



Vacuum assisted closure and local drug delivery systems in spinal infections: A review of current evidence



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ABSTRACT

Background: Spinal infections are still showing increased incidence throughout the years as our surgical capabilities increase, coupled with an overall aging population with greater number of chronic comorbidities. The management of spinal infection is of utmost importance, due to high rates of morbidity and mortality, on top of the general difficulty in eradicating spinal infection due to the ease of hematogenous spread in the spine. We aim to summarize the utility of vacuum-assisted closure (VAC) and local drug delivery systems (LDDS) in the management of spinal infections.

Methods: A narrative review was conducted. All studies that were related to the use of VAC and LDDS in Spinal Infections were included in the study.

Results: A total of 62 studies were included in this review. We discussed the utility of VAC as a tool for the management of wounds requiring secondary closure, as well as how it is increasingly being used after primary closure as prophylaxis for surgical site infections in high-risk wounds of patients undergoing spinal surgery. The role of LDDS in spinal infections was also discussed, with preliminary studies showing good outcomes when patients were treated with various novel LDDS.

Conclusions: We have summarized and given our recommendations for the use of VAC and LDDS for spinal infections. A treatment algorithm has also been established, to act as a guide for spine surgeons to follow when tackling various spinal infections in day-to-day clinical practice.

Introduction

Spinal infections are still a major problem in the developing world and are showing an increase in developed countries [1,2]. This may be related to our improved diagnostic capabilities with the advancement in technology, as well as the increasing burden of chronic conditions due to an aging population. As surgical techniques continue to evolve, patients with poorer comorbidities are also increasingly considered for surgery now. With this increase in surgical volume, the incidence of postoperative surgical site infections (SSIs) have also likewise increased. Spine surgery has also been commonly described to be a significant risk factor for spinal infections [3,4].

Spinal infections can be classified based on the pathophysiology of the infection as well as the route of spread of the responsible pathogen.

The spine can be infected due to contiguous spread from an adjacent infection. The infection can also originate from a distant site and reach the spine through hematogenous spread. More commonly, spinal infections are caused by direct inoculation such as from prior surgery or trauma [5]. The current literature regarding vacuum-assisted closure (VAC) and local drug delivery systems (LDDS) have not been established specifically for primary spine infection because antibiotic treatment alone in primary spine infection is shown to have up to 90% resolution rate [6]. Nonetheless, the use of VAC and LDDS has been described extensively for postoperative surgical site infections in spine surgery and have shown clear wound healing benefits compared with dressings alone [7,8].

Postoperative SSIs following spinal surgery still remain an unsolved problem. They have been described to be a wound infection that occurs

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within 30 days of an operative procedure or within 1 year if an implant was left in place [9]. Postoperative SSIs can be defined as superficial, deep, or organ space infection according to the United States Center for Disease Control and Prevention [10]. The incidence of postoperative SSIs in spinal surgery has been described to be between 1 to 16%, depending on the patient profile, type of spine surgery, approach, and usage of instrumentation [11,12]. Postoperative SSIs have been shown to cause increased morbidity, mortality, readmission, reoperation, and length of hospital stay [13,14]. Likewise, the treatment costs for patients exponentially increases and their overall outcomes are poorer [15]. Hence, surgical site care is of utmost importance in spine surgery. Prompt diagnosis and aggressive treatment of postoperative SSIs are also required, as they have been shown to have improved outcomes [16].

The standard available treatment or intervention for postoperative SSIs ranges from antibiotics alone or surgical debridement in association with antibiotics and removal of instrumentation or implants if necessary [17]. Superficial wound infections are commonly treated conservatively with antibiotics alone. However, if deep or organ space infection occurs, wound revision with irrigation and debridement is commonly required [18]. In these cases where the infection is worse, more advanced solutions have been described as adjuncts after extensive surgical debridement is done. These include VAC, antibiotic cement, temporary implantation of local tissue flap coverage, continuous suction irrigation, and hyperbaric oxygen therapy [18].

In recent years, the VAC system has been shown to allow for the effective management of SSIs with predictable outcomes. The VAC system has also demonstrated the ability to be used for infection prophylaxis, reducing the incidence of SSIs by up to 50% after application for closed incisions [19]. There also have been demonstrations of the use of LDDS such as antibiotic cement either in the form of beads [20,21] or a strut graft [22] and the use of Closed Suction Irrigation Systems (CSIS), with or without drug delivery, to assist in the successful management of SSIs [23].

