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Antibiotics and bacteriophage therapy in surgical site infection prevention and treatment: a structured evidence-mapping review with descriptive safety and outcome summaries

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Abstract:

Aim. Surgical site infection (SSI) remains a major postoperative complication and contributes to prolonged wound care, antibiotic exposure, antimicrobial resistance and healthcare costs. Bacteriophage therapy has re-emerged as a targeted antibacterial approach, but the available clinical literature includes very different contexts, ranging from routine antibiotic prophylaxis to salvage treatment of chronic, biofilm-associated or implant-related infections.

Materials and methods. This article is presented as a structured evidence-mapping review with descriptive safety and outcome summaries, not as a full systematic review or meta-analysis. A complete database screening log, duplicate-removal record, full-text exclusion list and prospectively documented PRISMA flow counts were not available. Therefore, the findings should be interpreted as an evidence map based on an extracted source set rather than as an exhaustive systematic synthesis of all available literature. Clinical sources were classified by clinical purpose: SSI prevention, treatment of established infection, chronic wound/diabetic foot infection and prosthetic joint/implant-associated infection. Outcomes were separated into negative prevention outcomes, such as SSI incidence, and positive treatment outcomes, such as wound healing, bacterial eradication or clinical resolution. Methodological confidence was considered according to study design using principles consistent with RoB 2, ROBINS-I, JBI checklists, AMSTAR 2 and GRADE.

Results. Antibiotic-only prophylaxis studies reported variable SSI or wound-infection rates, with a descriptive event summary of 11.17% in general-surgery prophylaxis. Phage evidence was concentrated mainly in treatment settings, where endpoints included infection resolution, eradication, reduced bacterial burden or wound healing. Phage-only chronic-wound studies showed an 80.9% descriptive success/healing/burden-reduction signal, whereas phage-only orthopedic evidence was based mainly on very small case reports or case series. One small phage-plus-antibiotic prophylaxis study reported 13.63% SSI in the intervention group. These descriptive summaries are not directly comparable across prevention and treatment categories and should not be interpreted as comparative efficacy estimates.

Conclusion. Antibiotic prophylaxis remains the most established approach for SSI prevention. Current clinical evidence suggests that bacteriophage therapy may be a promising adjunct for selected complicated, resistant or biofilm-associated infections, but its role in routine SSI prevention remains insufficiently defined. Available safety data indicate a generally favorable short-term tolerability signal, although this conclusion is limited by small samples, heterogeneous reporting and scarce standardized microbiome or resistance surveillance. Larger prospective controlled studies with reproducible search and reporting frameworks are needed before broad perioperative implementation can be recommended.

Keyword: Bacteriophages, Surgical Wound Infection, Antibiotic Prophylaxis, Anti-Bacterial Agents, Drug Resistance, Bacterial, Wound Healing.

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Introduction

Surgical site infection remains a clinically important postoperative problem because it increases morbidity, length of hospital stay, antibiotic exposure and healthcare costs. Standard perioperative antibiotic prophylaxis is effective in many surgical contexts; however, inappropriate agent selection, incorrect timing or unnecessarily prolonged use may contribute to adverse drug reactions and antimicrobial resistance. Complicated wound and implant-associated infections increasingly involve multidrug-resistant organisms and biofilm-related persistence, creating a clinical need for carefully evaluated adjunctive strategies.

Bacteriophage therapy has re-emerged as a targeted antibacterial approach, particularly in infections that are difficult to manage with conventional antibiotics alone. Phages can be applied topically, locally, intra-articularly, intravenously or in combination with antibiotics. The biological rationale is attractive because phages may target specific bacterial pathogens, including organisms embedded in biofilm. Nevertheless, the current clinical literature is heterogeneous: some studies address SSI prevention, while many phage publications describe salvage therapy for established, chronic or resistant infections.

The scientific gap addressed in this review is therefore not the general existence of phage literature, but the lack of a clinically structured map that separates prevention from treatment and interprets antibiotic-only, phage-only and phage-plus-antibiotic approaches through a common safety and resistance framework. This distinction is essential, because an SSI rate after a standardized operation cannot be directly compared with a wound-healing or bacterial-eradication rate in a chronic infection case series.

