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# Awareness and potential utilization of bacteriophages for therapeutic purposes among doctors in Saudi Arabia

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## ABSTRACT

Antimicrobial resistance (AMR) presents a significant global health challenge, necessitating alternative therapeutic strategies beyond conventional antibiotics. Phage therapy offers a promising alternative due to its high specificity for bacteria, ability to access complex infection sites, minimal off-target effects, and synergistic potential with antibiotics. This study aims to evaluate the awareness and possible adoption of phage therapy among doctors in Saudi Arabia to inform future research and its clinical integration. An anonymous online survey was distributed via email by the Saudi Commission for Health Specialties (SCFHS) and further promoted through local networks of clinicians. The inclusion criteria include active doctors who are working in Saudi Arabia and registered with the SCFHS. The survey yielded 102 valid responses from over 20 specialties and subspecialties. Results revealed doctors' significant concerns about AMR's impact on their practice and a moderate familiarity with phage therapy. Key pathogens identified for phage therapy included methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas*, *Klebsiella*, *Escherichia coli*, *Mycobacterium*, and *Streptococcus* species. Priority clinical conditions were infections in immunocompromised patients, diabetic foot infections, blood infections, and infective endocarditis. Despite limited awareness of AMR alternatives, there was optimism about phage therapy's future role. Enhancing research, development, and access to phage therapy could provide major clinical and economic benefits.

**Keywords:** Antibiotic resistance, bacteriophages, phage therapy, antibiotic alternatives, doctor awareness

## INTRODUCTION

Bacteriophages, or phages, are viruses that can specifically target and destroy bacteria with no threat to human cells. The term "bacteriophage" originates from the Greek words "bakterion" (bacterium) and "phagein" (to eat), literally meaning "bacteria eater".[1,2] Their discovery is attributed to both Frederick W. Twort (1915) and Félix d'Herelle (1917), with independent observations occurring around the same time. The work of these researchers provided evidence for the therapeutic potential of phages against bacterial infections in both humans and animal models.[3-5]

Despite its promising early results, phage therapy faced decline in Western countries following the mid-20th century, while its clinical application persisted in certain regions of the former Soviet Union,

particularly Georgia, Poland, and Russia.[6] The clinical introduction of penicillin in the 1940s ushered in the antibiotic era, marking a turning point in antimicrobial therapy. Since then, antibiotics have become the cornerstone of modern medicine for both preventing and treating infectious diseases. This widespread adoption of antibiotics eclipsed phage therapy as a viable treatment option, relegating it to the periphery of medical research for several decades.[6-8]

However, antimicrobial resistance (AMR) emerged as a critical global health crisis, not only by prolonging illnesses and increasing deaths, but also by escalating healthcare costs. The selective pressure imposed by the widespread and inappropriate use of antibiotics has driven the emergence of AMR bacteria.[9-11] This occur when bacteria evolve mechanisms to counteract the effects of antibiotics, rendering them ineffective.[12] It exacts a significant human cost, contributing to nearly 5 million deaths every year and potential escalation to 10 million deaths by 2050.[13] Furthermore, the discovery of new antibiotic classes has slowed in recent decades, significantly increasing the challenge, as no new class of antibiotics has been introduced since 1970s.[14] This highlights the immediate necessity for developing alternative therapeutic approaches to mitigate the impact of antibiotic resistance.

As the limitations of antibiotics become more apparent, phage therapy is re-emerging as a viable treatment strategy. The unique biological attributes of phages make them promising therapeutic candidates for addressing bacterial infections.[15,16] Unlike broad-spectrum antibiotics, phages are highly specific by which they can target specific harmful bacteria without harming the commensal microbiota.[17] Although phage resistance can arise, their narrow host range can limit the development of widespread phage resistance as bacteria must undergo specific genetic adaptations to evade phage infection. Nevertheless, phages can evolve rapidly in response to bacterial resistance, producing new phage variants capable of re-infecting resistant bacterial strains again. This co-evolutionary process can potentially maintain the effectiveness of phage therapy over time.[18-20] Additionally, the combination of phages and antibiotics can enhance the antibacterial efficacy through synergistic effects, reducing the likelihood of bacterial resistance during treatment.[21] Moreover, phages often demonstrate superior penetration of bacterial biofilms compared to antibiotics, offering a potential advantage in treating established infections and reducing the need for complex and multidisciplinary treatment regimens.[22,23]

Despite the global resurgence of interest in phage therapy as a potential weapon against multidrug-resistant (MDR) pathogens, its use in the Middle East, including Saudi Arabia, remains limited.[24] In contrast to countries like the US and those in Eastern Europe that have explored phage therapy for compassionate use and even commercially, Saudi Arabia lacks a regulatory framework and clinical experience with this approach.[6,24] Therefore, this research assessed the awareness and potential utilization of phage therapy among doctors in Saudi Arabia. Understanding the current knowledge base of healthcare professionals will be crucial for developing a future roadmap for phage therapy research and implementation in the Kingdom. The findings of this study could inform the development of strategies to promote the adoption of phage therapy as a viable treatment option in Saudi Arabia.

