BMJ Open

Single-stage surgery with antibiotic-loaded hydrogel-coated implants versus two-stage surgery for chronic periprosthetic hip joint infection in French tertiary referral hospitals: the SINBIOSE-H non-inferiority, randomised, controlled trial study protocol

Bertrand Boyer ,[1,2] Celine Cazorla,[3,4] Anne Carricajo,[5,6] Carine Labruyere,[7] Céline Chapelle,[8,9] Emilie Presles,[10] Paul Zufferey ,[11] Elisabeth Botelho-Nevers[12]

To cite: Boyer B, Cazorla C, Carricajo A, *et al*. Single-stage surgery with antibiotic-loaded hydrogel-coated implants versus two-stage surgery for chronic periprosthetic hip joint infection in French tertiary referral hospitals: the SINBIOSE-H non-inferiority, randomised, controlled trial study protocol. *BMJ Open* 2025;**15**:e085146. doi:10.1136/bmjopen-2024-085146

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-085146).

Received 06 February 2024
Accepted 24 January 2025

For numbered affiliations see end of article.

Correspondence to
Dr Bertrand Boyer;
bertrand.boyer@chu-st-etienne.fr

ABSTRACT

Introduction Chronic hip prosthetic joint infection (PJI) treatment needs non-conservative surgery. The recommended treatment follows a two-stage protocol. Between the two surgeries, full-weight bearing is prohibited, and joint stiffness and pain are rather usual complications. The single-stage procedure is thought to be less susceptible to late functional complications with a shorter, single hospital stay. However, infection control could be less efficient; the protocol highly relies on antibiotics and has a list of contra-indications. Most of these contra-indications are directly related to the biofilm formation. As no randomised control trial has ever compared single-stage versus two-stage surgery on infection treatment, the level of evidence for recommending one procedure over the other is low. An antibiotic-loaded hydrogel coating (Defensive Antiadhesive Coating (DAC), Novagenit SRL) has been proven to mechanically prevent biofilm formation while allowing a prolonged intra-articular antibiotic release. The addition of this biofilm inhibitor to a single-stage surgery might stand as a promising strategy for PJI. Moreover, using this device to prevent biofilm formation could expand one-stage surgery to patients who are in theory contra-indicated to one-stage surgery.

Methods and analysis SINBIOSE-H is a Prospective Randomized Open, Blinded End-point clinical trial that will include patients with a chronic hip PJI as defined by the Musculoskeletal Infection Society (MSIS), with at least one theoretical contra-indication for single-stage surgery. Patients needing a cemented implant will not be included. 440 patients will be randomised in two groups: the experimental group is composed of single-stage procedure associated with the use of biofilm inhibitor (DAC) loaded with topical antibiotics, and the control group is composed of two-stage procedure without biofilm inhibitor. The primary objective will be to demonstrate that single-stage surgery with antibiotic-loaded hydrogel-coated implants is non-inferior to two-stage surgery for chronic hip PJI treatment. The secondary objectives will be to demonstrate that single-stage surgery with antibiotic-loaded hydrogel-coated implants is superior to two-stage surgery on the prevention of functional complications, patient satisfaction scores, death rate, postoperative complications or early revision surgery for any cause other than infection. Based on a failure rate of two-stage surgery of 20% and a reduction of the infection rate using the DAC biofilm inhibitor from 3 to 0.7%, with a non-inferiority margin of 1.35 and power set at 90%, we estimated to enrol 420 patients.