The aim of this revised review is to provide a structured evidence map and safety-oriented descriptive synthesis of clinical evidence on antibiotic-only, phage-only and phage-plus-antibiotic strategies, while explicitly distinguishing prophylactic SSI outcomes from treatment outcomes in established infection.

Materials and Methods

Review design

This manuscript was revised as a structured evidence-mapping review with descriptive safety and outcome summaries. It is not presented as a full systematic review or meta-analysis, because the complete database search log, duplicate-removal record, full-text exclusion list and prospectively documented PRISMA flow counts were not available in the extracted dataset. PRISMA 2020 principles informed transparent reporting, but no formal PRISMA flow diagram is included for this version. Therefore, the findings should be interpreted as an evidence map based on an extracted source set rather than as an exhaustive systematic synthesis of all available literature.

Review question

The guiding question was: In surgical patients or patients with surgical, chronic wound, diabetic foot, prosthetic joint or other complicated infections, what clinical outcomes and safety signals have been reported for antibiotic-only, phage-only and phage plus-antibiotic strategies?

Information sources and search concepts

The evidence map was based on the clinical sources already extracted for the manuscript and their cited bibliographic records. Search concepts were organized around four domains: surgical site infection, antibiotic prophylaxis or therapy, bacteriophage therapy, and safety or antimicrobial resistance. Core search terms included combinations of: surgical site infection, wound infection, antibiotic prophylaxis, bacteriophage, phage therapy, chronic wound, diabetic foot infection, prosthetic joint infection, implant-associated infection, antimicrobial resistance, adverse events and microbiome. Because the search was not prospectively logged with database-specific strings, the present review should not be regarded as an exhaustive or fully reproducible systematic search. For a future full systematic review, the same concepts should be converted into database-specific strings and prospectively logged across PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library and Google Scholar.

Eligibility criteria

Eligible sources included human clinical studies, comparative studies, randomized or non-randomized trials, systematic reviews, meta-analyses, case series, case reports and N-of-1 reports if

they provided extractable clinical outcome or safety information related to antibiotic-only, phage-only or phage-plus-antibiotic strategies. Eligible clinical fields included routine perioperative prophylaxis, SSI treatment, chronic or diabetic foot wound infection, prosthetic joint infection and mixed complicated infection.

Sources were excluded from the evidence synthesis if they were purely in vitro or animal studies, did not report clinical outcomes, did not describe an antibacterial intervention relevant to the review question, lacked extractable outcome or safety information, or were editorials without original or review-level clinical data.

Classification of prevention and treatment evidence

To address the main methodological concern, sources were classified by clinical purpose before synthesis. Prevention studies were those in which the outcome was SSI or postoperative wound infection after a defined operation or prophylactic exposure. Treatment studies were those in which patients already had chronic, complicated, implant-associated or resistant infection and the reported outcome was clinical resolution, wound healing, bacterial eradication, reduced bacterial burden, recurrence-free survival or ongoing infection. Chronic wound/diabetic foot and prosthetic joint/implant-associated studies were additionally analyzed as separate clinical subgroups.

Data extraction and outcome direction

Extracted variables included study/source, year, clinical setting, design type, intervention class, sample size when available, comparator when available, endpoint definition, event count, reported rate, adverse events, serious adverse events and resistance or microbiome signals. Outcomes were not merged as equivalent effects unless they had the same clinical direction. Negative prevention outcomes included SSI or wound infection. Positive treatment outcomes included wound healing, bacterial eradication, clinical resolution or bacterial-burden reduction. Ongoing infection, recurrence or failure were treated as negative treatment outcomes.

Methodological quality and certainty approach

Because the included sources represented different designs, quality was assessed narratively rather than by a single numerical score. Randomized studies were interpreted using RoB 2 principles; non-randomized comparative studies using ROBINS-I principles; case reports and case series using JBI checklist principles; and systematic reviews or meta-analyses using AMSTAR 2 principles. Overall certainty was summarized using GRADE logic, considering design, consistency, directness, precision and publication bias. The rating was not used to exclude studies, but to guide interpretation.