## MATERIALS AND METHODS

### Research setting and participants

This study employed a cross-sectional design to assess the awareness and potential use of phages as a therapeutic option among doctors in Saudi Arabia. The survey instrument was adapted from previously published tools to align with the unique context of Saudi Arabian healthcare professionals.[25,26] Inclusion criteria: Active practitioners working in Saudi Arabia who are registered with the Saudi Commission for Health Specialties (SCFHS). Exclusion criteria: Non-active doctors, those not practicing in Saudi Arabia, healthcare workers other than doctors, and individuals not registered with the SCFHS.

**Data collection**

An anonymous online survey was developed using the SCFHS Qualtrics Survey Platform. It was distributed via email by the Health Research Centre of SCFHS to a selected group of licensed doctors registered in their database and was further disseminated through local networks of clinicians to increase participation. The survey was available from 9th July to 27th August 2024 and only licenced individuals registered with the SCFHS were granted access to the survey link. This measure ensured that the survey was directed exclusively to eligible participants and maintained data integrity by restricting participation to the intended population.

Prior to starting the survey, participants were required to provide informed consent. Failure to provide consent resulted in immediate questionnaire termination. To prevent duplicate responses, participants were allowed to complete the survey only once.

**Research tools**

The survey instrument consisted of fourteen items, utilizing a combination of closed-ended response formats, including tick boxes and rating scales, with options for open-ended comments. It was designed for rapid completion to optimize response rates among time-constrained participants with an estimated completion time of three to four minutes. Moreover, the closed-ended questions facilitated statistical analysis, enabling the identification of correlations or patterns within the data.

Demographic information regarding participants' professional rank, degree, specialty, experience, and work status were collected in questions one through five. Questions six and seven assessed participants' perceptions of antibiotic resistance. Respondents rated their concern about antibiotic resistance on a five-point Likert scale and estimated the number of patients who experienced treatment-resistant infections within the past year. Questions eight to ten explored the respondents' knowledge, attitudes, and perceived clinical need for phage therapy.

In question eleven, participants were asked to prioritize bacterial genera and species for phage therapy development. The provided list encompassed high-priority pathogens identified in the 2024 World Health Organization (WHO) Bacterial Priority Pathogens List, along with *Helicobacter pylori* and *Campylobacter* spp. from the 2017 edition.[27,28] An optional open-ended box was also included to allow respondents to suggest other priority bacterial targets. Subsequently, in question twelve, respondents were asked to prioritize clinical conditions for phage therapy from a predetermined list, with an open-ended option for additional conditions.

Question thirteen aimed to explore the physicians' knowledge and awareness of alternative strategies to combat AMR beyond phage therapy. Finally, the last open-ended question allowed participants to provide additional insights not captured by the structured questionnaire format, allowing for the expression of diverse perspectives and unexpected information relevant to the study objectives.

**Data analysis**

After data collection, the dataset was exported into an electronic format compatible with Microsoft Excel for computer-based analysis. Data entry was followed by careful quality control measures to ensure accuracy. These procedures included error checking, verification using methods such as frequency analysis and cross-tabulation, and manual correction wherever necessary. Statistical analyses were conducted using IBM SPSS Statistics (version 29.0.2.0), focusing on descriptive statistics, including the calculation of means, standard deviations, and frequencies. Finally, data visualization was carried out using Microsoft Excel.

**Ethical approval and informed consent**

Ethical approval for the study design and data collection was granted by the Local Committee of Research Ethics at Shaqra University (HAPO-01-R-128) (Ref.#: ERC_SU_S_202400024). To ensure participant privacy and confidentiality, informed consent was obtained from all participants, who were also informed of their right to withdraw from the study at any time without consequence. The collected data were initially stored and managed by the Health Research Centre of SCFHS before being securely transferred to the study investigator for extraction and analysis.

## RESULTS

### Demographic characteristics

A total of 186 responses were initially received for the study survey. However, after applying the inclusion criteria, only 102 responses were considered valid. Responses were excluded if participants either disagreed with the study (6 respondents) or failed to complete the survey questions (76 respondents). Additionally, two responses from individuals no longer active in practice were excluded. The demographic characteristics are detailed in Table 1. Consultants made up the largest group of respondents (30.4%), followed by registrars (24.5%) and residents (20.6%). Senior registrars, general practitioners, and training residents accounted for the remaining participants.

The most common specialties among participants were dentistry, general practice, pediatrics, surgery, and internal medicine (18.6%, 14.7%, 9.8%, 7.8%, and 6.9%, respectively), representing over half of the participants from a total of 22 specialties and subspecialties.

In terms of education level, the majority of participants held a board fellowship, MD, or MBBS degree (31.4%, 28.4%, and 26.5%, respectively), with the remainder holding other postgraduate degrees or professional qualifications. Additionally, participants exhibited a diverse range of professional experience, with most having more than five years of clinical practice.

### Attitudes towards antibiotic resistance

Participants reported a high level of concern about the influence of AMR on their clinical decisions and treatment regimens, with a moderate degree of variability in responses, as indicated by a mean Likert scale score of 3.87 (SD = 1.12) (Figure 1A). Additionally, a substantial proportion of respondents (33.3%) reported encountering 1 to 5 patients with antibiotic-resistant infections, followed by 21.6% who encountered 6 to 10 such cases. Notably, 16.7% of respondents had not encountered any AMR cases in their practice during the past year. However, five respondents (4.9%) reported over 100 AMR cases, with two of these reporting exceptionally high numbers (1000 and 1200 patients, respectively) (Figure 2A).