In our manuscript, we aim to discuss the evolution of the role of VAC in the management of SSIs over the past decade. We also like to explore the incorporation of newer LDDS techniques such as CSIS in the management of more complex spinal infections.

Methods

A narrative review was conducted for this paper using PubMed, Medical Literature Analysis and Retrieval System Online (MEDLINE), The Cochrane Library, and Scopus databases through 14 June 2023. The keywords used were “Spine” AND “Infect*” AND (“VAC” OR “drug delivery”). A total of 62 articles were shortlisted (Figure).

Inclusion criteria for the review were studies with discussion on the use of VAC or LDDS in spinal infection. All studies that had no description regarding the surgical procedure performed, no use of VAC or LDDS, and not in English were excluded. The articles were selected in 2 stages. Firstly, the abstracts identified by the above searches were downloaded and the list was screened using the inclusion and exclusion criteria. Next, the full texts of the shortlisted abstracts were downloaded and assessed for eligibility. The reference lists of the publications were then hand-searched for additional relevant studies. This process was repeated twice by our senior authors independently.

The concept of our treatment algorithm for the use of VAC and/or LDDS in spinal infections was done as an expert opinion by the 2 senior spine surgeons in this manuscript, with experiences from treating and observing patients with spinal infection.

Discussion

History of the VAC system

VAC was first described in the 1980s by Kostiuhenko and Davydov et al. [24] for the management of wounds with high amounts of exudates

or pus. Through their studies, they demonstrated that the use of VAC allowed for shortened healing time and hospital stays in their cohort. Both postulated that VAC affected the healing time as it reduced the overall bacterial burden in the wounds, in turn stabilizing the immune processes in patients.

Morykwas and Argenta et al. [25] thereafter described in 1997 what we know today as the modern VAC, establishing the technique of placing an open-cell foam dressing into the wound cavity and applying a controlled sub-atmospheric pressure over it. In their landmark study, they provided the biochemical evidence that VAC reduced bacterial counts in the wound bed, hence justifying the extension of the use of VAC to wounds that are potentially difficult to heal or already poorly healing. The optimal pressures of up to 125 mm Hg for VAC that were suggested in their paper for wound healing are still adhered to up to this day, with further studies also showing that these pressures produce a flattened cell morphology that can augment fibroblast ability to release energy in the form of adenosine triphosphate (ATP), promoting cellular migration and increased collagen filling of the wound defect [19,25,26].

Since then, VAC has been used extensively in the field of orthopedics [27]. Indications for its usage include open fractures with soft tissue defects requiring serial debridement and infected wounds. More recently, closed incision VAC (ciVAC) has been described in the literature for incisions that are at high risk of complications such as breakdown or hematoma formation after primary closure [28]. Newer models of VAC devices have also been introduced, with the ability for the instillation of fluids into the wound sites during the therapy regimen [29]. In spine surgery, the use of VAC lies the majority in the management of SSI postoperatively. The ciVAC system has been shown to be able to reduce the incidence of SSI after primary closure in abdominal and cardiothoracic surgeries [30,31]. However, the usage of ciVAC for the prevention of SSI following spinal surgery has not been currently established.

As VAC is likely to find its place in postoperative SSIs in spinal surgery, it is imperative to review the current evidence regarding the use of VAC in this setting, taking into account recent advancements in therapy modalities.

VAC for secondary wound closure in spinal surgery

VAC has been previously established in the management of postoperative SSIs following spinal surgery, especially for cases with deep soft tissue defects or exposed hardware. VAC is based on the theory that negative pressure leads to an increase in skin perfusion [32]. The system is a closed one that applies negative pressure to the surface of the wound. It involves an open-cell foam dressing that fills the wound, an airtight adhesive drape, and a vacuum pump that creates and maintains negative pressure. An optimal negative pressure of 125 mmHg has been shown to allow the formation of granulation tissue without compromising perfusion to the wound [25,28]. The airtight seal also ensures stability of the wound environment and prevents bacterial colonization. There has not been a consensus on the exact mechanism in which VAC affects wound healing. Theorized mechanisms include VAC being able to remove third-space fluid from wound areas, in turn resulting in a decrease in tissue turgidity and capillary afterload, promoting improved capillary circulation and local oxygenation [33,34]. Various experimental studies have also shown that VAC reduces the overall bacterial load in the wound and the potential for bacterial colonization. VAC has also been shown to exert contractile forces that promote the approximation of wound edges [29]. The microdeformation caused by the collapse of the wound edges into the wound dressing by the negative pressure environment has also been thought to promote wound healing through inhibition of apoptosis, promotion of cellular proliferation, and stimulation of angiogenesis [8].

