

SYSTEMATIC REVIEW

Antimicrobial resistance and antimicrobial stewardship: an update

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Abstract

Objective The aim of this narrative review is to examine the historical evolution of antimicrobial treatments, the rise of antimicrobial resistance (AMR) and the implementation of antimicrobial stewardship (AMS) over time. It explores whether AMR remains a concern in wound care, the development of new antibiotics and alternative antimicrobial therapies, and the benefits observed following AMS initiatives.

Materials and methods The Medline (PubMed) electronic literature database was searched for the relevant studies. The search revealed 2940 potential articles, screening for relevance identified 203 articles, which were reviewed.

Results Despite the emergence of AMS strategies, our review found that AMR remains a significant issue with regard to wound care and healthcare more generally. AMR is an increasing problem with resistance being widespread and being seen in non-antibiotic antimicrobials, such as silver. The identification of new antibiotics is lacking and, despite the development of newer treatments with current antibiotics (including combination therapies), there is a strong push for new, non-antibiotic therapies, such as photodynamic therapy and phage therapy.

Conclusion Alongside the development of new treatments, updating current AMS procedures and enhancing their implementation (resulting in a reduction in antimicrobial use) are identified as important areas in the battle against AMR. In addition, the implementation of AMS procedures corresponded with a decrease in levels of antimicrobial resistant microorganisms. As well as reducing levels of resistant microorganisms, this review revealed additional benefits of the introduction of AMS procedures, including a reduction in costs (surgical antibiotic prophylaxis costs), and a reduction in patient morbidity and mortality.

Keywords antimicrobial resistance, antimicrobial stewardship, dialkylcarbamoyl chloride, WHO-prioritised wound pathogens

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Introduction

Wounds disrupt the skin barrier and expose the body to infection, usually caused by bacteria such as *Pseudomonas aeruginosa*, *Staphylococcus aureus* and others.¹ Microbial biofilms, which provide protection to bacteria, complicate wound healing by being resistant to antimicrobial agents and the immune system.²

The history and importance of antimicrobials

Antimicrobial agents have been used for centuries, with the discovery of penicillin in 1928 marking a major milestone (Figure 1). However, antimicrobial resistance (AMR),

accelerated by the overuse of antibiotics, is now a global health threat.³ New antibiotic discoveries have stalled since 1987, leaving limited treatment options.^{4,5} AMR leads to increased morbidity, mortality and health care costs.⁶

Treating wound infection

AMR occurs when microorganisms develop the ability to withstand treatments that once effectively controlled them.⁹ AMR occurs when microorganisms develop resistance through mutations or acquisition of resistance genes, rendering standard treatments ineffective.² Wound care involves a combination of strategies, such as debridement (removal of dead tissue) and antimicrobial therapy.¹⁰

Antimicrobial dressings containing substances such as silver, iodine, honey and PHMB are common in wound care.¹¹ Known for its antimicrobial properties, silver is widely used,¹² but its overuse has raised concerns about durability and environmental impacts.¹³

Silver-resistant bacteria have emerged, including some found in wounds,¹⁴ necessitating close monitoring of silver-based treatments. Silver nanoparticles (NAg) are effective against bacteria,¹⁵ but resistance has also been observed in WHO priority pathogens.^{15,16} While silver-based dressings have been promoted for wound healing,^{17,18} the evidence supporting their efficacy is mixed,¹⁹ and increasing resistance to silver warrants re-evaluation of their use in minimising AMR.²⁰

An alternative approach to minimise the emergence of AMR includes dressings without active antimicrobial ingredients, such as hydrogels, and DACC-coated dressings.^{21,22} These dressings help remove microorganisms from wounds without the risk of contributing to AMR,²³ making them valuable in treating infections.

Antimicrobial stewardship

The goal of AMS is to optimise the use of antimicrobials to reduce resistance and improve patient outcomes.²⁴ First mentioned and subsequently incorporated into guidelines in the 1990s,^{25,26} AMS emphasises correct antimicrobial prescribing, regular evaluation of practices, and improved diagnostics.²⁴ Several guidelines, consensus documents and other important resources have been developed promoting AMS and for combating AMR.²⁷⁻³⁰

Global efforts against AMR

Global health organisations such as the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the European Center for Disease Prevention and Control (ECDC) have developed policies and strategies to combat AMR.²⁷⁻³⁰ In 2015, WHO adopted the Global Action Plan (GAP) on AMR,²⁷ which focuses on raising awareness, reducing infection rates and optimising the use of antimicrobial agents. By 2023, 178 countries had aligned their national action plans with the GAP.³