Ethics and dissemination The protocol is in accordance with ethical principles established by the Helsinki World Medical Assembly and its amendments and will be conducted in accordance with the recommendations of International Conference on Harmonisation Good Clinical Practice. A core information and informed consent form will be provided. The written approval of the Ethics Committee (EC)/Institutional Review Board (IRB) together with the approved subject information/informed consent forms must be filed in the study files. Written informed consent must be obtained before any study-specific procedure takes place. The data will be saved on the

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Patients will be followed for at least 2 years, thus preventing missing late infections.
⇒ An adjudication committee will ensure the safety of the study.
⇒ Prospective, open randomised study with blind evaluation.
⇒ Limitation: non-double-blinded.

internal network in a secured directory, dedicated to the study. At the end of the research, all documents (case report files, investigator files, etc) will be archived and stored for 15 years in each centre. Data on SAEs will be included in the study documentation file. All data and documents will be made available if requested by relevant authorities. The EC and IRB were submitted and approved in France (CPP Ile De France X, 93602 AULNAY-SOUS-BOIS). Ethics approval covers all centres.

Trial registration number The study is registered on clinicaltrials.org under NCT04251377 (EUDRACT NUMBER, 2019-A01491-56; trial sponsor, St Etienne University Hospital Center; date of the last version, 24 February 2006).

INTRODUCTION

Periprosthetic joint infection (PJI) is a devastating complication, associated with substantial patient morbidity and an economic burden for healthcare facilities.[1]

The biofilm protects the pathogen from both the host immune response and antibiotics; after 4 weeks, the infection is considered chronic, and the treatment needs the complete removal of all implants.[2]

Anti-microbial-resistant pathogens, absence of identification or immunodeficiency are factors associated with a high rate of failure in PJI.[3]

Chronic PJI surgical treatment includes two different strategies: single-stage and two-stage procedures.

In two reviews of cohorts,[4 5] two-stage surgery was found to have a higher rate of success than single-stage surgery, usually around 10%, and is considered the reference treatment with infection control in mind. This surgery is however associated with joint stiffness and often bedsore complication issues, which also have a risk of re-infection.[6]

Single-stage surgery is thought to offer a better and a quicker rehabilitation for the patient,[7] as well as lower hospital costs. However, the implantation of a new set of implants and the quickness of the formation of the biofilm imply that single-stage surgery strongly relies on the antibiotic treatment.

Because of the risks regarding infection control, expert consensus has contra-indicated single-stage surgery if one or more of the following features is found:[8] the presence of damaged soft tissues or a sinus tract, an unknown pathogen, a difficult-to-treat micro-organism, a severe immunosuppression and each time a bone graft is necessary.[9 10] The Infectious Diseases Society of America nevertheless classes the evidence of this expert consensus as C-III,[11] as there has never been any randomised control study comparing single versus two-stage surgery on infection control, the only randomised controlled trial (INFORM trial)[12 13] focusing on patient-reported outcome measures.

Defensive Antibacterial Coating (DAC, Novagenit SRL, Mezzolombardo, Italy)[14] is a biofilm inhibitor that can safely be combined with antibiotics.[15] Two randomised controlled studies have already proven the efficacy of DAC for primary prevention of a bone and joint infection,[16 17] with rather short follow-ups and focusing on infection prevention, not PJI treatment. Therefore, we propose a randomised control trial to compare single-stage surgery with antibiotic-loaded hydrogel-coated implants versus two-stage surgery for chronic hip PJI in patients who are 'usually' contra-indicated to one-stage surgery.[8]

Our hypothesis is that the strategy combining DAC gel with topical antibiotics and single-stage surgery is non-inferior to two-stage surgery of PJI treatment, while providing better functional and patient satisfaction results.

The primary objective is to demonstrate that single-stage surgery with antibiotic-loaded hydrogel-coated implants is non-inferior to two-stage surgery of chronic hip PJI treatment.

The secondary objectives will be to demonstrate that single-stage surgery with antibiotic-loaded hydrogel-coated implants is superior to two-stage surgery on the prevention of functional complications, patient satisfaction scores, death rate, postoperative complications or early revision surgery for any cause other than infection.

