

Removal of instrumentation for postoperative spine infection: systematic review

Andrew Hersh, AB, Robert Young, BS, Zach Pennington, BS, Jeff Ehresman, BS, Andy Ding, BA, Srujan Koppurapu, BS, BA, Ethan Cottrill, MS, Daniel M. Sciubba, MD, and Nicholas Theodore, MD

Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, Maryland

OBJECTIVE Currently, no consensus exists as to whether patients who develop infection of the surgical site after undergoing instrumented fusion should have their implants removed at the time of wound debridement. Instrumentation removal may eliminate a potential infection nidus, but removal may also destabilize the patient's spine. The authors sought to summarize the existing evidence by systematically reviewing published studies that compare outcomes between patients undergoing wound washout and instrumentation removal with outcomes of patients undergoing wound washout alone. The primary objectives were to determine 1) whether instrumentation removal from an infected wound facilitates infection clearance and lowers morbidity, and 2) whether the chronicity of the underlying infection affects the decision to remove instrumentation.

METHODS PRISMA guidelines were used to review the PubMed/MEDLINE, Embase, Cochrane Library, Scopus, Web of Science, and ClinicalTrials.gov databases to identify studies that compared patients with implants removed and patients with implants retained. Outcomes of interest included mortality, rate of repeat wound washout, and loss of correction.

RESULTS Fifteen articles were included. Of 878 patients examined in these studies, 292 (33%) had instrumentation removed. Patient populations were highly heterogeneous, and outcome data were limited. Available data suggested that rates of reoperation, pseudarthrosis, and death were higher in patients who underwent instrumentation removal at the time of initial washout. Three studies recommended that instrumentation be uniformly removed at the time of wound washout. Five studies favored retaining the original instrumentation. Six studies favored retention in early infections but removal in late infections.

CONCLUSIONS The data on this topic remain heterogeneous and low in quality. Retention may be preferred in the setting of early infection, when the risk of underlying spine instability is still high and the risk of mature biofilm formation on the implants is low. However, late infections likely favor instrumentation removal. Higher-quality evidence from large, multicenter, prospective studies is needed to reach generalizable conclusions capable of guiding clinical practice.

<https://thejns.org/doi/abs/10.3171/2020.12.SPINE201300>

KEYWORDS surgical site infection; instrumented fusion; systematic review; complication

SPINAL infections account for 2% to 7% of all musculoskeletal infections and have an estimated mortality of 2% to 4%.^{1,2} The incidence of infection has been rising in recent decades, partly due to improved diagnostic accuracy, an aging patient population, and increased use of instrumentation.^{2,3} Surgical site infections (SSIs) occur in 2% to 20% of cases of instrumented fusion, and SSIs are associated with increased morbidity and mortality, greater healthcare costs, longer length of stay (LOS), patient dissatisfaction, and poorer outcomes.^{4,5} Additionally, SSIs

have been linked to sepsis, multiorgan failure, pseudarthrosis, chronic pain, permanent disability, and death.^{6–8}

The most common cause of spine infections is *Staphylococcus aureus*, which accounts for 30% to 80% of spinal infections.^{2,3} Other common pathogens include beta-hemolytic streptococci, the gram-negative bacilli, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Enterobacter*.⁵ Several of these pathogens, including *S. aureus*, *Staphylococcus epidermidis*, *P. aeruginosa*, and *E. coli*, are particularly troublesome. These pathogens are capable

ABBREVIATIONS CNS = coagulase-negative *Staphylococcus*; IV = intravenous; LOS = length of stay; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*; SSI = surgical site infection.

SUBMITTED July 14, 2020. **ACCEPTED** December 14, 2020.

INCLUDE WHEN CITING Published online July 9, 2021; DOI: 10.3171/2020.12.SPINE201300.

of producing biofilm, a network of adherent bacterial cells embedded in a slimy extracellular matrix.^{9–11} Implants are coated with serum proteins that facilitate the formation of biofilms and bacterial adherence. The bacteria in these biofilms reduce their metabolism and alter their gene expression to confer greater resistance to host immunity and antibiotics, enabling the establishment of a persistent infection that is not readily treated.^{12,13}

Because of these biofilms, some surgeons and infectious disease specialists recommend the routine removal of implants in the case of SSI.¹⁴ However, on the whole, the field remains divided regarding whether infected instrumentation must be removed. To address this, we reviewed the current literature on instrumentation removal in patients with SSI. Our primary objectives were to determine 1) whether instrumentation removal from an infected wound facilitates infection clearance and lowers morbidity, and 2) whether the chronicity of the underlying infection affects the decision to remove instrumentation.

Methods

A systematic review was conducted between June 10, 2020, and June 25, 2020, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using the PubMed/MEDLINE, Embase, Cochrane Library, Scopus, Web of Science, and ClinicalTrials.gov databases. Search queries are included in Table 1. The bibliographies of studies meeting the inclusion/exclusion criteria were also reviewed to identify additional studies.

Studies were included if there were full-text English translations available and the study was primary literature (case series, cohort study, randomized controlled trial, or case-control study) that included ≥ 10 patients with SSIs after instrumented spine surgery, of whom ≥ 5 had undergone washout with instrumentation removal and ≥ 5 had undergone washout without removal. Both pediatric and adult populations were considered, and all instrumentation types were included (e.g., interbody fusion cages, interbody fixation cages, pedicle screw/rod systems). Studies were excluded if they 1) discussed nonspine instrumentation, such as baclofen pumps; 2) removed instrumentation for reasons other than infection, such as implant loosening; 3) the original indication for surgery was infection (e.g., spondylodiscitis, Pott's disease); or 4) did not include both patients who had retained instrumentation and patients who underwent removal of instrumentation at the time of wound washout. Single-arm studies were excluded to prevent differences in the treating surgeons or institutions from potentially confounding the results obtained from comparing patients that had their instrumentation removed to those who had their instrumentation retained.

Eligible studies were screened against these criteria by two reviewers (R.Y. and A.D.) using the Covidence systematic review application, with a third reviewer (A.H.) serving as a referee in cases of disagreement. Studies meeting all inclusion/exclusion criteria then underwent data extraction to identify relevant details using Microsoft Excel. Details extracted included study design, sample size, sample

demographics, indication for the index procedure, antibiotic regimen used, and postoperative outcomes. Postoperative outcomes of interest were mortality, occurrence of sepsis, occurrence of delirium, hospitalization LOS, readmission rate, discharge disposition (e.g., home, acute inpatient rehabilitation unit, subacute rehabilitation unit, skilled nursing facility), rate of repeat wound washout, and changes in curvature.

Results

We identified 8764 unique articles, of which 162 underwent full-text review; 15 were found to meet criteria for inclusion in the qualitative analysis. The PRISMA diagram in Fig. 1 elaborates on the articles found, excluded, and included. All included studies were retrospective comparative studies and were classified as level III studies according to the North American Spine Society guidelines.¹⁵ A total of 878 patients were included across the 15 studies, with the average age ranging from 6.3 to 66.3 years and the average study follow-up ranging from 1.5 years to more than 7 years (Table 2). Six studies investigated pediatric populations,^{16–21} and the remaining 9 investigated adult populations.^{22–30}

Indications for the index procedures were scoliosis ($n = 7$ studies), degenerative spondylolisthesis/spondylolysis ($n = 1$), thoracolumbar spinal stenosis ($n = 1$), spinal trauma ($n = 1$), degenerative thoracolumbar disease ($n = 1$), and osteoporotic vertebral collapse ($n = 1$). Surgical procedures were classified as posterior/posterolateral fusion ($n = 7$), transforaminal lumbar interbody fusion ($n = 1$), and growing-rod surgery ($n = 1$). Twelve of the 15 studies included patients originally treated with thoracic/thoracolumbar ($n = 11$) or lumbar/lumbosacral ($n = 5$) fusion,^{16–23,25,26,28} and 3 studies did not specify the instrumented region.^{24,27,29} All but one reported the cultured organism.^{16–28,30} In 11 studies, *S. aureus* was the most commonly implicated pathogen, followed by coagulase-negative staphylococcal species, including *S. epidermidis*.^{19–21,23–30}

A total of 292 patients (33%) had their instrumentation removed at the time of wound washout; of these, 39 had partial removal (Table 3). Seven studies examined implant management as a function of time between index procedure and readmission for operative management of infection.^{16,18,25,26,28–30} Five of these studies documented rates of instrumentation removal for early and late infections, finding that 17 (11%) of 160 patients with early infections underwent instrumentation removal compared with 99 (58%) of 172 with late infections.^{16,18,21,26,30} Pull ter Gunne et al. also examined instrumentation removal practices as a function of infection depth.²⁴ In their series, only 1 (2%) of 48 patients with an isolated superficial infection underwent removal of instrumentation, compared with 12 (14%) of 84 patients with deep infections. Across the included studies, there was no consensus antibiotic agent or treatment schedule, suggesting that antibiotic therapy may be best dictated by the isolated bacterial strain as opposed to the decision to remove the spinal instrumentation.