Synthesis strategy

Formal comparative meta-analysis was not performed because of substantial clinical and methodological heterogeneity. Instead, descriptive event summaries were calculated within clearly defined subgroups and interpreted alongside source design, endpoint direction, publication status and methodological confidence. The term “descriptive event summary” in this manuscript refers only to pragmatic aggregation within an evidence category and should not be interpreted as a formal comparative effect estimate. Prevention endpoints and treatment-success endpoints were not combined as equivalent outcomes.

Results

Evidence base and study selection

Twenty-four sources were included in the extracted evidence base. These sources covered antibiotic prophylaxis, phage-only therapy, phage-plus-antibiotic therapy, chronic wound/diabetic foot infection, prosthetic joint infection, emergency abdominal surgery and other complicated infections. Because screening counts were not available, the selection process is described narratively rather than as a PRISMA flow diagram. Publication status and evidence type were added to Table 1 to distinguish peer-reviewed studies, reviews, case reports, case series, reporting guidance and preprint evidence.

Table 1. Characteristics of the included evidence sources

Source	Clinical setting / design	Intervention and comparator	Endpoint used in this review	Methodological comment	Publication status / evidence type
Marni et al., 2020 [1]	Cesarean/postoperative wound infection; comparative prophylaxis study	Cefazolin/ceftriaxone timing strategies	Postoperative wound infection / SSI	Prevention evidence; useful for SSI-rate mapping but procedure-specific.	Peer-reviewed comparative prophylaxis study
Mushtaq et al., 2021 [2]	Cesarean section; prophylactic antibiotic timing	Preoperative versus postoperative antibiotic timing	Wound infection rate	Prevention evidence; contextual heterogeneity limits transferability.	Peer-reviewed comparative prophylaxis study
Rubalskii et al., 2020 [3]	Cardiothoracic surgery-related critical infections; case series	Individualized phage therapy, often with antibiotics	Infection resolution / eradication	Treatment evidence; small uncontrolled sample.	Peer-reviewed case series
Simpson et al., 2023 [4]	Cardiac and peripheral vascular infections; systematic review	Phage therapy across vascular/cardiac contexts	Resolution, safety and eradication signals	Review-level evidence; heterogeneous included studies.	Peer-reviewed systematic review
Migliorini et al., 2025 [5]	Hip/knee prosthetic joint infection; review/analysis	Phage therapy with or without antibiotics	Ongoing infection / clinical success	Treatment evidence; endpoint definitions vary.	Peer-reviewed review / analysis
Vasu and Sagar, 2018 [6]	Clean surgery prophylaxis; randomized comparative trial	Single-dose ceftriaxone versus postoperative ciprofloxacin/metronidazole	Postoperative wound infection and minor ADRs	Prevention evidence with direct clinical comparator.	Peer-reviewed randomized comparative trial
Narayanasamy et al., 2020 [7]	XDR Pseudomonas limb-threatening infection; case report	Antibiotics, drug monitoring and debridement	Clinical cure and nephrotoxicity signal	Treatment evidence; not SSI prophylaxis.	Peer-reviewed case report
LaVergne et al., 2018 [8]	MDR Acinetobacter craniectomy site infection; case report	Phage therapy in severe infection	Clinical response and tolerability	Very low-certainty treatment evidence.	Peer-reviewed case report
Nath, 2025 [9]	Pan-drug-resistant Klebsiella PJI; case report	Phage therapy	Clinical response / safety	Very low-certainty treatment evidence; single case.	Case report; peer-review status to verify before submission
Doub et al., 2022 [10]	Recalcitrant PJI; case series	Adjunctive phage plus antibiotics	Clinical outcome and adverse events	Low-certainty uncontrolled treatment evidence.	Peer-reviewed case series
Dedrick et al., 2019 [11]	Disseminated drug-resistant Mycobacterium infection; N-of-1	Engineered bacteriophages	Microbiological and clinical response	Mechanistically important but indirect to SSI prevention.	Peer-reviewed N-of-1 / case report
Parshin et al., 2023 [12]	Emergency abdominal surgery; prophylaxis	Polyvalent bacteriophages plus standard management versus comparison	SSI incidence	Small prevention study; important but requires replication.	Clinical study; peer-review status to verify before submission
Duplessis and Biswas, 2020 [13]	Chronic wounds/diabetic foot; review and trial preparation	Topical phage therapy	Healing and bacterial-burden outcomes	Treatment-oriented; not directly comparable with SSI prevention.	Peer-reviewed review and trial-preparation article
Sadigursky et al., 2019 [14]	Orthopedic surgery; systematic review/meta-analysis	Intrawound vancomycin powder versus control	SSI events	Prevention evidence; antibiotic-based local prophylaxis.	Peer-reviewed systematic review / meta-analysis

