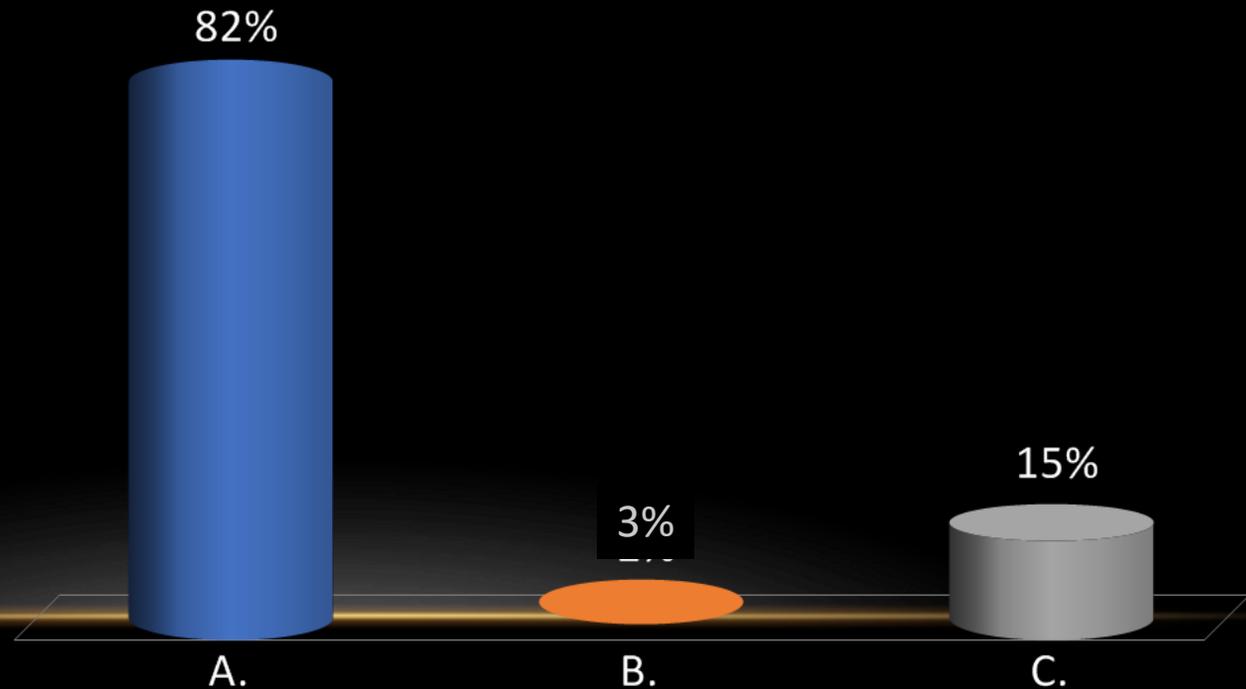
- **Meta-analysis 6, Prospective/Randomized 1, Retrospective 20**
- **Moderate evidence suggesting different recommendations regarding the duration of antibiotic treatment by IDSA & ICG.**



Recommendation: There is some disagreement between what the International Consensus Group (ICG) recommends and the Infectious Diseases Society of America (IDSA) guidelines regarding the duration of antibiotic treatment for different infective organisms. The difference between the two organizations resides on the duration of oral antibiotic therapy following a pathogen-specific intravenous (IV) antimicrobial therapy.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Is the type, dose, route of administration and duration of antimicrobial treatment influenced by the type of infective organism causing PJI?

RESEARCHED BY:

Aboltins, Craig A

Yombi, Jean

Marculescu, Camelia



Literature:

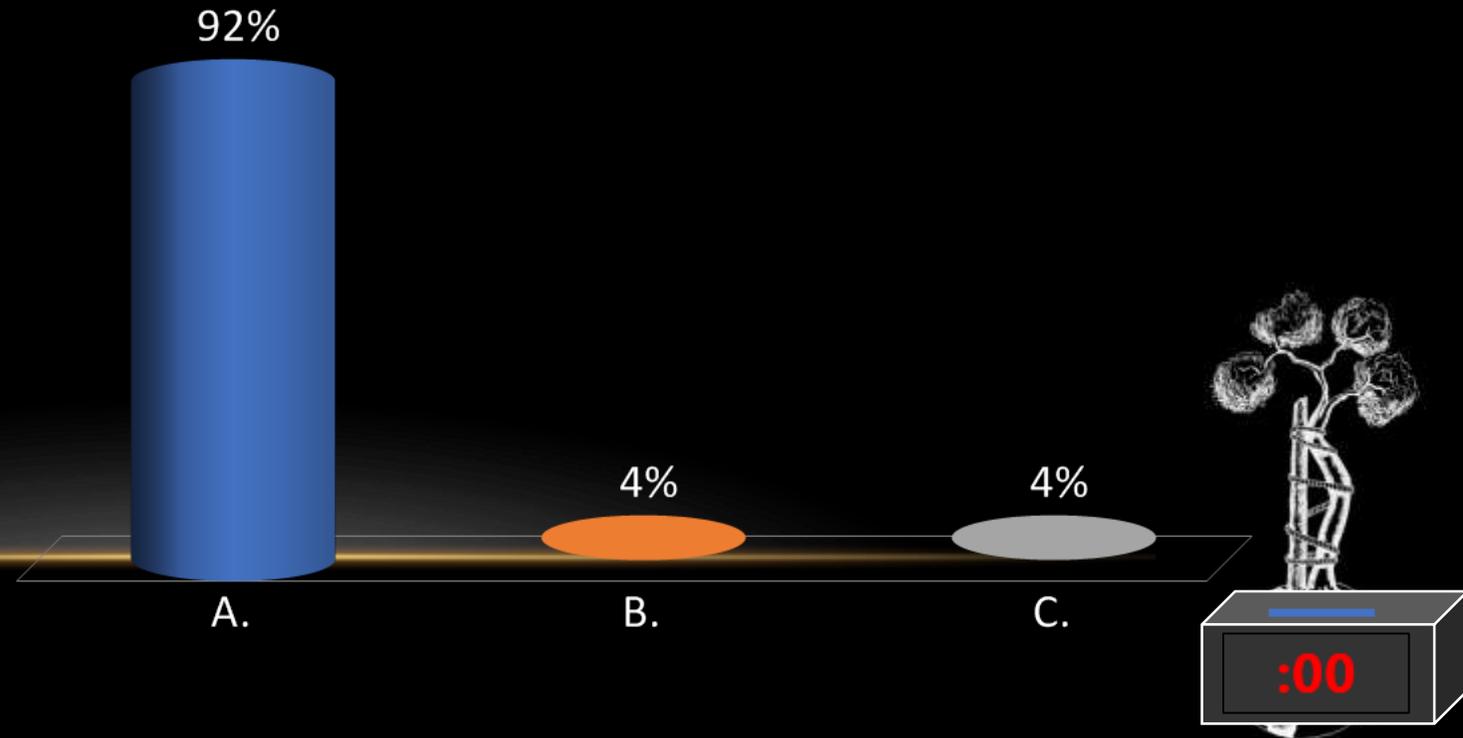
- Meta-analysis 0, Prospective/Randomized 0, Retrospective 28
- No high quality evidence exists: studies are heterogenous and retrospective
- Optimal duration of total antibiotic therapy ranges from 6/52 – 3/12
- Multiple studies report longer (but varied) duration of antibiotics for rapidly-growing mycobacteria (3-112/52)



Recommendation: The duration, dose, route of administration, and the type of antibiotic administered to patients with PJI is determined by the type of infective organism(s) isolated.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 5: When a patient undergoes aseptic revision and intraoperative culture(s) grow an organism, should patients be treated with antibiotic therapy?

RESEARCHED BY:



Carlos A. Higuera MD, United States of America

Barry Brause MD,
United States of America



Literature:

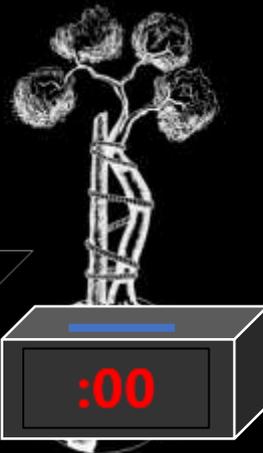
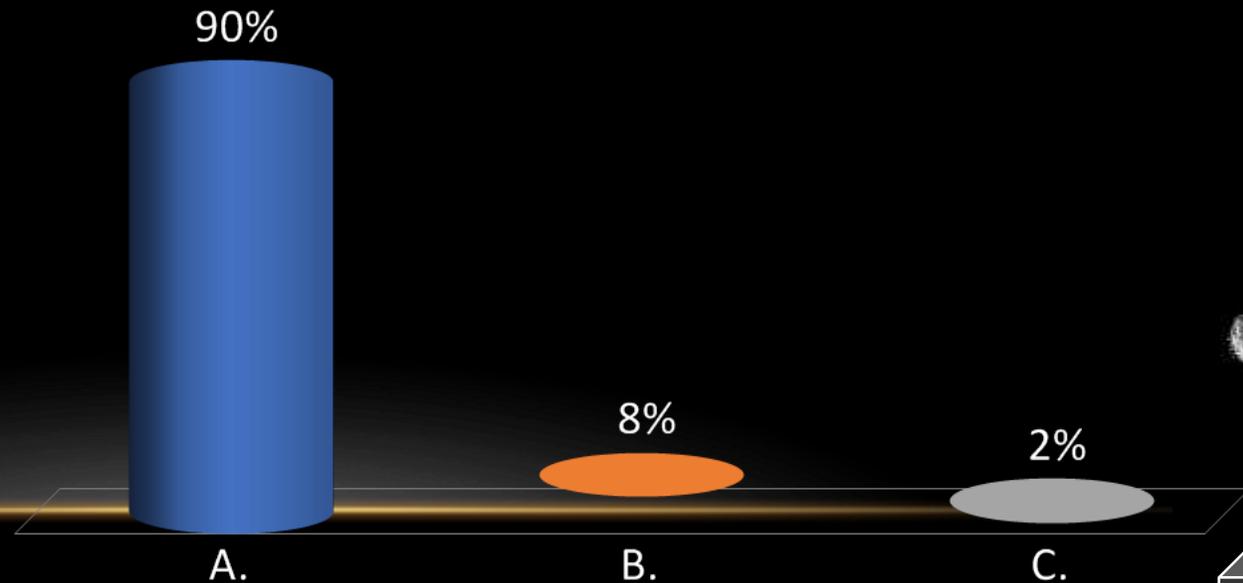
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 13**
- Atkins et al. prospectively found that when 3 or more operative cultures are obtained, a single positive culture reflected PJI due to that organism 13.3% of the time; two positive cultures were indicative of PJI in 20.4% of patients and 3 or more cultures positive for the same organism signified a PJI in 94.8% of patients
- If two or more operative cultures grow the same microbe, then treatment for prosthetic joint infection (PJI) would be appropriate, as per the MSIS and the Consensus Conference criteria for the diagnosis of PJI (Parvizi et al.)
- Several issues with the literature prohibit solid conclusions including lack of standardization, lack of prospective controlled studies, etc