Postwashout outcome data were limited, with no studies reporting on discharge disposition, rates of delirium, rates of sepsis, or return to ambulatory care. Only one

TABLE 1. Database search queries for systematic review

Database	Search Queries
PubMed	<p>("instrumentation" [Subheading] OR "prostheses and implants"[mesh:noexp] OR "internal fixators"[mesh:noexp] OR "bone plates"[mesh] OR "instrumentation"[tiab] OR "instrumented"[tiab] OR "instrument"[tiab] OR "instruments"[tiab] OR "hardware"[tiab] OR "screw"[tiab] OR "screws"[tiab] OR "rod"[tiab] OR "rods"[tiab] OR "cage"[tiab] OR "cages"[tiab] OR "plate"[tiab] OR "plates"[tiab] OR "implant"[tiab] OR "implants"[tiab] OR "internal fixator"[tiab] OR "internal fixators"[tiab] OR "device"[tiab] OR "devices"[tiab])</p> <p>AND</p> <p>("Orthopedic Procedures"[Mesh:noexp] OR "neurosurgical procedures"[mesh:noexp] OR "neurosurgery"[mesh:noexp] OR "spine"[mesh:noexp] OR "cervical vertebrae"[mesh] OR "thoracic vertebrae"[mesh] OR "lumbar vertebrae"[mesh] OR "sacrum"[mesh] OR "cervical"[tiab] OR "thoracic"[tiab] OR "lumbar"[tiab] OR "sacrum"[tiab] OR "sacral"[tiab] OR vertebra*[tiab] OR "spine"[tiab] OR "spinal"[tiab] OR "neurosurgery"[tiab] OR "neurosurgical"[tiab] OR "spines"[tiab] OR interverteb*[tiab] OR orthopedic*[tiab] OR orthopaedic*[tiab] OR "disk"[tiab] OR "disks"[tiab] OR "disc"[tiab] OR "discs"[tiab])</p> <p>AND</p> <p>("Infection"[Mesh:NoExp] OR "prosthesis-related infections"[mesh:noexp] OR "Bone Diseases, Infectious"[Mesh:NoExp] OR "gram-positive bacterial infections"[mesh:noexp] OR "osteomyelitis"[mesh:noexp] OR "Epidural Abscess"[Mesh] OR "spondylitis"[mesh:noexp] OR "osteodiscitis"[tiab] OR "infections"[tiab] OR "epidural abscess"[tiab] OR "epidural abscesses"[tiab] OR "spondylitis"[tiab] OR "discitis"[tiab] OR "diskitis"[tiab] OR "spondylodiscitis"[tiab] OR "spondylodiscitis"[tiab] OR "Surgical Wound Infection"[MeSH] OR "Surgical Wound Dehiscence"[Mesh] OR ("surgical wound"[mesh] OR "surgical site"[tiab] OR "surgical sites"[tiab] OR "surgical wound"[tiab] OR "surgical wounds"[tiab]) AND ("infection"[mesh:noexp] OR infection*[tiab] OR dehiscence*[tiab]))</p> <p>AND</p> <p>("wound healing"[mesh] OR "Second-Look Surgery"[Mesh] OR "heal"[tiab] OR "healing"[tiab] OR "Anti-Bacterial Agents"[mesh:noexp] OR "debridement"[mesh] OR "biofilms"[mesh] OR "extracellular polymeric substance matrix"[mesh] OR "anti-bacterial agents"[pharmacological action] OR antibacterial*[tiab] OR "anti bacterial"[tiab] OR antibiotherap*[tiab] OR "anti bacterials"[tiab] OR antibiotic*[tiab] OR "anti biotic"[tiab] OR "anti biotics"[tiab] OR antimycobacterial*[tiab] OR "anti mycobacterial"[tiab] OR "anti mycobacterials"[tiab] OR "bacteriocide"[tiab] OR "bacteriocides"[tiab] OR "extracellular polymeric substance"[tiab] OR "washout"[tiab] OR "washouts"[tiab] OR "debridements"[tiab] OR "removal"[tiab] OR "revision"[tiab] OR "revisions"[tiab] OR "second look"[tiab] OR "second looks"[tiab] OR "second surgery"[tiab] OR "second surgeries"[tiab] OR "remove"[tiab] OR "removing"[tiab] OR "conservative"[tiab] OR "surgical management"[tiab] OR "surgical treatment"[tiab] OR "surgical treatments"[tiab] OR "biofilm"[tiab] OR "biofilms"[tiab] OR "bio film"[tiab] OR "bio films"[tiab])</p> <p>AND</p> <p>(randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR randomised [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR study [ti] OR groups [tiab] OR "retrospective studies"[mesh] OR "prospective studies"[mesh] OR "observational study"[pt] OR "longitudinal studies"[mesh] OR "retrospective"[tiab] OR "prospective"[tiab] OR "observational"[tiab] OR "longitudinal"[tiab] OR "follow up study"[tiab] OR "follow up studies"[tiab] OR "randomization"[tiab] OR "random"[tiab] OR "randomisation"[tiab] OR "evaluation studies"[pt] OR "evaluation study"[tiab] OR "evaluation studies"[tiab] OR "comparative effectiveness research"[mesh] OR "comparative study"[pt] OR "cohort studies"[mesh] OR "comparative"[tiab] OR "cohort"[tiab] OR "Case-Control Studies"[Mesh] OR "case control"[tiab] OR "case reports"[pt] OR "case report"[tiab] OR "case reports"[tiab]) NOT ("animals"[mesh] NOT ("animals"[mesh] AND "humans"[mesh]))</p>

CONTINUED ON PAGE 379 »

study, performed by Khoshbin et al.,¹⁸ reported LOS. The LOS in their study was 13.3 days in patients with instrumentation removed compared with 20.4 days in patients without removal, although this result was not statistically significant. Six studies reported rates of reoperation or need for additional washouts.^{16,18,21,22,27,29} All 6 of these studies found that reoperation rates were higher in patients undergoing instrumentation removal; however, 3 of these studies did not specify whether the reoperations were for repeat washout or to replace the removed instrumentation.^{21,22,27} Only Hey et al. and Chen et al. reported mortality rates, and both found mortality rates to be higher in patients who underwent instrumentation removal.^{25,27} However, the results were not statistically significant for

Hey et al., and Chen et al. noted that the higher rate in the instrumentation removal group may have resulted from perioperative malnutrition, immunosuppression, and delayed treatment.

Eight studies reported additional outcomes. Kowalski et al. noted similar rates of 2-year survival free of treatment failure, defined as recurrent infections necessitating unanticipated debridement and/or antimicrobial therapy, between patients with instrumentation removed (84%) and patients with instrumentation retained (80%).³⁰ In contrast, Cho et al. found higher rates of treatment failure at 2 years in patients with late infections who did not undergo instrumentation removal compared with those who underwent removal of the infected implants (44% vs