METHODS AND ANALYSIS

The SINBIOSE-H study is a multicentre, Prospective Randomized Open, Blinded End-point phase III non-inferiority trial comparing a single stage with biofilm inhibitor and topical antibiotic strategy to two-stage surgery in chronically infected hip arthroplasties. Centres are all PJI referral centres from university hospital centres in France.

Inclusion criteria are a patient over 18 years old with social security affiliation diagnosed with a chronic hip PJI, according to the MSIS[18] criteria: either two positive periprosthetic cultures with phenotypically identical organisms or a sinus tract communicating with the joint or at least three of the five minor criteria, that is, elevated serum C-reactive protein (CRP) and erythrocyte sedimentation rate, elevated synovial fluid white blood cell count, elevated synovial fluid polymorphonuclear neutrophil percentage, positive histological analysis of periprosthetic tissue and a single positive culture.

Non-inclusion criteria are hypersensitivity to hydrogel components, pregnancy, a life expectancy lower than 3 months, the expected use of a cemented implant by the surgical team (for the treatment surgical protocol) or a patient unable to give informed consent/under guardianship or curatorship.

Patients will be randomised into two groups (figure 1).

The experimental group will be composed of single-stage surgeries with DAC and topical antibiotics. Surgery consists of the removal of implants, all joint tissues and a thorough lavage followed by a new set of implants coated with antibiotic-loaded hydrogel and topical antibiotics, during the same surgery. Immediately after the pathogen sampling, during the surgery, systemic antibiotic treatment is introduced for a total of 12 weeks.

The control group will be receiving the standard of care (SOC), that is, two-stage surgery. The first surgery consists in the complete removal of all implants, a wide synovectomy and a thorough lavage +/-an antibiotic-infused hip

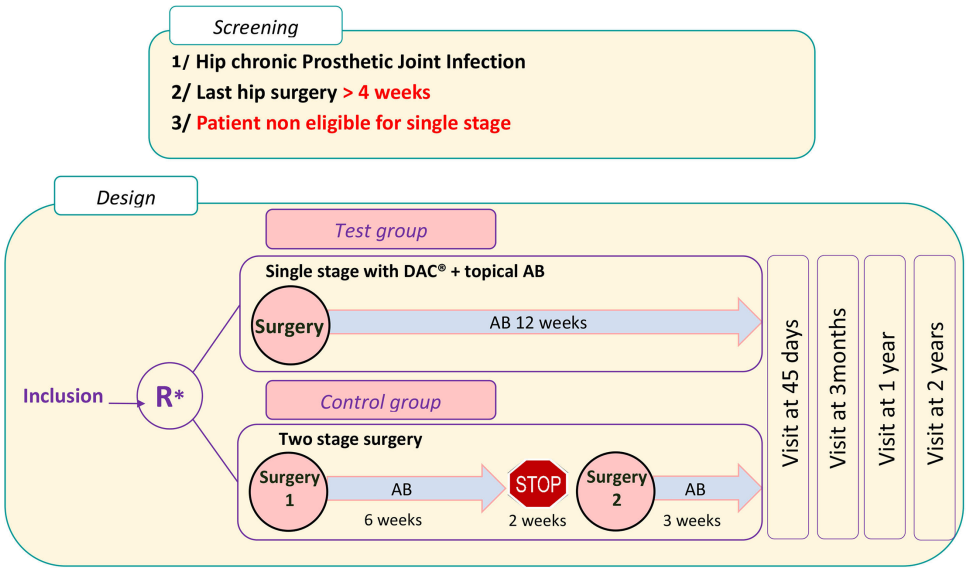

Figure 1 SINBIOSE-H protocol. AB, antibiotics; DAC, Defensive Antiadhesive Coating; *R, randomisation the day before surgery.

spacer. Systemic antibiotics will be introduced during the surgery after the removal of implants and the realisation of microbiological samples, for a duration of 6 weeks. If no clinical and biological sign of infection is found after 6 weeks of antibiotic treatment, an antibiotic-free window of 2 weeks might be set. An amendment was authorised to allow the centres which do not perform an antibiotic-free window to follow an alternative (figure 2). At 8 weeks, the second surgery will be performed, consisting in the removal of the spacer, a new set of microbiological samples, a wide synovectomy, a thorough lavage and finally the implantation of a new set of implants. Systemic antibiotics will be re-introduced for 3 weeks.