Cammuso et al., 2025 [15]	Life-threatening PJI; N-of-1/preprint	Phage therapy adjunct or salvage	Clinical outcome / safety	Preprint and single-patient evidence; interpret cautiously.	Preprint / N-of-1; not peer-reviewed at time of citation
Schoeffel et al., 2022 [16]	MRSA knee/hip PJI; case report	Salvage phage therapy	Recurrence-free survival / clinical resolution	Very low-certainty treatment evidence.	Peer-reviewed case report
Kanikovskyi et al., 2025 [17]	Wound infection; clinical experience	Bacteriophages in complex treatment	Bacterial-burden reduction / wound outcome	Treatment evidence; endpoint differs from SSI incidence.	Clinical experience article; peer-review status to verify before submission
Young et al., 2023 [18]	Diabetic foot infection; case series	Phage therapy, often adjunctive	Clinical response and absence of reported adverse effects	Small treatment subgroup.	Peer-reviewed case series
Parshin et al., 2023 [19]	Emergency abdominal surgery complications; treatment	Polyvalent bacteriophages as adjunct	Resistant isolate detection and clinical treatment signals	Treatment evidence; SSI counts not consistently extractable.	Clinical study; peer-review status to verify before submission
Groenen et al., 2024 [20]	Incisional wound irrigation; systematic review/network meta-analysis	Wound irrigation strategies including antibiotics	SSI prevention and resistance concerns	Prevention evidence; indirect to phage therapy.	Peer-reviewed systematic review / network meta-analysis
Ali et al., 2023 [21]	General/plastic surgery; review	Antibiotic prophylaxis and alternatives	Current practices and resistance concerns	Narrative/review evidence; broad context.	Narrative review; peer-review status to verify before submission
Fedorov et al., 2023 [22]	Periprosthetic hip infection; clinical study	Phage-antibiotic combination	Short-term outcome and reversible adverse events	Treatment evidence; relatively focused but non-routine prophylaxis.	Peer-reviewed clinical study
Ramirez-Sanchez et al., 2021 [23]	Staphylococcus aureus PJI; case report	Bacteriophage therapy with antibiotics	Clinical and microbiological outcome	Very low-certainty treatment evidence.	Peer-reviewed case report
Page et al., 2021 [24]	Reporting guideline	PRISMA 2020 statement	Reporting framework	Methodological guidance, not clinical outcome evidence.	Reporting guideline / methodological statement

Methodological quality and certainty of evidence

The evidence base was methodologically uneven. Antibiotic prophylaxis was supported by more conventional perioperative studies and systematic reviews, whereas most phage evidence came from case reports, case series, N-of-1 trials or small non-randomized cohorts in severe or salvage contexts. For this reason, high apparent success rates in phage-only treatment studies should be interpreted as hypothesis-generating rather than as proof of comparative superiority.

Prevention evidence: SSI and wound-infection incidence

Prevention evidence should be interpreted separately from treatment evidence. In prevention studies, the unfavorable event is SSI or postoperative wound infection. Antibiotic-only prophylaxis remains the best-established preventive approach, although reported rates vary widely by procedure, patient risk, timing, agent and local infection-control context. Descriptive percentages in this section are not directly comparable with treatment-success outcomes from chronic wound, diabetic foot or implant-associated infection studies.