» CONTINUED FROM PAGE 378

TABLE 1. Database search queries for systematic review

Database	Search Queries
Embase	<p>(devices/de OR implant/de OR internal fixator/de OR bone plates/de OR instrumentation:ti,ab OR instrumented:ti,ab OR instrument:ti,ab OR instruments:ti,ab OR hardware:ti,ab OR screw:ti,ab OR screws:ti,ab OR rod:ti,ab OR rods:ti,ab OR cage:ti,ab OR cages:ti,ab OR plate:ti,ab OR plates:ti,ab OR implant:ti,ab OR implants:ti,ab OR internal fixator:ti,ab OR internal fixators:ti,ab)</p> <p>AND</p> <p>(Orthopedic surgery/de OR neurosurgery/de OR spine/de OR cervical spine/de OR thoracic spine/de OR lumbar spine/de OR sacrum/de OR cervical:ti,ab OR thoracic:ti,ab OR lumbar:ti,ab OR sacrum:ti,ab OR sacral:ti,ab OR vertebra*:ti,ab OR spine:ti,ab OR spinal:ti,ab OR neurosurgery:ti,ab OR neurosurgical:ti,ab OR spines:ti,ab OR interverteb*:ti,ab OR orthopedic*:ti,ab OR orthopaedic*:ti,ab OR disk:ti,ab OR disks:ti,ab OR disc:ti,ab OR discs:ti,ab)</p> <p>AND</p> <p>(Infection/de OR osteomyelitis/de OR Epidural Abscess/de OR spondylitis/de OR diskitis/de OR osteomyelitis:ti,ab OR infection:ti,ab OR infectious:ti,ab OR osteodiskitis:ti,ab OR osteodiscitis:ti,ab OR infections:ti,ab OR epidural abscess:ti,ab OR epidural abscesses:ti,ab OR spondylitis:ti,ab OR discitis:ti,ab OR diskitis:ti,ab OR spondylodiscitis:ti,ab OR spondylodiskitis:ti,ab OR Surgical Infection/de OR Wound Dehiscence/de OR ((surgical wound/de OR surgical site:ti,ab OR surgical sites:ti,ab OR surgical wound:ti,ab OR surgical wounds:ti,ab) AND (infection/de OR infection*:ti,ab OR dehiscence*:ti,ab)))</p> <p>AND</p> <p>(wound healing/de OR Second Look Surgery/de OR heal:ti,ab OR healing:ti,ab OR Antibiotic Agent/de OR debridement/de OR biofilm/de OR extracellular polymeric substance:ti,ab OR antibacterial*:ti,ab OR anti bacterial:ti,ab OR antibiotherap*:ti,ab OR anti bacterials:ti,ab OR antibiotic*:ti,ab OR anti biotic:ti,ab OR anti biotics:ti,ab OR antimycobacterial*:ti,ab OR anti mycobacterial:ti,ab OR anti mycobacterials:ti,ab OR bactericide:ti,ab OR bacteriocides:ti,ab OR washout:ti,ab OR washouts:ti,ab OR debridements:ti,ab OR removal:ti,ab OR revision:ti,ab OR revisions:ti,ab OR second look:ti,ab OR second looks:ti,ab OR second surgery:ti,ab OR second surgeries:ti,ab OR remove:ti,ab OR removing:ti,ab OR conservative:ti,ab OR surgical management:ti,ab OR surgical treatment:ti,ab OR surgical treatments:ti,ab OR biofilm:ti,ab OR biofilms:ti,ab OR bio film:ti,ab OR bio films:ti,ab)</p> <p>AND</p> <p>(randomized controlled trial/de OR controlled clinical trial/de OR randomized:ti,ab OR randomised:ti,ab OR placebo:ti,ab OR drug therapy:ti,ab OR randomly:ti,ab OR trial:ti,ab OR study:ti OR groups:ti,ab OR retrospective studies/de OR prospective studies/de OR observational study/de OR longitudinal studies/de OR retrospective:ti,ab OR prospective:ti,ab OR observational:ti,ab OR longitudinal:ti,ab OR follow up study:ti,ab OR follow up studies:ti,ab OR randomization:ti,ab OR random:ti,ab OR randomisation:ti,ab OR evaluation study/de OR evaluation study:ti,ab OR evaluation studies:ti,ab OR comparative effectiveness/de OR comparative study/de OR cohort analysis/de OR comparative:ti,ab OR cohort:ti,ab OR Case Control Study/de OR case control:ti,ab OR case report/de OR case report:ti,ab OR case reports:ti,ab) NOT (animal/exp NOT (animal/exp AND human/exp))</p>
Cochrane Library	<p>(([mh ^"prostheses and implants"] OR [mh ^"internal fixators"] OR [mh "bone plates"] OR "instrumentation":ti,ab OR "instrumented":ti,ab OR "instrument":ti,ab OR "instruments":ti,ab OR "hardware":ti,ab OR "screw":ti,ab OR "screws":ti,ab OR "rod":ti,ab OR "rods":ti,ab OR "cage":ti,ab OR "cages":ti,ab OR "plate":ti,ab OR "plates":ti,ab OR "implant":ti,ab OR "implants":ti,ab OR "internal fixator":ti,ab OR "internal fixators":ti,ab OR "device":ti,ab OR "devices":ti,ab)</p> <p>AND</p> <p>(([mh ^"Orthopedic Procedures"] OR [mh ^"neurosurgical procedures"] OR [mh ^"neurosurgery"] OR [mh ^"spine"] OR [mh "cervical vertebrae"] OR [mh "thoracic vertebrae"] OR [mh "lumbar vertebrae"] OR [mh "sacrum"] OR "cervical":ti,ab OR "thoracic":ti,ab OR "lumbar":ti,ab OR "sacrum":ti,ab OR "sacral":ti,ab OR vertebra*:ti,ab OR "spine":ti,ab OR "spinal":ti,ab OR "neurosurgery":ti,ab OR "neurosurgical":ti,ab OR "spines":ti,ab OR interverteb*:ti,ab OR orthopedic*:ti,ab OR orthopaedic*:ti,ab OR "disk":ti,ab OR "disks":ti,ab OR "disc":ti,ab OR "discs":ti,ab)</p> <p>AND</p> <p>(([mh ^"Infection"] OR [mh ^"prosthesis-related infections"] OR [mh ^"Bone Diseases, Infectious"] OR [mh ^"gram-positive bacterial infections"] OR [mh ^"osteomyelitis"] OR [mh "Epidural Abscess"] OR [mh ^"spondylitis"] OR [mh "discitis"] OR "osteomyelitis":ti,ab OR "infection":ti,ab OR "infectious":ti,ab OR "osteodiskitis":ti,ab OR "osteodiscitis":ti,ab OR "infections":ti,ab OR "epidural abscess":ti,ab OR "epidural abscesses":ti,ab OR "spondylitis":ti,ab OR "discitis":ti,ab OR "diskitis":ti,ab OR "spondylodiscitis":ti,ab OR "spondylodiskitis":ti,ab OR [mh "Surgical Wound Infection"] OR [mh "Surgical Wound Dehiscence"] OR (([mh "surgical wound"] OR "surgical site":ti,ab OR "surgical sites":ti,ab OR "surgical wound":ti,ab OR "surgical wounds":ti,ab) AND ([mh ^"infection"] OR infection*:ti,ab OR dehiscence*:ti,ab)))</p> <p>AND</p> <p>(([mh "wound healing"] OR [mh "Second-Look Surgery"] OR "heal":ti,ab OR "healing":ti,ab OR [mh ^"Anti-Bacterial Agents"] OR [mh "debridement"] OR [mh "biofilms"] OR [mh "extracellular polymeric substance matrix"] OR "anti-bacterial agents":ti,ab OR antibacterial*:ti,ab OR "anti bacterial":ti,ab OR antibiotherap*:ti,ab OR "anti bacterials":ti,ab OR antibiotic*:ti,ab OR "anti biotic":ti,ab OR "anti biotics":ti,ab OR antimycobacterial*:ti,ab OR "anti mycobacterial":ti,ab OR "anti mycobacterials":ti,ab OR "bactericide":ti,ab OR "bacteriocides":ti,ab OR "extracellular polymeric substance":ti,ab OR "washout":ti,ab OR "washouts":ti,ab OR "debridements":ti,ab OR "removal":ti,ab OR "revision":ti,ab OR "revisions":ti,ab OR "second look":ti,ab OR "second looks":ti,ab OR "second surgery":ti,ab OR "second surgeries":ti,ab OR "remove":ti,ab OR "removing":ti,ab OR "conservative":ti,ab OR "surgical management":ti,ab OR "surgical treatment":ti,ab OR "surgical treatments":ti,ab OR "biofilm":ti,ab OR "biofilms":ti,ab OR "bio film":ti,ab OR "bio films":ti,ab)</p>

CONTINUED ON PAGE 380 »