The primary outcome measure is a clinically diagnosed infection relapse of the periprosthetic joint, that is, recurrence of infection by the same organism(s) and/or re-infection with a new organism up to 2 years postrandomisation (according to MSIS criteria[18]).

Secondary endpoints are functional scores (Harris Hip Score (HHS), Postel-Merle d'Aubigné (PMA) score, Hip Dysfunction and Osteoarthritis Outcome Score (HOOS)), Oxford-12 patient satisfaction score, death rate, postoperative complications and revision surgery for any cause other than infection, measured at 2 years postrandomisation.

Measures taken to avoid biases

The randomisation will be done centrally by an interactive web response system (IWRS).

Confusion bias will be limited by setting up a control group: two-stage surgery.

Evaluation biases will be limited despite the use of an open-label design by including an independent adjudication committee (iCAC) unaware of the surgery assignment to review the primary clinical endpoint in order to standardise the adjudication and blindly assess the efficacy and safety. This independent adjudication committee will be composed of physicians not involved in the study. The time and number of visits will also be standardised. All concomitant medication or any procedure that could modify the management of patients will be recorded.

To limit the number of incomplete outcome data (ie, the attrition bias), we first try to limit the number of lost-to-follow-up patients. Second, the statistical analysis will be performed on the per-protocol population (non-inferiority design) and on an intention-to-treat basis.

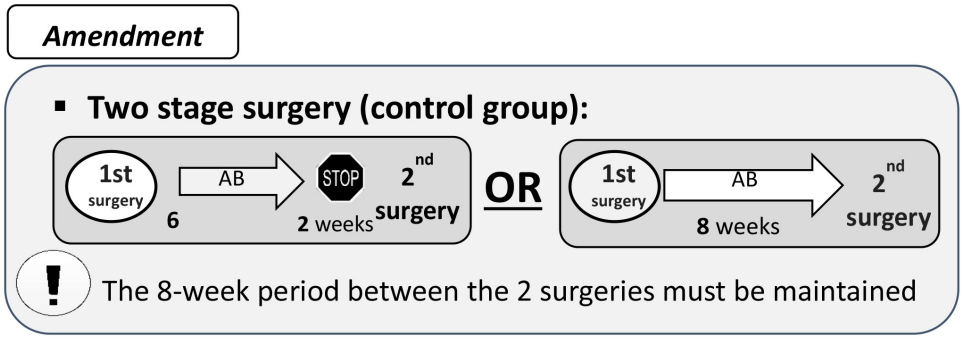

Figure 2 Amendment concerning the control group. Additional content: consent form (translated from French with DeepL).

The study protocol will be recorded in a public registry of randomised clinical trials with all endpoints (primary and secondary) to show the lack of reporting bias.

Description of the device

DAC (Novagenit SRL, Mezzolombardo, Italy; BC-NG002_ kit DAC_EN_27.02.2017; CE 0426) is a biofilm inhibitor. The DAC kit is a class III sterile disposable medical device composed of one sterile DAC syringe containing 300 mg of dry powder. In the operating room sterile field, mixing 5 mL of a solution of sterile water and topical antibiotics with the DAC powder results in the formation of a gel composed of hyaluronic acid of low molecular weight and poly-lactic acid, loaded with the chosen antibiotics. DAC gel is bio-absorbable within 72 hours.

DAC gel is applied on the surface of the implants before implantation. 5 mL is enough for standard implants (stem and cup). For larger implants, two doses will be necessary.

Its only contra-indication is the concomitant use of surgical cement, due to the exothermic quality of the cement polymerisation, degrading the gel.