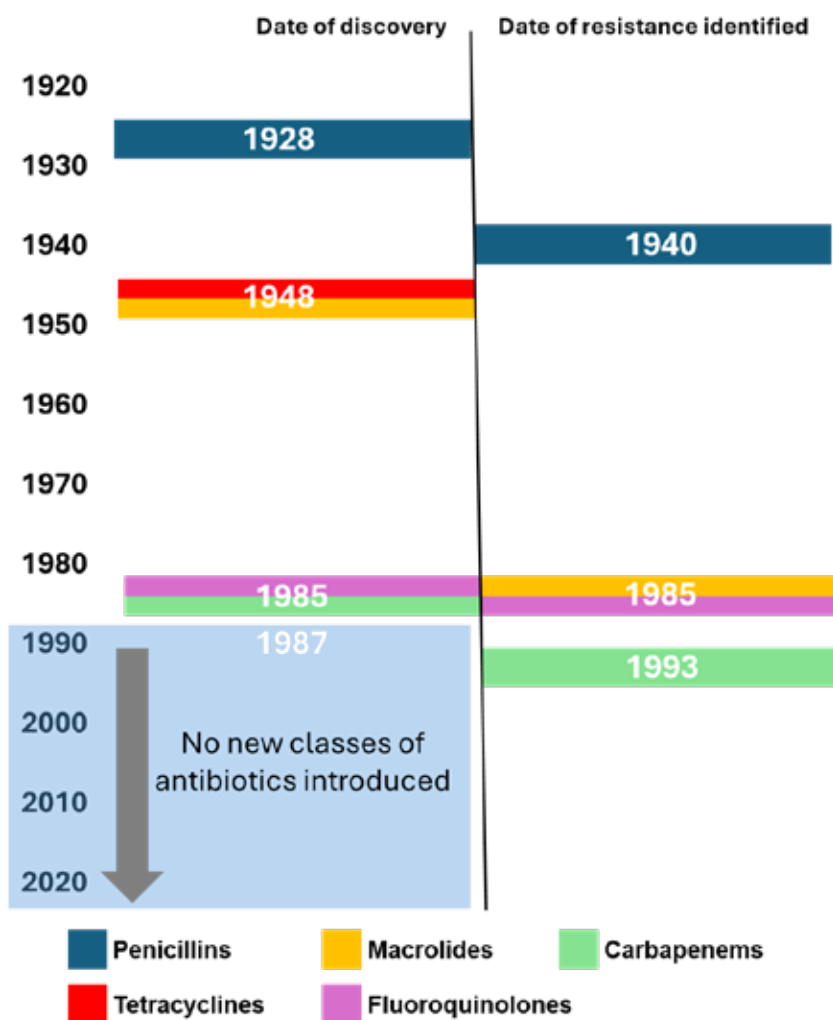


Figure 1. Antibiotic class discovery and resistance timeline^{7,8}

This global effort includes improving antimicrobial prescribing practices, improving diagnostic methods, and promoting multidisciplinary collaboration. WHO developed the AWaRe (Access, Watch, Reserve) classification system that provides guidelines for the correct use of antibiotics, helping to reduce the number of inappropriate prescriptions.²⁹ In addition, the WHO list of priority bacterial pathogens, updated in 2024,³¹ helps address the evolving challenges of AMR.

Despite new antibiotics and adjuvants, multidrug-resistant organisms such as ESKAPE pathogens (*Enterococcus faecium*, *S. aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *P. aeruginosa* and *Enterobacter* spp.) remain significant therapeutic challenges,³² highlighting the continued need for global collaboration and innovation in the fight against AMR.³¹

AIM: A narrative review to compare and contrast the history of antimicrobial treatments with the development of AMR and the instigation of AMS past, present and future. To explore:

- whether AMR still an issue in wound care
- if new antibiotics are being developed to challenge the development of AMR
- if new antimicrobial agents (excluding antibiotics) or other antimicrobial therapies are being developed to challenge the development of AMR
- what benefits have been identified post-AMS implementation

Methods

Inclusion criteria: This review includes primary published research articles of any study design: randomised control trials (RCTs), non-randomised controlled trials, prospective, retrospective, case series studies, and pre-post studies. Any study focusing on use of antimicrobial treatments and the development of AMR and the instigation of AMS was included.

Exclusion criteria: Articles that did not match these types of studies, and studies not written in the English language.

Electronic searches: The literature search was conducted in MEDLINE (via PubMed) between January 2019 and May 2024. In addition, reference lists were screened. Wound journals not listed in MEDLINE that were published within the date range were screened manually. The keywords included in the search included:

- #1: “antimicrobial” AND (“wounds” OR “injury” OR “diabetic foot ulcer*” OR “venous leg ulcer*” OR “pressure ulcer*” OR “pressure sore*”) OR “burn*” OR “surgical wound*”
- #2: “resistance” OR “stewardship”
- #3: “infection”
- #4: #1 AND #2 AND #3

Study selection: Article titles and abstracts were assessed by two authors (MR and AR) according to the inclusion and exclusion criteria. The full-text versions of potentially relevant studies were obtained and screened against the inclusion criteria. Following screening of the full text articles, consensus between reviewers in relation to the studies to be included was then obtained.

Data extraction: Descriptive data were extracted from the full text versions and added to a pre-designed data extraction table recording author and year, country, setting, design, population, sample and intervention.

Study inclusion: The study selection process is illustrated in the PRISMA flow diagram (Figure 2). The initial search identified 2940 potential articles, and no other articles were identified from other sources, giving a total of 2940 articles to screen. Following review of the abstracts against the inclusion criteria 238 articles were screened for full-text eligibility after title/abstract screening, and from this, 203 articles were found to be eligible for inclusion in the narrative review.

Results and discussion

Characteristics of included studies: An overview of the wound types featured in the reviewed studies indicated that surgical site infections (44.3%, 58/131) was the largest wound infection recorded in the papers followed by burn wounds (11.5%, 15/131). Chronic wounds were identified in 15 (7.4%) studies, with three-quarters of these studies (66.7%, 10/15) relating to diabetic foot ulceration. Thirty-six (16.7%, 34/203) papers were laboratory-based studies. Thirty-nine (19.2%, 39/203) studies did not specify wound type in enough detail to be assigned to any specific group.

