The gold standard for treating chronic periprosthetic joint infection is still considered to be double-stage exchange revision. The purpose of this review is to analyse the difference in terms of eradication rates and functional outcome after single- and double-stage prosthetic exchange for chronic periprosthetic joint infection around the knee.

We reviewed full text articles written in English from 1992 to 2018 reporting the success rates and functional outcomes of either single-stage exchange or double-stage exchange for knee arthroplasty revision performed for chronic infection. In the case of double-stage exchange, particular attention was paid to the type of spacer: articulating or static.

In all, 32 articles were analysed: 14 articles for single-stage including 687 patients and 18 articles for double-stage including 1086 patients. The average eradication rate was 87.1% for the one-stage procedure and 84.8% for the two-stage procedure. The functional outcomes were similar in both groups: the average Knee Society Knee Score was 80.0 in the single-stage exchange group and 77.8 in the double-stage exchange. The average range of motion was 91.4° in the single-stage exchange group and 97.8° in the double-stage exchange group.

Single-stage exchange appears to be a viable alternative to two-stage exchange in cases of chronic periprosthetic joint infection around the knee, provided there are no contra-indications, producing similar results in terms of eradication rates and functional outcomes, and offering the advantage of a unique surgical procedure, lower morbidity and reduced costs.

Keywords: eradication rate; functional outcome; periprosthetic joint infection; single-stage exchange; total knee replacement; two-stage exchange

Introduction

Prosthetic joint infection (PJI) remains one of the most serious complications of knee prosthesis implantation. Its incidence is reported as between 0.5% and 2.0% according to the risk factors.¹⁻⁴ It is the commonest reason for total knee arthroplasty (TKA) revision in the United States.⁵ Of these revisions, 25% are due to infectious disease and the cost per case is 50,000 US dollars.⁴⁻⁷ Today there are now two options for the treatment of delayed PJI around the knee: single- and two-stage revision arthroplasty.⁸

Two-stage revision is considered as the gold standard for revision in cases of PJI for knee arthroplasty. It was originally described by Insall et al in 1983⁹ and secondly modified through the development of static spacers¹⁰ and then articulating spacers in 2001.¹¹

Single-stage exchange for periprosthetic joint infection is not a truly new technique: it was first described by Buchholz in the 1970s at the Endo Klinik in Hamburg and reported by Borden and Gearen⁸ in 1987 and Göksan and Freeman¹² in 1992. The recent literature on the subject tends to suggest this as an alternative for revision in delayed infected knee arthroplasty. The main benefits are a single surgical procedure, a shorter period of antibiotic treatment and reduced costs.

The comparison of the two procedures ideally requires prospective, randomized, controlled trials but they are time-consuming and difficult to set up. The results of each case series are controversial, and the performance of single-stage compared to two-stage exchange remains unclear. In order to clarify this question, we performed a systematic review of the available literature comparing single- and double-stage exchange for delayed PJI around the knee, published between 1992 and 2018.

Cite this article: EJORT Open Rev 2019;4:495-502.
DOI: 10.1302/2058-5241.4.190003
Materials and methods

A thorough systematic review of the literature was performed to identify articles reporting on one- or two-stage exchange in knee arthroplasty for periprosthetic joint infection. Articles written in English published from 1992 to 2018 were reviewed. The depth of details described in the materials and methods of each article varied markedly, making it impossible to perform a meta-analysis. Instead of this, a descriptive review of the results is presented. The international databases were searched and included: EMBASE; PubMed/Medline; Medline Daily Update; Medline In-Process and other non-indexed citations; Google Scholar; SCOPUS; CINAHL; Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews; NHS Health Technology Assessment.

The Mesh terms used for our research were based on the ones described by Jämsen et al for their own review: “periprosthetic joint infection”, “single-stage exchange”, “two-stage exchange”, “knee arthroplasty revision”, “prosthesis-related infections”, “direct exchange arthroplasty”, “knee joint infection”, “revision knee replacement”.

The inclusion criteria were the following:

- Articles written fully or with an abstract in English
- Articles reporting infectious outcomes of either single-stage or double-stage exchange arthroplasty
- Articles reporting functional outcomes of either single-stage or double-stage exchange arthroplasty: range of motion or Knee Society Score (KSS), or Oxford Knee Score (OKS) or Hospital for Special Surgery Knee Score (HSS)
- Study design classifiable as: randomized controlled trial; comparative prospective study; prospective case series with no comparison group; comparative retrospective study; retrospective study with no control group
- The study population had to be 10 or more and cases with a minimum follow-up of six months (note that most studies use at least one year follow-up)
- The following information should have been reported: number of patients, type of treatment, and number of recurrent infections after treatment

Our principal aim was to compare the rate of recurrence of infection after one- and two-stage exchange and the second was to explore the differences in terms of functional outcomes. Knee Society Score (KSS), Oxford Knee Score and the Hospital for Special Surgery Knee Score (HSS) were used to measure the clinical outcomes in most studies. The pre- and post-operative range of motion (ROM) were frequently reported.