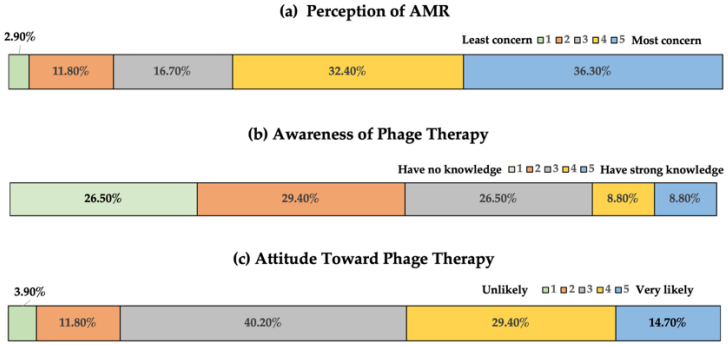


**Figure 1:** Stacked bar graphs representing responses to three survey questions based on a five-point Likert scale (A) Respondents' attitudes toward the impact of AMR on clinical decision-making and treatment strategies., (B) prior knowledge of phage therapy, and (c) belief in the effectiveness of phage therapy as a solution to AMR infections.

**Table 1:** Demographic characteristics of the participants

| Demographic data | | Frequency (*N*= 102) | Percentage |
|---|---|---|---|
| **Professional Rank** | Consultants | 31 | 30.4% |
| | Senior registrars | 13 | 12.7% |
| | Registrars | 25 | 24.5% |
| | Training residents | 5 | 4.9% |
| | Residents | 21 | 20.6% |
| | General practitioners | 7 | 6.9% |
| **Specialty** | Anesthetics | 4 | 3.9% |
| | Cardiology | 1 | 1.0% |
| | Clinical pathology | 4 | 3.9% |
| | Dentist/Prosthodontist/Orthodontics | 19 | 18.6% |
| | Dermatology | 1 | 1.0% |
| | Diabetes and endocrinology | 1 | 1.0% |
| | General practice/Family medicine | 15 | 14.7% |
| | Hematology and Hematopathology | 2 | 2.0% |
| | Infectious diseases | 3 | 2.9% |
| | Intensive care medicine | 2 | 2.0% |
| | Internal medicine | 7 | 6.9% |
| | Microbiology | 5 | 4.9% |
| | Nephrology/Urology | 4 | 3.9% |
| | Obstetrics and gynecology | 4 | 3.9% |
| | Pediatrics and neonatology | 10 | 9.8% |
| | Palliative medicine | 3 | 2.9% |
| | Psychiatry | 2 | 2.0% |
| | Surgery | 8 | 7.8% |
| | Radiology | 1 | 1.0% |
| | Respiratory medicine | 1 | 1.0% |
| | Ophthalmology | 2 | 2.0% |
| | Orthopedics/Rheumatology | 3 | 2.9% |
| **Degree** | Board, fellowship | 32 | 31.4% |
| | MD[1] | 29 | 28.4% |
| | MBBS[2] | 27 | 26.5% |
| | MSc[3] | 7 | 6.9% |
| | BDS[4] | 4 | 3.9% |
| | Diploma | 1 | 1.0% |
| | MCPS[5] | 1 | 1.0% |
| | MRCS Part 2[6] | 1 | 1.0% |
| **Years of experience** | 1 - 5 | 35 | 34.3% |
| | 6 - 10 | 30 | 29.4% |
| | 11 -15 | 14 | 13.7% |
| | 16 -20 | 17 | 16.7% |
| | 20 < | 6 | 5.9% |

[1]MD (Doctor of Medicine), [2]MBBS (Bachelor of Medicine, Bachelor of Surgery), [3]MSc (Master of Science), [4]BDS (Bachelor of Dental Surgery), [5]MCPS (Membership of the College of Physicians and Surgeons), [6]MRCS Part 2 (Membership of the Royal College of Surgeons, Part 2)

**Awareness and perception of phage therapy**

A moderate level of prior knowledge about phage therapy was observed among respondents, with a significant degree of variability in responses (mean = 2.4; SD = 1.2). Despite this, participants expressed a positive attitude towards phage therapy to address AMR infections, as reflected by a mean score of 3.4 (SD = 0.1) (Figure 1B, 1C). Additionally, 39% of participants believed that none of the AMR cases they encountered could benefit from phage therapy, while the remaining respondents reported an average of 25 patients per year who might potentially benefit from phage therapy due to antibiotic treatment failures (Figure 2B).

Participants assessed the perceived importance of various pathogens and conditions for phage therapy development using a four-point Likert scale and a weighted scoring system. Responses indicating uncertainty were assigned a score of zero, while high-priority items received three points. Cumulative scores (CS) were calculated for each pathogen and condition, establishing a priority ranking as shown in Figure 3 and 4.