In this study, topical antibiotics will be added to the reconstituted DAC gel preparation and decided prior to surgery. The following antibiotics that have been found to be compatible with the hydrogel are gentamicin, vancomycin, daptomycin, meropenem, rifampicin and ciprofloxacin.[15]

Study procedure for a patient

Patients will be selected during a consultation with the orthopaedic surgeon and/or the infectious disease doctor. During this visit, eligibility criteria of consecutive patients with chronic infection of a Total Hip Arthroplasty (THA) will be assessed.

At Visit zero (V0) or Inclusion, the study will be presented to the patient and the consent form will be distributed. A period of at least 2 days will be set, for the patient to have the time to process the information and give the clearest and most enlightened consent. Written informed consent will be obtained before inclusion in the study.

After inclusion, a blood sample set (BSS), composed of complete blood count, CRP, hepatic and pancreatic workup, and serum creatinine, will be obtained, as well as blood culture (aerobic and anaerobic), a site aspiration (ultrasound guided if necessary) and an anteroposterior (AP) view of the pelvis.

At V1, patients will be randomised as close to the surgery as possible, with the patient informed of his allocation group.

At V2, set at the end of hospital stay for the 'single-stage surgery group' or at the end of the first hospital stay for the 'two-stage surgery group'; BSS, AP view, outcome assessments (recurrence of infection, surgery complications, surgery revision), adverse event (AE) and serious AE (SAE) assessments, date of discharge and antibiotics at discharge will be recorded.

The next follow-up visits for the two groups will be the same (V3 or 45 days after randomisation (AR), V4 or 3 months AR, V5 or 1 year AR, V6 or 2 years AR). At each visit, the following exams will be realised (usual postoperative care): BSS and AP view and at V5 and V6 clinical and quality of life scores (HHS, PMA, HOOS and SF-12).

The total duration of follow-up for one patient will be 24 months after the inclusion.

Sample size

Based on studies focusing on contra-indications for single stage[19–22] (antibiotic-resistant pathogens, immunodepressed patients, etc), so using only two-stage surgery, we estimated the expected failure rate of two-stage surgery in these cases at 20%.

Based on the available studies using the DAC biofilm inhibitor,[15–17 23] with a reduction of the infection rate from 3% to 0.7% (primary surgery) or even from 13.4% to 0% (revision surgery),[17] we expect the addition of the biofilm inhibitor and antibiotics to lower the failure rate of single-stage surgery alone. In series choosing single stage for every patient, failure rates were often lower than 15% (Jenny *et al*[24] conducted a single-stage without biofilm inhibitor series with a failure rate of 8%, with every chronically infected total hip patient enrolled; Lange's cohort review[4] showed an average failure rate of 13% for single-stage.

A failure rate of single-stage and biofilm inhibitor of 15%, in patients contra-indicated for single-stage, seems a fair estimation, as many of the contra-indications are based on biofilm-related issues.

As the benefits of single stage are important[7 10 24 25] (length of hospital stay, functional benefit, etc), we chose a non-inferiority margin of 1.35 for the relative risk. Power was set at 90% and one-sided alpha level at 0.025.

With these values, we calculated that we would need to include 420 patients (210 per group) to have a 90% power showing the non-inferiority of single-stage and biofilm inhibitor on infection control at 2 years, at a one-sided alpha level of 0.025.

As the follow-up is quite short (24 months), an estimation of 5% of patients lost to follow-up seems fair. So we plan to randomise 440 patients, 220 in each group.

Statistical methods for primary and secondary outcomes

Data will be processed and analysed using SAS-WINDOWS software V.9.4 (SAS Institute Inc., Cary, NC, USA). Qualitative data will be presented as the number and the percentage of patients in each treatment group. Quantitative data will be presented as mean and SD, range, median and IQR by treatment group.