In order to perform this analysis, the data we reviewed were:

- Number of patients
- Single- or double-stage exchange
- In case of double-stage exchange, the kind of spacer: static or articulating
- The rate of eradication of infection
- The functional knee score: KSS, OKS, HSS
- The range of motion after the whole procedure

Results

Thirty-two original articles describing the management of periprosthetic joint infection around the knee were included: 14 articles for the single-stage exchange procedure and 18 for the two-stage procedure. Our review reported the results of 1773 surgical procedures: 687 for one-stage exchange and 1086 for two-stage exchange. The range in the number of cases was from 10 to 177 and the range of follow up was from six months to 10.5 years.

Eradication rate

The eradication rate after the one-stage procedure ranged from 67% to 100% with an average rate of 87.1%. The eradication rate after the double-stage procedure ranged from 54% to 100% with an average rate of 84.8%. In the double-stage exchange group, 34.5% of patients underwent the procedure with a static spacer and 65.5% with an articulating spacer. The eradication rate was higher in the articulating spacer group compared with the static spacer group: 92.5% vs 74%. The results are reported in Table 1.

Functional outcomes

The functional outcomes were similar in both groups. The studies reporting single-stage exchange gave a Knee Society Score ranging from 72 to 88 with an average score of 80. The studies reporting double-stage exchange reported a Knee Society Score ranging from 63.8 to 86.0 with an average score of 77.8. The average range of motion was 91.4° (76°–100°) in the single-stage group and 97.8° (86°–112°) in the double-stage group. The results are reported in Table 2.

Discussion

Our study reported no statistical difference between the single-stage exchange group and the two-stage exchange in terms of functional outcome and eradication rates. Considering the fact that single-stage exchange is much more comfortable for the patients and allows the hospital to reduce the costs associated with periprosthetic joint infection, single-stage exchange appears to be a viable alternative to double-stage exchange surgery. However, some of the studies were small with very short (six months) follow-up.
Recently, Kunutsor et al.\(^{14}\) performed a meta-analysis comparing single- and two-stage exchange for knee revision in cases of infectious disease. Their article included 10 studies for single-stage (423 patients), and 18 studies for double-stage exchange (5129 patients). They reported lower re-infection rates for single-stage exchange compared with two-stage exchange: 7.6% (95% CI 3.4–13.1) vs 8.8% (95% CI 7.2–10.6). As in our review, the functional outcomes were similar in terms of clinical score and range of motion. The knee society knee score was 80.3 (74.8–86.5) in the single-stage group and 82.1 (76.0–86.0) in the double-stage exchange group. The average range of motion was 97.5° (93.8°–100.5°) in the one-stage revision group and 97.8° (93.7°–104.0°) in the two-stage revision group.

Nagra et al.\(^{15}\) published their review in 2016 including 231 patients: 46 single-stage and 185 double-stage with a minimum of two years follow up. The rate of re-infection was 4.3% in their single-stage group, and 13.5% in the double-stage but without statistically significant difference: OR −0.06 (95% CI −0.13 to 0.01). In their subgroup analyses, the studies performed after 2000 reported significantly better rates for the single-stage group (OR −0.08; 95% CI −0.20 to 0.00). Considering the functional outcomes they reported the results of Haddad et al.\(^{16}\) with an increase of 56 points in the Knee Society Score for single-stage compared with 45 points for the two-stage revision group.

In 2012, Romanò et al.\(^{17}\) published a systematic review. Their results included a comparison between static and articulating spacers in cases of two-stage revision. In their review, 204 patients underwent single-stage exchange in six studies from 1966 to 2011 and 1421 patients underwent two-stage exchange in 38 studies. The eradication rate was higher in the two-stage exchange group: 89.8% with 40 months of follow-up versus 81.9% with 44 months of follow-up in the single-stage exchange group. In cases of two-stage revision, they recommended using an articulating spacer to improve the eradication rate: 91.2% versus 87.0% in cases of static spacer.