*Staphylococcus* species, including methicillin-resistant *S. aureus* (MRSA), were identified as the highest-priority pathogens for phage therapy development, followed by *Pseudomonas*, *Klebsiella*, *Escherichia coli*, *Mycobacterium*, and *Streptococcus* species (259, 232, 227, 223, 222, and 220 CS, respectively). Conversely, *Acinetobacter baumannii*, *Neisseria*, and *Campylobacter* were identified as the lowest-scored pathogens for phage therapy development (182, 182, and 166 CS, respectively) (Fig 3). Moreover, participants suggested additional pathogens suitable for phage therapy, which are detailed in Table S1.

Regarding underlying conditions, infections in patients with suppressed immunity, diabetic foot infections, blood infections, and infective endocarditis were deemed critical targets for phage therapy applications (267, 265, 264, and 259 CS, respectively). In contrast, skin and soft tissue infections, cystic fibrosis, and gastrointestinal tract infections were assigned lower priorities (217, 215, and 208 CS, respectively) (Figure 4). Participants also suggested additional conditions for phage therapy, including eye infections (n=2), surgical site infections (n=2), central nervous system infections including meningitis (n=4), necrotizing fasciitis (n=1), and upper respiratory tract infections (n=1). However, some responses were excluded due to redundancy with the predetermined list or irrelevance.

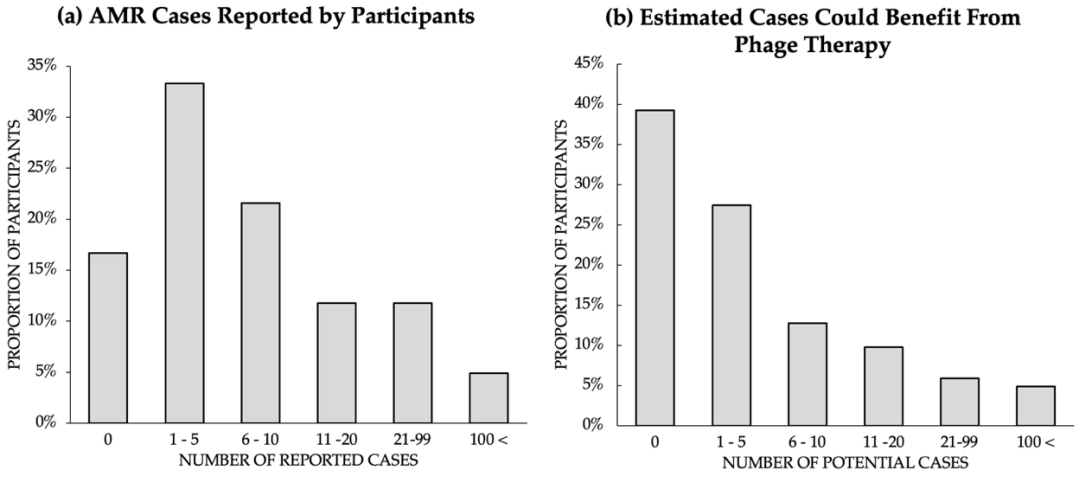


**Figure 2:** Doctors' estimates of (A) the number of patients who experienced treatment-resistant infections in the past year, and (B) the number of patients with AMR infections who could potentially benefit from phage therapy.