Figure 3 summarises the number of articles in each of the six review discussion areas. Sixty-nine (34.0%) articles related to describing new wound pathogens, with 36/203 (17.7%) detailing the use of new antibiotic therapies (such as, antimicrobial agent combinations). Non-antibiotic (“new treatment”) therapies were summarised in 40/203 (19.7%) studies.

Updates to AMS processes and implementation were described in 23/203 (11.3%), and 18/203 (8.9%) articles, respectively, and a demonstration of the benefits of AMS in wound care was described in 19/203 (9.4%) articles.

Emerging antimicrobial resistant organisms: Recent studies have investigated the rise of AMR in humans by analysing global data and using models.³³⁻³⁵ These studies examine how factors, such as antimicrobial use, population size and mobility influence the emergence of AMR. By incorporating these factors, the researchers developed predictive models to estimate the global risk of developing AMR. These studies suggest that AMR emergence is positively correlated with antibiotic consumption in humans, particularly for WHO critical priority and high priority

pathogens.³⁴ Mendelsohn et al³⁵ found that human travel may also play a role in AMR emergence. Interestingly, Allel et al³⁴ presented data to suggest that reducing the rate of antibiotic consumption alone will not be sufficient to combat rising worldwide prevalence of AMR.

Emerging resistance to antibiotics is not the only concern in the fight against infection, particularly in wound care. Silver (in the form of antimicrobial silver ions (Ag⁺), a

widely used antimicrobial agent of the last 20+ years is an important tool in the fight against wound infection.³⁶ Found in wound care products (such as bandages, creams, wound dressings) in several different forms (silver nitrate, silver sulfadiazine, nanocrystalline silver), and offering different ways of delivering silver ions,³⁷ concern has been raised by the emergence of silver resistance including in microorganisms with clinical significance.^{13,38,39} An increasing