» CONTINUED FROM PAGE 379

TABLE 1. Database search queries for systematic review

Database	Search Queries
Scopus	<p>TITLE-ABS("instrumentation" OR "prostheses and implants" OR "internal fixators" OR "bone plates" OR "instrumentation" OR "instrumented" OR "instrument" OR "instruments" OR "hardware" OR "screw" OR "screws" OR "rod" OR "rods" OR "cage" OR "cages" OR "plate" OR "plates" OR "implant" OR "implants" OR "internal fixator" OR "internal fixators" OR "device" OR "devices")</p> <p>AND</p> <p>TITLE-ABS("Orthopedic Procedures" OR "neurosurgical procedures" OR "neurosurgery" OR "spine" OR "cervical vertebrae" OR "thoracic vertebrae" OR "lumbar vertebrae" OR "sacrum" OR "cervical" OR "thoracic" OR "lumbar" OR "sacrum" OR "sacral" OR vertebra* OR "spine" OR "spinal" OR "neurosurgery" OR "neurosurgical" OR "spines" OR interverteb* OR orthopedic* OR orthopaedic* OR "disk" OR "disks" OR "disc" OR "discs")</p> <p>AND</p> <p>TITLE-ABS("Infection" OR "prosthesis-related infections" OR "gram-positive bacterial infections" OR "osteomyelitis" OR "Epidural Abscess" OR "spondylitis" OR "discitis" OR "osteomyelitis" OR "infection" OR "infectious" OR "osteodiskitis" OR "osteodiscitis" OR "infections" OR "epidural abscess" OR "epidural abscesses" OR "spondylitis" OR "discitis" OR "diskitis" OR "spondylodiscitis" OR "spondylodiscitis" OR "Surgical Wound Infection" OR "Surgical Wound Dehiscence") OR (TITLE-ABS("surgical wound" OR "surgical site" OR "surgical sites" OR "surgical wound" OR "surgical wounds") AND TITLE-ABS("infection" OR infection* OR dehiscence*))</p> <p>AND</p> <p>TITLE-ABS("wound healing" OR "Second-Look Surgery" OR "heal" OR "healing" OR "Anti-Bacterial Agents" OR "debridement" OR "biofilms" OR "extracellular polymeric substance matrix" OR "anti-bacterial agents" OR antibacterial* OR "anti bacterial" OR antibiotherap* OR "anti bacterials" OR antibiotic* OR "anti biotic" OR "anti biotics" OR antimycobacterial* OR "anti mycobacterial" OR "anti mycobacterials" OR "bactericide" OR "bacteriocides" OR "extracellular polymeric substance" OR "washout" OR "washouts" OR "debridements" OR "removal" OR "revision" OR "revisions" OR "second look" OR "second looks" OR "second surgery" OR "second surgeries" OR "remove" OR "removing" OR "conservative" OR "surgical management" OR "surgical treatment" OR "surgical treatments" OR "biofilm" OR "biofilms" OR "bio film" OR "bio films")</p> <p>AND</p> <p>TITLE-ABS("randomized controlled trial" OR "controlled clinical trial" OR "randomized" OR "randomised" OR "placebo" OR "drug therapy" OR "randomly" OR "trial" OR "study" OR "groups" OR "retrospective studies" OR "prospective studies" OR "observational study" OR "longitudinal studies" OR "retrospective" OR "prospective" OR "observational" OR "longitudinal" OR "follow up study" OR "follow up studies" OR "randomization" OR "random" OR "randomisation" OR "evaluation studies" OR "evaluation study" OR "evaluation studies" OR "cohort" OR "case report" OR "case reports" OR "comparative" OR "case control")</p>
Web of Science	<p>TS=("instrumentation" OR "prostheses and implants" OR "internal fixators" OR "bone plates" OR "instrumentation" OR "instrumented" OR "instrument" OR "instruments" OR "hardware" OR "screw" OR "screws" OR "rod" OR "rods" OR "cage" OR "cages" OR "plate" OR "plates" OR "implant" OR "implants" OR "internal fixator" OR "internal fixators" OR "device" OR "devices")</p> <p>AND</p> <p>TS=("Orthopedic Procedures" OR "neurosurgical procedures" OR "neurosurgery" OR "spine" OR "cervical vertebrae" OR "thoracic vertebrae" OR "lumbar vertebrae" OR "sacrum" OR "cervical" OR "thoracic" OR "lumbar" OR "sacrum" OR "sacral" OR vertebra* OR "spine" OR "spinal" OR "neurosurgery" OR "neurosurgical" OR "spines" OR interverteb* OR orthopedic* OR orthopaedic* OR "disk" OR "disks" OR "disc" OR "discs")</p> <p>AND</p> <p>TS=("Infection" OR "prosthesis-related infections" OR "gram-positive bacterial infections" OR "osteomyelitis" OR "Epidural Abscess" OR "spondylitis" OR "discitis" OR "osteomyelitis" OR "infection" OR "infectious" OR "osteodiskitis" OR "osteodiscitis" OR "infections" OR "epidural abscess" OR "epidural abscesses" OR "spondylitis" OR "discitis" OR "diskitis" OR "spondylodiscitis" OR "spondylodiscitis" OR "Surgical Wound Infection" OR "Surgical Wound Dehiscence") OR (TS=("surgical wound" OR "surgical site" OR "surgical sites" OR "surgical wound" OR "surgical wounds") AND TS=("infection" OR infection* OR dehiscence*))</p> <p>AND</p> <p>TS=("wound healing" OR "Second-Look Surgery" OR "heal" OR "healing" OR "Anti-Bacterial Agents" OR "debridement" OR "biofilms" OR "extracellular polymeric substance matrix" OR "anti-bacterial agents" OR antibacterial* OR "anti bacterial" OR antibiotherap* OR "anti bacterials" OR antibiotic* OR "anti biotic" OR "anti biotics" OR antimycobacterial* OR "anti mycobacterial" OR "anti mycobacterials" OR "bactericide" OR "bacteriocides" OR "extracellular polymeric substance" OR "washout" OR "washouts" OR "debridements" OR "removal" OR "revision" OR "revisions" OR "second look" OR "second looks" OR "second surgery" OR "second surgeries" OR "remove" OR "removing" OR "conservative" OR "surgical management" OR "surgical treatment" OR "surgical treatments" OR "biofilm" OR "biofilms" OR "bio film" OR "bio films")</p> <p>AND</p> <p>TS=("randomized controlled trial" OR "controlled clinical trial" OR "randomized" OR "randomised" OR "placebo" OR "drug therapy" OR "randomly" OR "trial" OR "study" OR "groups" OR "retrospective studies" OR "prospective studies" OR "observational study" OR "longitudinal studies" OR "retrospective" OR "prospective" OR "observational" OR "longitudinal" OR "follow up study" OR "follow up studies" OR "randomization" OR "random" OR "randomisation" OR "evaluation studies" OR "evaluation study" OR "evaluation studies" OR "cohort" OR "case report" OR "case reports" OR "comparative" OR "case control")</p>

CONTINUED ON PAGE 381 »

» CONTINUED FROM PAGE 380

TABLE 1. Database search queries for systematic review

Database	Search Queries
ClinicalTrials.gov	Surgical Site Infection/instrumentation Surgical Site Infection/implant Surgical Site Infection/fixator Surgical Site Infection/device

7%).²⁶ In this study, failure was defined as infection-related death, need for additional surgical debridement, infection recurrence, or the occurrence of a new infection at the surgical site. However, pseudarthrosis rates are reported as being higher in patients who undergo instrumentation removal. Khoshbin et al. found that rates were nearly 40 percentage points higher in the instrumentation removal group (38% vs 0%), and Chen et al. found that rates were three times higher in the group undergoing instrumentation removal (60% vs 19.5%).^{18,25} Despite these higher pseudarthrosis rates, Chang et al. reported that patients undergoing instrumentation removal and revision had greater correction in their segmental lordotic angle (7.1° vs 1.3°). The authors also found that patients undergoing

instrumentation removal reported significantly higher satisfaction scores.²³

Discussion

SSIs are common after spine surgery, occurring in 2% to 20% of cases of instrumented fusion.^{4,5} Postoperative deep wound infections have been found to prolong hospitalization by nearly 10 days,³¹ increase healthcare costs,³² increase mortality rates,^{33,34} increase readmission rates,³⁵ and produce poorer patient-reported outcomes.⁷ Ambiguity remains as to whether patients undergoing reoperation for SSI should undergo simultaneous instrumentation removal, or if it is safe to preserve the implants. Here, we sought

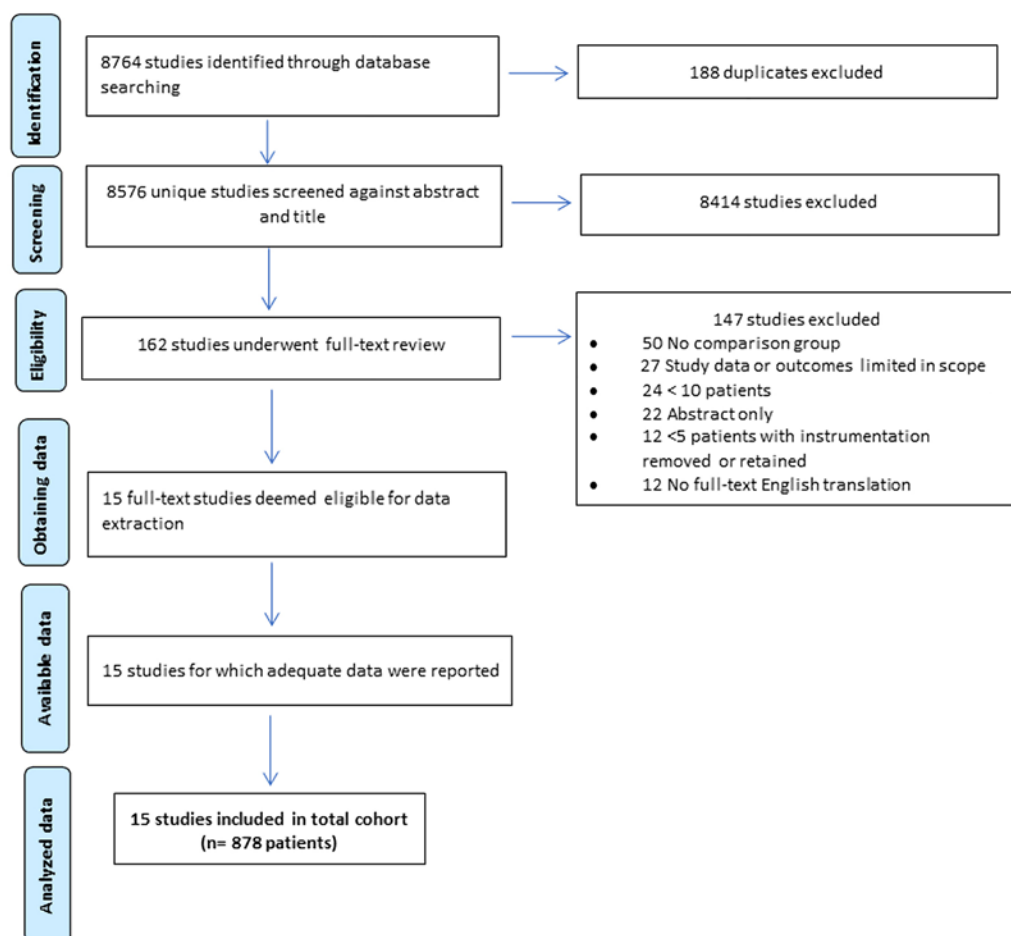


FIG. 1. PRISMA diagram outlining the results of the search query. Figure is available in color online only.