Jämsen et al.\(^{13}\) in 2009 published a systematic review in which they included 31 articles from 1980 to 2005: 154 cases underwent single-stage exchange with eradication rates ranging from 73% to 100%; 956 cases underwent two-stage exchange with eradication rates ranging from 82% to 100%. The lowest rates were reported for the series with two-stage exchange using an articulating spacer as reported by Romanò et al.\(^{17}\) Their functional results were similar to ours with no difference in terms of clinical score or range of motion between the single- and two-stage revision groups.

| Author            | Single/double stage | Year | Revue                  | Patients | FU   | Eradication rate % |
|-------------------|---------------------|------|------------------------|----------|------|---------------------|
| Buechel et al.\(^{39}\) | Single             | 2004 | American Journal of Orthopedics | 22       | 10.2 | 90.9                |
| Göksan and Freeman\(^{12}\) | Single             | 1992 | JBJS Br                | 18       | 5.0  | 77.0                |
| Jenny et al.\(^{20}\) | Single             | 2013 | Clinical Orthopedics   | 47       | 3.0  | 87.0                |
| Silva et al.\(^{24}\)  | Single             | 2002 | Clinical Orthopedics   | 37       | 4.0  | 89.2                |
| Singer et al.\(^{17}\) | Single             | 2012 | Clinical Orthopedics   | 63       | 24.0 | 95.0                |
| Tibrewal et al.\(^{20}\) | Single             | 2014 | BI                    | 50       | 10.5 | 92.0                |
| Jenny et al.\(^{19}\) | Single             | 2016 | Knee                  | 130      | 3.2  | 81.0                |
| Antony et al.\(^{41}\) | Single             | 2015 | Infectious Disease    | 37       | 1.0  | 89.0                |
| Zahar et al.\(^{47}\) | Single             | 2013 | Clinical Orthopedics   | 70       | 9.0  | 93.0                |
| Massin et al.\(^{23}\)  | Single             | 2016 | KSSTA                 | 108      | 3.5  | 77.0                |
| Bauer et al.\(^{15}\)  | Single             | 2004 | Clinical Orthopedics   | 30       | 4.5  | 67.0                |
| Castellani et al.\(^{34}\)  | Single             | 2015 | Clinical Orthopedics   | 28       | 6.5  | 100.0               |
| Haddad et al.\(^{16}\) | Single             | 2015 | Clinical Orthopedics   | 44       | 5.4  | 98.0                |
| Cuckler et al.\(^{43}\)  | Double             | 2005 | JOA                   | 24       | 2.8  | 92.0                |
| Durbzhakula et al.\(^{34}\)  | Double             | 2004 | JOA                   | 24       | 2.8  | 92.0                |
| Fehring et al.\(^{47}\)  | Double             | 2000 | Clinical Orthopedics   | 55       | 3.0  | 90.0                |
| For et al.\(^{22}\)  | Double             | 2018 | JOA                   | 56       | 3.3  | 54.0                |
| Frank et al.\(^{18}\)  | Double             | 2017 | Clinical Orthopedics   | 57       | 1.0  | 88.0                |
| Hofmann et al.\(^{48}\)  | Double             | 2005 | Clinical Orthopedics   | 50       | 6.0  | 88.0                |
| Hsu et al.\(^{30}\)  | Double             | 2007 | JOA                   | 28       | 2.0  | 87.0                |
| Huang et al.\(^{50}\)  | Double             | 2006 | JOA                   | 21       | 4.5  | 96.5                |
| Jämsen et al.\(^{23}\)  | Double             | 2006 | International Orthopedics | 34      | 2.8  | 85.0                |
| Lichstein et al.\(^{22}\)  | Double             | 2016 | Clinical Orthopedics   | 121      | 3.7  | 94.0                |
| Mortazavi et al.\(^{27}\)  | Double             | 2011 | Clinical Orthopedics   | 117      | 3.8  | 72.0                |
| Siebel et al.\(^{11}\)  | Double             | 2002 | Acta Orthopedica Belgica | 10      | 1.5  | 100.0               |
| Massin et al.\(^{23}\)  | Double             | 2016 | KSSTA                 | 177      | 55.0 | 69.0                |
| Bauer et al.\(^{15}\)  | Double             | 2006 | RCOT                  | 77       | 4.5  | 67.0                |
| Castellani et al.\(^{34}\)  | Double             | 2017 | HSS Journal           | 52       | 1.0  | 84.0                |
| Haddad et al.\(^{19}\) | Double             | 2015 | Clinical Orthopedics   | 74       | 6.5  | 93.0                |

Note. FU, follow up; ER, eradication rate.
Selection criteria for single-stage surgery

The above studies are encouraging when considering single-stage exchange in cases of periprosthetic joint infection around the knee. However, many of them do not describe comparable patient groups and the criteria for selection of single- or two-stage revision are not defined precisely.

Following Gehrke et al., we consider that each procedure should be performed considering various selection criteria and considering contra-indications. Single-stage exchange should not be considered in any of the following situations:

- Failure of \( \geq 2 \) previous one-staged procedures.
- Infection spreading to the neurovascular bundle.
- Unclear pre-operative bacterial specification.
- Non-availability of appropriate antibiotics.
- High antibiotic resistance.
- Sinus tract with unclear bacterial specification.