VAC has been applied successfully in a wide variety of wounds undergoing secondary healing. Ploumis et al. [35] showed in their retro-

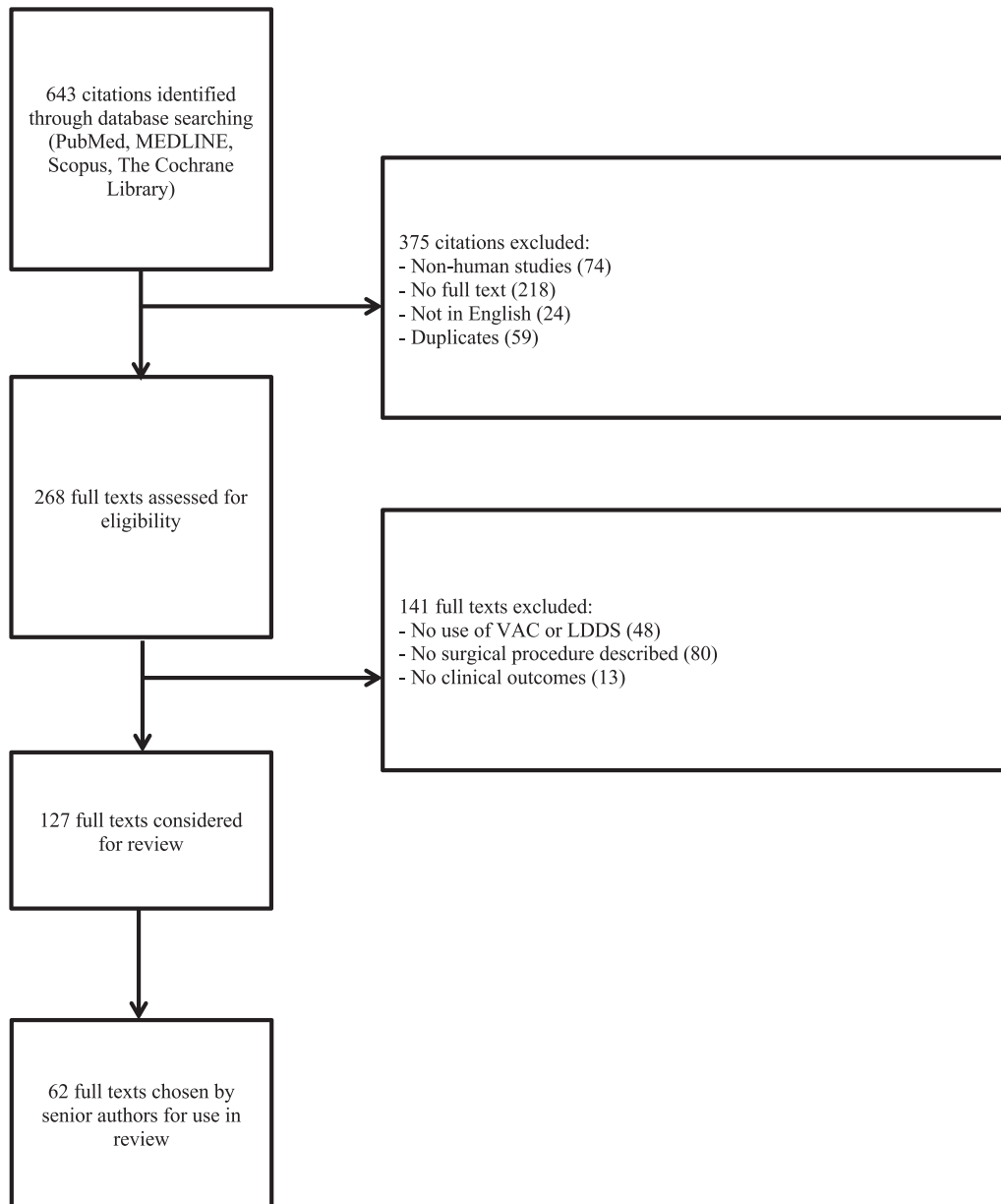


Figure. Flow diagram of the review and selection of cases.