Table 2. Narrative quality and certainty assessment

Evidence category	Main designs	Quality framework applied	Overall certainty	Reason for rating
Antibiotic-only SSI prophylaxis	Randomized or comparative prophylaxis studies; systematic reviews/meta-analyses	RoB 2 / ROBINS-I / AMSTAR 2 principles	Moderate, but procedure- and regimen-dependent	Directly relevant to SSI prevention, but heterogeneous across operations and antibiotic protocols.
Phage-plus-antibiotic SSI prophylaxis	One small prophylaxis-oriented clinical study	ROBINS-I / design-based appraisal	Low	Potentially relevant to SSI prevention but limited by single-study evidence and small denominator.
Phage-only treatment of chronic or complicated infections	Case reports, case series, review syntheses	JBI checklist / AMSTAR 2 principles	Low to very low	Useful for feasibility and safety signals; high risk of selection and publication bias.
Phage-plus-antibiotic treatment of PJI or complicated SSI	Case series, observational studies, case reports	ROBINS-I / JBI principles	Low	Clinically relevant for salvage therapy; limited standardization of routes, dosing and co-interventions.
Microbiome and resistance outcomes	Inconsistently reported across designs	GRADE logic for indirectness and imprecision	Very low	Most conclusions remain inferential because direct microbiome monitoring was rarely performed.

Table 3. Prevention studies: SSI and wound-infection outcomes

Clinical field	Intervention class	Studies / N / events	Descriptive event summary	Interpretation
General surgery prophylaxis	Antibiotic only	17 / 22,544 / 2,519	11.17% SSI or wound infection	Negative prevention outcome: event = infection. Individual examples ranged from 0% postoperative infection to 28.4% wound infection [1,2].
General surgery / emergency abdominal prophylaxis	Phage plus antibiotic	1 / 44 / 6	13.63% SSI	Negative prevention outcome: single small study; comparison group had 31.81% SSI, but replication and standardized safety reporting are limited [12].
Orthopedic surgery prophylaxis	Antibiotic/local antibiotic strategy	2 / 3,131 / 65	2.08% SSI	Negative prevention outcome: topical vancomycin powder example reported 64/3,131 SSI events versus 144/3,839 controls, but pathogen-pattern shifts require attention [14].

Treatment evidence: healing, eradication, resolution or ongoing infection

Treatment evidence refers to patients who already had infection. These studies often report favorable outcomes such as wound healing, infection resolution or bacterial eradication. Such positive

outcomes should not be numerically compared with SSI incidence from prophylaxis studies, because the direction and clinical meaning of the endpoint are different.

Table 4. Treatment studies: clinical resolution, eradication, healing or ongoing infection

Clinical field	Intervention class	Studies / N / events	Descriptive treatment summary	Interpretation
Orthopedic PJI / implant-associated infection	Phage only	6 / 6 / 5	83.3% favorable outcome	Positive treatment outcome; based on very small case-report/series evidence and endpoints such as healing or cessation of drainage [15,16].
Orthopedic PJI / implant-associated infection	Phage plus antibiotic	15 / 91 / 20	22.0% unfavorable/ongoing infection signal in extracted field	Endpoint definitions varied; one 53-patient analysis reported ongoing infection in 4/53 (7.5%) [5].
Diabetic foot and chronic wound infection	Phage only	4 / 299 / 242	80.9% healing or bacterial-burden reduction	Positive treatment outcome; includes 242/273 partial or complete wound healing in one component study [17].
Diabetic foot and chronic wound infection	Phage plus antibiotic	1 / 10 / 9	90% favorable outcome	Positive treatment outcome; single small subgroup, and safety reporting emphasized absence of adverse effects [18].
Mixed or other complicated infection	Phage only	3 / 46 / 33	71.7% infection resolution/eradication signal	Positive treatment outcome; influenced by small case series and review-level syntheses [3,4].
Mixed or other complicated infection	Phage plus antibiotic	2 / 129 / 86	Not reliable for SSI pooling	Treatment evidence supports adjunctive use, but SSI event counts were not consistently extractable [19].

General surgery prophylaxis

In general surgery prophylaxis, antibiotic-only studies showed wide variability in SSI or wound-infection outcomes. One report described 0% postoperative infection across different ceftriaxone/cefazolin timing strategies, whereas another cohort reported 28.4% wound infection in the overall population [1,2]. This range reflects major differences in operation type, patient risk, timing, definitions and local context.

A single phage-plus-antibiotic prophylaxis study reported fewer SSIs in the phage-supplemented group (6/44, 13.63%) than in the comparison group (14/44, 31.81%) and described a tendency toward normalization of microbial patterns [12]. However, this evidence is based on one small study and cannot establish routine phage prophylaxis. Replication in prospective trials with standardized SSI definitions, adverse-event monitoring, microbiome assessment and resistance surveillance is required.

