

## Clinician-driven research priorities in bone and joint infection: perspectives of orthopaedic surgeons and infectious diseases physicians

Bone and joint infections (BJI) are a significant challenge for healthcare systems worldwide, but there are significant challenges in performing high quality BJI research, including heterogeneous presentations, low patient numbers at individual sites and ingrained clinical opinions. BJI research should be focused on specific, clinically relevant questions and driven by clinician- and patient-specific priorities. We aimed to determine clinicians' research priorities by surveying a diverse group of doctors with a specific interest in this area at a national BJI conference.

In March 2020, the inaugural Australasian Bone and Joint Infection conference was held in Newcastle, Australia. The meeting was attended by approximately 200 delegates including practicing clinical specialists and trainees in the fields of infectious diseases (ID), orthopaedic surgery and clinical microbiology. Prior to the conference, we asked all registered delegates to nominate two key BJI research priorities. We compiled these into a list of the eight most commonly suggested priorities and asked conference delegates to rank these in terms of priority (1 being the highest, and 8 being the lowest). For each of the eight topics, we assigned a score of 8 each time a delegate ranked it as number 1, 7 for number 2, 6 for number 3, down to 1 for number 8. We then summed the total score for each topic. This takes into account the number of votes each topic received as well as the priority given.

We received a total of 69 responses (42 ID physicians/trainees, 24 orthopaedic consultants/trainees and 3 from other backgrounds). The research question given the highest priority by clinicians overall was one versus two-stage revision for prosthetic joint infection (Table 1). There was a clear difference in research priorities between the ID and orthopaedic cohort, with ID physicians favouring questions relating to the choice or duration of antibiotics, and orthopaedic surgeons favouring questions of surgical strategy (Table 1). This difference emphasizes the need for increased and continuing dialogue and collaboration between these two key specialties in this field. A brief summary of the existing literature and proposed research for each of top three research priorities follows.

- (1) Which is the superior surgical strategy for chronic prosthetic joint infection: one-stage or two-stage revision?

Whilst the traditional approach of two-stage revision arthroplasty is considered the standard of care, there is emerging evidence of

successful outcomes following single stage revision arthroplasty. Several systematic reviews have suggested that barring significant contra-indications, a single stage revision arthroplasty has comparable patient reported outcomes, postoperative range of motion and re-infection rates to two-stage revision arthroplasty.<sup>1–3</sup> Several small trials addressing this question are in fact currently recruiting (<https://clinicaltrials.gov/ct2/show/NCT03435679>,  $n = 96$ ; <http://www.isrctn.com/ISRCTN10956306>,  $n = 142$ ) and will help contribute to answering this question.

- (2) Which is the superior surgical strategy for acute prosthetic joint infection: one-stage revision or debridement, antibiotics with implant retention (DAIR)?

In contrast to one-stage versus two-stage revision, there has been less focus on the comparison of one-stage versus DAIR in treating acute periprosthetic joint infections. Currently no RCT exists to compare one-stage vs. DAIR and this presents a priority for future research. There is a wide range of reported treatment success with DAIR (11%–100%),<sup>4</sup> but these are generally lower than for a one-stage revision.

- (3) What is the optimal duration of antibiotic therapy for native large joint septic arthritis?

Traditionally, a 4-to-6-week course of antibiotics has been considered as standard treatment for native joint septic arthritis (NJSa), extrapolating from the practice in acute osteomyelitis.<sup>5</sup> However, shorter courses are often successfully used, and there is no clear evidence that such a long course is actually needed.<sup>6</sup> Existing RCT data in children suggest a 10-day total treatment duration is non-inferior to 30-days,<sup>7</sup> but this question remains unresolved in adults. A recent RCT did address this, randomizing adults with NJSa to 2 versus 4 weeks of intravenous antibiotics following drainage and irrigation,<sup>8</sup> with a cure rate in the 2-week group (99%) non-inferior to that of the 4-week group (97%). However, an important caveat is that 99 of the 154 enrolled patients had infection of the small joints of the hand, and hence these results cannot be extrapolated to the more common presentation of hip or knee NJSa.