spective review that VAC was an effective adjunct treatment in degenerative spinal surgery and spine tumor surgery for closing spinal wounds even after repeated debridement procedures. Van Rhee et al. [36] also published a prospective case series that demonstrated the utility of VAC in the pediatric scoliosis population. VAC has also been demonstrated to allow for preservation of hardware after SSIs, reducing the overall cost and morbidity associated with hardware removal [26,37]. However, it is notable that patients with mixed pathogen growth in their wound culture required a significantly greater number of revision surgeries before definitive wound healing. Knowing this can in turn help guide patient's expectations before surgery and allow the surgical team to plan ahead on the aggressiveness of debridement required. VAC is also advantageous for use in large wounds as they are able to stimulate granulation tissue in the wound bed, before secondary closure or fitting of a reconstructive graft for definitive wound closure [38,39].

This directly demonstrates VAC's utility and versatility in various aspects of spinal surgery, especially in cases where SSI wounds are large and not amenable to primary closure.

Use of VAC for prophylaxis of SSIs after primary wound closure

In recent years, ciVAC has been introduced as prophylaxis for SSIs postspinal surgery. Prior literature has established the use of ciVAC in other aspects of orthopedic surgery such as in lower limb trauma or total joint arthroplasty to reduce the risk of SSIs postsurgery [40,41]. Studies have shown that VAC provides increased wound perfusion, mechanical properties, and tensile strength when applied to closed surgical wounds [28].

Closed surgical wound healing is a major challenge in certain high-risk groups of spine surgery patients. This includes patients who have posterior open surgery across the cervicothoracic junction, thoracic kyphosis due to metastatic disease, high-energy trauma, or multilevel revision reconstruction surgery [19]. Dyck et al. [19] demonstrated in their retrospective proof of concept study that such high-risk patients who underwent ciVAC had up to 50% reduction in the rate of SSI after spine surgery as compared with regular dressings. The use of ciVAC is also supported by Adogwa et al. [42] who showed in their retrospective cohort study that ciVAC significantly reduced the incidence of postoper-

active wound infection (10.63 % vs. 14.91 %; $p=.04$), wound dehiscence (6.38% vs. 12.28%; $p=.02$), and reoperation rates for patients undergoing long-segment spine fusions for idiopathic scoliosis. More recently, Mehkri [43] showed in his study that the use of ciVAC resulted in a two-fold decrease in SSI, with mean infection-related cost savings of \$163,492 per 100 patients.

The effectiveness of ciVAC has since been reinforced by a recent meta-analysis done by Chen et al. [44] that showed that ciVAC was able to significantly reduce postoperative SSI in spinal fusion surgery (OR: 0.399; 95% CI: 0.198, 0.802). However, Naylor et al. [45] reported in their study that ciVAC usage in select high-risk patients after taking into account their medical comorbidities, surgical approach, and diagnosis resulted in no significant difference in the incidence of wound dehiscence or SSI compared with the non-ciVAC group (5.7% vs. 5.6%; $p=.03$). The use of ciVAC is also not without increased costs and appropriate patient selection is paramount to justify these costs [46]. Mueller et al. [46] showed in their prospective study that the overall SSI rate was significantly lower with ciVAC dressing as compared with the standard dressing (3.4 vs. 10.9%, $p=.02$). However, there was no statistical difference in infection rate for decompression alone procedures on subgroup analysis when ciVAC was used (4.2 vs. 9.1%; $p=.63$), compared with when ciVAC was used in those who underwent instrumentation (3.2 vs. 11.4%; $p=.03$). This correlates with the analysis by Cizik et al. [47] that the complexity of the surgery, which can be interpreted through the spine surgical invasiveness index (SSII), is a significant risk factor for postoperative SSIs.

Taking into account the above factors, ciVAC may be a valuable asset for higher-risk procedures such as those with instrumentation, but clear evidence is yet to appear to support the blanket use of ciVAC in spine surgery. The SSII can also be considered for use preoperatively to guide the selection of patients who potentially require ciVAC postoperatively, if their SSII scores are high. This prevents unnecessary costs from being incurred by patients who are undergoing routine spine surgery.