The primary analysis will be performed on per-protocol analysis and will be confirmed on intention to treat population. No imputation of missing data is planned. Time-to-event infection outcome will be estimated by competitive risk analysis using the Kalbfleisch and Prentice method, accounting for death as a competing risk with primary endpoint. Patients will be censored at their last available

follow-up. Cumulative incidences and corresponding 95% CIs will be calculated. Treatment effect will be estimated by the HR and its 95% CI by proportional hazards model using the Fine and Gray method, considering competing risks. Prior to this estimation, the proportionality of the risks will be checked. For the primary efficacy endpoint, the non-inferiority margin for the 95% CI of the HR comparing single-stage surgery with biofilm inhibitor to two-stage surgery will be 1.35. In case of imbalance between groups at inclusion, an adjusted analysis on the unbalanced covariate will be performed for the primary endpoint, with a multivariate model, using the Fine and Gray method. No subgroup analysis is planned.

To compare postoperative complications and early revision surgery, the same statistical methods as the statistical analysis of the primary endpoint will be performed (model considering competing risks).

Time-to-death will be estimated by the Kaplan–Meier method. A log-rank test between two treatment groups will be done. The HR and its 95% CI will be estimated by Cox model.

Regarding functional scores and satisfaction scores, a repeated measures analysis of variance (ANOVA) will be performed if the Normal distribution was checked (with a Shapiro–Wilk test). In the case of non-Normality, a Friedman test will be done. If repeated measures ANOVA is statistically significant, post hoc tests will be run. A p value less than 0.05 will be considered significant.

A statistical analysis plan will be written blinded to the data and define the role of the blind review committee.

Start and end dates

The study started on September 2022 and is supposed to end on September 2027.

Patient and public involvement

Patients or the public were involved in the design, conduct, reporting or dissemination plans of our research

ETHICS AND DISSEMINATION

The protocol is in accordance with ethical principles (Helsinki 1964 and its amendments) and will be conducted in accordance with the recommendations of International Conference on Harmonisation Good Clinical Practice.

A core information and informed consent form will be provided. The written approval of the Ethics Committee (EC)/Institutional Review Board (IRB) together with the approved subject information/informed consent forms is filed in the study files. Written informed consent must be obtained before any study-specific procedure takes place. Participation in the study and date of informed consent given by the subject should be documented appropriately in the subject's files.

The EC and IRB were submitted and approved in France (CPP Ile De France X, 93602 AULNAY-SOUS-BOIS). Ethics approval covers all centres.

The randomisation will be done centrally by an IWRS.

Data recording will be done under the responsibility of the investigator, by a member of his team.

The data file and the corresponding formats and labels will be reviewed and saved in SAS format. The data will be saved on the internal network of the University Hospital in a directory dedicated to the study, directory accessible only to the statistician. The internal network is secured by a firewall that protects the network from outside intrusion. A proxy server also controls Internet navigation, and anti-virus software examines all files and pages copied from external servers to the University Hospital. Anyone wishing to connect to the network must first identify with a username and a password provided by the University Hospital IT services.

As data entry will be made on an electronic case report form, terminal controls will be programmed according to the data management manual and therefore impose the correction data since data entry.

Depending on specifications, data validation will eventually be performed for statistical analysis, and correction requests are issued to the investigator or the study nurse, who will complete and correct data results.

The base gel will be decided by mutual agreement between the statistician of the study, the principal investigator and project manager.

At the end of the research, all documents (case report files, investigator files, etc) will be archived and stored for 15 years in each centre. Once data processing is completed, the computer data will be stored temporarily on a library to which access is restricted to only authorised personnel by the sponsor. Once the final report of the research is completed or published and within a maximum of 5 years after the end of the research, the data on the computer will be archived on external hard disk for 15 years.