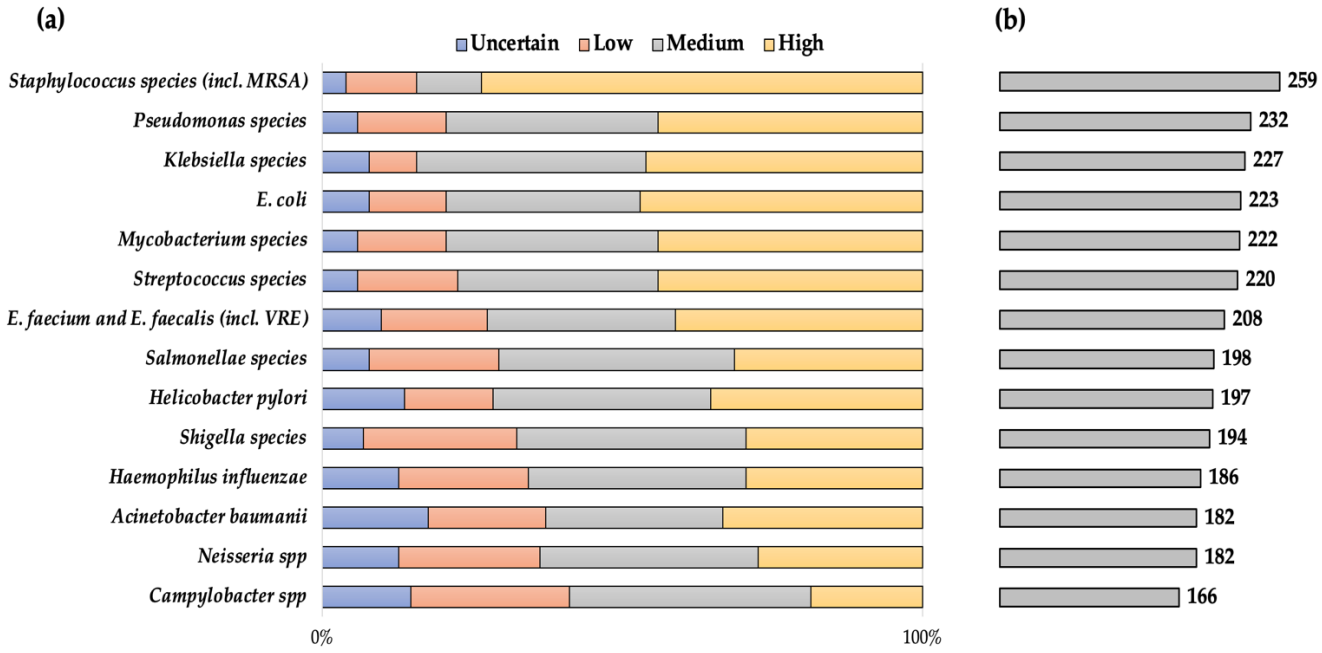


**Figure 3:** Comparison of the perceived importance of various pathogens for phage therapy development. (A) A diverging stacked bar chart shows the distribution of participant ratings across a four-point Likert scale. (B) A bar chart represents the weighted scores assigned to each pathogen, reflecting their overall importance based on the Likert scale responses (uncertain= 0, low= 1, medium= 2, high=3). Cumulative scores (CS) were calculated for each pathogen, establishing a priority ranking model. MRSA= methicillin resistance *S. aureus*; VRE= vancomycin resistant Enterococci.

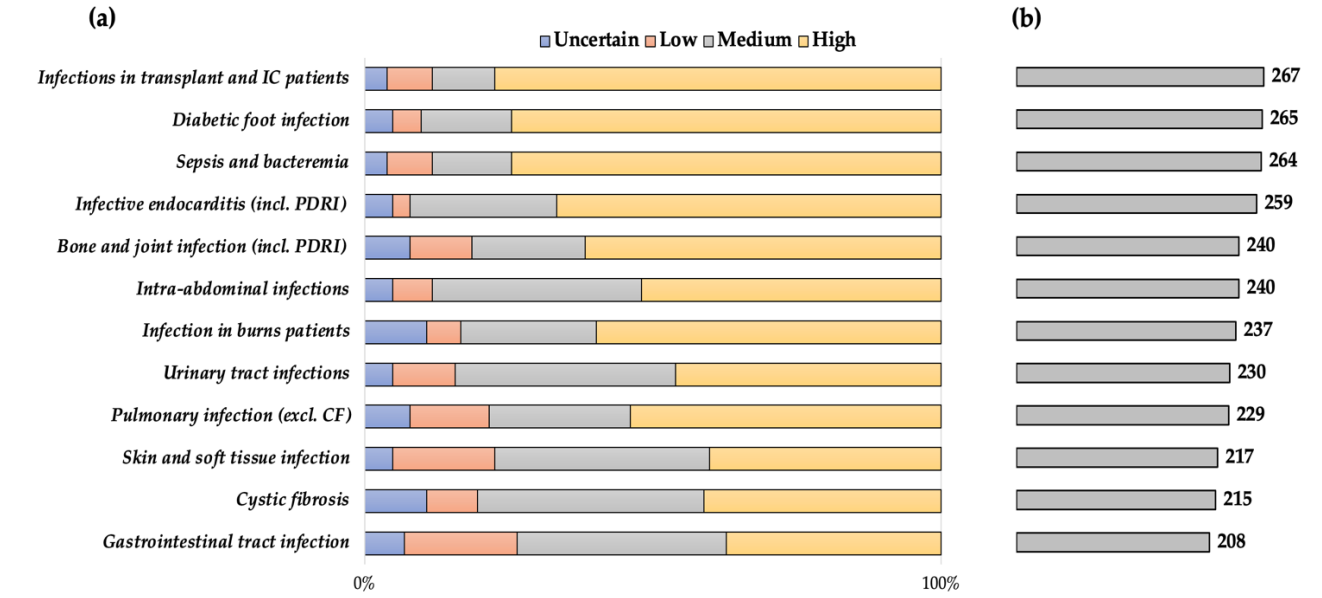


**Figure 4:** Comparison of the perceived importance of various clinical conditions for phage therapy development. (A) A diverging stacked bar chart shows the distribution of participant ratings across a four-point Likert scale. (B) A bar chart represents the weighted scores assigned to each condition, reflecting their overall importance based on the Likert scale responses (uncertain= 0, low= 1, medium= 2, high=3). Cumulative scores (CS) were calculated for each condition, establishing a priority ranking model. IC= intensive care; PDRI= prosthetic device-related infections; CF= cystic fibrosis.