Recommendation: Antibiotic therapy is recommended if two or more cultures isolate the same organism, as per the MSIS and the International Consensus Group (ICG) criteria for prosthetic joint infection. Antibiotic therapy may not be required when a single intraoperative culture isolates an organism. There may be circumstances when a single positive culture combined with other tests may indicate the presence of infection and treatment would be indicated.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 6: When should rifampin be added to the regimen of antibiotics for management of patients with PJI undergoing surgical treatment?

RESEARCHED BY:

Katherine Belden MD, United States of America

Werner Zimmerli MD, Switzerland



Literature:

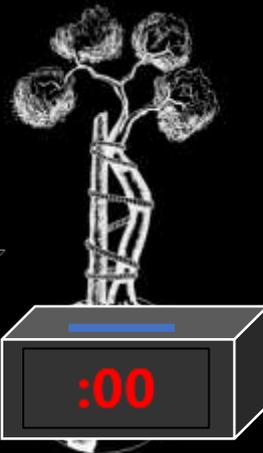
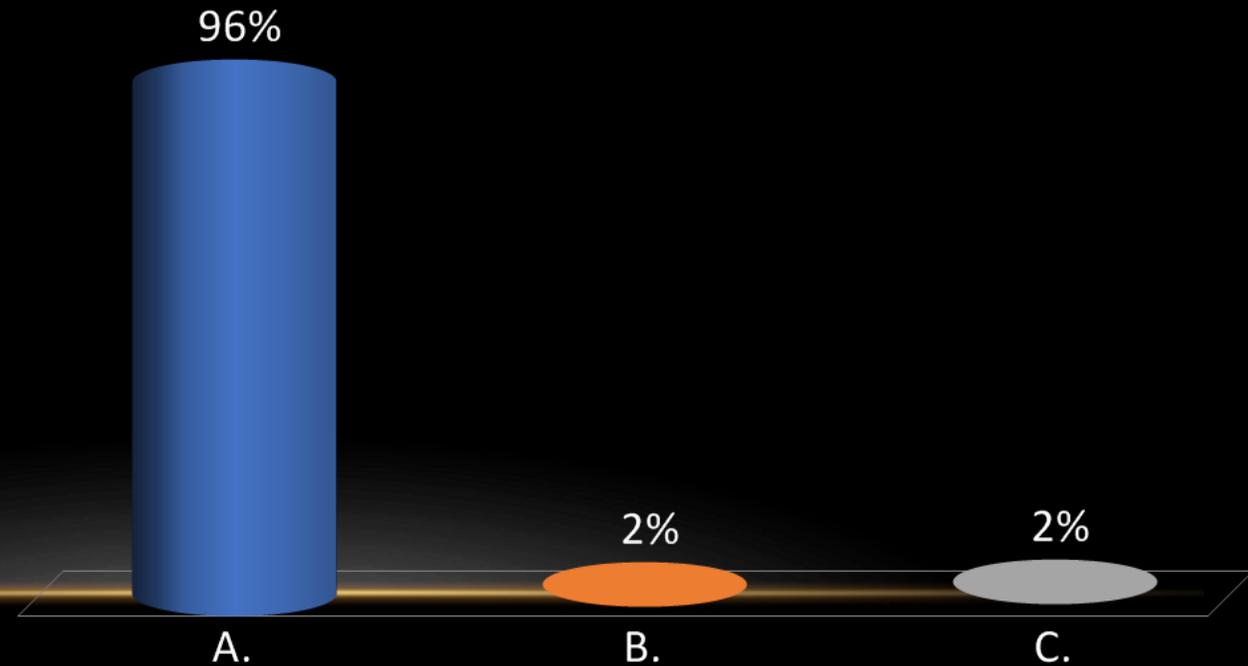
- **Meta-analysis 1, Prospective/Randomized 1, Retrospective 25**
- A randomized controlled study by Zimmerli et al. showed that among 24 patients with methicillin-susceptible *Staphylococcus aureus* (MSSA)- or coagulase-negative staphylococcus (CNS)-PJI with stable implants and a short duration of infection managed with DAIR, those able to tolerate long-term (3-6 months) combination therapy with ciprofloxacin-rifampin achieved cure at a higher rate than those treated with ciprofloxacin-placebo
- The Infectious Diseases Society of America (IDSA) PJI and MRSA management guidelines recommend the use of rifampin combination therapy (2-6 weeks of pathogen specific iv. antimicrobial therapy plus rifampin followed by 3-6 months of rifampin plus an oral companion drug) in the treatment of staphylococcal PJI/hardware infection in patients managed with debridement or single stage exchange



Recommendation: Rifampin should be considered in the treatment of Staphylococcal PJI in patients managed surgically with debridement and implant retention (DAIR) or single-stage exchange, where activity against biofilm is required. Rifampin should only be used in combination therapy, with the best reported combination appearing to be with a fluoroquinolone.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 7: What is the optimal antibiotic therapy in cases of culture-negative PJI?

RESEARCHED BY:

Harriet Hughes MD, United Kingdom

Gina Ann Suh MD, United States of America



Literature:

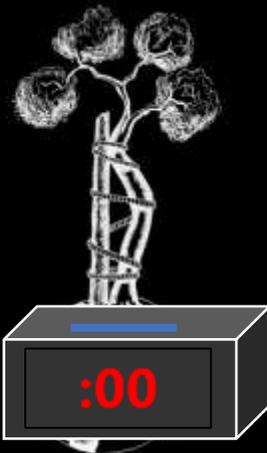
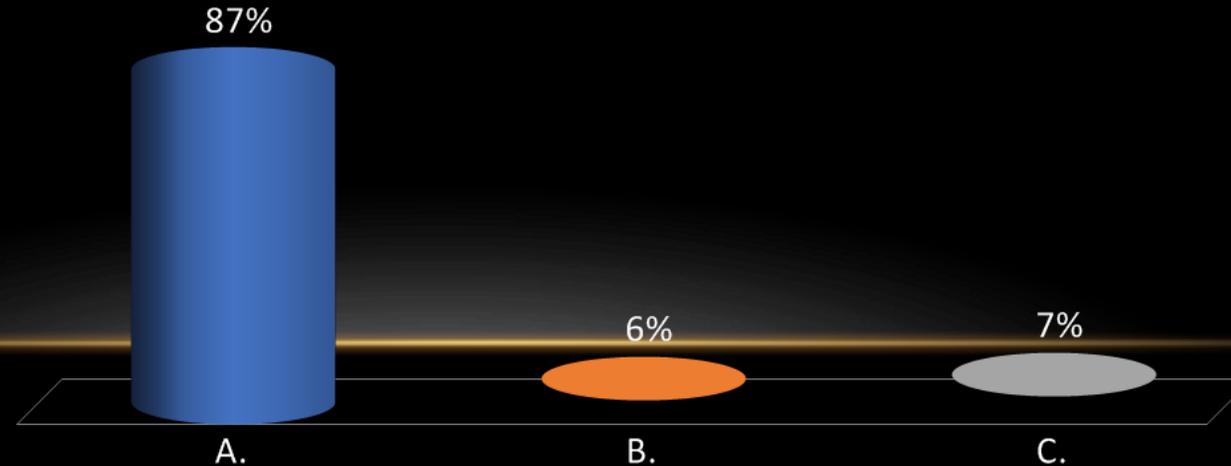
- **Meta-analysis 2, Prospective/Randomized 0, Retrospective 17**
- A recent systematic review by Yoon et al. evaluated clinical studies related to culture-negative PJI.
 - In the majority of these studies glycopeptides (vancomycin) were used followed by cephalosporins, beta-lactams, quinolones or combination therapy. Duration of intravenous antibiotics for CN PJI was usually 6 weeks.
- If all attempts to isolate the infecting organism fails then strategies employed in choosing an antibiotic regimen for CN PJI must be individualized based on risk factors, previous history, and local epidemiology
 - The antibiotic treatment of CN PJI usually includes broad spectrum antibiotics with a prolonged intravenous phase.



Recommendation: In patients with true CN PJIs, the antibiotics should be selected to have broad spectrum activity against both gram-positive and gram-negative organisms. In addition, the exact choice should relate to the known modern epidemiology in that country.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 8: What antibiotic therapy and duration of treatment should be used in Enterococcal PJI?