Data on SAEs will be included in the study documentation file. All data and documents will be made available if requested by relevant authorities. Records should be maintained to verify the existence of each patient in the study and should contain the full name, last known address, telephone number and other pertinent information of each patient. Notwithstanding the foregoing, the investigator should contact the sponsor to obtain written permission to dispose study-related records including information on the method of such disposal or, at the sponsor's discretion, the archiving of such records by the sponsor.

Dissemination of the results will be made through the Bone and Joint Infection Referral Centre Network.

Author affiliations
[1]SAnté INgéniérie BIOlogie St-Etienne, Saint-Priest-en-Jarez, France
[2]Department of Orthopedics, St Etienne University Hospital Center, Saint-Priest-en-Jarez, France
[3]Department of Infectious Diseases, CIC-1408, Saint-Priest-en-Jarez, France
[4]Department of Infectious Diseases and Hygiene, St Etienne University Hospital Center, Saint-Priest-en-Jarez, France
[5]Department of Microbiology, CIC1408, Saint-Priest-en-Jarez, France

[6]Department of Microbiology, Centre International de Recherche en Infectiologie, Lyon, France
[7]Unité de Recherche Clinique Innovation et Pharmacologie, Saint-Priest-en-Jarez, France
[8]Université Jean Monnet, Saint-Étienne, France
[9]Unité de Recherche Clinique Innovation et Pharmacologie, Saint-Etienne, France
[10]Inserm CIC1408, Saint-Etienne University Hospital Centre, Saint-Etienne, France
[11]University Hospital of Saint-Etienne, Saint-Priest-en-Jarez, France
[12]Service d'Infectiologie, CIC-1408 INSERM Vaccinologie, CHU St. Etienne, Saint-Etienne, France

X Bertrand Boyer @boyer_bertrand

Contributors BB was responsible for writing the manuscript, is the chair of the steering committee and is the guarantor. CCa was responsible for the study's compliance with infectious disease recommendations; AC was responsible for the study's compliance with microbiology recommendations; PZ designed the study's methodology; CL is the project manager of the study; CCh and EP are responsible for the statistical analysis; EBN corrected the manuscript and co-designed the methodology. DeepL was used for the English translation of the consent form given to the patient (originally in French). No AI was used for the rest of the manuscript.

Funding This work was supported by France Direction Générale de l'Offre de Soins, grant number 2022-A02513-40.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer-reviewed.

ORCID iDs
Bertrand Boyer http://orcid.org/0000-0001-6427-9491
Paul Zufferey http://orcid.org/0000-0003-2899-1195