**Table 2:** Qualitative analysis of suggested alternatives to antibiotics, other than phage therapy

| Specialty of respondents | Level of AMR concern | Level of prior PT knowledge | AMR Cases from last year | Cases could benefit from PT last year | Suggested Alternative | Analysis |
|---|---|---|---|---|---|---|
| Family medicine | 5 | 2 | 20 | 20 | Probiotics | Not a primary treatment for AMR infections but may help support gut microbiota balance |
| Anesthetics | 5 | 4 | 10 | 0 | Multi-drug therapy | Not alternative. Multi-drug therapy involves using multiple antibiotics to treat infections |
| Anesthetics | 5 | 3 | 2 | 2 | Prophylaxis | It is a preventive measure not a therapeutic option. Typically based on antibiotics |
| Nephrology | 4 | 3 | 3 | 10 | New type of Ab | Developing novel antibiotics remains a significant challenge. |
| Clinical Pathology | 2 | 2 | 32 | 2 | Gene therapy | Gene-based approaches to combat infections rely on engineered phages or antimicrobial peptides. The latter can be considered as a potential alternative. |
| Pediatrics and neonatology | 4 | 4 | 12 | 12 | Research and development of new antimicrobials and gene therapy. | Discussed at the above mentioned analysis |
| Infectious diseases | 5 | 3 | 35 | 5 | Monoclonal antibodies | Good alternative designed to specifically target microbial surface proteins and neutralize toxins, thereby helping the immune system to clear the infection. |
| Surgery | 4 | 2 | 25 | 2 | | |
| General practice | 4 | 3 | 15 | 15 | Antimicrobial stewardship program | It is not alternative, but an antibiotic-based program to ensure the effective use of antibiotics |
| Infectious diseases | 5 | 4 | 20 | 4 | | |

**Beyond phage therapy**

While phage therapy has emerged as a potential solution to the escalating challenge of AMR, participants demonstrated limited knowledge of other alternative therapeutic approaches. Only a minority (9.8%) suggested potential alternatives, although many of these options are either not distinct from traditional antibiotic-based strategies or are misconstrued (Table 2).

Finally, an open-ended question inviting additional comments was included at the end of the survey. Although only 7 respondents provided relevant feedback, their responses revealed a predominant theme of optimism regarding the future implementation of phage therapy as a treatment option (Table S2).

## DISCUSSION

Given the escalating global crisis of AMR, exploring alternative therapeutic strategies, such as phage therapy, is imperative. While recent studies in Western countries, including the UK, Canada, and Australia, as well as Korea in East Asia, have shed light on health professionals' attitudes and knowledge

regarding phage therapy, data from the Middle East, particularly Saudi Arabia, remain limited.[24-26,29,30] Therefore, this study attempted to bridge the knowledge gap by investigating the current landscape of phage therapy awareness in Saudi Arabia. By doing so, it may contribute to a broader understanding of the global perception and potential adoption of this promising therapeutic approach.

The study aimed to capture insights from a cohort of doctors regarding their awareness and attitudes toward phage therapy. Responses from 102 doctors who met the inclusion criteria were successfully obtained, surpassing those reported in similar studies, where the highest number was 92 respondents.[25,26,29,30] However, the response rate for this study cannot be calculated, as respondents were encouraged to forward the survey to colleagues, preventing an accurate calculation.

A significant proportion of participants were excluded due to incomplete surveys, which can be attributed to various factors. It has been observed that physicians, as busy professionals, often prioritize patient care and other clinical responsibilities over research participation. The demanding nature of their schedules and the burden of heavy workloads likely contributed to the incomplete responses observed in this study.[31,32] These challenges are well-documented in survey-based research involving healthcare professionals and underscoring the need for strategies to enhance both participation and completion rates within this demographic.[33]

Clinicians from a wide range of specialties were included in this study, similar to the UK study by Simpson et al. (2023), providing a broader perspective on the issues explored, whereas other relevant studies specifically targeted infectious disease physicians.[25,26,29,30] Saudi doctors expressed high levels of concern about the impact of AMR infections on their clinical decisions, comparable to those in the UK (3.87 vs. 3.9, respectively). This is further supported by a recent study from Saudi Arabia, which found that over 87% of physicians believe AMR is a major problem.[34] In terms of direct encounters with AMR, five respondents from three specialties (infectious diseases/microbiology, paediatrics, and radiology) reported encountering over 100 cases each, with a combined total of approximately 2,900 antibiotic-resistant infections. Excluding these outliers, the remaining respondents estimated a total of 926 AMR cases, with an average of 9.5 patients per doctor, closely aligning with the 8.6 patients per clinician reported by Simpson et al (2023). These findings highlight the ongoing need for effective strategies to combat AMR infections globally.

In the absence of established phage therapy practices in Saudi Arabia, this study serves as a foundational effort to evaluate physicians' perceptions of this re-emerging treatment option. The increasing global acceptance and integration of phage therapy, along with growing research interest in bacteriophages within Saudi academic circles, indicates a favourable potential for the future development and clinical application of phage therapy in the region.[24,35] We reported a moderate level of awareness about phage therapy, consistent with findings from similar research in Australia and Korea.[26,30] This suggests that despite increasing global attention to antimicrobial resistance, familiarity with phage therapy remains limited among healthcare professionals in these regions. Conversely, a higher level of awareness was observed among UK physicians, possibly reflecting regional differences in exposure to or education about phage therapy. This variation may indicate the influence of national or local initiatives on the dissemination of information regarding emerging therapies like phage therapy.[24,36,37]