TABLE 2. Population characteristics of included studies

Authors & Year	No. of Patients	Age, yrs*	% Female	FU*	Surgery Type	Surgery Indication (%)	Spine Region (%)	Infectious Organism (%)
Bémer et al., 2008 ²²	68	43	72	1 yr‡	Posterolat fusion	Scoliosis (82), burst fracture (6), spinal stenosis (3)	Thoracolumbar	<i>P. acnes</i> (100)
Cahill et al., 2010 ²¹	61	12.1	NR	2 yrs	Posterior fusion	Scoliosis: neuromuscular (70), idiopathic (8), syndromic (8)	Thoracolumbar	MSSA (25), <i>S. epidermidis</i> (20), MRSA (16), <i>P. aeruginosa</i> (16)
Chang et al., 2019 ²³	32	66.3	44	2 yrs‡	Transforaminal lumbar interbody fusion	Spondylolysis, degenerative spondylolisthesis	Lumbar	<i>S. aureus</i> , <i>P. acnes</i> , <i>S. viridans</i>
Chen et al., 2015 ²⁵	51	57.2	NR	7.3 yrs	Posterior spinal instrumentation	Spinal stenosis/spondylolisthesis (55), spinal trauma (20), narrow/collapsed disc space (16)	Lumbosacral (75), thoracolumbar junction (22)	<i>S. aureus</i> (57), <i>E. coli</i> (14), <i>S. epidermidis</i>
Cho et al., 2018 ²⁶	102	63	49	2.7 yrs†	NR	NR	Lumbosacral (87), thoracic (18), cervical (5)	<i>S. aureus</i> (100)
Glottzbecker et al., 2016 ¹⁷	82	13.7	59	2.8 yrs†	Posterior spinal fusion	Scoliosis: neuromuscular (48), syndromic (23), idiopathic (23)	Thoracolumbar	NR
Hey et al., 2018 ²⁷	20	52.6	72	2 yrs‡	NR	NR	NR	<i>S. aureus</i> (60), <i>K. pneumoniae</i> (15)
Ho et al., 2007 ¹⁶	53	14.3	NR	NR	Posterior spinal fusion	Idiopathic scoliosis (40), cerebral palsy (23), spina bifida (6)	Thoracolumbar	CNS (47), <i>S. aureus</i> (17), polymicrobial (15), <i>Enterococcus</i> (6)
Ishii et al., 2013 ²⁸	29	65	31	Varied	Posterior lumbar interbody fusion, posterior spinal fusion	Thoracolumbar degenerative disease (52), osteoporotic vertebral collapse (34)	Thoracolumbar	MRSA, methicillin-resistant <i>S. epidermidis</i>
Kabirian et al., 2014 ²⁰	42	6.3	40	5.3 yrs	Growing-rod surgery	Scoliosis: neuromuscular (40), congenital (26), syndromic (29)	Thoracolumbar	MSSA (57), MRSA (5)
Khanna et al., 2018 ²⁹	67	62	66	3.1 yrs	NR	NR	NR	<i>S. epidermidis</i> (39), <i>S. aureus</i> (25)
Khoshbin et al., 2015 ¹⁸	35	15.1	66	3.5 yrs	Pediatric spinal fusion	Scoliosis: idiopathic (49), neuromuscular (31), congenital (20)	Thoracic (26), lumbosacral (6)	Gram-positive (49), gram-negative (14), polymicrobial (14)
Kowalski et al., 2007 ³⁰	81	56	43	2 yrs‡	NR	NR	Thoracic (42), cervical (15), lumbosacral (43)	<i>S. aureus</i> (26), polymicrobial (23), CNS (15), <i>P. acnes</i> (9)
Messina et al., 2014 ¹⁹	23	14.8	NR	1.5 yrs	Posterior spinal fusion	Scoliosis: adolescent idiopathic (43), neuromuscular (43)	Thoracolumbar	<i>S. aureus</i> (35), <i>Enterobacter</i> (22), <i>P. aeruginosa</i> (17)
Pull ter Gunne et al., 2010 ²⁴	132	56.4	56	4.2 yrs	NR	NR	NR	<i>S. aureus</i> (65), <i>E. faecalis</i> (15), MRSA (11), <i>E. coli</i> (11)

FU = follow-up; NR = not reported.

* All ages and follow-up reported are averages unless otherwise noted.

† Median.

‡ Minimum.

to summarize the existing evidence by systematically reviewing published studies that compare outcomes between patients undergoing wound washout and instrumentation removal with patients undergoing wound washout alone.

We identified 15 studies including a total of 878 patients, of whom 292 underwent instrumentation removal. All stud-

ies were level III evidence studies, and the patient populations were highly heterogeneous, which precluded a quantitative meta-analysis. Additionally, limited data were found on relative rates of mortality, sepsis, delirium, and need for repeat washout. The data that were available suggested that rates of reoperation, pseudarthrosis, and death were higher

TABLE 3. Comparison of mortality, reoperation rates, and morbidity between patients who underwent instrumentation removal and those with retained instrumentation at the time of surgical wound revision

Authors & Year	% Removed (n)*	PO/IV Antibiotics %	2nd Washout or Reop	Mortality	Other Outcomes	Recommendation
Bémer et al., 2008 ²²	32% (22) complete, 44% (30) partial	Clindamycin-ofloxacin (28), clindamycin-levofloxacin (15), amoxicillin (7), cloxacillin (7)	Partial removal: 67% (20); retained: 6% (1)	NR	NR	Remove; otherwise antibiotics 3–6+ mos
Cahill et al., 2010 ²¹	54% (33): 25% (8) early, 86% (25) late	NR	Removed: 2.3 avg reops; retained: 1.6 avg reops	NR	Removed: deformity progression 23 hrs (9 hrs pre-removal, 14 hrs post-removal); retained: deformity progression 2 hrs	Retention in early infections; consider removal in late & <i>S. epidermidis</i> infections
Chang et al., 2019 ²³	47% (15)	4- to 6-wk IV followed by 6-wk PO	NR	NR	Removed: segmental lordotic angle 7.1°, lumbar lordosis 30.5°, VAS 0.07, Kirkaldy-Willis overall satisfaction 86.7%; retained: segmental lordotic angle 1.3°, lumbar lordosis 28.1°, VAS 0.12, Kirkaldy-Willis overall satisfaction 41.2%	Removal, unless diagnosed <30 days + no endplate erosion on MRI + small extent of infection + low-virulent pathogens
Chen et al., 2015 ²⁵	20% (10)	NR	NR	Removed: 20% (2); retained: 5% (2)	Removed: union 2, pseudarthrosis 6; retained: solid fusion 33, pseudarthrosis 8	Retention in early infections; removal in late infections
Cho et al., 2018 ²⁶	19% (19): 6% (3) early, 31% (16) late	MRSA: IV vancomycin (58) or teicoplanin (17); MSSA: IV cefazolin (17), nafcillin (7), or vancomycin (2), followed by PO antibiotics (41), 41 days	NR	NR	Removed: 2-yr survival free of treatment failure 93% (late infection); retained: 2-yr survival free of treatment failure 62% (early infection), 56% (late infection)	Removal for <i>S. aureus</i> infections, recommend rifampin-based combination therapy
Glottzbecker et al., 2016 ¹⁷	10% (8)	6 wks	NR	NR	NR	Retention in early infections†
Hey et al., 2018 ²⁷	35% (7)	Cefazolin (80), vancomycin (10), cloxacillin (10), 6–8 wks	Removed: 14% (1); retained: 15% (2)	Removed: 14% (1); retained: 7.6% (1)	NR	Retention, even in deep infections
Ho et al., 2007 ¹⁶	19% (10): 3% (1) early, 41% (9) late	Varied	Removed: 20% (2); retained: 47% (20)	NR	Removed: loss of correction in coronal plane: thoracic curve 9°, lumbar curve 3°; sagittal plane: thoracic kyphosis change 15°, lumbar lordosis change 8°. Retained: NR	Balance benefits of removal w/ chance of progressive deformity
Ishii et al., 2013 ²⁸	66% (19)	Varied; IV several wks until normalized level (<0.3 mg/dL) of CRP → PO antibiotics several mos	NR	NR	NR	Retention in early infections
Kabirian et al., 2014 ²⁰	Partial: 21% (9); total: 31% (13)	NR	NR	NR	Partial removal: final fusion (5), treatment terminated (2), continued lengthening (1), completed lengthening (1); total removal: final fusion (5), treatment terminated (6), continued lengthening (2); retained: continued lengthening (12), final fusion (4), treatment terminated (3), completed lengthening and no final fusion (1)	Avoid partial or total removal unless infection cannot be otherwise managed

CONTINUED ON PAGE 384 »

» CONTINUED FROM PAGE 383

TABLE 3. Comparison of mortality, reoperation rates, and morbidity between patients who underwent instrumentation removal and those with retained instrumentation at the time of surgical wound revision

Authors & Year	% Removed (n)*	PO/IV Antibiotics %	2nd Washout or Reop	Mortality	Other Outcomes	Recommendation
Khanna et al., 2018 ²⁹	37% (25)	Implants removed: 70.4 days; retained w/ suppression: 36.8 days; retained w/o suppression: 26.6 days	Removed: 2.8 avg washouts; retained: 1.4 avg washouts	NR	NR	Retention in early infections; removal in late infections
Khoshbin et al., 2015 ¹⁸	60% (21): 25% (4) early, 89% (17) late	Regimen not specified; 117.9 days	Removed: 29% (6), avg 1.14 washouts; retained: 14% (2), avg 1.07 washouts	NR	Removed: pseudarthrosis 8, Cobb angle 40°, % coronal loss in the thoracic curve 69.5, curve progression rate: 5.8°/yr; retained: pseudarthrosis 0, Cobb angle 33°, % coronal loss in main thoracic curve 50, curve progression rate 0.2°/yr	Consider a trial of retention "irrespective of timing or depth of infection"
Kowalski et al., 2007 ³⁰	41% (33): 3% (1) early, 63% (32) late	β-lactam (41), vancomycin (28), combination (17); parenteral: 41 days	NR	NR	Removed: 2-yr survival free of treatment failure 84%; retained: 2-yr survival free of treatment failure 80% w/ PO antimicrobial suppression therapy, 33% w/o PO therapy	Retention in early infections; removal in late infections
Messina et al., 2014 ¹⁹	22% (5)	Regimen NR, median 131 days	NR	NR	NR	Retention, long courses of antibiotics
Puller et al., 2010 ²⁴	17% (13): 2% (1) superficial; 16% (12) deep	Superficial: PO 1st-gen cephalosporin, modified based on culture results, 21.9 days; deep: vancomycin + gentamicin, modified based on culture, 40.6 days	NR	NR	NR	Retention, irrespective of superficial or deep infection, except in cases of instrumentation failure or loosening

Avg = average; CRP = C-reactive protein; gen = generation; IV = intravenous; PO = by mouth; VAS = visual analog scale.