Potential complications of use of VAC

VAC has indeed shown clear advantages in reducing and managing SSIs postspinal surgery. However, they are not without potential complications. Jones et al. reported two cases of hemorrhage during VAC placement in his cohort, highlighting that VAC should be used in caution in patients with spine injuries or bleeding diathesis due to risk of increased bleeding or failure of primary closure [48]. VAC is also contraindicated for use in the presence of malignant tumor in the wound, exposed neurovascular structures or presence of necrotic tissue with eschar [49]. Hence, the use of VAC in spinal wounds with exposed dura was also a controversial topic due to concerns of cerebrospinal fluid leak or dural tears. However, several recent studies [26,39,50] have shown the safety and efficacy of VAC even in wounds with exposed dura. Importance should be placed on a watertight dural closure before initiation of VAC therapy [50]. Incorporating the usage of VAC whitefoam [26,39] and reduced pressures [26,50] have also shown to be able to allow wound healing even in cases with exposed dura, as long as the dura is closed appropriately without any subsequent CSF leak.

Recommendation on VAC

We recommend that VAC can be used for SSIs postspinal surgery, especially when the wound defects are large, as it is able to address varying wound defect sizes and shapes. Patient-related (age, diabetes, obesity, malnutrition, and malignancy) and procedure-related (deformity correction, multiple surgical levels, instrumentation, and blood loss) factors can increase a patient's risk for developing an SSI [51,52,53] and should be taken into consideration when planning for the use of ciVAC as prophylaxis after primary closure. ciVAC should, however, not be used

routinely, as there has yet to be robust cost benefit analysis regarding its usage and may in turn result in greater cost burden to the patient without any added clinical benefits.

Local drug delivery systems (LDDS)

LDDS allows high drug concentrations to be achieved at the site requiring anti-microbial action, reducing the risk of systemic exposure and toxicity [54]. Various factors have to be considered for LDDS to be applied successfully in clinical practice, including but not limited to: antimicrobial spectrum; release properties from chosen delivery systems; solubility; as well as local and systemic toxicity [54,55]. Antibiotic bone cement (ABC) has been used in both trauma and arthroplasty subspecialties of orthopedic surgery as a successful LDDS for treatment of SSI [56]. Polymethylmethacrylate (PMMA) has also been established as a suitable vector for delivery of antibiotics as heat generated by curing bone cement has shown to have negligible effects on antibiotic concentration and activity [55]. The exothermic reaction of cement solidification in PMMA also provides additional thermal debridement and may increase the permeability of the biofilm to local antibiotic penetration [54]. However, the application of such LDDS in spinal surgery has still been limited.

For spinal infections that require surgery, various case series have described the use of antibiotic loaded calcium sulfate beads for the treatment of patients with spondylodiscitis [19,21]. Ramey et al. [22] also described the use of a PMMA strut graft as the LDDS in treatment of patients with spinal osteomyelitis. Gentamicin, tobramycin, vancomycin, and clindamycin are the most widely used in ABC [20,57]. Gentamicin and tobramycin covers for gram negative bacteria whereas vancomycin and clindamycin covers for gram positive bacteria. They are commonly used in combination with antibiotic bone cement to allow for broad spectrum antimicrobial cover. However, gentamicin has recently been shown to have slightly higher degradation with heat and should be avoided in use with ABC if possible [58]. Tang et al. [20] used a mixture of ABC with 0.5 g of vancomycin hydrochloride with cefoperazone and sulbactam sodium for both gram positive and gram-negative coverage respectively. In their study, antibiotic loaded calcium sulfate beads were described to be safe in managing spondylodiscitis.

In terms of SSI prophylaxis, the use of vancomycin powder intraoperatively has been currently established as the gold standard for use in instrumented spine surgery to reduce rates of SSI [58]. Hey et al. [58] showed in his paper that there was a statistically significant reduction in postoperative SSIs in the group treated with vancomycin as compared with the group without (0.9% vs. 6.3%, $p=.049$). A meta-analysis done by Luo et al. [59] also demonstrated the significant reduction in postoperative SSIs in posterior spinal surgery when vancomycin powder was used intra-operatively.

The role of CSIS

Various groups have since also introduced the concept of CSIS as a drug delivery system, but there has yet to be a consensus regarding the application of these LDDS in current clinical practice. Rohmiller et al. [60] was the first to describe the technique of CSIS for use in SSIs after posterior spinal surgery involving instrumentation. The technique involves one inflow catheter containing sterile normal saline placed in the deep fascia in the cephalad portion of the wound and 2 to 3 outflow catheters placed in the superficial and deep fascia in the caudal portion of the wound. The overlying fascia, subcutaneous fat and skin are then closed securely over the suction system. The study established that CSIS allowed for complete healing of postoperative spinal SSI wounds post-debridement and primary closure. Even for cases in their cohort that had repeated SSI postindex debridement, serial CSIS was done after repeat debridement, which eventually resulted in complete resolution of infection without requiring any removal of implants.