RESEARCHED BY:

Randi Silibovsky MD

Michael Kheir MD

Kang-il Kim MD



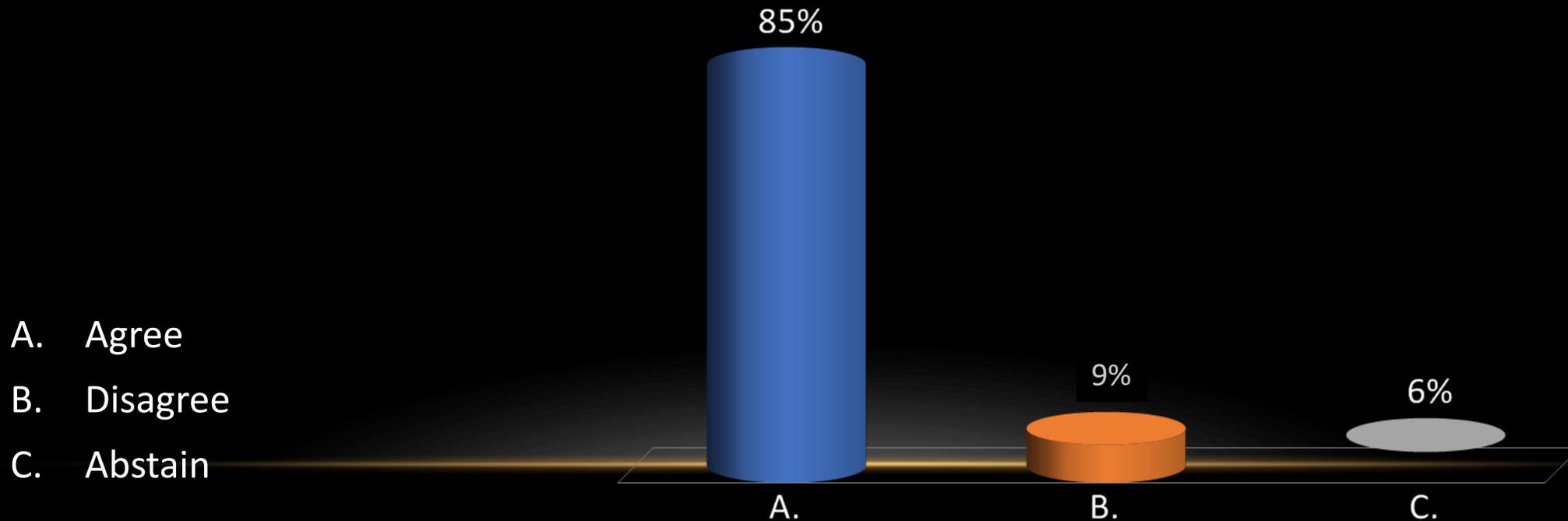
Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 14**
- There is a lack of high quality randomized, controlled, prospective comparative treatment studies
- Raymond et al. (1995) reviewed 19 cases of septic arthritis caused by *E. Faecalis*.
 - 11/19 were PJI.
 - 14 cases were treated with a PCN (11/19) or Glycopeptide (3/19).
 - Aminoglycoside was also used to treat 7 of these 14 (4/7 were PJI)
- El Helou et al. (2008) reviewed 50 Enterococci-induced PJI cases.
 - No statistical difference in clinical outcomes between patients receiving combo abx therapy vs monotherapy (P = 0.1)

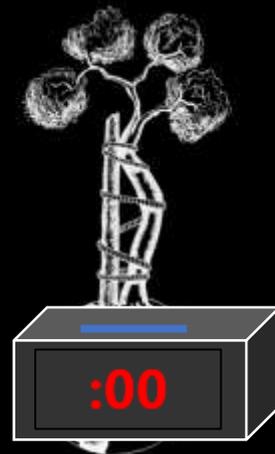


Recommendation: Based on the limited available evidence, combination antimicrobial therapy should be considered for the treatment of Enterococcal PJI, at least during the first weeks of treatment. Antibiotics should be tailored according to the susceptibility of the infective microorganism.

Level of Evidence: Limited



- A. Agree
- B. Disagree
- C. Abstain



Question 9: What are the indications for utilizing Fosfomycin, Tigecycline and Daptomycin, either instead of other antibiotics or in conjunction with other antibiotics for the management of PJI?

RESEARCHED BY:

Jose L. Del Pozo MD

Alex Soriano MD



Literature:

- Meta-Analysis 0
- Prospective/Randomized 3
- Retrospective 43

P: prospective cohort. RCT: randomized control trial. R: retrospective cohort. PJI: prosthetic joint infection. MRSA: methicillin-resistant *S. aureus*. DAIR: debridement and implant retention. 2S: 2-stage exchange. 1S: 1-stage exchange.

¹ Remission was calculated over 11 patients because one patient died after complete treatment for an unrelated cause.

² Only 14 patients who had been on daptomycin for ≥50% of the course of antibiotic treatment were considered evaluable.

³ Only 18 patients were analyzed for clinical and microbiological cure since two patients had to withdraw because of serious adverse effects, one related to rifampin and the other one to daptomycin.

Author, year	Type of study	Nº of patients/ type of PJI - surgical treatment	Dose, duration	Rifampin (%)	Adverse events related with daptomycin (%)	Follow-up months	MRSA n/total (%)	Remission n/total evaluated (%)
Rao[16] ¹ , 2006	P	12 / 5 early acute-DAIR 7 chronic-2S	4 mg/kg, 6 weeks	0	0	9 (range 7-13)	7/12 (58.3)	5/11 (45.5)
Byren[17], 2012	RCT	75 / chronic-2S	6 mg/kg vs. 8 mg/kg vs. control, 6 weeks	0	CPK >500u/L 6 mg/kg: 16% 8 mg/kg: 21.7% control: 8%	5-7	3/25 (12) 7/24 (30.4) 3/25 (12)	6mg/kg: 14/24 (58) 8mg/Kg:14/23 (61) control: 8/21 (38)
Corona[18] ² , 2012	R	20/ 8 early acute-5 DAIR and 3 2S 12 chronic-9 2S and 3 1S	6.6 mg/kg (median), 6.4 weeks	yes:8 (40)	CPK: 1 (12.5)	20 (range 12-41)	1/14 (7.1)	Acute infection: 5/6 (83.3) Chronic infection: 5/7 (71.4)
				no:12 (60)	CPK: 1 (8.3) Eosinophilic pneumonia: 1(8.3)			
Jugun[19], 2013	P	16 osteoarticular infection (6 with PJI)	8.15 mg/kg (median) + rifampin 600 mg/d, 7.3 (range 2-17) weeks	16 (100)	0	15.8 (range 12.4-30)	3/6 (50)	totally or partially removed: 3/3 (100) DAIR: 3/3 (100)
Lora-Tamayo ³ [20], 2014	R	20 Early acute-DAIR	10 mg/kg + rifampin 600 mg/d, 6 weeks	20 (100)	Rhabdomyolysis: 1 (5)	25 (range 24.4-32.3)	10/18 (55.5)	Daptomycin + Rifampin: 9/18 (50) Control group: 15/44 (34)
Chang[22], 2017	R	16 / 5 early acute-DAIR 11 chronic-2S	8.3 mg/kg, 2 weeks	0	0	27	10/16 (62.5)	2S: 10/11 (91) DAIR: 4/5 (80)

Table 1. Summary of the clinical experience with daptomycin in PJI including case series with more than 5 cases.

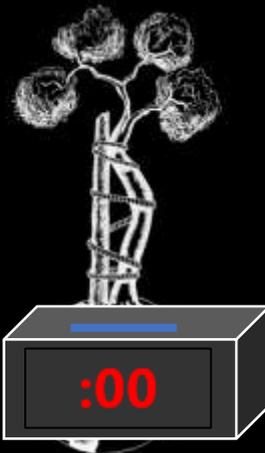
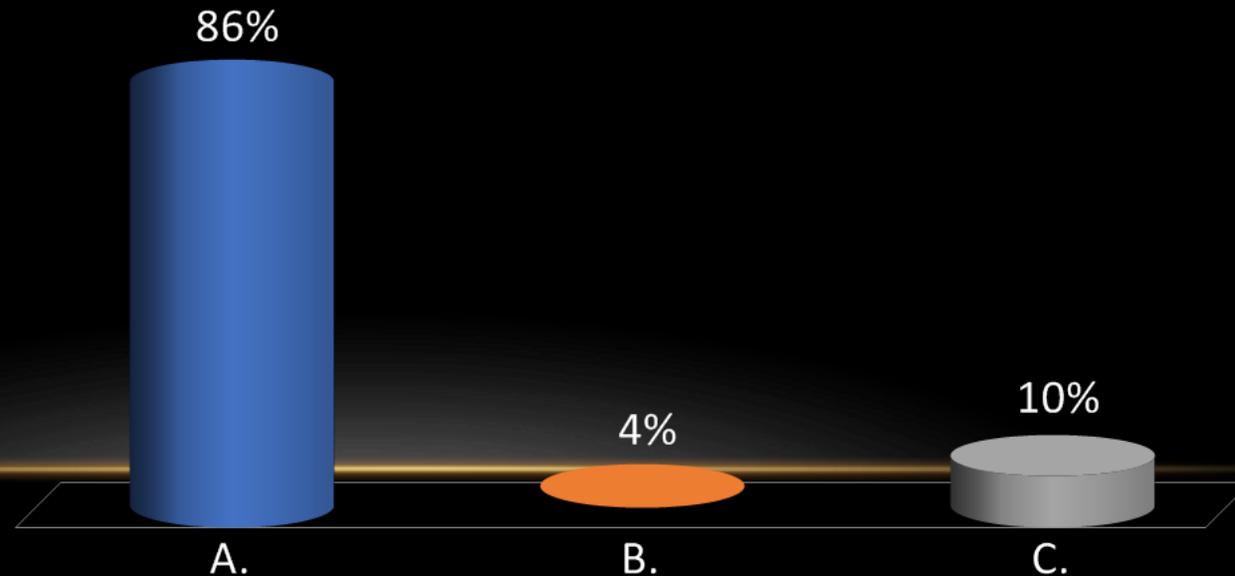
Recommendation:

- **DAPTOMYCIN:** Daptomycin is an alternative treatment for patients with PJIs caused by methicillin-resistant *Staphylococcus aureus* (MRSA).
- **FOSFOMYCIN:** Although there is no clinical experience using fosfomycin in PJIs, it could be considered in infections due to multi-drug resistant gram-positive (MDR-GP) or gram-negative bacteria (GNB) as a part of a combination regimen with daptomycin, rifampin or tigecycline when the microorganism is susceptible.
- **TIGEYCYLINE:** Tigecycline could be considered for the treatment of MDR-GP or -GNB as a part of a combination regimen when the microorganism is susceptible.