* Early/late refers to the timing of the infection.

† Study population identified only early infections.

in the group that underwent instrumentation removal at the time of the initial washout. However, given the retrospective nature of the study and the small sample sizes, it is unclear whether this relationship was causal, and if so, the direction of the causality. Consistent with this, only three studies recommended that implants be uniformly removed at the time of wound washout.^{22,23,26} In contrast, 5 studies favored retaining the original instrumentation, when possible.^{18–20,24,27} One study was inconclusive and suggested a careful balance between the benefits and risks of removal.¹⁶ The remaining 6 studies tailored their recommendations to the timing of infection, favoring instrumentation retention in early infections and removal in late infections.^{17,21,25,28–30}

Biofilms and Surgical Instrumentation

Standard practice during surgical wound debridement involves irrigating the wound with copious amounts of saline and removing dead or necrotic tissue.³⁶ In the case of instrumented fusion, wound washouts also may include removal of local bone graft material and instrumentation. The latter point is one of contention. Many patients experiencing wound infection may still have not achieved fu-

sion, in which case instrumentation removal can lead to increased morbidity, including spinal column destabilization and vertebral column collapse. Mechanical back and radicular pain, pseudarthrosis, and neurological injury can potentially occur after removal.^{12,37–39} Nevertheless, many bacterial species are known to be capable of adhering to implants on which they form antibiotic-resistant biofilms that can function as a nidus for chronic infection. Therefore, some argue that implants in an infected wound should be removed or replaced at the time of washout.⁵ Consequently, the decision of whether to remove implanted instrumentation rests on the competing pressures of eliminating a potential infection nidus and avoiding destabilization of the instrumented spine.

The ability of certain bacteria, notably *S. aureus*, *S. epidermidis*, and enterococci, to form biofilms is well documented in the orthopedic surgery literature.^{26,40} Steps in biofilm formation begin with a foreign body reaction in response to the implants.⁴¹ This inflammatory reaction leads to the formation of granulation tissue and fibrous encapsulation of the implant, creating a zone of immune suppression. Bacteria within the wound can adhere to the implant

through passive and active adhesion and can proliferate on its surface. Passive adhesion relies on interactions between capsular polysaccharides and charged groups on the metal surface, whereas active adhesion is mediated by adhesins and fibronectin-binding proteins that cling to serum proteins and extracellular matrix components deposited on the material by host tissues. Once the proliferating bacteria reach a critical density, they release extracellular signaling factors that trigger biofilm formation.⁴¹ The resultant biofilm resists penetration by systemic antibiotics and may also contain bacteria-produced enzymes that favor antibiotic degradation.^{42–46} Therefore, many argue that once the infection has progressed to the stage of biofilm formation, the implants must be removed to clear the infection.^{47,48} Several studies in the present review support this argument favoring instrumentation removal. Ho et al. reported that patients with retained implants had a nearly 50% chance of persistent infection requiring additional washouts, compared with 20% of patients who had their implants removed during the first washout.¹⁶ Similarly, Cho et al. found that those undergoing washout for *S. aureus*-related infection had a 30-percentage-point higher rate of infection clearance at 2 years postwashout if their instrumentation was removed at the time of washout.²⁶ Given the proclivity of *S. aureus* to form biofilms,⁴¹ the authors conjectured that the presence of biofilm on the implants contributed to lower infection clearance rates in patients with retained instrumentation.²⁶

Biomechanical work has demonstrated that pedicle screw instrumentation contributes significantly to stability in the newly instrumented spine.⁴⁹ The gradual formation of bridging bone across the instrumented levels produces a fusion mass that is then primarily responsible for the biomechanical properties of the spine. However, local bacterial proliferation and the resultant inflammatory response are noted to inhibit new bone formation through a combination of osteoblast inactivation and apoptosis.⁵⁰ Several in vitro studies of *S. aureus* have demonstrated decreased osteoblast activity in the presence of *S. aureus* as well as molecular markers of increased osteoblast death.^{51–54} Additionally, other in vitro studies have demonstrated that *S. aureus* increases osteoclastogenesis, setting up a dynamic of decreased bone formation and increased bone resorption.^{55–57} This dynamic may help account for the relatively high rates of pseudarthrosis seen in this population. Consequently, it seems likely that in the setting of SSI, the patient's spine may be increasingly reliant on the implanted instrumentation. Removal would therefore be destabilizing and subject the patient to increased risk of neurological injury.

Chronicity and SSI Management

Based on the results identified in our review, these two opposing pressures concerning the decision to remove instrumentation seem to be best reconciled by considering the chronicity of the infection. Although biofilms have been demonstrated in vitro to form over the course of hours,⁵⁸ early biofilms are relatively unstable and still susceptible to host immune defenses and systemically delivered antibiotics.⁵⁹ Consequently, in early infections—that is, those occurring within 1 month of treatment—wound debridement with implant retention and treatment with

systemic antibiotics is likely reasonable and avoids unnecessary destabilization of the healing spine. In contrast, in delayed infections, biofilms are likely mature and therefore resistant to systemic antibiotic therapy. Additionally, mature biofilms have been demonstrated in vivo to erode the underlying metal of titanium alloy (Ti6Al4V) spine rods.⁶⁰ Therefore, the original instrumentation may not only be an infection nidus impervious to systemic therapy, but it may also be structurally compromised to the point that retention places the patient at increased risk of instrumentation failure. Consequently, in delayed infections, implant replacement seems reasonable.

Six studies that categorized patients presenting with early or late infections concluded that retention is best suited for early infections, whereas removal is favored in late infections, constituting the most common recommendation across the identified studies.^{17,21,25,28–30} This recommendation is also supported in the total joint arthroplasty literature.⁶¹ As an example, Zimmerli et al. published an algorithm for the management of periprosthetic joint infections after joint arthroplasty, using time as one of the key determinants for guiding management.⁴⁰ They favored instrumentation retention in cases of early infection, defined as a symptomatic period of ≤ 3 weeks. For infections with longer symptomatic periods or those caused by antibiotic-resistant organisms, instrumentation removal was recommended. When minimal local tissue damage was present, a one-stage exchange was recommended, whereas in those with more extensive tissue damage or a resistant organism, a two-stage exchange was recommended with an initial washout, followed 2 to 8 weeks later by reimplantation. However, this algorithm was based on low-quality data, underlining the need for additional studies.

Other authors have proposed different treatment algorithms. The algorithm suggested by Abbey et al. is based largely on the depth of the SSI.⁶² However, they noted that in practice it is often difficult to differentiate superficial and deep infections. Therefore, they advocated for treating most infections as deep infections, using an aggressive approach that includes immediate wound debridement, followed by 4 to 8 weeks of intravenous antibiotics. Patients were then placed under close clinical monitoring, and those with potential implant infection were treated with suppressive antibiotics for 3 to 9 months, until bone fusion was achieved. Once the fusion is deemed successful, the patient's implants can be removed, or the patient can be followed clinically for signs of recurrent infection. In their algorithm, Abbey et al. considered the risks of treatment failure to outweigh the risks of overtreatment. In contrast, Kabirian et al. concluded that implant removal after growing-rod surgery should be considered only as a last resort.²⁰ In cases in which implant removal was favored, they recommended trying to retain at least one implant to allow for continued correction of the scoliotic deformity during treatment of the underlying infection.

Two studies in this review that investigated the pediatric population also favored differential treatment based on chronicity of infection.^{17,21} However, 3 studies favored retention.^{18–20} These findings suggest that the decision to retain or remove instrumentation may vary between pediatric and adult populations. Neuromuscular disorders, in-

cluding scoliosis, constitute a leading cause for instrumentation in children, and Khoshbin et al. noted that removal can have significant adverse outcomes on spinal alignment in these children.^{18,63} However, these findings are based on a small number of studies, and additional research is needed to clarify whether treatment algorithms should vary not just by chronicity of infection but also by patient age.