Jenny el al. published a study in 2016 in which they claimed the opposite: they compared a single-stage revision group without selection criteria (54 cases) with another one including only selected patients (77 cases). The selection criteria were: good general patient condition, non-acute infection, responsible pathogens sensitive to standard antibiotic treatment, and good bone stock without the need for bone grafting. In their study the rate of infection-free patients at 38 months’ follow-up was 85% in the group without selection and 78% in the selected group. Their conclusion was that selection of patients for single-stage exchange does not improve the eradication rate. Jenny et al. previously published on the subject a series describing 47 patients who underwent single-stage exchange for revision knee arthroplasty: the minimum follow-up was three years, the eradication rate was 87%, and 56% of the patients had a Knee Society Score of more than 150 points. Their findings were similar to ours: single-stage exchange gave the same results as double-stage exchange, but no benefits were demonstrated in functional outcomes.

Table 2. Functional outcomes of single- and double-stage exchange

| Author                | Year | Revue                     | Patients | Follow up (yrs) | KSS before | KSS after | HSS before | HSS after | OKS before | OKS after | ROM before | ROM after |
|-----------------------|------|---------------------------|----------|----------------|------------|-----------|------------|-----------|------------|-----------|------------|-----------|
| Buechel et al.        | 2004 | American Journal of Orthopedics | 22       | 10.2           | 79.5       |           |            |           |            |           |            |           |
| Göksan and Freeman    | 1992 | JBJS Br                   | 18       | 5.0            |            |           |            |           |            |           |            |           |
| Jenny et al.          | 2013 | Clinical Orthopedics      | 47       | 3.0            | 85.0       |           |            |           |            |           | 100.0     |           |
| Silva et al.          | 2002 | Clinical Orthopedics      | 37       | 4.0            | 72.0       | 14.5      |            | 34.5      |            |           |           |           |
| Singer et al.         | 2012 | Clinical Orthopedics      | 63       | 24.0           |            |           |            |           |            |           |           |           |
| Tiberwal et al.       | 2014 | BJJ                       | 50       | 10.5           |            |           |            |           |            |           |           |           |
| Jenny et al.          | 2016 | The Knee                  | 130      | 3.2            |            |           |            |           |            |           |           |           |
| Antony et al.         | 2015 | Infectious Disease        | 37       | 1.0            |            |           |            |           |            |           |           |           |
| Zahar et al.          | 2015 | Clinical Orthopedics      | 70       | 9.0            |            | 35        | 69.6       | 50        | 76.0       |           |           |           |
| Baker et al.          | 2013 | KSSTA                     | 33       | 0.6            |            |           |            |           |            |            | 24.9      |           |
| Massin et al.         | 2016 | KSSTA                     | 108      | 3.5            |            |           |            |           |            |           | 97.0      |           |
| Bauer et al.          | 2006 | RCOT                      | 30       | 4.5            | 75.5       |           |            |           |            |           | 92.5      |           |
| Castellani et al.     | 2017 | HSS Journal               | 14       | 1.0            |            |           |            |           |            |           |           |           |
| Haddad et al.         | 2015 | Clinical Orthopedics      | 28       | 6.5            | 32         | 88.0      |            |           |            |           |           |           |
| Cuckler et al.        | 2005 | Journal of Arthroplasty    | 44       | 5.4            | 36         | 84.0      |            |           |            |           | 112.0     |           |
| Durbakhula et al.     | 2004 | Journal of Arthroplasty    | 24       | 2.8            |            | 82.0      | 104.0      |           |           |           |           |           |
| Feiring et al.        | 2000 | Clinical Orthopedics      | 55       | 3.0            |            | 83.0      | 102.0      |           |           |           |           |           |
| Ford et al.           | 2018 | Journal of Arthroplasty    | 56       | 3.3            |            |           |           |           |            |           |           |           |
| Frank et al.          | 2017 | Clinical Orthopedics      | 57       | 1.0            |            |           |           |           |            |           |           |           |
| Hofmann et al.        | 2005 | Clinical Orthopedics      | 50       | 6.0            |            |           |           |           |            |           | 104.0     |           |
| Hsu et al.            | 2007 | Journal of Arthroplasty    | 28       | 2.0            |            |           | 86.0       |           |           |           |           |           |
| Huang et al.          | 2006 | Journal of Arthroplasty    | 21       | 4.5            | 60         | 80.0      | 97.6       |           |           |           |           |           |
| Jämsen et al.         | 2006 | International Orthopedics  | 34       | 2.8            | 38         | 80.0      | 100.0      |           |           |           |           |           |
| Lichstein et al.      | 2016 | Clinical Orthopedics      | 121      | 4.0            | 36         | 86.0      | 100.0      |           |           |           |           |           |
| Mortazavi et al.      | 2017 | Clinical Orthopedics      | 117      | 3.8            |            |           |           |           |            |           |           |           |
| Siebel et al.         | 2002 | Acta Orthopaedica Belgica | 10       | 1.5            | 39         | 63.8      | 86.5       |           |           |           |           |           |
| Baker et al.          | 2013 | KSSTA                     | 89       | 0.6            |            |           |            |           |            |           | 22.8      |           |
| Massin et al.         | 2016 | KSSTA                     | 177      | 5.5            |            |           |            |           |            |           | 91.0      |           |
| Bauer et al.          | 2006 | RCOT                      | 77       | 4.5            |            |           | 74.8       |           |            |           | 93.0      |           |
| Castellani et al.     | 2017 | HSS Journal               | 52       | 1.0            |            |           |           |           |            |           |           |           |
| Haddad et al.         | 2015 | Clinical Orthopedics      | 74       | 6.5            | 31         | 76.0      |           |           |           |           |           |           |