Level of Evidence

- **Daptomycin: Moderate**
- **Fosfomycin: Limited**
- **Tigecycline: Limited**

- A. Agree
- B. Disagree
- C. Abstain



5.10 – Treatment: Antimicrobials (Two-Stage)



Question 1:

- a) What is the optimal length of administration for antibiotic treatment following resection arthroplasty?
- b) What is the optimal mode of administration for antibiotic treatment following resection arthroplasty?

RESEARCHED BY:

Oscar Murillo MD, Spain

Scott R. Nodzo MD, United States of America

Anne Lachiewicz MD, United States of America



Literature:

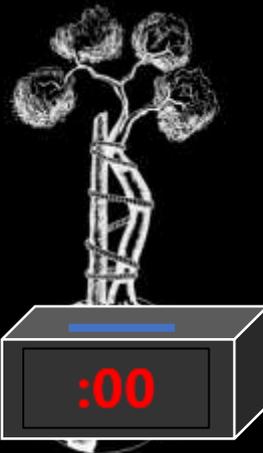
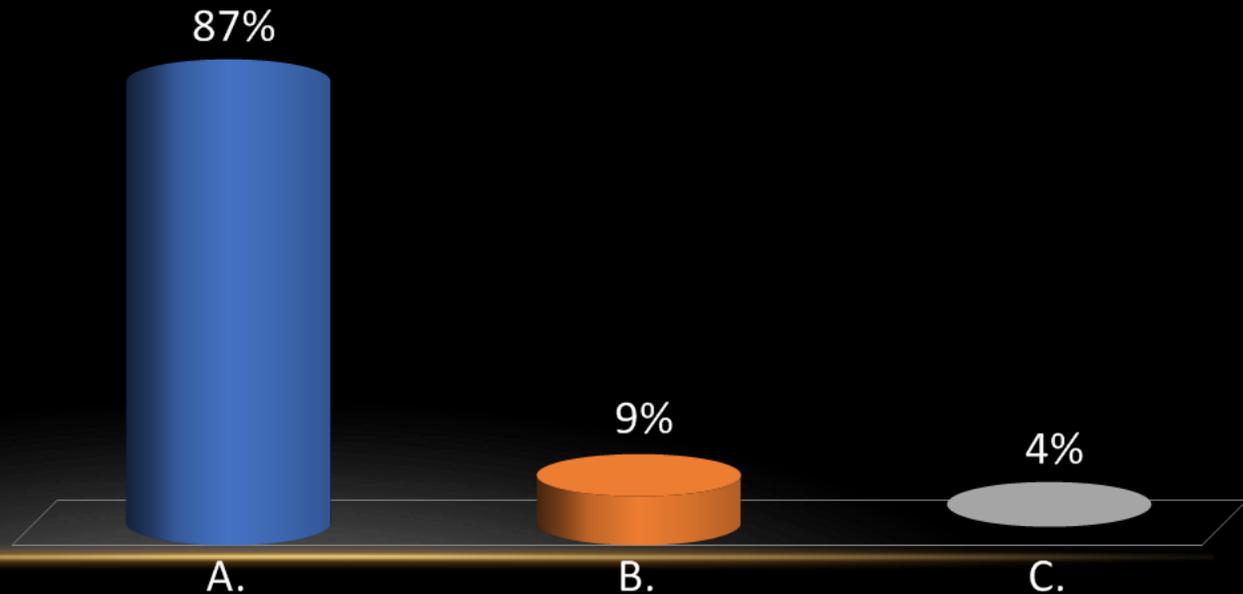
- Meta-analysis 1, Prospective/Randomized 0, Retrospective 21
- Current literature mostly consists of retrospective reviews and has not found prolonged antibiotic therapy beyond six weeks to significantly increase success rates
 - Prolonged use may increase the rate of antibiotic related complications and expenses.
 - Many published studies have reported success rates ranging from 88-100% with a combination of oral and intravenous (IV) antibiotic administration of six weeks or less
- To delegates' knowledge, no publication has compared the efficacy of oral-only versus IV-only antibiotics after resection arthroplasty
 - An increasing number of clinicians and surgeons are using a combination approach of IV and oral antibiotics following resection arthroplasty, including some using a rifampicin antibiotic as a companion drug



Recommendation: Antimicrobial therapy should be individualized and based on the sensitivity profile of the microorganism, patient tolerance, and drug side effect profile. There is no conclusive evidence supporting the exact length of antibiotic therapy after resection arthroplasty. We recommend treatment for two to six weeks. Either intravenous, oral antibiotics, or a combination are acceptable for treatment following resection arthroplasty as long as the oral agent has adequate bioavailability and can achieve a concentration at the site of infection to eradicate the infecting organism, if used alone.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: Does extended oral antibiotic prophylaxis following reimplantation reduce the risk of future failure? If so, what type of antibiotic should be administered and for how long?

RESEARCHED BY:



Viktor Janz MD,
Germany



Craig J Della Valle MD,
USA



Linda I Suleiman MD, USA



Literature:

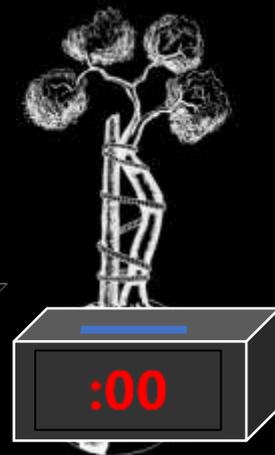
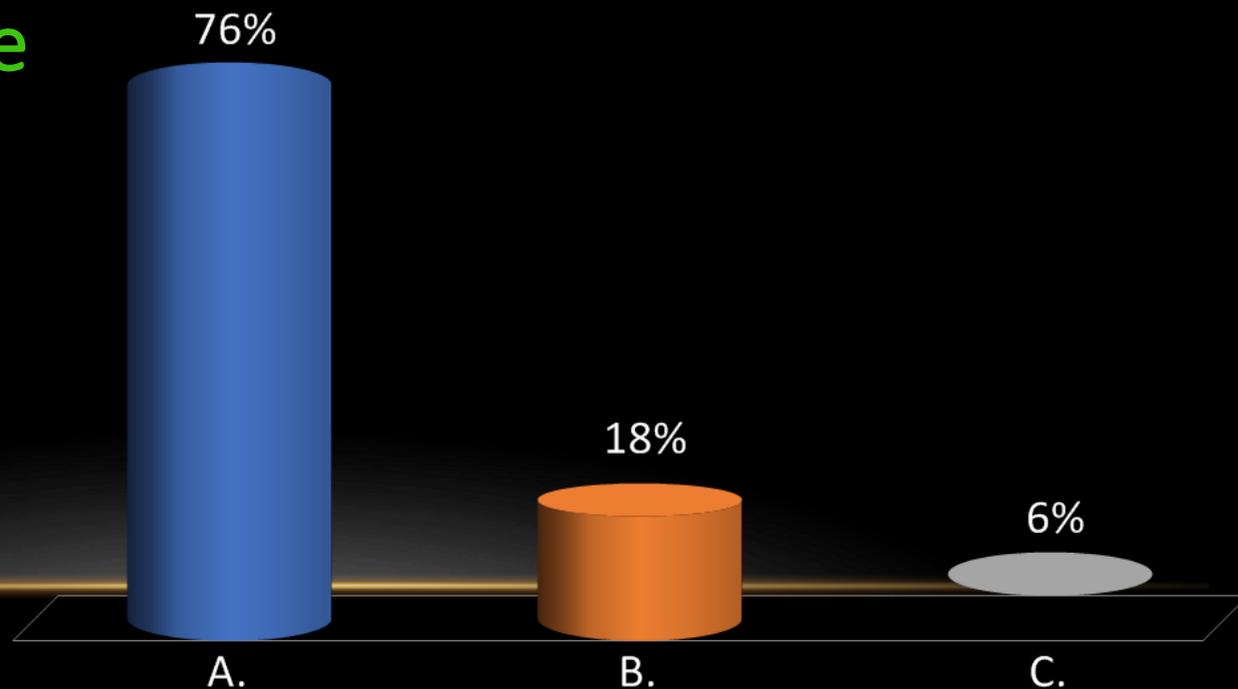
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 2**
- Frank et al. conducted a multicenter RCT examining the role of prolonged (3 months) prophylactic oral antibiotics following reimplantation patients undergoing revision TJA (n=107).
 - The rate of reinfection was 19% in the control group vs. 5% in the prolonged antibiotic treatment group (p=0.0162).
- Two retrospective studies
 - Zywiell et al (n=28) - found that the risk of reinfection with extended oral antibiotics was 4% vs.16% in the control cohort receiving routine antibiotics
 - Johnson et al - found 13.6% vs. 0% rates of reinfection in the routine perioperative antibiotic group compared to patients treated with oral antibiotics for 14 days following a two-stage exchange, respectively



Recommendation: Possibly. There is emerging evidence that administration of three months of oral antibiotic directed towards the original infecting organism following re-implantation reduces the risk of early failure secondary to periprosthetic joint infections.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 3: When is the optimal time to change IV antibiotic(s) to an oral agent(s) after a resection arthroplasty as part of two-stage exchange?