Attitudes towards phage therapy were generally positive across the studies compared. Clinicians in Australia, Canada, and the UK demonstrated significant interest in exploring phage therapy as a potential solution to AMR, while Korean clinicians expressed a strong willingness to use phage formulations if regulatory safety standards were met.[25,26,29,30] In this study, these positive attitudes were also a major theme in respondents' answers and comments (Figure 1C, Table S2). The findings highlight a shared enthusiasm for this therapeutic approach, despite varying levels of awareness. Moreover, the

consistent positive attitudes suggest a growing openness among clinicians to integrate phage therapy into clinical practice, particularly if further evidence supports its efficacy and safety.[35,38]

*Staphylococcus* species, particularly MRSA, emerged as the highest-priority pathogen for phage therapy development, followed by *Pseudomonas, Klebsiella, E. coli*, and *Mycobacterium*. These results align closely with findings from similar research conducted in the UK.[25] Notably, *A. baumannii*, despite being a critical focus in global discussions on AMR, was ranked among the lowest priorities in this work. This contrasts with surveys targeting infectious disease specialists, such as those conducted in Korea and Australia, which identified a broader range of ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter* species), including *A. baumannii* and *E. faecium*, as top priorities for phage therapy.[26,30] The obvious divergence may reflect the differing clinical priorities across specialties, with infectious disease specialists likely focusing more on well-recognized MDR pathogens. For instance, in this study, opportunistic pathogens such as *Nocardia, Burkholderia,* and *Stenotrophomonas* were highlighted as priorities primarily by infectious disease clinicians (Table S1). These variations emphasize the need for a tailored approach to phage therapy development, considering both the broader cross-specialty perspectives and the specific challenges encountered within individual clinical disciplines.

Another key focus of this study was to identify the clinical priorities for phage therapy development. Our findings closely align with previous research conducted in Australia and Korea, highlighting the critical need for phage therapy to address infections in immunocompromised individuals, diabetic foot infections, blood infections, and infective endocarditis.[26,30] However, this study also revealed some differences in prioritization compared to the other relevant studies. For instance, bone and joint infections, including those associated with prosthetic devices, were identified as high priorities in the Korean study but received lower emphasis in our findings. Similarly, cystic fibrosis-related lung infections were ranked as top priorities in both the Australian and Korean studies; however, they were considered of lower urgency in our research.[26,30] These discrepancies may reflect variations in clinician populations, clinical settings, and the awareness about specific conditions across regions, underscoring the importance of tailoring phage therapy approaches to local epidemiological trends and clinical needs.

Despite recognizing phage therapy as a potential strategy against AMR, participants, limited awareness of other alternative therapeutic approaches was observed. Only a small fraction suggested alternatives, many of which were either conventional antibiotic-based strategies or misconstrued as true alternatives (Table 2). For instance, probiotics were mentioned for their role in supporting gut microbiota balance, but they are not considered primary treatments for AMR infections.[39] Similarly, multi-drug therapy, a conventional approach involving the use of multiple antibiotics to treat infections, and prophylaxis, a preventive measure, were cited, although neither represents a distinct alternative to antibiotics. Another frequently mentioned option, antimicrobial stewardship programs, focuses on optimizing the use of antibiotics and reducing resistance, but it does not offer a therapeutic alternative to antibiotics themselves.[40]

In contrast, promising alternatives such as antimicrobial peptides (AMPs) and monoclonal antibodies hold potential for addressing AMR infections. AMPs are naturally occurring molecules with broad-spectrum activity against bacteria, fungi, and viruses. They exert their bactericidal effect by interacting with negatively charged microbial membranes, which increases permeability and leads to cell lysis or leakage of intracellular contents, ultimately causing cell death. Moreover, AMPs have the potential to synergize with antibiotics, enhancing the elimination of complex bacterial infections, including those involving biofilms.[41,42] Monoclonal antibodies, on the other hand, target specific microbial surface proteins or neutralize toxins, assisting the immune system clear infections.[43] These emerging therapies,

along with the ongoing development of phage therapy, offer valuable options for combating AMR, either as complementary treatments with antibiotics or as stand-alone therapies in the future.

A notable limitation of this study is the relatively small sample size, despite our efforts to enhance it and mitigate potential biases by distributing the survey broadly through the SCFHS and local networks of health professionals. This limitation reduces the strength of our statistical analyses and may affect the generalizability of the findings. Specifically, the uneven distribution of respondents across various specialties may bias the results toward the experiences of more heavily represented groups and underrepresent those from less-represented specialties. Additionally, variations in study contexts and target groups precluded direct comparisons with other studies in certain aspects. To address these limitations, a collaborative research model involving multiple researchers across different countries could help minimize variability and errors, thereby strengthening the generalizability and robustness of future studies.

## CONCLUSION

This study provides valuable insights into the awareness and willingness of clinicians in Saudi Arabia to adopt phage therapy, marking a significant first step in exploring its potential within the Middle East. While current knowledge of phage therapy is limited, the shared enthusiasm among clinicians, especially in light of the growing AMR crisis, suggests a promising future for phage-based treatments. This positive reception of the study underscores the importance of continued research and the development of a regulatory framework to support the clinical integration of phage therapy in Saudi Arabia. These efforts will be crucial in addressing the escalating AMR burden and expanding treatment options.

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Nil

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**Conflicts of interest**

The author declares no conflict of interest relevant to this article.