REFERENCES

1 Trentinaglia MT, Van Der Straeten C, Morelli I, *et al*. Economic Evaluation of Antibacterial Coatings on Healthcare Costs in First Year Following Total Joint Arthroplasty. *J Arthroplasty* 2018;33:1656–62.
2 Jacqueline C, Caillon J. Impact of bacterial biofilm on the treatment of prosthetic joint infections. *J Antimicrob Chemother* 2014;69 Suppl 1:i37–40.
3 McPherson EJ, Woodson C, Holtom P, *et al*. Periprosthetic total hip infection: outcomes using a staging system. *Clin Orthop Relat Res* 2002;8–15.
4 Lange J, Troelsen A, Thomsen RW, *et al*. Chronic infections in hip arthroplasties: comparing risk of reinfection following one-stage and two-stage revision: a systematic review and meta-analysis. *Clin Epidemiol* 2012;4:57–73.
5 Kunutsor SK, Whitehouse MR, Blom AW, *et al*. Re-Infection Outcomes following One- and Two-Stage Surgical Revision of Infected Hip Prosthesis: A Systematic Review and Meta-Analysis. *PLoS One* 2015;10:e0139166.
6 Reina N, Delaunay C, Chiron P, *et al*. Infection as a cause of primary total hip arthroplasty revision and its predictive factors. *Orthopaed Traumatol: Surg Res* 2013;99:555–61.
7 De Man FHR, Sendi P, Zimmerli W, *et al*. Infectiological, functional, and radiographic outcome after revision for prosthetic hip infection according to a strict algorithm. *Acta Orthop* 2011;82:27–34.
8 Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004;351:1645–54.
9 Zeller V, Lhotellier L, Marmor S, *et al*. One-stage exchange arthroplasty for chronic periprosthetic hip infection: results of a large prospective cohort study. *J Bone Joint Surg Am* 2014;96:e1.
10 Klouche S, Leonard P, Zeller V, *et al*. Infected total hip arthroplasty revision: One- or two-stage procedure? *Orthopaed Traumatol: Surg Res* 2012;98:144–50.
11 Osmon DR, Berbari EF, Berendt AR, *et al*. Executive Summary: Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of Americaa. *Clin Infect Dis* 2013;56:1–10.
12 Strange S, Whitehouse MR, Beswick AD, *et al*. One-stage or two-stage revision surgery for prosthetic hip joint infection--the INFORM trial: a study protocol for a randomised controlled trial. *Trials* 2016;17:90.
13 Blom AW, Lenguerrand E, Strange S, *et al*. Clinical and cost effectiveness of single stage compared with two stage revision for hip prosthetic joint infection (INFORM): pragmatic, parallel group, open label, randomised controlled trial. *BMJ* 2022;379:e071281.
14 Romanò CL, Trentinaglia MT, De Vecchi E, *et al*. Cost-benefit analysis of antibiofilm microbiological techniques for peri-prosthetic joint infection diagnosis. *BMC Infect Dis* 2018;18:154.
15 Drago L, Boot W, Dimas K, *et al*. Does implant coating with antibacterial-loaded hydrogel reduce bacterial colonization and biofilm formation in vitro? *Clin Orthop Relat Res* 2014;472:3311–23.
16 Malizos K, Blauth M, Danita A, *et al*. Fast-resorbable antibiotic-loaded hydrogel coating to reduce post-surgical infection after internal osteosynthesis: a multicenter randomized controlled trial. *J Orthop Traumatol* 2017;18:159–69.
17 Romanò CL, Malizos K, Capuano N, *et al*. Does an Antibiotic-Loaded Hydrogel Coating Reduce Early Post-Surgical Infection After Joint Arthroplasty? *J Bone Jt Infect* 2016;1:34–41.
18 Parvizi J, Tan TL, Goswami K, *et al*. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. *J Arthroplasty* 2018;33:1309–14.
19 Ji B, Zhang X, Xu B, *et al*. The fate of immunocompromised patients in the treatment of chronic periprosthetic joint infection: a single-centre experience. *Int Orthop* 2018;42:487–98.
20 Leung F, Richards CJ, Garbuz DS, *et al*. Two-stage total hip arthroplasty: how often does it control methicillin-resistant infection? *Clin Orthop Relat Res* 2011;469:1009–15.
21 Kim S-J, Huh J, Odrobina R, *et al*. Systemic review of published literature on Candida infection following total hip arthroplasty. *Mycopathologia* 2015;179:173–85.
22 Wolf M, Clar H, Friesenbichler J, *et al*. Prosthetic joint infection following total hip replacement: results of one-stage versus two-stage exchange. *Int Orthop* 2014;38:1363–8.
23 Capuano N, Logoluso N, Gallazzi E, *et al*. One-stage exchange with antibacterial hydrogel coated implants provides similar results to two-stage revision, without the coating, for the treatment of peri-prosthetic infection. *Knee Surg Sports Traumatol Arthrosc* 2018;26:3362–7.
24 Jenny J-Y, Lengert R, Diesinger Y, *et al*. Routine one-stage exchange for chronic infection after total hip replacement. *Int Orthop* 2014;38:2477–81.
25 Ilchmann T, Zimmerli W, Ochsner PE, *et al*. One-stage revision of infected hip arthroplasty: outcome of 39 consecutive hips. *Int Orthop* 2016;40:913–8.