RESEARCHED BY:

José Cordero-Ampuero MD, Spain

Marc Nijhof MD, Netherlands

Katherine Belden MD, United States of America



Literature:

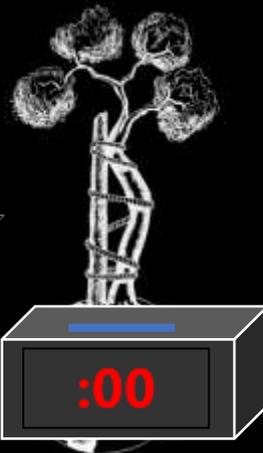
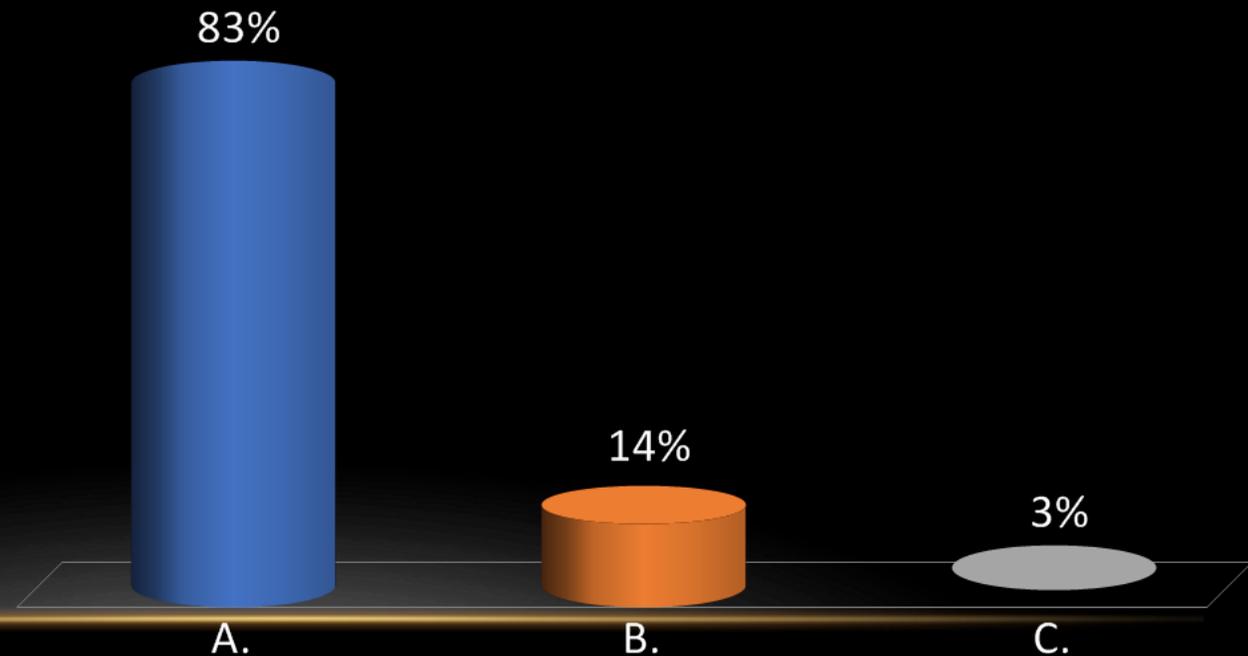
- **Meta-analysis 0, Prospective/Randomized 3, Retrospective 12**
- The recently published OVIVA randomized controlled trial concluded that PO antibiotic therapy was non-inferior to IV therapy when used during the first 6 weeks in the treatment of bone and joint infection as assessed by treatment failure within 1 year of randomization.
- Darley et al showed retrospectively that 10-14 days of IV antibiotic therapy followed by 6-8 weeks of PO therapy was successful in 17 patients who underwent 2-stage resection arthroplasty for management of prosthetic hip infection
 - Ciriviri et al. and Ascione et al. showed similar results



Recommendation: There is evidence to support pathogen-specific, highly bioavailable oral antibiotic therapy as an appropriate choice after resection arthroplasty in a two-stage treatment of PJI after an initial intravenous antibiotic period of at least 5-7 days.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 4: Can short term (two weeks or less) antibiotic treatment be considered following resection arthroplasty for chronic PJI?

RESEARCHED BY:



Henk Eijer MD,
Switzerland



Brian de Beaubien MD,
USA

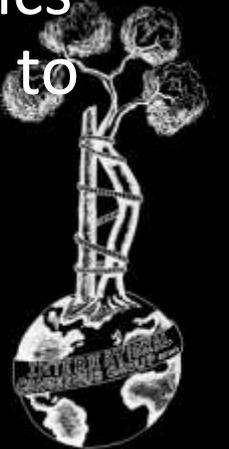


Ian Stockley MD,
United Kingdom



Literature:

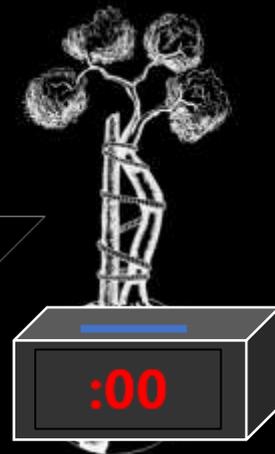
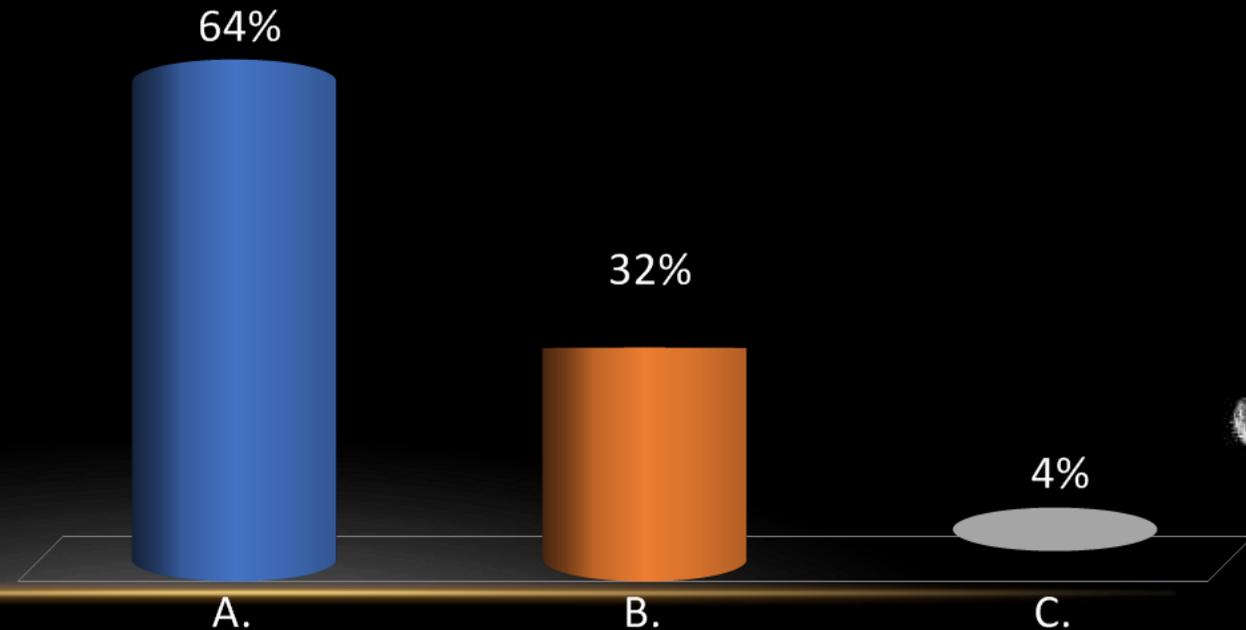
- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 9**
- Rationale of using a shortened duration of systemic antibiotics is based on the high local levels of antibiotic that can be achieved following elution from antibiotic-loaded cement, with local tissue levels of antibiotic above the mean inhibitory concentration for commonly infecting organisms
- Multiple studies exploring short-term (<2 week) courses of antibiotics show promising results with infection eradication rates comparable to when much longer course of antibiotic treatment were used



Recommendation: Yes. Following an aggressive debridement and insertion of antibiotic loaded cement spacer or beads, a short-term course of less than 2 weeks of systemic antibiotic therapy can be considered. Several studies show promising results with infection eradication rates comparable to when a much longer course of antibiotic treatment is used.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



5.11 – Treatment: Antimicrobial Suppression



Question 1: Is there a role for administration of prolonged oral antibiotics following primary total joint arthroplasty?