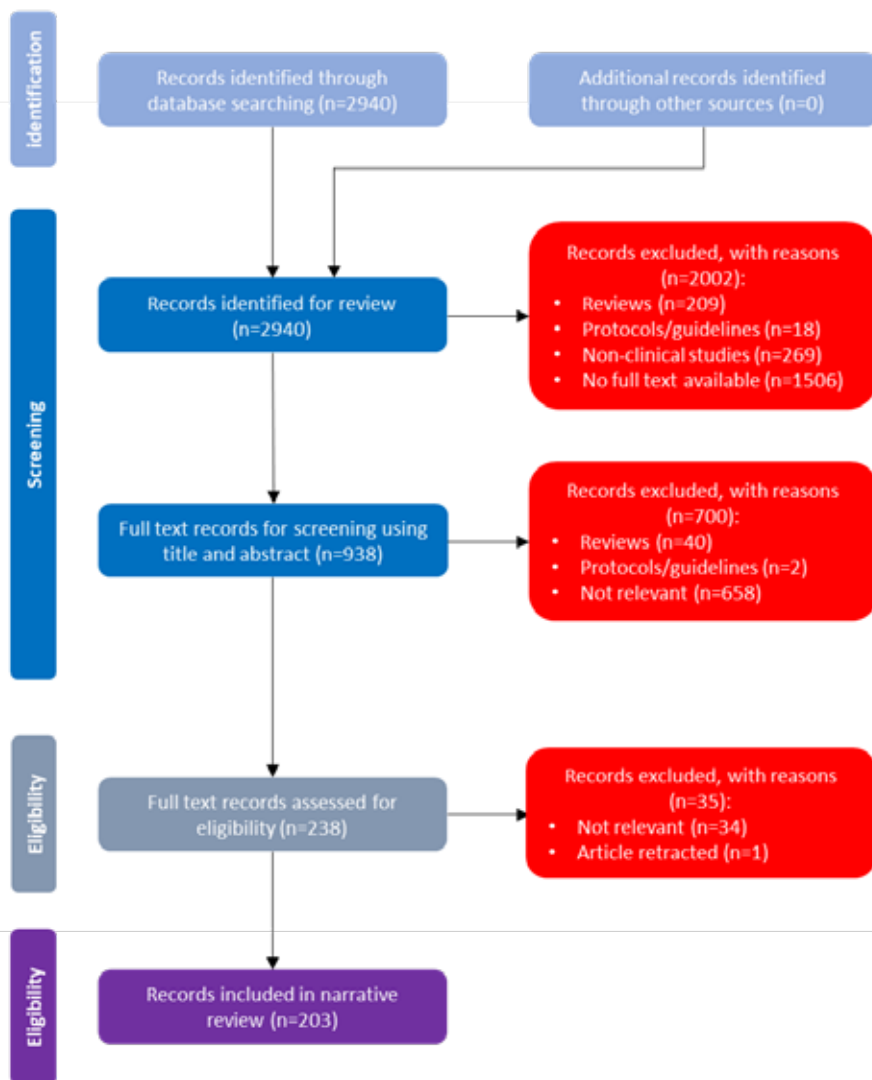


Figure 2. PRISMA flow diagram of literature review

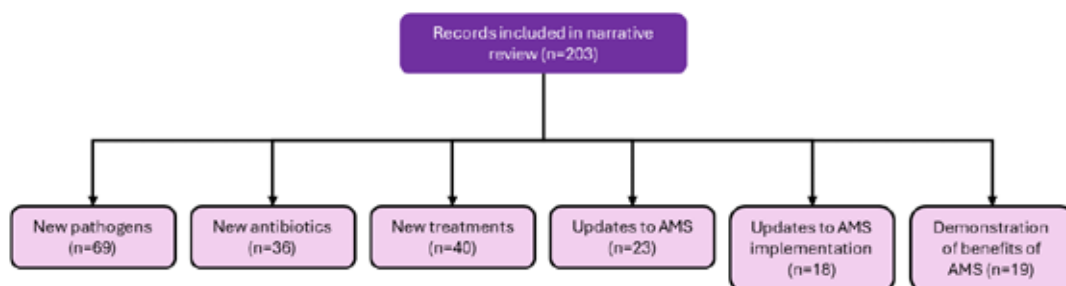


Figure 3. Breakdown of articles (n=203) into discussion areas

number of studies have shown silver resistance in bacteria including (but not exclusively) *P. aeruginosa*, *S. aureus*, and *A. baumannii*, examples of ESKAPE microorganisms that are also examples of WHO priority pathogens.^{16,40} To avoid further selection and spread of silver-resistant bacteria with a high potential for healthcare-associated infections, the use of silver-based products needs to be controlled, and the silver resistance monitored.⁴¹

This review identified 69 articles⁴²⁻¹¹⁰ related to the emergence of pathogens exhibiting AMR, with the description of the identification of antimicrobial resistant pathogens being the highest proportion of articles in this group (see Figure 4).

Antimicrobial resistant microbes were isolated from various clinical situations including several different wound types (including surgical site infections,^{43,51,54,55,77,107} burn wounds,^{52,60,72,101,108,110} traumatic wounds,⁶⁷ a bite wound,⁵³ and studies where wounds were not specified,^{81,83,88,92,93,99,100,103,104,106} and other non-wound conditions (including peritonitis,⁶⁴ intestinal colonisation,⁹⁴ and meningitis¹⁰⁵). Both gram-positive (such as *S. aureus*, *S. epidermidis*, *E. faecalis*, *E. faecium*) and gram-negative (*Escherichia coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*) bacteria resistant to antimicrobials were identified.

Resistance to antibiotics such as beta-lactam antibiotics (for example carbapenems and penicillin's), and the isolation of extended spectrum beta-lactamase (ESBL)- and metallo-beta-lactamase (MBL)-producing microorganisms was observed in microorganisms isolated from a variety of different wound types (for example carbapenems in SSI,^{47,82} burn wounds⁷² and wounds generally,^{73,88} ESBL in SSI,^{47,82} burns,⁵⁶ and unspecified wounds,^{97,106} and MBL in wounds¹⁰⁴).

Several studies identified microorganisms with multi-drug resistance (such as SSI,^{43,54,74,80} burn wounds,⁶⁰ and studies with undefined wounds^{92,93}). In one multicentre study in patients undergoing surgical procedures several gram-positive and gram-negative bacteria were isolated that showed resistance to numerous antimicrobials (such as penicillin, tetracycline, cefoxitin). Several of the microorganisms (for example *S.*

aureus) exhibited 100% multi-drug resistance (MDR).⁴³ Zhao et al⁵¹ report the appearance of AMR (ESBL-producing and carbapenem-resistant) in a hypervirulent *Klebsiella pneumoniae* found in SSIs, which is a microorganism that can cause life-threatening infections. Tchakal-Mesbahi et al⁵² document the emergence of a new antibiotic-resistant *P. aeruginosa* in burn patients.

Several studies indicate an increase in frequency in AMR and increased resistance rates (Figure 4 shows results of a study of the trend of AMR of *K. pneumoniae* from a number of sample types (including wound swabs) in patients between 2016 and 2020 found that there was a significant increase in carbapenem resistance rates, increasing from around 45% in 2016 to over 80% in 2020,⁴⁷ as well as an increase in the rate of ESBL-producing *K. pneumoniae* since 2017. Additionally, pathogens were showing increasing levels of resistance (meaning the level of resistance was increasing and microorganisms were becoming less susceptible to the antimicrobials). Sana et al⁶² concluded from their cross-sectional study of intensive care patients that there was a rapid increasing resistance profile in *A. baumannii*. In another cross-sectional study, swabs taken from 140 patients with diabetic foot ulcers found an overall increase in bacterial resistance to antimicrobial agents.¹⁰²

Together, these studies indicate that resistance to antimicrobial agents in microorganisms found in several different wound types is common, and that this resistance covers a wide range of antimicrobials. In addition, this resistance is an increasing problem and, consequently, the options for effective antimicrobials are becoming more limited.

The development of new antibiotics/treatment regimens

The current situation with regards to the development of AMR has been highlighted by the WHO³ as an emerging crisis and that the development of new antimicrobial agents is an imperative. In 2022 WHO published a document,¹¹¹ titled *2021 Antibacterial agents in clinical and preclinical development: an overview and analysis* stating that a number of antibiotics were at various stages of development. However, the number of microorganisms becoming resistant to treatment with current antibiotics is rising. With few new antimicrobial agents being developed there is a necessity for the urgent development of new classes of antibiotics to avoid a major global health crises.

More recently, WHO released its updated *Bacterial Priority Pathogens List (BPPL) 2024* which prioritises 24 pathogens (including *A. baumannii*, *P. aeruginosa*, *S. aureus*, and *E. faecium*) and provides guidance on the development of new and necessary treatments to stop the spread of AMR.³¹

Thirty-six papers¹¹²⁻¹⁴⁷ related to the identification and use of new antibiotics or AMS-driven changes to the use of current antimicrobials for the management of AMR (see Figure 5).