Table
Algorithm on management of spinal infection.

Type of spinal infection	Treatment options
Superficial spinal infection	1st line: IV antibiotics, regular wound dressing 2nd line: Surgical debridement, keep in view VAC and/or LDDS depending on etiology as well presence of instrumentation
Deep or organ space involvement	1st line: Surgical debridement, VAC and/or LDDS depending on etiology as well presence of instrumentation

CSIS with VAC for secondary wound closure

Chen et al. [23] described the novel application of VAC with CSIS to treat SSIs in spinal surgery. In their study, normal saline was similarly used as the lavage fluid and replaced daily. The application of VAC with CSIS showed significant decrease in wound size from 23.5 to 13.2 cm² after 1 week of treatment. Average wound healing time and hospital stay of patients in this cohort was 17 and 33 days, respectively. This is comparable to previous studies which used only VAC for postoperative SSIs requiring secondary closure in spine surgery [35,61]. However, the wounds of patients undergoing CSIS may require more frequent dressing changes due to the moist environment, inadvertently increasing overall costs for the patient.

CSIS with ciVAC after primary wound closure

Shi et al. [62] studied the novel use of CSIS in addition to ciVAC for prophylaxis of early deep SSIs after primary wound closure. Like the previous CSIS studies prior, normal saline was used as the irrigation fluid, but the study also added 80 mg gentamicin for every 500 mL of normal saline used as a form of LDDS. Their cohort had a mean hospital stay of 30.4 days and all of the patients were cured of early deep SSI with implant retention.

CSIS in ciVAC is however not without potential complications. The continuous irrigation system restricts the patient's movement and ability to undergo physical rehabilitation postsurgery. Moreover, the irrigation fluid has a possibility of leaking from either the inflow or outflow tubes, causing the dressings to be wet and likely requires more frequent dressing change with an increased risk of infection.

Recommendation on LDDS

We recommend that vancomycin powder be used intra-operatively in all cases of spinal surgery as prophylaxis for SSIs. Currently, CSIS has been shown to be beneficial for wound healing in SSIs in spinal surgery and there has also been various case reports on novel techniques of LDDS use in tackling different primary spinal infections.

However, the current literature for LDDS are limited to small case series and there is still a lack of prospective comparative studies to establish the role of LDDS in wound healing. Regarding CSIS, there is also no evidence to show whether the irrigation fluid, combined with drug delivery has superior outcomes to that of without drug delivery. Taking this into account, the use of LDDS in spine surgery patients should be individualized based on each center's expertise. More prospective studies will have to be done to further establish the role of LDDS for wound management in SSIs postspinal surgery.

Algorithm on management

In this review, we also describe an algorithm that spine surgeons can adopt when managing spinal infections (Table).

Limitations

There is a wide variety of etiology of spinal infections, and treatment of spinal infections are also closely affected by the primary etiology. In this study, the discussion of LDDS is limited by the lack of high-quality

prospective studies comparing the various treatment modalities. Moreover, there is also bound to be heterogeneity in the paper due to the various etiology of spinal infections quoted in various literature.

Conclusion

VAC has been well established in the management of spinal infections and should be considered for routine use in cases of deep or organ space involvement whenever possible. The increase in use of VAC for prophylaxis of SSIs has to be weighed against its cost-effectiveness. We suggest the use of VAC for prophylaxis only in high-risk spine surgeries as discussed in our manuscript.

The use of LDDS in spinal infections has yet to be readily adopted in spine surgery and the literature has been limited to small case series. Further larger scale studies can be conducted to support the outcomes proposed in our manuscript. Nonetheless, we propose that vancomycin powder can be used in all cases of spine surgery for prophylaxis against SSI. ABC as a LDDS has also shown clear benefits in use for SSI and can be used effectively in SSIs. However, the use of the type of LDDS such as bone cement or CSIS should be dependent on each center's expertise. With the publication of this review highlighting its merits, the amount of evidence is bound to continue rising in the near future to guide the selection of type of LDDS in spinal infection.

As summarized in this manuscript, both VAC and LDDS have important utilities in the management of spine infection and should be in the armamentarium of any spine surgeon when tackling spine infections.

Declaration of Competing Interests

None

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2023.100266.

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