RESEARCHED BY:

Massimo Franceschini MD, Italy

Rafael Franco-Cendejas MD, Mexico



Literature:

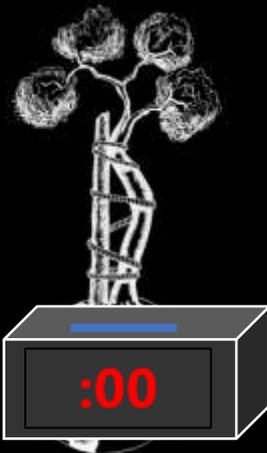
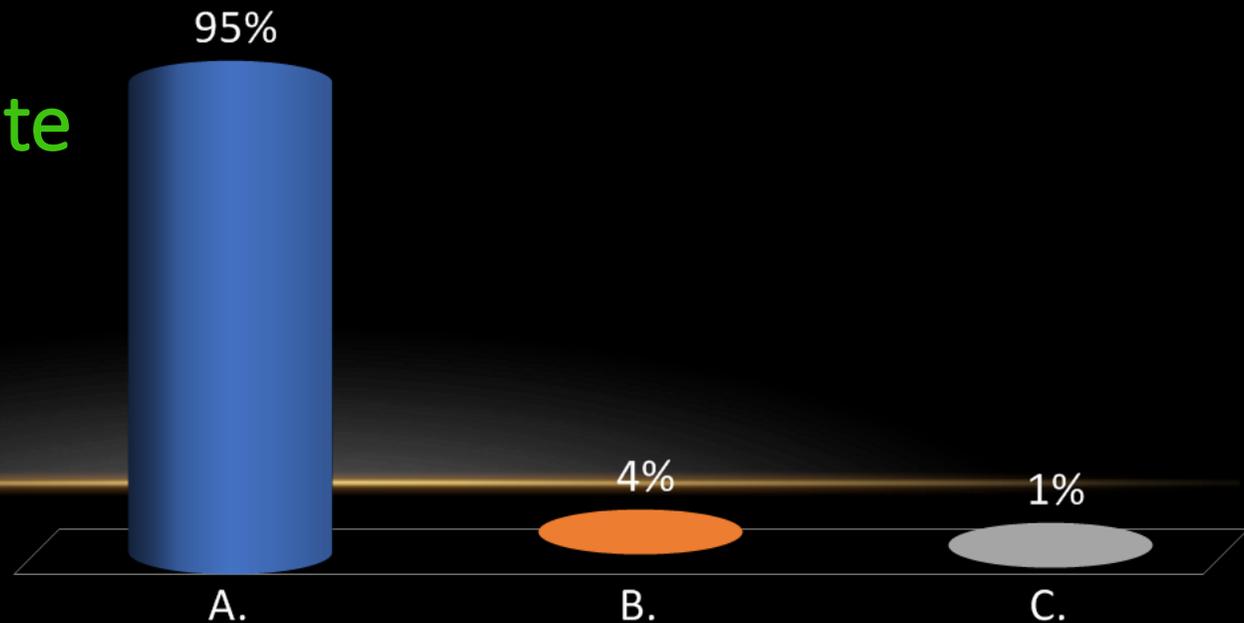
- **Meta-analysis 1, Prospective/Randomized 1, Retrospective 10**
- A systematic review by Thornley et al. evaluated the evidence for postoperative antibiotic prophylaxis and its role for reduction of SSIs among patients undergoing primary THA/TKA. The pooled estimate demonstrated that prolonged postoperative antibiotic prophylaxis did not significantly reduce the rate of SSIs (OR 0.01, 95% CI 0.00-0.02).
 - The quality of this evidence was determined to be low however
- The only study demonstrating benefit to the administration of prolonged oral antibiotics was a small, unpublished study presented to the American Association of Hip and Knee Surgeons



Recommendation: No. The administration of prolonged oral antibiotics in the context of perioperative prophylaxis after primary total joint arthroplasty is not recommended. Continuing antibiotic prophylaxis longer than 24 hours after wound closure has not proven to be beneficial; indeed, it may contribute to the development of antimicrobial resistance, carries risk, and adds to cost.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 2: What is the role of oral suppression antibiotics after reimplantation in patients with negative cultures after 14 days of incubation?

RESEARCHED BY:



John Segreti MD,
United States of America

Angela Hewlett MD, United
States of America



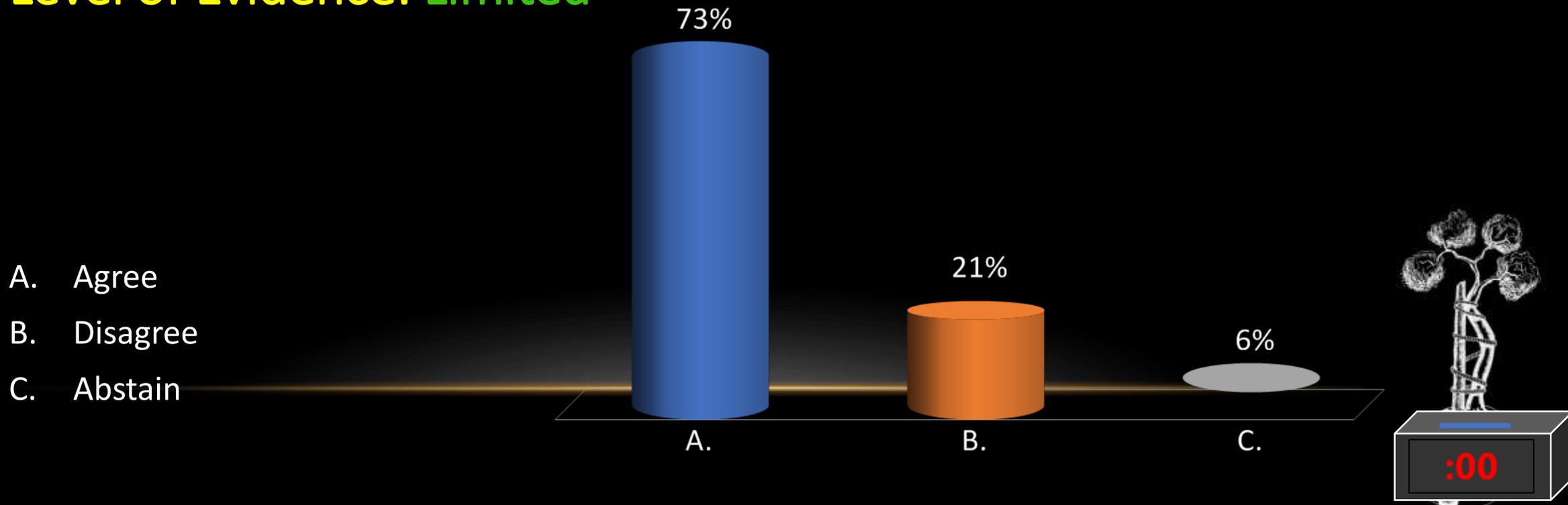
Literature:

- **Meta-analysis 0, Prospective/Randomized 1, Retrospective 3**
- One RCT and three retrospective studies evaluated the role of antibiotics in two-stage revision
 - Three of these studies found reduced rates of reinfection in the group of patients who received oral antibiotics following reimplantation, one study found no difference
 - Follow-up period and antibiotic choice varied between studies
- These studies may represent a signal that oral antibiotics after reimplantation may be of benefit; however there is a definite need to confirm these findings with further study.



Recommendation: There may be a role for the administration of oral antibiotics to decrease reinfection rates following reimplantation in patients with negative cultures, but further study is necessary.

Level of Evidence: Limited



Question 3: Which patients should be considered for administration of longterm suppressive oral antibiotic instead of surgical treatment in patients with chronic PJI?

RESEARCHED BY:

Eric Senneville MD, France



Literature:

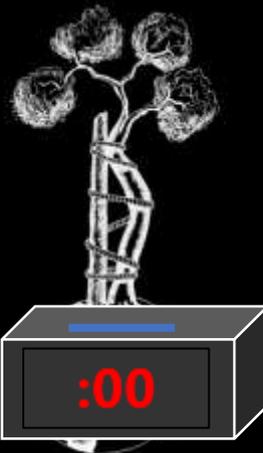
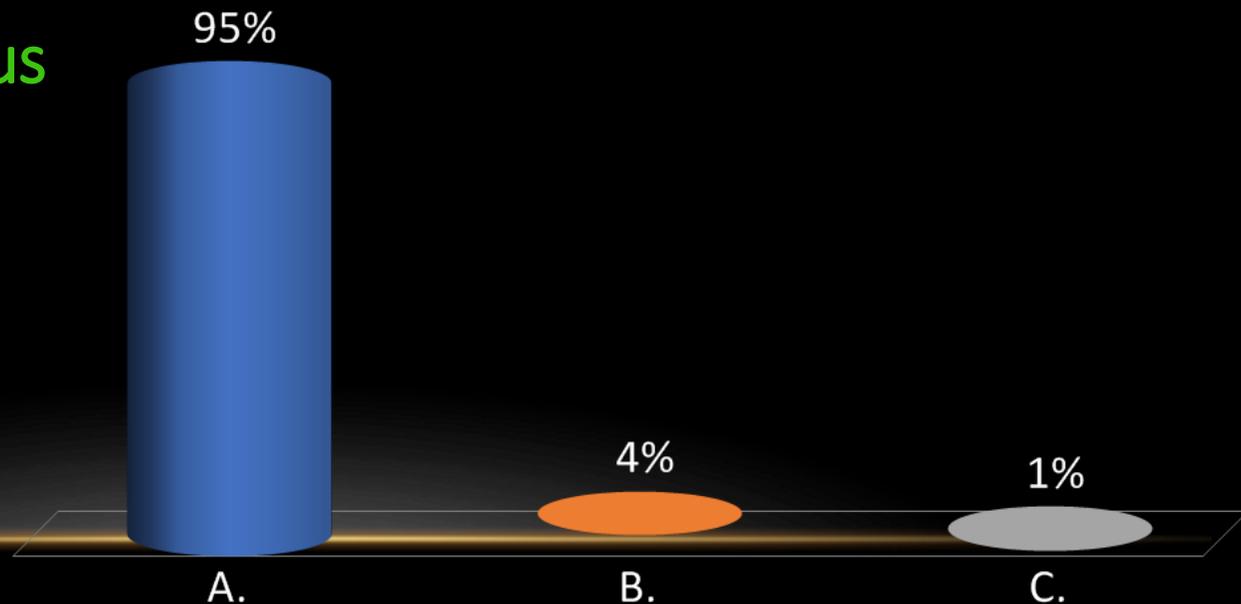
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 6**
- After an extensive literature search was conducted to examine the role of suppressive antibiotics instead of surgical intervention no such study could be identified
- The indications for the use of long term suppressive antibiotics is not well known or well-studied in the literature. In the absence of evidence, the delegates advocate that suppressive antibiotics instead of surgical intervention may be an option
 - (i) for patients in whom surgery is contraindicated because of the patient's general condition,
 - (ii) when surgery is not expected to improve the functional outcome for patient, such as those with multiple prior failures, and
 - (III) for patients who refuse surgery.