Orthopedic prosthetic joint and implant-associated infections

Orthopedic prophylaxis evidence included antibiotic-based local preventive strategies, such as intrawound vancomycin powder, with 64 (2.04%) SSI events in an intervention group versus 144 (3.75%) in controls [14]. These data address prevention rather than treatment of established PJI.

In contrast, phage-only and phage-plus-antibiotic orthopedic reports usually involved patients with established, difficult-to-treat or recurrent PJI. Reported outcomes included clinical resolution,

recurrence-free survival, cessation of drainage, bacterial eradication or ongoing infection [5,15,16, 22,23]. The apparent success in some reports is clinically important, but the certainty remains low because many publications are uncontrolled case reports, case series or N-of-1 experiences.

Diabetic foot and chronic wound infection

In chronic wound and diabetic foot infection, phage therapy was used mainly as treatment rather than prophylaxis. One component study reported partial or complete wound healing in 242/273 patients (89%), while another described bacterial-burden reduction below a clinically relevant threshold in the main group [13,17]. These outcomes reflect wound management and microbial control in already established disease, not SSI prevention after a standardized operation.

For phage-plus-antibiotic chronic-wound evidence, one small subgroup suggested favorable clinical outcomes and did not report adverse effects [18]. The small denominator and incomplete standardization of outcome definitions limit the strength of inference.

Safety, microbiome and resistance signals

Table 5. Safety, microbiome and resistance signals by intervention class

Intervention class	Common adverse events	Serious adverse events	Microbiome / resistance signal	Safety interpretation
Antibiotic only	Minor rash and nausea/vomiting in one prophylaxis study [6].	Colistin-associated nephrotoxicity was described in a treatment case report, with creatinine increase and improvement after dose reduction [7].	Direct microbiome outcomes were rarely measured; resistance concerns were noted for commonly used antibiotic classes and wound-irrigation practices [20, 21].	Safety is agent-, dose- and patient-dependent; stewardship remains essential.
Phage only	Usually absent, mild or transient; examples included localized allergic symptoms, mild febrile reaction, mild transaminitis or brief hypotension [8,9,13,16].	Severe events were not clearly attributable to phages in the extracted excerpts; severe underlying disease often confounded interpretation [8].	Direct microbiome outcomes were rarely measured. Phage resistance was reported in a subset of non-responders in one synthesis; other case reports described preserved sensitivity [3,4, 11].	Available data suggest favorable short-term tolerability, but evidence is mostly low-certainty.
Phage plus antibiotic	Reported signals included reversible liver-function test elevation, fever/chills and transient administration reactions [5,10,15,22].	Serious phage-attributed toxicity requiring withdrawal was not consistently described; some systemic reactions were reversible [10,22].	Microbiome disruption was rarely directly reported. One phage-supplemented group showed lower antibiotic-resistant isolate detection at day 7 [19,23].	Promising adjunctive safety signal, but systematic monitoring is needed.

Mixed and other complicated infections

Mixed complicated infections included cardiothoracic, vascular, transplant, biofilm-associated and other recalcitrant infections. Examples included 70.3% infection resolution among evaluable cases and complete eradication of target bacteria in 7/8 patients in an individualized phage series [3,4]. These findings support the feasibility of phage therapy in selected severe infections but remain indirect for routine SSI prevention.

In emergency abdominal surgery complications, adjunctive polyvalent phage therapy was associated with differences in resistant isolate detection during follow-up, but extractable SSI event counts were not consistently available [19]. Therefore, these data are better interpreted as treatment and resistance-ecology signals rather than as definitive SSI-prevention evidence.