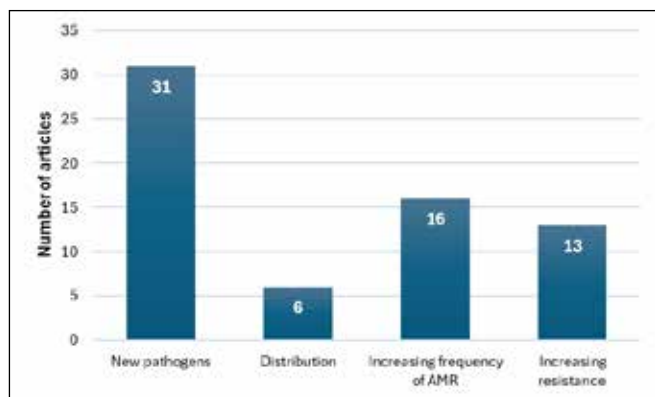


Figure 4. New pathogens, number of articles describing new pathogens exhibiting AMR, their distribution, and increasing frequency and incidence of AMR

Articles about the combined use of two or more antimicrobials, or switching between antimicrobials, made up the largest group of articles about agents being used to combat resistant microorganisms. Combination therapy is described for several conditions including tuberculosis, pneumonia, and several wound-related issues, such as surgical site infections, diabetic foot ulceration (DFU) and other general wounds.

For example, Wang et al¹⁴⁰ described a study in renal transplant patients where tigecycline combination therapy was found to be a potential option for treating Carbapenem-resistant gram-negative bacteria infections. Additionally, in a case of patient with an open craniocerebral injury, a series of *in vitro* and *in vivo* tests showed that tigecycline combined with aminoglycosides had good synergistic effects against carbapenem-resistant *K. pneumoniae*, and that bacterial resistance selection was suppressed.¹³⁰ In a multicentre cohort study of patients (with a variety of infections including wound infections) treated for MDR *P. aeruginosa* several antimicrobial combination therapies offered potential for treatment of infections.¹³⁵ Two studies in our review described newly discovered antibiotics and their potential use against infections.^{139,141}

Other studies reported changes in antimicrobial therapy duration (such as reduced prophylactic duration),^{115,126} changes in dosage,¹¹⁶ and timing of antimicrobial agents application are at least as effective or improve treatment of infection compared with previous treatments.¹¹⁹ Maruo et al,¹¹⁶ rather than using systemic high-dose antibiotics to treat patients with fracture-related infection after osteosynthesis, treated these infections with continuous local antibiotic perfusion thus reducing the overall dosage applied to patients and minimising patient adverse events. Another study examining infection after osteosynthesis,¹¹⁹ compared the use of immediate combination antibiotic therapy with postponed targeted antibiotic therapy. They observed overall success rates for both modalities, and no additional bacterial resistance was reported. The use of novel delivery systems such as aerosolisation¹²⁹ or nebulisation¹⁴³ were reported.

Although the development of new antibiotics to address the increasing problem of AMR are lacking, studies show that the development of combination therapies with current antimicrobial agents, and the application of AMS principles, such as reducing antimicrobial agent usage through changes in parameters such as duration, dosage, and timing of usage have the potential to be as effective as current antimicrobial therapy practices while reducing the use of antimicrobials.

Emerging new treatments

With the increasing emergence of antimicrobial agents' resistance in increasing numbers of microorganisms there has been an increase in the research and development of potential antimicrobial agents – excluding agents such as antibiotics – in the fight against AMR. For example, the development of bacterial viruses (phages), which were originally developed for the treatment of bacterial infections

before the discovery of penicillin,^{148,149} for treatment of drug-resistant pathogens. In addition, photodynamic therapy is being used whereby photosensitised drug-resistant bacteria are killed by light irradiation.^{150,151} Development work is also underway on the identification of other potential antimicrobial agents, such as novel metal ions¹² and plant-derived agents^{152,153} for use against antimicrobial resistant microorganisms. They are at various stages in development and clinical use.

Forty papers^{5,154-192} related to the use of new treatments for the management of antimicrobial resistant (see Figure 6). Bacterial phage technology and 'biological' agents (such as a group of agents including antibacterial peptides, and efflux pump inhibitors) were the largest group of antimicrobial agents reported. Other groups of antimicrobial treatments, including photodynamic therapies, were also reported.

Bacterial phages were active against resistant microorganisms in a number of laboratory-based studies,^{154,184} as well as a number of clinical studies in patients with SSIs^{160,182} or DFUs.^{161,187} Green et al¹⁶⁰ reported on the use of customised bacterial phage therapy in 12 patients (including patients with sternal wounds) to improve difficult-to-treat AMR infections and associated bacterial eradication and clinical improvement. Other phage-mediated antimicrobial activity was shown in AMR *K. pneumoniae*,^{154,181} MDR strains of *P. aeruginosa*,¹⁶¹ and carbapenem-resistant *A. baumannii*.¹⁸⁴

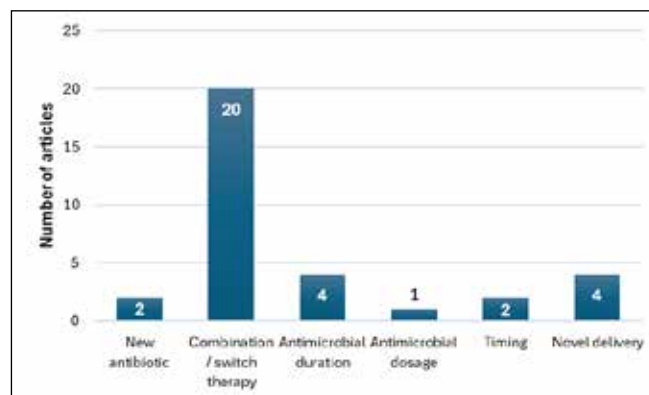


Figure 5. New antibiotic/treatment regimens for use against antimicrobial agent resistant microorganisms