The chemical structure, surface roughness, hydrophobicity, and surface-free energy of implants have all been shown to impact bacterial adherence and biofilm formation.^{58,64,65} Several researchers have found that titanium implants resist bacterial adhesion better than stainless steel implants, potentially due to the smoother structure of titanium and its ability to form a thick surface oxide layer.^{66,67} Similarly, pure tantalum has been shown to resist *S. aureus* adhesion better than titanium and stainless steel.⁶⁸ Implant material can also affect the host response to infection, including immune activation and phagocytosis of bacteria. For example, silicone is associated with greater complement activation and a higher infection risk compared with polyvinylchloride and complement component C3 preferentially binds smooth rather than rough titanium surfaces.^{69,70} Therefore, the choice of instrumentation may affect the likelihood of its removal in the setting of infection. However, only two studies specified the metal type in patients with removed or retained instrumentation.^{23,26} Glotzbecker et al. did not specify how frequently a given metal was removed or retained, but they did recommend considering removal for patients with infected stainless steel implants.¹⁷ Similarly, Kabirian et al. found that patients experiencing deep infections had more commonly undergone instrumentation with stainless steel implants.²⁰ Therefore, the composition of the implant and its propensity to support biofilm progression should be considered when deciding whether to remove it.

The decision to remove instrumentation may also affect the choice of antibiotic agent, route of administration, and dosing regimen. Khanna et al. divided their cohort into 4 groups: removal, reinstrumentation, retention with antibiotic suppression, and retention without suppression.²⁹ The patients with retention without suppression did not have any recurrent infections, suggesting that lifelong suppression may not be required with infected retained instrumentation. These patients predominantly presented with early infections, suggesting that infection chronicity impacts the decision to retain instrumentation, which in turn impacts the duration of antibiotics. However, Khanna et al. cautioned that their results may suffer from selection bias, as those patients taken off antibiotics likely presented with a better prognosis.

Limitations

Limitations to the present study include both the heterogeneous patient populations and lack of consistent outcome measurements across studies. Large, multicenter prospective studies are needed to evaluate directly the impact of instrumentation removal on mortality, sepsis, readmission rates, reoperation rates, delirium, and long-term quality-of-life data. Another limitation stems from the heterogeneity in the infecting organisms and the antibiotic regimens used in patients with retained and removed

instrumentation. The lack of a consistent treatment methodology confounds any potential differences in treatment failure rates between the two groups, creating the possibility that instrumentation removal has no effect on ultimate outcomes. To this end, it is possible that those studies finding no difference between the groups may have had a low prevalence of biofilm formation, whereas those favoring instrumentation removal may have had high rates of implant biofilm formation. The studies identified by the present review are also all small, level III studies, with medium to high potential for selection bias. There is also a high risk of publication bias, and most studies did not report criteria for treatment selection, which may have further compounded existing selection bias. The overall medium to high bias restricts our ability to generalize the conclusions of the present study to the broader spine population. To address this, future studies involving large cohorts are necessary to evaluate the impact of implant management strategy on infection clearance in patients presenting with deep wound infections. Additionally, most of the studies failed to consider other determinants of infection clearance, such as medical comorbidities (e.g., diabetes mellitus), patient age, and concurrent use of immune-modulating drugs.

Conclusions

SSIs after instrumented spinal fusion are common and are associated with poor outcomes, including increased mortality, pseudarthrosis, and functional disability. The debate about whether instrumentation should be removed at the time of wound debridement or if retention can be safely pursued without increasing the risk for chronic infection is ongoing. The quality of current literature on this topic remains poor, and no clear consensus was identified; however, the most common approach favors retention in the setting of early infections, where underlying spine instability is still high and the risk of mature biofilm formation on the implants is low. In contrast, the high risk of mature biofilm formation in late infections potentially favors instrumentation removal at the time of debridement with either immediate or delayed replacement depending on the underlying infectious agent and level of spine stability. Higher-quality evidence from large, multicenter, prospective studies is needed to reach generalizable conclusions capable of guiding clinical practice.

Acknowledgments

We would like to thank Carrie Price for her assistance with structuring the literature search for the present review. Ethan Cottrill receives an F30 grant from National Institute on Aging (unrelated).

References

1. Tyrrell PN, Cassar-Pullicino VN, McCall IW. Spinal infection. *Eur Radiol.* 1999;9(6):1066–1077.
2. Duarte RM, Vaccaro AR. Spinal infection: state of the art and management algorithm. *Eur Spine J.* 2013;22(12):2787–2799.
3. Lener S, Hartmann S, Barbagallo GMV, et al. Management of spinal infection: a review of the literature. *Acta Neurochir (Wien).* 2018;160(3):487–496.
4. Gerometta A, Rodriguez Olaverri JC, Bitan F. Infections in spinal instrumentation. *Int Orthop.* 2012;36(2):457–464.

5. Kasliwal MK, Tan LA, Traynelis VC. Infection with spinal instrumentation: review of pathogenesis, diagnosis, prevention, and management. *Surg Neurol Int.* 2013;4(6)(suppl 5): S392–S403.
6. Chaudhary SB, Vives MJ, Basra SK, Reiter MF. Postoperative spinal wound infections and postprocedural diskitis. *J Spinal Cord Med.* 2007;30(5):441–451.
7. Weinstein MA, McCabe JP, Cammisa FP Jr. Postoperative spinal wound infection: a review of 2,391 consecutive index procedures. *J Spinal Disord.* 2000;13(5):422–426.
8. Weiss LE, Vaccaro AR, Scuderi G, et al. Pseudarthrosis after postoperative wound infection in the lumbar spine. *J Spinal Disord.* 1997;10(6):482–487.
9. Donlan RM. Biofilm formation: a clinically relevant microbiological process. *Clin Infect Dis.* 2001;33(8):1387–1392.
10. Schaber JA, Triffo WJ, Suh SJ, et al. *Pseudomonas aeruginosa* forms biofilms in acute infection independent of cell-to-cell signaling. *Infect Immun.* 2007;75(8):3715–3721.
11. Sharma G, Sharma S, Sharma P, et al. *Escherichia coli* biofilm: development and therapeutic strategies. *J Appl Microbiol.* 2016;121(2):309–319.
12. Yin D, Liu B, Chang Y, et al. Management of late-onset deep surgical site infection after instrumented spinal surgery. *BMC Surg.* 2018;18(1):121.
13. Hickok NJ. What are biofilms? *Spine (Phila Pa 1976).* 2018; 43(7):S7–S8.
14. Atesok K, Vaccaro A, Stippler M, et al. Fate of hardware in spinal infections. *Surg Infect (Larchmt).* 2020;21(5):404–410.
15. Levels of evidence for primary research question. North American Spine Society. Accessed January 22, 2021. <https://www.spine.org/Portals/0/Assets/Downloads/ResearchClinicalCare/LevelsofEvidence.pdf>
16. Ho C, Skaggs DL, Weiss JM, Tolo VT. Management of infection after instrumented posterior spine fusion in pediatric scoliosis. *Spine (Phila Pa 1976).* 2007;32(24):2739–2744.
17. Glotzbecker MP, Gomez JA, Miller PE, et al. Management of spinal implants in acute pediatric surgical site infections: a multicenter study. *Spine Deform.* 2016;4(4):277–282.
18. Khoshbin A, Lysenko M, Law P, Wright JG. Outcomes of infection following pediatric spinal fusion. *Can J Surg.* 2015; 58(1):006014–6014.
19. Messina AF, Berman DM, Ghazarian SR, et al. The management and outcome of spinal implant-related infections in pediatric patients: a retrospective review. *Pediatr Infect Dis J.* 2014;33(7):720–723.
20. Kabirian N, Akbarnia BA, Pawelek JB, et al. Deep surgical site infection following 2344 growing-rod procedures for early-onset scoliosis: risk factors and clinical consequences. *J Bone Joint Surg Am.* 2014;96(15):e128.
21. Cahill PJ, Warnick DE, Lee MJ, et al. Infection after spinal fusion for pediatric spinal deformity: thirty years of experience at a single institution. *Spine (Phila Pa 1976).* 2010; 35(12):1211–1217.
22. Bémer P, Corvec S, Tariel S, et al. Significance of *Propionibacterium acnes*-positive samples in spinal instrumentation. *Spine (Phila Pa 1976).* 2008;33(26):E971–E976.
23. Chang CW, Fu TS, Chen WJ, et al. Management of infected transforaminal lumbar interbody fusion cage in posterior degenerative lumbar spine surgery. *World Neurosurg.* 2019; 126:e330–e341.
24. Pull ter Gunne AF, Mohamed AS, Skolasky RL, et al. The presentation, incidence, etiology, and treatment of surgical site infections after spinal surgery. *Spine (Phila Pa 1976).* 2010;35(13):1323–1328.
25. Chen SH, Lee CH, Huang KC, et al. Postoperative wound infection after posterior spinal instrumentation: analysis of long-term treatment outcomes. *Eur Spine J.* 2015;24(3):561–570.
26. Cho OH, Bae IG, Moon SM, et al. Therapeutic outcome of spinal implant infections caused by *Staphylococcus aureus*: a retrospective observational study. *Medicine (Baltimore).* 2018;97(40):e12629.
27. Hey HWD, Ng Li WN, Kumar N, et al. Spinal implants can be retained in patients with deep spine infection: a cohort study. *J Orthop Trauma Rehabil.* 2018;24(1):34–38.
28. Ishii M, Iwasaki M, Ohwada T, et al. Postoperative deep surgical-site infection after instrumented spinal surgery: a multicenter study. *Global Spine J.* 2013;3(2):95–102.
29. Khanna K, Janghala A, Sing D, et al. An analysis of implant retention and antibiotic suppression in instrumented spine infections: a preliminary data set of 67 patients. *Int J Spine Surg.* 2018;12(4):490–497.
30. Kowalski TJ, Berbari EF, Huddleston PM, et al. The management and outcome of spinal implant infections: contemporary retrospective cohort study. *Clin Infect Dis.* 2007;44(7):913–920.
31. Aleem IS, Tan LA, Nassr A, Riew KD. Surgical site infection prevention following spine surgery. *Global Spine J.* 2020; 10(1)(suppl):92S–98S.
32. Blumberg TJ, Woelber E, Bellabarba C, et al. Predictors of increased cost and length of stay in the treatment of postoperative spine surgical site infection. *Spine J.* 2018;18(2): 300–306.
33. Veeravagu A, Patil CG, Lad SP, Boakye M. Risk factors for postoperative spinal wound infections after spinal decompression and fusion surgeries. *Spine (Phila Pa 1976).* 2009; 34(17):1869–1872.
34. Petilon JM, Glassman SD, Dimar JR, Carreon LY. Clinical outcomes after lumbar fusion complicated by deep wound infection: a case-control study. *Spine (Phila Pa 1976).* 2012; 37(16):1370–1374.
35. Bernatz JT, Tuetting JL, Anderson PA. Thirty-day readmission rates in orthopedics: a systematic review and meta-analysis. *PLoS One.* 2015;10(4):e0123593.
36. Hegde V, Meredith DS, Kepler CK, Huang RC. Management of postoperative spinal infections. *World J Orthop.* 2012; 3(11):182–189.
37. Kim JI, Suh KT, Kim SJ, Lee JS. Implant removal for the management of infection after instrumented spinal fusion. *J Spinal Disord Tech.* 2010;23(4):258–265.
38. Fang XT, Wood KB. Management of postoperative instrumented spinal wound infection. *Chin Med J (Engl).* 2013; 126(20):3817–3821.
39. Tominaga H, Setoguchi T, Kawamura H, et al. Risk factors for unavoidable removal of instrumentation after surgical site infection of spine surgery: a retrospective case-control study. *Medicine (Baltimore).* 2016;95(43):e5118.
40. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med.* 2004;351(16):1645–1654.
41. Arciola CR, Campoccia D, Montanaro L. Implant infections: adhesion, biofilm formation and immune evasion. *Nat Rev Microbiol.* 2018;16(7):397–409.
42. Percival SL, McCarty SM, Lipsky B. Biofilms and wounds: an overview of the evidence. *Adv Wound Care (New Rochelle).* 2015;4(7):373–381.
43. Schierle CF, De la Garza M, Mustoe TA, Galiano RD. Staphylococcal biofilms impair wound healing by delaying reepithelialization in a murine cutaneous wound model. *Wound Repair Regen.* 2009;17(3):354–359.
44. Chusri S, Sompetch K, Mukdee S, et al. Inhibition of *Staphylococcus epidermidis* biofilm formation by traditional Thai herbal recipes used for wound treatment. *Evid Based Complement Alternat Med.* 2012;2012:159797.
45. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. *Science.* 1999; 284(5418):1318–1322.
46. Stewart PS, Costerton JW. Antibiotic resistance of bacteria in biofilms. *Lancet.* 2001;358(9276):135–138.
47. Ahmed R, Greenlee JDW, Traynelis VC. Preservation of spinal instrumentation after development of postoperative