Discussion:

This revised evidence map highlights a central methodological issue: antibiotic-only prophylaxis studies and many phage studies answer different clinical questions. Antibiotic prophylaxis studies usually evaluate the prevention of SSI after a defined operation, whereas phage studies commonly describe treatment of established, complicated, resistant or biofilm-associated infection. Therefore, descriptive percentages in this review are useful for mapping evidence but should not be interpreted as direct comparative efficacy estimates. The evidence map is based on an extracted source set and should not be read as an exhaustive systematic synthesis of all available literature. The most clinically mature evidence remains antibiotic prophylaxis for SSI prevention. However, antibiotic use requires stewardship because benefits depend on agent selection, correct timing, dose, duration, local microbiology, renal function and surgical risk. The review also shows that antibiotic adverse effects range from minor postoperative symptoms to clinically important toxicity in treatment contexts [6,7]. Bacteriophage therapy appears most clinically developed as an individualized adjunct for selected complicated infections, including PJI, chronic wounds and multidrug-resistant infections. Available reports suggest possible benefit in infection resolution, wound healing, bacterial eradication and reduction of bacterial burden. Nevertheless, many of these data are derived from uncontrolled case reports, case series or small observational experiences, which are vulnerable to selection bias, publication bias and confounding by concurrent antibiotics or surgery. Safety conclusions also require caution. The available data point toward a favorable short-term tolerability profile, but reporting is not standardized and denominators are often small. Preprints, case reports and single-center clinical experiences were retained for mapping purposes but interpreted with lower methodological confidence than controlled or review-level evidence. Future studies should prospectively record adverse events, infusion or local reactions, liver and renal function, inflammatory response, microbiome change, emergence of phage resistance and bacterial resistance to antibiotics. For clinical practice, the current evidence supports phage therapy as a potential adjunct in carefully selected complicated, resistant or biofilm-associated infections, preferably with microbiological confirmation, phage-susceptibility testing and multidisciplinary oversight. The evidence does not yet support replacing standard perioperative antibiotic prophylaxis with phage therapy in routine surgery.

Limitations

- The review was based on an extracted evidence dataset; complete database search records, screening counts and full-text exclusion reasons were not available.
- The evidence base combines different clinical purposes, including SSI prevention and treatment of already established infection; these categories were separated in the revised synthesis, but residual heterogeneity remains.
- Descriptive event summaries combine studies with different definitions, routes of administration, dosing schedules, pathogens, surgical contexts and follow-up durations.
- Much phage evidence comes from case reports, case series and N-of-1 experiences, which may overestimate benefit because of selection and publication bias.
- Microbiome outcomes, phage-resistance emergence and antibiotic-resistance ecology were inconsistently measured, limiting firm conclusions about collateral ecological effects.
- Several references include preprint or early clinical evidence; such sources should be interpreted cautiously and updated before final journal submission if newer peer-reviewed versions become available. Publication status was added to the evidence table, but journal peer-review status should be rechecked before final submission, especially for preprint and 2025 sources.

Conclusions

Antibiotic prophylaxis remains the best-established strategy for SSI prevention. Bacteriophage therapy, alone or combined with antibiotics, shows promising treatment signals in selected complicated wound, implant-associated and chronic infections. However, these treatment outcomes should not be interpreted as equivalent to SSI-prevention rates. Available safety evidence suggests a generally favorable short-term tolerability profile for phage-based interventions, but this conclusion is limited by small samples, heterogeneous study designs, inconsistent adverse-event reporting and the inclusion of some preprint or very low-certainty case-based evidence. Prospective controlled

trials with standardized SSI definitions, microbiological endpoints, phage-susceptibility testing, resistance surveillance, adverse-event monitoring and microbiome assessment are required before broad perioperative implementation can be recommended.

Authors' contribution

Nilufar Saidmurodova: conceptualization, methodology, data curation, evidence synthesis, original draft preparation and manuscript revision. Sur'at Gulyamov: supervision, scientific validation, critical review and editing. Both authors approved the final version of the manuscript.

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Ethics approval

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Consent for publication.

Not applicable.

Data Availability Statement

No new datasets were generated during this review. Extracted summary data used for the descriptive synthesis are presented in the tables and references of this manuscript.

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Conflict of interest

The authors declare no conflicts of interest.

Abbreviations

SSI	Surgical site infection
PJI	Prosthetic joint infection
MRSA	Methicillin-resistant Staphylococcus aureus
VRSA	Vancomycin-resistant Staphylococcus aureus
ADR	Adverse drug reaction
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
GRADE	Grading of Recommendations Assessment, Development and Evaluation
JBI	Joanna Briggs Institute

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