Note: KSS, Knee Society Score; HSS, Hospital for Special Surgery Score; OKS, Oxford Knee Score; ROM, range of motion.
Today the choice between single- and two-stage exchange remains, in most cases, the decision of the surgeon and depends on the habits of the institution. In order to help surgeons choose wisely, the Infectious Disease Society of America has published guidelines explaining what the present indications are for single- and two-stage exchange for periprosthetic joint infection (Fig. 1).

**Types of spacers**

In the case of two-stage exchange, the studies so far are unanimous: the articulating spacer improves the eradication rates and the functional outcomes compared with static spacers. Lichteinstein et al. reported the results of 121 infected TKAs treated with two-stage exchange and articulating spacer from 1999 to 2011. The median range of motion was 100° (60°–139°) and 94% patients were free of infection at 3.7 years of follow-up. The results of Romanò et al. showed an eradication rate of 91.2% for articulating spacers vs 87.0% in cases treated with a static spacer as mentioned previously.

An alternative to the cement spacer is described by Jämsen et al. using re-sterilized prosthetic components as spacers. In their study, 24 patients underwent exchange with this kind of spacer compared with 10 patients in a control group with a static spacer. The rate of re-infection was similar in the two groups. During the interim period, the patients with re-sterilized prosthetic spacers had a greater range of motion: mean 89°±18° vs 17°±13° (p < 0.001) in patients with cement spacers.

Finally, the last advantage of the articulating spacer is that it can be left in place if the patient is medically unfit for repeated surgery. Siddiqi et al. published a series of 29 patients who underwent only the first stage of a double-stage exchange and kept their spacer. Their results showed 79.3% success, 13.8% chronic wound drainage and 6.9% requiring a later multiple-spacer exchange.

**Risks factors for PJI**

The risks factors for PJI are well known, Pulido et al. described them as high American Society of Anesthesiologists (ASA) score, obesity, blood transfusion, atrial fibrillation, myocardial infarction, urinary infection or longer hospital stay, whereas Bohl et al. cited great age, male gender, diabetes, high blood pressure, smoking habit, high operating time and pneumonia. Considering the choice between single-stage surgery or double-stage for PJI around the knee, we must consider the risk factors of recrudescence of the infection. Massin et al. described the global risk factors of failure for PJI as fistula, gram-negative bacteria and two-stage exchange with a static spacer. Silva et al. reported factors associated with successful single-stage exchange as gram-positive organism, absence of sinus tract, aggressive debridement of infected tissue, antibiotics-impregnated cement and long-term antibiotic therapy, whereas rheumatoid arthritis and corticosteroid were associated with higher rates of failure. Mortazavi et al. published a series of 117 patients who underwent two-stage exchange to identify the risks factor for failure. Their rate of failure was 28% with three identified risks factors: negative culture and methicillin-resistant organism and increased operative time.

---

The patient has:**

- THA
- Good soft tissue
- Identity of the organisms determined preoperatively
- Good bone stock
- Susceptible to oral agents with high oral bioavailability
- Use of antibiotics impregnated bone cement for fixation
- No bone grafting required

**Types of spacers**

The patient has:**

- Poor soft tissue, OR
- Difficult to treat micro-organisms, AND
- No prior two-stage exchange for infection or prior two-stage exchange and reason for failure AND
- Delayed reimplantation technically feasible, AND
- Anticipated good functional outcome

---

*Uncommonly performed in the U.S.*

**Relative indications see text**

---

*Fig. 1 Guidelines of the Infectious Disease Society of America*
Infectious organism
The infectious agent also needs to be known to be able to choose between single- and double-stage exchange. In their series, Ford et al described 68.75% of Staphylococci with higher risks of re-offending bacteria in cases of Coagulase negative or Methicillin resistant organism. The results of Klatte et al on single-stage exchange with fungal infection do not encourage us to perform these procedures in the presence of fungal infection.