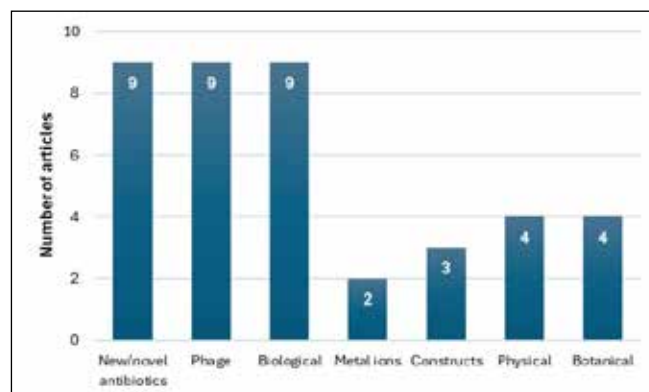


Figure 6. Antimicrobial treatments used against antimicrobial resistant microorganisms

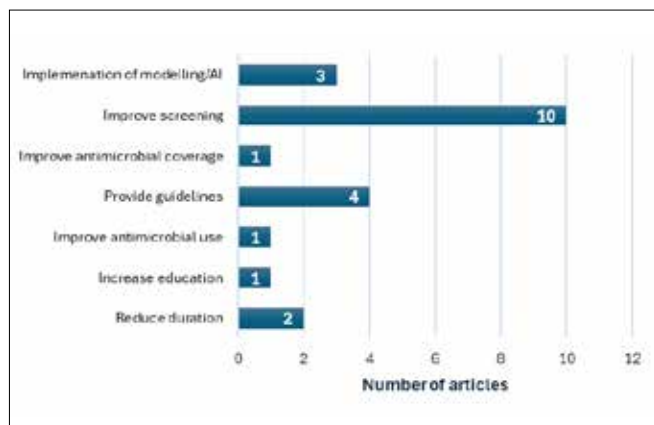


Figure 7. Major areas identified related to updates to AMS practices

There was also positive laboratory^{162,172} — and clinical^{163,178} — based antimicrobial activity reported in several different non-antibiotic antimicrobial agents, termed ‘biologicals’ (Figure 6). In one study, antibacterial peptides were found to be effective in reducing antimicrobial resistant microorganisms in patients with sternal wound infections — and reducing length of hospital stay and reducing costs.¹⁶³ Laboratory-based studies have demonstrated a pentapeptide conjugate with potent activity against MDR clinical isolates of both gram-positive and gram-negative bacteria species belonging to the ESKAPE group of pathogens.¹⁷²

In physical antimicrobial therapy, antimicrobial photodynamic therapy has been shown to have antimicrobial activity against clinical strains from diabetic foot ulcers¹⁵⁶ and prophylactic photodynamic disinfection therapy for spinal SSIs.¹⁶⁶ Using organic light-emitting diodes (OLED) as the light source, and methylene blue as a photosensitiser for the microorganisms, Piksa et al¹⁵⁶ identified these were effective against pathogens and opportunistic bacteria regardless of drug resistance. Antimicrobial agents for treatment of AMR microorganisms based upon the use of metal ions, botanically derived compounds, and constructs are being developed. Nanoparticle forms of silver¹⁶⁵ and zinc¹⁶⁹ have been shown to exhibit potent antibacterial effects for multi-drug resistant *P. aeruginosa*, and carbapenem-resistant *K. pneumoniae*. Electro-fabricated copper-alginate matrices,¹⁵⁸ and antimicrobial nanofibre mats^{171,185} are examples of various forms of constructed matrices that have shown antimicrobial activity against drug resistant microorganisms.

A number of studies have provided further evidence for the mode of action of the antimicrobial effect of DACC-coated dressings and its wide spectrum effect (including WHO-prioritised microorganisms). Additional clinical studies have provided evidence of new applications, such as in treating wounds in paediatric patients, and extended the evidence relating to their use in treating surgical site infections. Evidence also shows that DACC-coated wound dressings can aid in the binding of biofilms, and how this technology can align and support AMS in the prevention of AMR.^{21,23}

The use of non-antibiotic-dependent antimicrobial therapies in the fight against AMR is a promising area with enormous potential for supporting AMS practices. These therapies, particularly those independent of the AMR of microorganisms, offer treatments with broad action potential across multiple resistant microorganisms. Those therapies that minimise the likelihood of subsequent emergence of resistance offer the best potential.

Updates to AMS practices

With the inappropriate use of antimicrobial agents driving the acquisition of antimicrobial resistant pathogens both in hospitals and within the wider community,¹⁹³ it has been reported that 30–50% of hospital antibiotics are considered unnecessary or inappropriate.¹⁹⁴ Laboratory and clinical studies examining AMR in microorganisms have important implications for the updating of AMS processes for minimising the development of AMR.