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## Supplementary materials

**Table S1:** Analytical review of respondents' additional comments regarding pathogens for which they advocate the development of phage therapy.

| Specialty of respondents | Suggested pathogen | Type | Class | Primary Diseases | Antibiotic Treatment | Phage Therapy Potential | Comment |
|---|---|---|---|---|---|---|---|
| Obstetrics and gynaecology (*n*=2) | *Clostridium* spp. | Bacteria | Gram-positive | Clostridial infections (e.g., tetanus, botulism, gas gangrene) | Yes, but some strains are MDR and difficult to treat | Present | Spore-forming organisms that are highly resistant to many environmental factors, including antibiotics. |
| Clinical Pathology (*n*=1) | *Vibrio Cholerae* | Bacteria | Gram-negative | Cholera | Yes | Present | Resistant strains are relatively uncommon. |
| Infectious diseases (*n*=1) | *Nocardia* | Bacteria | Gram-positive | Nocardiosis (lung, skin, brain infections) | Yes, but can be challenging | Present | Common infection in immunocompromised patients. Mostly suitable to antibiotics. |
| Infectious diseases (*n*=2) | *Burkholderia* | Bacteria | Gram-negative | Pneumonia, bloodstream infections, skin infections | Yes, but often resistant | Present | Mostly affect immunocompromised patients especially the lung of cystic fibrosis patients. Often exhibit high antibiotic resistance due to their intrinsic mechanisms, efflux pumps, biofilm formation, horizontal gene transfer, and slow growth rate. |
| Infectious diseases (*n*=2) Paediatrics and neonatology (*n*=1) | *Stenotrophomonas* | Bacteria | Gram-negative | Pneumonia, urinary tract infections, bloodstream infections | Yes | Present | There is an increasing resistance to antibiotics like tigecycline and ticarcillin-clavulanic acid, while effective treatment options are widely available such as trimethoprim-sulfamethoxazole. |
| Infectious diseases (*n*=1) | *Actinomyces* | Bacteria | Gram-positive | Actinomycosis (jaw, lung, skin infections) | Yes | Present | Resistant strains are relatively uncommon |
| Microbiology (*n*=1) | *Proteus mirabilis* | Bacteria | Gram-negative | Urinary tract infections, wound infections | Yes | Present | Resistant strains are relatively uncommon |
| Anesthetics (*n*=1) | Meningococci (or *Neisseria meningitidis*) | Bacteria | Gram-negative | Meningitis, septicemia | Yes | Present | Resistant strains are relatively uncommon |
| Anesthetics (*n*=1) | Gonococci (or *Neisseria gonorrhoeae*) | Bacteria | Gram-negative | Gonorrhea | Yes | Present | Resistant strains are relatively uncommon |

| Specialty of respondents | Suggested pathogen | Type | Class | Primary Diseases | Antibiotic Treatment | Phage Therapy Potential | Comment |
|---|---|---|---|---|---|---|---|
| Obstetrics and gynecology (*n*=1) | *Salmonella* Typhi | Bacteria | Gram-negative | Typhoid fever | Yes | Present | Typically susceptible to antibiotics, but MDR strains have been detected. |
| General practice (*n*=1) | Vancomycin-resistant *Staphylococcus aureus* (VRSA) | Bacteria | Gram-positive | Skin infections, pneumonia, bloodstream infections | Difficult to treat | Present | Other FDA-approved options are still available (e.g. daptomycin, linezolid and ceftaroline) |
| Dentist (*n*=2) | *Klebsiella aeruginosa* | Bacteria | Gram-negative | Pneumonia, urinary tract infections, bloodstream infections | Yes, but often resistant | Present | MDR strain are very common, making infections difficult to treat |
| Pediatrics and neonatology (*n*=1) | *Candida albicans* | Fungi | Yeast | Thrush, vulvovaginal candidiasis, skin infections | Not effective | Absent | Antibiotics are not effective against fungi. Phages are only found in bacteria |
| Ophthalmology (*n*=1) | *Acanthamoeba* | Parasite | Amoeba | Keratitis (eye infection), granulomatous amebic encephalitis | Not effective | Absent | Antibiotics are not effective against parasites. Phages are only found in bacteria |

**Table S2:** Participant's feedback summary

| Specialty of respondent | Level of AMR concern | Level of prior PT knowledge | AMR Cases from last year | Cases could benefit from PT last year | Feedback |
|---|---|---|---|---|---|
| Rheumatology | 3 | 2 | 1 | 0 | New good rout in treatment |
| Obstetrics and gynecology | 5 | 3 | 0 | 0 | Phage Therapy is an innovative and a welcome idea. |
| Surgery | 5 | 3 | 8 | 0 | This is very innovative way to compete AMR |
| Obstetrics and gynecology | 3 | 3 | 20 | 1 | It will be necessary for addressing the growing problem of antibiotic-resistant infections. |
| Dentist | 3 | 2 | 2 | 10 | Good luck hope that research come to light for the benefits of human |
| General practice | 4 | 3 | 15 | 15 | Unique and innovative research. Kudos to the team to address this pressing issue in the medical fraternity. All the best. I hope we use phages in our daily practice. |
| Dentist | 2 | 1 | 0 | 0 | I find it interesting approach against AMR |