Periprosthetic joint infection in unicompartmental knee arthroplasty (UKA)
Chronic infection in UKA is not a common mode of failure. The three main reasons are loosening, wear and progression of osteoarthritis. Nevertheless, the incidence of infection in cases of failure for UKA should force us to consider it as a diagnosis option. Epinette et al describe it as the cause of 1.9% of failures and Sierra et al as 3%. The Society of Unicondylar Research reported it to be the cause of 10% of re-interventions after UKA. In their article, they claim that surgeons do not think about this diagnosis and thus, 40% of the failures of UKA have an incomplete PJ evaluation before re-intervention. They published a list of tools which should be used in case of UKA failure: An Erythrocyte Sedimentation Rate > 27 mm/H, C-Reactive Protein > 14 mg/mL and white blood cell count in synovial fluid 6200/µL is the cut-off value for which PJ should be considered. The white blood cell count in synovial fluid has a sensitivity of 90% and specificity of 96%.

Only one series has been published for infected UKA management: Labruyère et al reported nine cases of single-stage exchange of UKA to TKA. The average International Knee Society (IKS) knee score was 60 before surgery and 75 after surgery. The average IKS function score was 50 before surgery and 60 after surgery. They explained that in cases of PJ, cartilage and ligaments are so destroyed that a revision implant or rotating hinge is needed. Khan et al that in cases of PJI, cartilage and ligaments are so destroyed that a revision implant or rotating hinge is needed. They published a list of tools which should be used in case of a 'short double stage'. This involves closing the wound after debridement, the whole surgical team re-scrubbing and the use of new instruments for re-implantation.

In cases of double-stage exchange, the principles of debridement remain the same except for two differences: a second debridement may be necessary before re-implantation during the second stage, and bone loss needs to be considered after removal of the cement spacer. Calton et al demonstrated in their report that bone loss is caused directly by removal of the spacer. A small spacer and long period between two surgeries are directly correlated with higher bone loss.

Antibiotic therapy
Finally, a well conducted surgical procedure will be useless without a documented and wisely chosen antibiotic regime, guided by expert microbiologists. The length and timing of this antibiotic therapy still varies from one team to another. Osmon et al in their guidelines for the Infectious Disease Society of America recommend generally four to six weeks of IV antibiotic therapy followed by oral antibiotic therapy for a total of three months. Laffer et al considered that there is no need to have longer antibiotic therapy than six months. Recently, Frank et al performed a randomized controlled trial for double-stage exchange; the control group had no antibiotics after re-implantation and the other group had three months antibiotic therapy after re-implantation. The rates of re-infection were totally different: 19% of re-infection in the control group and 5% in the antibiotic group (hazard ratio, 4.37; 95% CI, 1.297–19.748; p = 0.0162).

Conclusions
The results of this systematic review should help us to decide whether single- or double-stage exchange is the most indicated procedure for chronic periprosthetic infection around the knee. Our results show that there are no clear benefits in terms of eradication rates or functional outcomes. Single-stage exchange appears to be a viable alternative to double-stage exchange, provided there are no contra-indications, with reduced morbidity and costs. The decision should be based upon the risk factors related to the patient and infectious organism and the contra-indication previously mentioned. In cases of double-stage exchange, articulating spacers show higher eradication rates and better functional outcomes.
ICMJE CONFLICT OF INTEREST STATEMENT
MO reports consultancy to Arthrex, Stryker and New-clip outside the submitted work.
JNA reports board membership of the Journal of Bone and Joint Surgery and consultancy to Zimmer, Adler and Symbios outside the submitted work.
CP declares no conflict of interest relevant to this work.

FUNDING STATEMENT
No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

LICENSE
© 2019 The author(s)
This article is distributed under the terms of the Creative Commons Attribution-Non Commercial 4.0 International (CC BY-NC 4.0) licence (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed.