In 23 papers^{195–217} identified in this review the improvement of microorganism screening was the largest area related to potential points for AMS procedures. A number of these studies highlight the importance of regular screening of patients for multidrug resistant (MDR) microorganisms. Yaacoub et al¹⁹⁹ retrospectively evaluated patients admitted with war-related injuries and found a high proportion of MDR microorganisms (including *Enterobacteriales*, methicillin-resistant *S. aureus* (MRSA), and *P. aeruginosa*). They proposed that regular screening for MDR bacteria coupled with antibiotic-sensitivity testing for an appropriate therapeutic approach to treatment.

To facilitate improved screening a number of screening methodologies for microorganisms are being developed and used clinically. For example, rapid PCR assays have been used for the detection of MRSA from clinical isolates of patients with DFUs,¹⁹⁸ a fluorescence-based assay is being developed to improve diagnostic accuracy of bacterial burden in patients with wounds and guide appropriate antimicrobial treatment,²¹⁰ laboratory studies have provided evidence of the use of novel biosensor technology to develop a whole cell bacteria (for example, MRSA, *P. aeruginosa*).²¹³

AMS-identified processes that can have an impact in reducing the onset of AMR have also been identified in this review, including suggestions for improving antimicrobial use,²⁰⁵ reducing the duration of use of antimicrobials,^{195,200} and improving antimicrobial coverage through the use of the full range of antibiotic classes.¹⁹⁷ Other studies have suggested improved education¹⁹⁶ and the development or updating of guidelines and practices to further enhance AMS practices.^{206,207} Within 10 weeks of implementing a quality improvement project to improve AMS practices, Konda et al²¹² observed a reduction in unindicated antibiotic usage.

Artificial intelligence is being assessed as a potential tool for the identification of AMR which can be applied to the improvement in AMS processes. Rothberg et al²⁰³ developed a logistic regression prediction model to identify risk of resistance in community-acquired pneumonia. In being able to predict infection by resistant pathogens the authors suggested that the integration of the model into clinical use could reduce unnecessary use of broad-spectrum antibiotics. Stracy et al²⁰⁹ used machine learning analyses of data related to urinary and wound infections to predict and minimise treatment-induced emergence of resistance.

Updating AMS practices with procedures, such as improved screening of microorganisms and changing antimicrobial use (such as reducing usage) are all aimed at minimising the opportunity for the emergence of AMR. Improved screening for bacteria also allows for timely identification of resistant microorganisms, including those with MDR.

Updates to AMS implementation

The emergence of AMR is being driven by inappropriate use of antibiotics. Antibiotic consumption in the outpatient setting represents 80% or more of total consumption,²¹⁸ and inappropriate prescribing accounts for up to 50%.²¹⁹ There are a number of key factors that are particularly important for the implementation of AMS programs (ASPs).²¹⁸

Eighteen articles²²⁰⁻²³⁷ were identified that related to updates to AMS implementation. Together, provision of practical training and education, along with the implementation of AMS guidelines were identified as the three main and important areas described in the literature related to the fight against AMR (Figure 8).

Several studies reinforced the opinion that, together, the training and education of healthcare professionals, the implementation of AMS guidelines as part of ASPs are key in the drive to minimise the emergence, as well as reduce the presence, of AMR.^{223,224,227} Sartelli et al²²³ identified that the behaviours of healthcare workers and the characteristics of their workplaces regarding ASPs is key to supporting best practices and for the promotion of behavioural change. As part of a microbiological assessment of 109 samples from

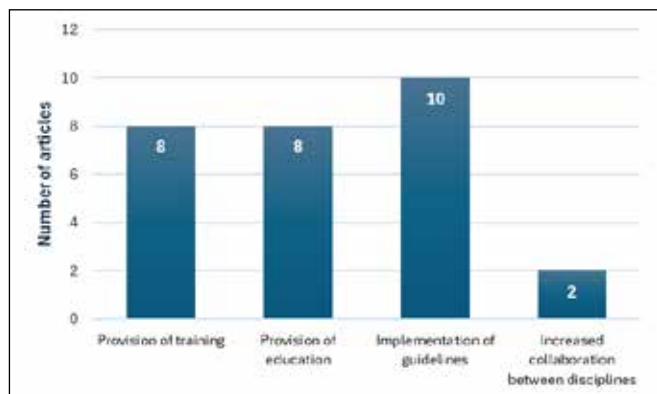


Figure 8. Major areas related to updates to AMS implementation

a variety of clinical sources (including wounds) where a high level of AMR was found, Bashir et al²²⁵ suggested that the input from healthcare professionals with the appropriate expertise (such as pharmacists) can play an important role in promoting the optimal use of antimicrobial agents, and in educating/training other healthcare professionals. For example, where ASPs have been implemented there is an improvement in prescribing practices of antibiotics for surgical prophylaxis; an improvement achieved by initiating educational interventions.²³⁴ It should be noted, however, that poor implementation of established AMS guidelines (related to areas such as prevention practices and protocols) can result in a lack of improvement in AMS-linked benefits such as reductions in antimicrobial prescribing.²²⁹ In a study evaluating the attitudes of infectious disease and critical care physicians towards AMS in ICUs, Vazquez Guillamet et al²²² found that clinicians placed great value on multidisciplinary ICU collaborations.

Alongside updating AMS practices, improvements in the implementation of AMS and ASPs offer benefits to reduce the emergence of resistant microorganisms to current antimicrobial agents. The improvement of AMS processes through better training and more effective education, as well as ensuring the effective delivery of AMS guidelines created to address AMR, aims to optimise all opportunities to help prevent the development of AMR, as well as providing effective treatment for AMR when it arises.