Recommendation: Long-term suppressive oral antibiotic instead of surgical treatment may be considered for patients who are not candidates for surgery, when surgery is not expected to improve the functional outcome for patient, and for patients who refuse surgery.

Level of Evidence: Consensus

- A. Agree
- B. Disagree
- C. Abstain



Section 6: Outcomes



Question 1: What is the definition of success of surgical treatment of a patient with PJI? What clinical, operative, microbiological and functional metrics should be considered?

RESEARCHED BY:

Yale A Fillingham MD
Craig J Della Valle MD
Linda I Suleiman MD
Bryan D Springer MD
Thorsten Gehrke MD
Stefano Bini MD
John Segreti MD

Antonia F Chen MD
Karan Goswami MD
Timothy L Tan MD
Noam Shohat MD
Claudio Diaz-Ledezma MD
Adam J Schwartz MD
Javad Parvizi MD



Literature:

- **Meta-Analysis 0, Prospective/Randomized 1, Retrospective 18**
- **A retrospective study performed by Gomez et al. in 2015 showed that of 87 cases that underwent spacer implantation without reimplantation, 72 (82.8%) underwent spacer retention.**
- **Tarabichi et al. demonstrated in a prospective study that next generation sequencing may be able to detect the presence, and phenotype, of microorganisms in the synovial space much better than conventional cultures can.**



Recommendation: The treatment of PJI typically does not have a dichotomous outcome. More commonly, the result is a gradient of success or failure. As such, the outcome-reporting tool has been organized into four tiers with each tier encompassing different levels of perceived success or failure. The outcomes reporting for the treatment of PJI are the following (definitions regarding items within each tier are explained in the rationale section):

Tier 1. Infection Control with no continued Antibiotic Therapy

Tier 2. Infection Control with patient on Suppressive Antibiotic Therapy

Tier 3. Need for reoperation and/or revision and/or spacer retention (Assigned to subgroups of A, B, C, D, E, and F based on the type of reoperation)

A. Aseptic Revision greater than 1 year from initiation of PJI treatment

B. Septic Revision (including DAIR) greater than 1 year from initiation of PJI treatment (excluding amputation, resection arthroplasty, and fusion)

C. Aseptic Revision less than or equal to 1 year from initiation of PJI treatment

D. Septic Revision (including DAIR) less than or equal to 1 year from initiation of PJI treatment (excluding amputation, resection arthroplasty, and fusion)

E. Amputation, Resection Arthroplasty, or Fusion

F. Retained Spacer

Tier 4. Death (Assigned to subgroups of A or B)

A. Death less than or equal to 1 year from initiation of PJI treatment

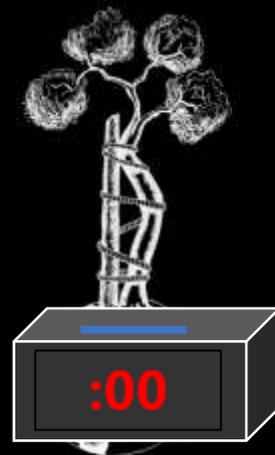
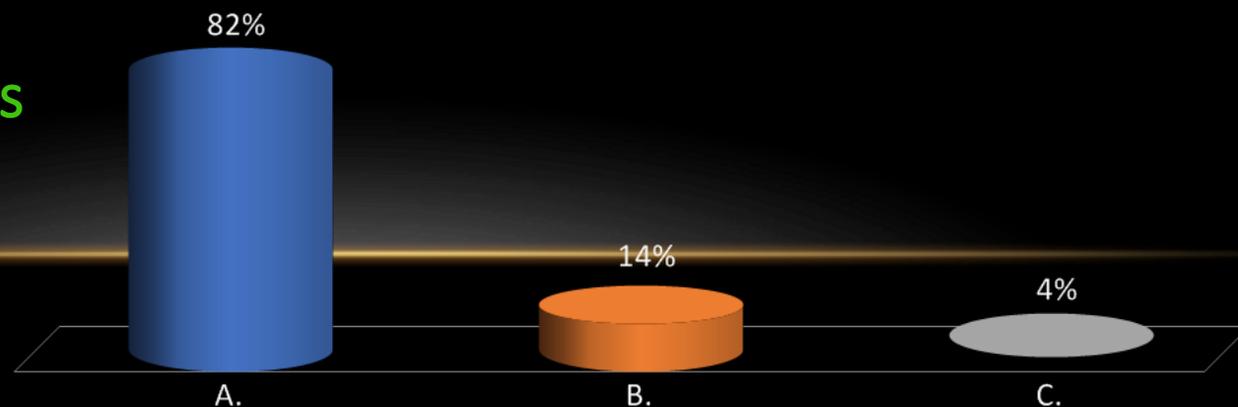
B. Death greater than 1 year from initiation of PJI treatment

Level of Evidence: Consensus

A. Agree

B. Disagree

C. Abstain



Question 2: Is there a minimum number of PJI procedures a surgeon should perform annually that qualifies them as experts in management of PJI?

RESEARCHED BY:



George Grammatopoulos
MD, UK



Paul M Courtney MD, USA



Guillem Bori MD, Spain

Literature:

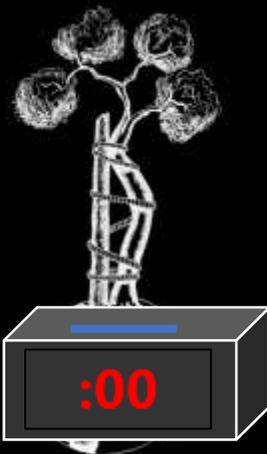
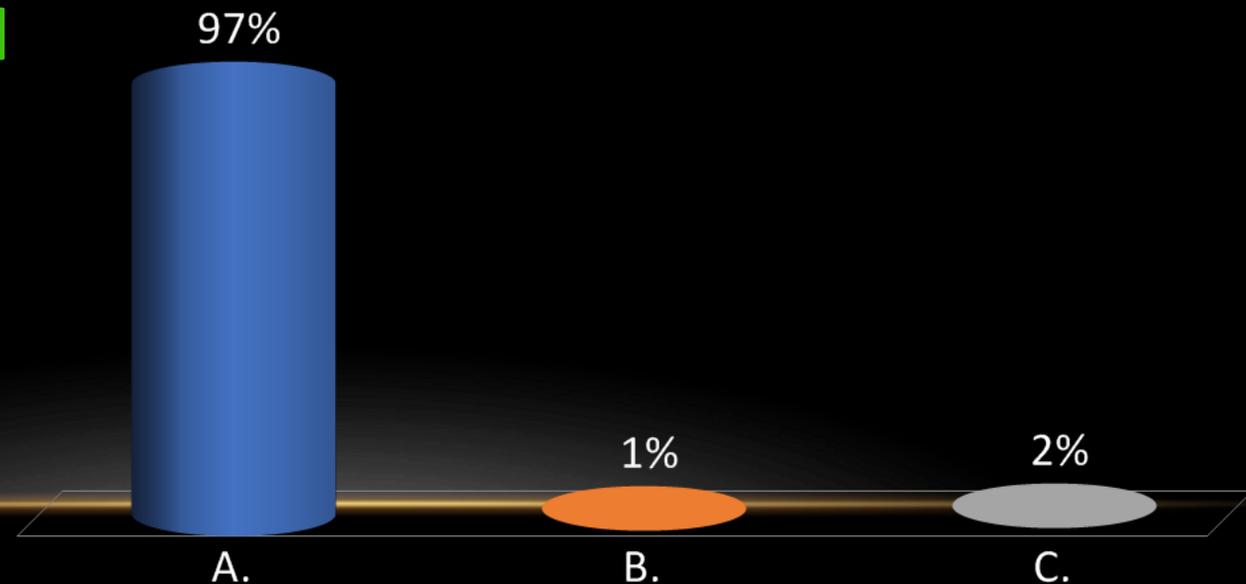
- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 13**
- Studies have reported that even among highly specific groups of experts, many institutions manage less than 50 PJI cases yearly
 - Similarly, two additional studies report surgeons managing about 3 cases per year
- The arthroplasty literature suggests that in primary hip arthroplasty, 35 cases per year is the optimal number above which complications reduce significantly



Recommendation: While the optimal number of PJI cases a surgeon needs to perform annually to improve outcomes has not been established in the literature, some data suggests that surgeons that care for more PJI patients will have better results than lower volume arthroplasty surgeons. Further studies are needed to identify the minimum number of PJI cases a surgeon should perform to reduce complications and improve outcomes.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain



Question 3: What tools (i.e. KLIC score) are available to help predict successful treatment with debridement, antibiotics, and implant retention (DAIR)? What are the accuracy of these tools?