REFERENCES
1. Pulido L, Ghanem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. J Orthop Res 2008;26:170–176.
2. Bohl DD, Sershon RA, Fillingham YA, Della Valle CJ. Incidence, risk factors, and sources of sepsis following total joint arthroplasty. J Arthroplasty 2016;31:2875–2879.e2.
3. Blom AW, Brown J, Taylor AH, Pattison G, Whitehouse S, Bannister GC. Infection after total knee arthroplasty. J Bone Joint Surg Br 2004;86:688–691.
4. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty 2012;27:61–65 e1.
5. Bozic KJ, Kurtz SM, Lau E, et al. The epidemiology of revision total knee arthroplasty in the United States. Clin Orthop Relat Res 2010;468:45–51.
6. Parvizi J, Pawsarat IM, Azzam KA, Joshi A, Hansen EN, Bozic KJ. Periprosthetic joint infection: the economic impact of methicillin-resistant infections. J Arthroplasty 2010;25:103–107.
7. Sculco TP. The economic impact of infected total joint arthroplasty. Instr Course Lect 1993;42:349–351.
8. Borden LS, Gearen PF. Infected total knee arthroplasty: a protocol for management. J Arthroplasty 1987;2:27–36.
9. Insall JN, Thompson FM, Brause BD. Two-stage reimplantation for the salvage of infected total knee arthroplasty. J Bone Joint Surg Am 1983;65:1087–1098.
10. Calton TF, Fehring TK, Griffin WL. Bone loss associated with the use of spacer blocks in infected total knee arthroplasty. Clin Orthop Relat Res 1997;345:148–154.
11. Goldstein WM, Kopplin M, Wall R, Berland K. Temporary articulating methylmethacrylate antibiotic spacer (TAMMAS): a new method of intraprostatic manufacturing of a custom articulating spacer. J Bone Joint Surg Am 2001;83-A:92–97.
12. Göksan SB, Freeman MA. One-stage reimplantation for infected total knee arthroplasty. J Bone Joint Surg Br 1992;74:78–82.
13. Jämsen E, Stogiannidis I, Malimavaara A, Pajamäki J, Puolakka T, Konttinen YT. Outcome of prosthesis exchange for infected knee arthroplasty: the effect of treatment approach. Acta Orthop 2009;80:67–77.
14. 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.
15. Nagra NS, Hamilton TW, Ganatra S, Murray DW, Pandit H. One-stage versus two-stage exchange arthroplasty for infected total knee arthroplasty: a systematic review. Knee Surg Sports Traumatol Arthrosc 2016;24:3106–3114.
16. Haddad FS, Sukeik M, Alazzawi S. Is single-stage revision according to a strict protocol effective in treatment of chronic knee arthroplasty infections? Clin Orthop Relat Res 2015;473:8–14.
17. Romano CI, Gala L, Logoluso N, Romano D, Drago L. Two-stage revision of septic knee prostheses with articulating knee spacers yields better infection eradication rate than one-stage or two-stage revision with static spacers. Knee Surg Sports Traumatol Arthrosc 2012;20:2445–2453.
18. Gehrke T, Zahar A, Kendorf D. One-stage exchange: it all began here. Bone Joint J 2013;95-B(11):77–81.
19. Jenny J-Y, Barbe B, Cazenave A, Roche O, Massin P; French Society for Hip and Knee Surgery (SFHG). Patient selection does not improve the success rate of infected TKA one-stage exchange. Knee 2016;23:1002–1005.
20. Jenny J-Y, Barbe B, Gaudias J, Boeri C, Argenson J-N. High infection control rate and function after routine one-stage exchange for chronically infected TKA. Clin Orthop Relat Res 2013;471:235–243.
21. Osmon DR, Berbari EF, Berendt AR, et al; Infectious Diseases Society of America. Executive summary: diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis 2013;56:1–10.
22. Lichstein P, Su S, Hedlund H, et al. Treatment of periprosthetic knee infection with a two-stage protocol using static spacers. Clin Orthop Relat Res 2016;474:120–125.
23. Jämsen E, Sheng P, Halonen P, et al. Spacer prostheses in two-stage revision of infected knee arthroplasty. Int Orthop 2006;30:257–261.
24. Siddiqi A, George NE, White PB, et al. Articulating spacers as a modified one-stage revision total knee arthroplasty: a preliminary analysis. Surg Technol Int 2018;32:239–248.
25. Massin P, Delory T, Lhotellier L, et al. Infection recurrence factors in one- and two-stage total knee prosthesis exchanges. Knee Surg Sports Traumatol Arthrosc 2016;24:3313–3319.
26. Silva M, Tharani R, Schmalzried TP. Results of direct exchange or debridement of the infected total knee arthroplasty. Clin Orthop Relat Res 2002;404:125–131.
27. Mortazavi SMJ, Vegari D, Ho A, Zmistowski B, Parvizi J. One-stage reimplantation of a femoral revision prosthesis for infected knee prosthesis: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc 2013;21:764–773.
28. Ford AN, Holzmeister AM, Rees HW, Belich PD. Characterization of outcomes of 2-stage exchange arthroplasty in the treatment of prosthetic joint infections. J Arthroplasty 2018;33:S224–S227.
29. Klatte TO, Kendorf D, Kamath AF, et al. Single-stage revision for fungal peri-prosthetic joint infection: a single-centre experience. Bone Joint J 2014;96-B:492–496.
30. Sierra RJ, Kassel CA, Wetters NG, Berend KR, Della Valle CJ, Lombardi AV. Revision of unicompartmental arthroplasty to total knee arthroplasty: not always a slam dunk! J Arthroplasty 2013;28:128–132.
31. Epinette J-A, Brunschweiler B, Mertl P, Mole D, Cazenave A; French Society for Hip and Knee. Unicompartmental knee arthroplasty modes of failure: wear is not the main reason for failure: a multicentre study of 418 failed knees. Orthop Traumatol Surg Res 2012;98:S124–S130.