- bacterial infections in patients undergoing spinal arthrodesis. *J Spinal Disord Tech*. 2012;25(6):299–302.
48. Collins I, Wilson-MacDonald J, Chami G, et al. The diagnosis and management of infection following instrumented spinal fusion. *Eur Spine J*. 2008;17(3):445–450.
 49. Brailovski V, Facchinello Y, Brummund M, et al. Ti–Ni rods with variable stiffness for spine stabilization: manufacture and biomechanical evaluation. *Shape Memory Superelasticity*. 2016;2(1):3–11.
 50. Josse J, Velard F, Gangloff SC. *Staphylococcus aureus* vs. osteoblast: relationship and consequences in osteomyelitis. *Front Cell Infect Microbiol*. 2015;5:85.
 51. Claro T, Widaa A, O'Seaghdha M, et al. *Staphylococcus aureus* protein A binds to osteoblasts and triggers signals that weaken bone in osteomyelitis. *PLoS One*. 2011;6(4):e18748.
 52. Widaa A, Claro T, Foster TJ, et al. *Staphylococcus aureus* protein A plays a critical role in mediating bone destruction and bone loss in osteomyelitis. *PLoS One*. 2012;7(7):e40586.
 53. Jin T, Zhu YL, Li J, et al. Staphylococcal protein A, Panton-Valentine leukocidin and coagulase aggravate the bone loss and bone destruction in osteomyelitis. *Cell Physiol Biochem*. 2013;32(2):322–333.
 54. Young AB, Cooley ID, Chauhan VS, Marriotti I. Causative agents of osteomyelitis induce death domain-containing TNF-related apoptosis-inducing ligand receptor expression on osteoblasts. *Bone*. 2011;48(4):857–863.
 55. Johansen LK, Iburg TM, Nielsen OL, et al. Local osteogenic expression of cyclooxygenase-2 and systemic response in porcine models of osteomyelitis. *Prostaglandins Other Lipid Mediat*. 2012;97(3–4):103–108.
 56. Trouillet-Assant S, Gallet M, Nauroy P, et al. Dual impact of live *Staphylococcus aureus* on the osteoclast lineage, leading to increased bone resorption. *J Infect Dis*. 2015;211(4):571–581.
 57. Somayaji SN, Ritchie S, Sahraei M, et al. *Staphylococcus aureus* induces expression of receptor activator of NF- κ B ligand and prostaglandin E2 in infected murine osteoblasts. *Infect Immun*. 2008;76(11):5120–5126.
 58. Koseki H, Yonekura A, Shida T, et al. Early staphylococcal biofilm formation on solid orthopaedic implant materials: in vitro study. *PLoS One*. 2014;9(10):e107588.
 59. Zimmerli W, Moser C. Pathogenesis and treatment concepts of orthopaedic biofilm infections. *FEMS Immunol Med Microbiol*. 2012;65(2):158–168.
 60. Ayers R, Patel V, Burger E, et al. Corrosion of titanium spinal explants is similar to that observed in oil field line pipe steel: evidence of microbial-influenced corrosion in vivo. *Orthopedics*. 2020;43(1):62–67.
 61. Cury RDPL, Cinagawa EHT, Camargo OPA, et al. Treatment of infection after total knee arthroplasty. *Acta Ortop Bras*. 2015;23(5):239–243.
 62. Abbey DM, Turner DM, Warson JS, et al. Treatment of post-operative wound infections following spinal fusion with instrumentation. *J Spinal Disord*. 1995;8(4):278–283.
 63. Mendenhall S, Mobasser D, Relyea K, Jea A. Spinal instrumentation in infants, children, and adolescents: a review. *J Neurosurg Pediatr*. 2019;23(1):1–15.
 64. Katsikogianni M, Missirlis YF. Concise review of mechanisms of bacterial adhesion to biomaterials and of techniques used in estimating bacteria-material interactions. *Eur Cell Mater*. 2004;8:37–57.
 65. Teughels W, Van Assche N, Sliepen I, Quirynen M. Effect of material characteristics and/or surface topography on biofilm development. *Clin Oral Implants Res*. 2006;17(suppl 2):68–81.
 66. Metsmakers WJ, Schmid T, Zeiter S, et al. Titanium and steel fracture fixation plates with different surface topographies: Influence on infection rate in a rabbit fracture model. *Injury*. 2016;47(3):633–639.
 67. McEvoy JP, Martin P, Khaleel A, Dissanayake S. Titanium Kirschner wires resist biofilms better than stainless steel and hydroxyapatite-coated wires: an in vitro study. *Strateg Trauma Limb Reconstr*. 2019;14(2):57–64.
 68. Schildhauer TA, Robie B, Muhr G, Köller M. Bacterial adherence to tantalum versus commonly used orthopedic metallic implant materials. *J Orthop Trauma*. 2006;20(7):476–484.
 69. Rochford ETJ, Richards RG, Moriarty TF. Influence of material on the development of device-associated infections. *Clin Microbiol Infect*. 2012;18(12):1162–1167.
 70. Mödinger Y, Teixeira GQ, Neidlinger-Wilke C, Ignatius A. Role of the complement system in the response to orthopedic biomaterials. *Int J Mol Sci*. 2018;19(11):E3367.

Disclosures

Dr. Sciubba: consultant for Baxter, DePuy Synthes, Globus Medical, K2M, Medtronic, NuVasive, and Stryker; and unrelated grant support from Baxter Medical, North American Spine Society, and Stryker. Dr. Theodore: royalties from Globus Medical and DePuy Synthes; stock ownership in Globus Medical; consultant for Globus Medical; and scientific advisory board/other office for Globus Medical.

Author Contributions

Conception and design: Theodore, Young. Acquisition of data: Hersh, Young, Ding, Kopparapu. Analysis and interpretation of data: Hersh. Drafting the article: Hersh. Critically revising the article: Pennington, Ehresman, Cottrill. Reviewed submitted version of manuscript: Theodore. Statistical analysis: Hersh. Administrative/technical/material support: Theodore, Sciubba. Study supervision: Theodore, Sciubba.

Correspondence

Nicholas Theodore: Johns Hopkins University School of Medicine, Baltimore, MD. theodore@jhmi.edu.