RESEARCHED BY:

Ayman Ebied MD, Egypt

Gregory Polkowski MD, United States of America



Literature:

- **Meta-analysis 0, Prospective/Randomized 0, Retrospective 23**
- The KLIC-score (Tornero et al) was validated by Jimenez-Garrido et al. in a cohort of 30 patients with acute post-operative or acute hematogenous PJI Z
- Buller et al published a nomogram scoring system based on their retrospective regression analysis of 309 hip or knee PJI treated with DAIR, however it has not been validated to delegates' knowledge

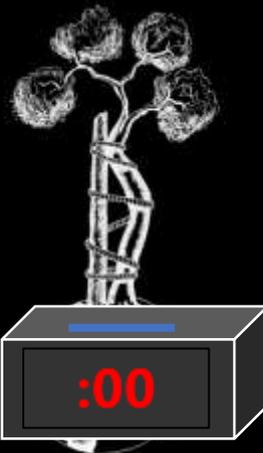
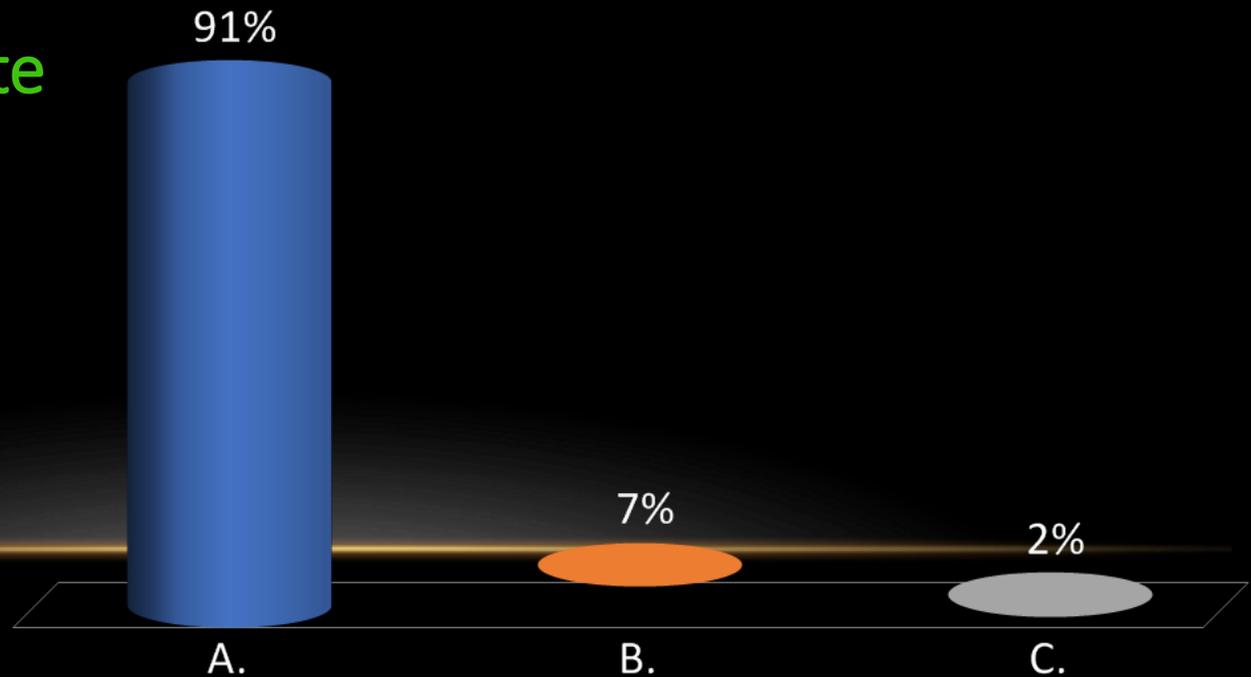
Variable		Score
K	Chronic renal failure (Kidney), glomerular filtration rate <30 ml/min	2
L	Liver cirrhosis	1.5
I	Index surgery = revision surgery or indicated for femoral neck fracture	1.5
C	Cemented prosthesis	2
C	C-reactive protein > 11.5 mg/dl	2.5



Recommendation: Two prognostic scoring systems have been published, and only one has been validated. While several studies exist confirming the significance of the variables utilized by the two scoring systems, the body of literature is heterogeneous and conflicted such that general statements of their accuracy and applicability cannot be supported.

Level of Evidence: Moderate

- A. Agree
- B. Disagree
- C. Abstain



Question 4:

A) What is the optimal follow-up plan (schedule, exam maneuvers, labs, imaging) for patients being treated for PJI?

B) How frequently should the inflammatory biomarkers be measured after the resection arthroplasty performed as part of two-stage exchange?

RESEARCHED BY:

Tiziana Ascione MD, Italy

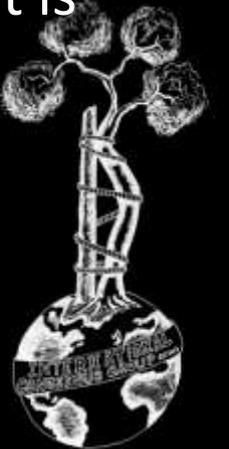
Ali Oliashirazi MD, United States of America

YiRong Zeng MD, China



Literature:

- **Meta-analysis 1, Prospective/Randomized 2, Retrospective 27**
- The overall recommendation for follow up visits are at 6 weeks, 3 months, 6 months, 12 months postoperatively – this schedule was utilized by a prospective study and a randomized control trial examining PJI treatment
- Follow-up of patients being treated for PJI needs to be individualized based on their needs and the clinical progress
 - Patients with PJI who have undergone surgical procedure may be at higher risk of complications and issues, and thus require more regular follow-up
- Inflammatory markers do not exactly determine the timing of reimplantation, it is important that the level of these inflammatory markers declines in the interim stage between resection and reimplantation

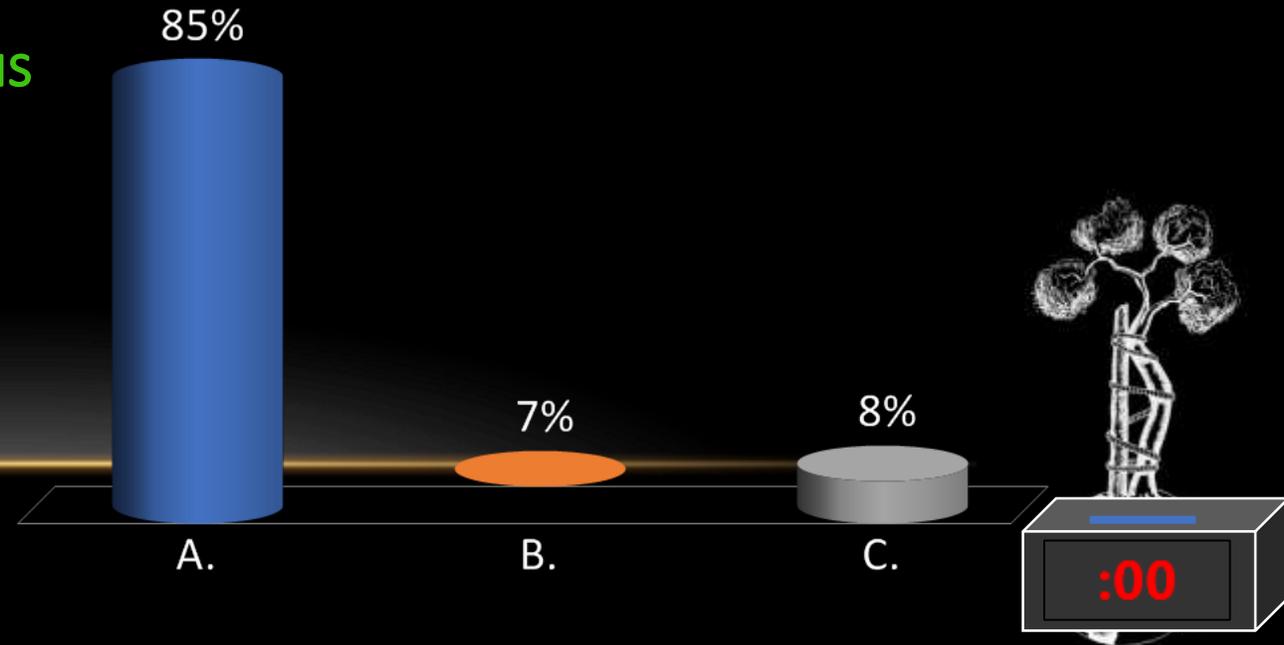


Recommendation: A) At present, there is no consensus regarding the optimal follow-up schedule for patients being treated for PJI and no specific research discussing this topic. In the absence of evidence, we recommend that the patients should be followed at 6 weeks postoperatively, 3 months, 6 months, 12 months, and annually thereafter, with adjustments being made based on individual circumstances. Inflammatory markers should be measured on a weekly basis after resection arthroplasty.

B) As of now there is no study to assess the frequency in which the biomarkers are needed to be checked during the course of a two-stage exchange for PJI. Most of the available studies have checked the available diagnostic battery of the tests including serum ESR and CRP and synovial fluid WBC, PMN, and LE at least once prior to the second stage (reimplantation). However, there is no unified protocol that provides recommendations on the timing of these tests. Future studies in this field are required to guide the orthopaedic community and help forming a consensus.

Level of Evidence: A) Consensus B) Consensus

- A. Agree
- B. Disagree
- C. Abstain



Question 5: Is there a benefit for the engagement of a multidisciplinary team for the management of patients with PJI?

RESEARCHED BY:



Kordo Saeed, MD



Chun Hoi Yan, MD



Literature:

- Meta-analysis 0, Prospective/Randomized 0, Retrospective 8
- A small number of retrospective studies suggest utilization of a multidisciplinary team may improve management of patients with PJI
- No high quality studies exist evaluating the effects of a multidisciplinary team on patient outcomes



Recommendation: The treatment of periprosthetic joint infection (PJI) takes a multidisciplinary approach with interaction between the orthopedic surgeon, anesthesiologist, infectious disease specialist, medical microbiologist, plastic surgeon, and ancillary service teams. It is demonstrated that centers with experience in the treatment of PJI, or those adopting standardized protocols, have improved outcomes with lower complications. Until further research demonstrates otherwise, patients with PJI should be cared for in centers using a multidisciplinary approach and experience in management of PJI.

Level of Evidence: Limited

- A. Agree
- B. Disagree
- C. Abstain