32. Society of Unicondylar Research and Continuing Education. Diagnosis of periprosthetic joint infection after unicompartmental knee arthroplasty. J Arthroplasty 2012;27:46–50.

33. Labruyère C, Zeller V, Lhotellier L, et al. Chronic infection of unicompartmental knee arthroplasty: one-stage conversion to total knee arthroplasty. Orthop Traumatol Surg Res 2015;101:553–557.

34. Khan Z, Nawaz SZ, Kahane S, Esler C, Chatterji U. Conversion of unicompartmental knee arthroplasty to total knee arthroplasty: the challenges and need for augments. Acta Orthop Belg 2013;79:699–705.

35. George DA, Haddad FS. One-stage exchange arthroplasty: a surgical technique update. J Arthroplasty 2017;32:S59–S62.

36. George DA, Haddad FS. Surgical management of periprosthetic joint infections: two-stage exchange. J Knee Surg 2014;27:279–282.

37. Laffer RR, Graber P, Ochsner PE, Zimmerli W. Outcome of prosthetic knee-associated infection: evaluation of 40 consecutive episodes at a single centre. Clin Microbiol Infect 2006;12:433–439.

38. Frank JM, Kayupov E, Moric M, et al; Knee Society Research Group. The Mark Coventry, MD, Award: oral antibiotics reduce reinfection after two-stage exchange: a multicenter, randomized controlled trial. Clin Orthop Relat Res 2017;475:56–61.

39. Buechel FF, Femino FP, D’Alessio J. Primary exchange revision arthroplasty for infected total knee replacement: a long-term study. Am J Orthop (Belle Mead NJ) 2004;33:90–98.

40. Tibrewal S, Malagelada F, Jeyaseelan L, Posch F, Scott G. Single-stage revision for the infected total knee replacement: results from a single centre. Bone Joint J. 2014;96-B(6):759–764.

41. Antony SJ, Westbrook RS, Jackson JS, Heydemann JS, Nelson JL. Efficacy of single-stage revision with aggressive debridement using intra-articular antibiotics in the treatment of infected joint prosthesis. Infect Dis (Athl) 2015;8:17–23.

42. Zahar A, Kendoff DO, Klatte TO, Gehrke TA. Can good infection control be obtained in one-stage exchange of the infected TKA to a rotating hinge design? 10-year results. Clin Orthop Relat Res 2016;474:81–87.

43. Bauer T, Piriou P, Lhotellier L, et al. Results of reimplantation for infected total knee arthroplasty: 107 cases. J Bone Joint Surg Am 2013;95:702–709.

44. Castellani L, Daneman N, Mubareka S, Jenkinson R. Factors associated with choice and success of one- versus two-stage revision arthroplasty for infected hip and knee prostheses. J Arthroplasty 2017;32:2228–231.

45. Cuckler JM. The infected total knee: management options. J Arthroplasty 2005;20:33–36.

46. Durbakula SM, Czajka J, Fuchs MD, Uhl RL. Antibiotic-loaded articulating cement spacer in the 2-stage exchange of infected total knee arthroplasty. J Arthroplasty 2004;19:768–774.

47. Fehringer TK, Odum S, Calton TF, Mason JB. Articulating versus static spacers in revision total knee arthroplasty for sepsis. The Ranawat Award. Clin Orthop Relat Res 2000;380:9–16.

48. Hofmann AA, Goldberg T, Tanner AM, Kurtin SM. Treatment of infected total knee arthroplasty using an articulating spacer: 2- to 12-year experience. Clin Orthop Relat Res 2005;125–131.

49. Hsu YC, Cheng HC, Ng TP, Chiu KY. Antibiotic-loaded cement articulating spacer for 2-stage reimplantation in infected total knee arthroplasty: a simple and economic method. J Arthroplasty 2007;22:1050–1066.

50. Huang H-T, Su J-Y, Chen S-K. The results of articulating spacer technique for infected total knee arthroplasty. J Arthroplasty 2006;21:1163–1168.

51. Siebel T, Kelm J, Porsch M, Regitz T, Neumann WH. Two-stage exchange of infected knee arthroplasty with an prosthesis-like interim cement spacer. Acta Orthop Belg 2002;68:150–156.

52. Baker P, Petheram TG, Kurtz S, et al. Patient reported outcome measures after revision of the infected TKR: comparison of single versus two-stage revision. Knee Surg Sports Traumatol Arthrosc 2013;21:2715–2720.