**Table 1** Research priorities as ranked by clinicians

Rank	Topic	Total score
All respondents (n = 69)		
1	Which is the superior surgical strategy for chronic prosthetic joint infection, one-stage or two-stage revision?	336.5
2	Which is the superior surgical strategy for acute prosthetic joint infection, one-stage revision or debridement, antibiotics with implant retention?	320.5
3	What is the optimal duration of antibiotic therapy for native large joint septic arthritis?	318
4	What is the role of adjunctive rifampicin for prosthetic joint infection treated with debridement and implant retention?	306
5	What is the optimal duration of antibiotic therapy for diabetic foot infection following debridement?	238
=6	What is the role of topical vancomycin powder as a prophylactic strategy for elective non-cemented hip and knee replacement?	154
=6	Is a 6 weeks antibiotic duration non-inferior to 12 weeks for pyogenic vertebral osteomyelitis	154
8	What is the optimal surgical irrigation fluid in treating acute prosthetic joint infection?	95
Infectious diseases physicians and trainees (n = 42)		
1	What is the role of adjunctive rifampicin for prosthetic joint infection treated with debridement and implant retention?	225
2	What is the optimal duration of antibiotic therapy for diabetic foot infection following debridement?	220
3	What is the optimal duration of antibiotic therapy for native large joint septic arthritis?	186
4	Which is the superior surgical strategy for chronic prosthetic joint infection, one-stage or two-stage revision?	180.5
5	Which is the superior surgical strategy for acute prosthetic joint infection, one-stage revision or debridement, antibiotics with implant retention?	168.5
6	Is a 6 weeks antibiotic duration non-inferior to 12 weeks for pyogenic vertebral osteomyelitis	143
7	What is the role of topical vancomycin powder as a prophylactic strategy for elective non-cemented hip and knee replacement?	83
8	What is the optimal surgical irrigation fluid in treating acute prosthetic joint infection?	39
Orthopaedic surgeons and trainees (n = 24)		
1	Which is the superior surgical strategy for chronic prosthetic joint infection, one-stage or two-stage revision?	152
2	Which is the superior surgical strategy for acute prosthetic joint infection, one-stage revision or debridement, antibiotics with implant retention?	129
3	What is the optimal duration of antibiotic therapy for native large joint septic arthritis?	120
=4	What is the role of adjunctive rifampicin for prosthetic joint infection treated with debridement and implant retention?	64
=4	What is the role of topical vancomycin powder as a prophylactic strategy for elective non-cemented hip and knee replacement?	64
6	What is the optimal surgical irrigation fluid in treating acute prosthetic joint infection?	50
7	What is the optimal duration of antibiotic therapy for diabetic foot infection following debridement?	16
8	Is a 6 weeks antibiotic duration non-inferior to 12 weeks for pyogenic vertebral osteomyelitis?	10

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**Joshua S Davis:** Conceptualization; data curation; formal analysis; methodology; project administration; supervision; writing – original draft; writing – review and editing. **Laurant Xi Kang:** Data curation; formal analysis; writing – original draft; writing – review and editing. **Laurens Manning:** Formal analysis; writing – review and editing. **David Dewar:** Conceptualization; methodology; writing – original draft; writing – review and editing.


**References**

- Pangaud C, Ollivier M, Argenson JN. Outcome of single-stage versus two-stage exchange for revision knee arthroplasty for chronic periprosthetic infection. *EFORT Open Rev.* 2019; **4**: 495–502.
- Kunutsor SK, Whitehouse MR, Lenguerrand E, Blom AW, Beswick AD, INFORM Team. Re-infection outcomes following

- one- and two-stage surgical revision of infected knee prosthesis: a systematic review and meta-analysis. *PLoS One* 2016; **11**: e0151537.
- George DA, Logoluso N, Castellini G *et al.* Does cemented or cementless single-stage exchange arthroplasty of chronic periprosthetic hip infections provide similar infection rates to a two-stage? A systematic review. *BMC Infect. Dis.* 2016; **16**: 553.
- Kunutsor SK, Beswick AD, Whitehouse MR, Wylde V, Blom AW. Debridement, antibiotics and implant retention for periprosthetic joint infections: a systematic review and meta-analysis of treatment outcomes. *J. Infect.* 2018; **77**: 479–88.
- Cortes-Penfield NW, Kulkarni PA. The history of antibiotic treatment of osteomyelitis. *Open Forum Infect. Dis.* 2019; **6**: ofz181.
- Mathews CJ, Kingsley G, Field M *et al.* Management of septic arthritis: a systematic review. *Postgrad. Med. J.* 2008; **84**: 265–70.
- Peltola H, Pääkkönen M, Kallio P, Kallio MJT, Osteomyelitis–Septic Arthritis (OM-SA) Study Group. Prospective, randomized trial of 10 days versus 30 days of antimicrobial treatment, including a short-term course of parenteral therapy, for childhood septic arthritis. *Clin. Infect. Dis.* 2009; **48**: 1201–10.
- Gjika E, Beaulieu JY, Vakalopoulos K *et al.* Two weeks versus four weeks of antibiotic therapy after surgical drainage for native joint bacterial arthritis: a prospective, randomised, non-inferiority trial. *Ann. Rheum. Dis.* 2019; **78**: 1114–21.

Joshua S Davis,\*† MBBS FRACP PhD 

Laurant Xi Kang,‡ MBBS 

Laurens Manning,§ MBBS FRACP PhD 

David Dewar,†‡ MBBS FRACS PhD

*\*School of Medicine and Public Health, The University of Newcastle, Newcastle, New South Wales, Australia, †Infection Research Program, Hunter Medical Research Institute, Newcastle,*

*New South Wales, Australia, ‡Department of orthopaedics, John Hunter Hospital, Newcastle, New South Wales, Australia and §Faculty of Health and Medical Sciences, University of Western Australia, Perth, Western Australia, Australia*

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