Benefits of AMS

The overall goal of AMS is better patient care, a reduction in the use of antimicrobial agents (particularly antibiotics), and the provision of cost-effective health care.²³⁸ ASPs are designed to provide guidance for the safe and cost-effective use of antimicrobial agents and to slow the emergence of resistant (including multi-drug resistant) microorganisms.²³⁹

Nineteen articles^{122,234,240-256} reported the benefits of AMS implementation. The reported reduction in antimicrobial use was identified as the most frequent benefit of the introduction of AMS (Figure 9). For example, in a quasi-experimental study in patients with spinal cord injury/disease, the implementation of AMS practices reduced the use of peri-procedure antimicrobial prophylaxis in patients

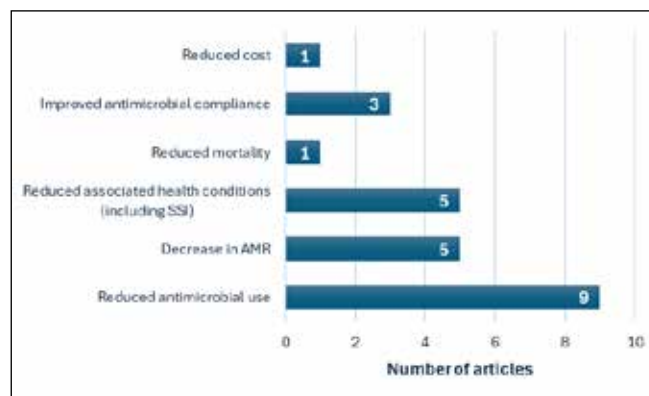


Figure 9. Benefits of AMS implementation

undergoing urological procedures.²⁴⁰ Additionally, a pre- and post-intervention study in patients undergoing surgical procedures, Abubakar et al²⁴⁹ showed that the implementation of AMS procedures (including audit and feedback processes) reduced the prescription of several antibiotics without affecting the rate of SSIs. In this study, AMS implementation also improved appropriate antimicrobial use compliance, a finding reported in several other studies.^{253,255}

The implementation of AMS procedures corresponded with a decrease in levels of antimicrobial resistant microorganisms. For example, Kawamura et al²⁴⁶ reported a reduction in transmission of MRSA SSI as seen by a decrease in orthopaedic MRSA SSIs after the introduction of active MRSA surveillance, preoperative decolonisation, and contact precautions. As well as reducing levels of resistant microorganisms, this review revealed additional benefits of the introduction of AMS procedures. As well as a

reduction in costs (surgical antibiotic prophylaxis costs),²⁴⁹ pharmacist-led interventions in individual patients treated with vancomycin for MRSA resulted in a decrease in levels of acute kidney injury and reduced 30-day mortality rates.²⁴⁷ Interestingly, interventions via ‘facility systems’ (infection control or AMS teams) alone did not show these benefits.²⁴⁷

The benefits of the introduction of AMS procedures appears to be reflected in a corresponding reduction in antimicrobial agent use in healthcare facilities leading to additional benefits, such as reduced healthcare costs and additional improved health outcomes.

Summary

The key points from this review are summarised in Table 1.

Conclusions

Despite AMS being instigated for over 20 years (with

Table 1. Overview of review findings

#	Discussion questions	Comments
1	Is antimicrobial resistance still an issue?	Resistance to antimicrobial agents in microorganisms remains an issue Resistance covers a wide range of antimicrobials Resistance is an increasing problem Options for effective antimicrobial are becoming more limited Emerging resistance to non-antibiotic agents such as silver in an increasing problem
2	Are new antibiotics/ treatment regimens being developed to challenge the development of AMR?	Development of new antibiotics to address the increasing problem of AMR are lacking Combination therapies with current antimicrobial agents being developed based on AMS
3	Are new antimicrobial agents (non-antibiotic) or other antimicrobial therapies being developed to challenge the development of AMR?	The use of non-antibiotic-dependent antimicrobial therapies (such as phytodynamic therapy, phage therapy) in the fight against AMR is a promising area with enormous potential These therapies offer treatments with broad action potential across multiple resistant microorganisms Therapies that minimise the likelihood of emergence of resistance offer the best potential (for example DACC)
4	What are the updates to AMS processes?	Updating AMS practices with procedures such as improved screening of microorganisms and changing antimicrobial use (such as reducing usage) are all aimed at minimising the opportunity for the emergence of AMR Improved screening for bacterial also allows for timely identification of resistant microorganisms including those with MDR
5	What are the updates to AMS implementation?	It offers benefits to reduce the emergence of resistant microorganisms to current antimicrobial agents The improvement of AMS processes through better training and more effective education, as well as ensuring the effective delivery of AMS guidelines created to address AMR, aim to optimise all opportunities to help prevent the development of AMR as well as providing effective treatment for AMR when it arises
6	What benefits have been identified post-AMS implementation?	A reduction in antimicrobial agent use Additional benefits include reduced healthcare costs and additional improved health outcomes

good effect in many cases and the additional benefits of development of strategies and protocols) this review indicates that AMR organisms are still emerging throughout healthcare in general and in wound care in particular. Furthermore, of particular interest to wound care practitioners is that microbial resistance to silver (a mainstay of wound infection treatment) is also emerging as a challenge to the treatment of wound infections.

Although some new antibiotics/combinations are being developed it is apparent that a new approach to treating wound infections is an imperative. As such, this review highlights several treatment options that might offer opportunities for treatment of antimicrobial resistant microorganisms. However, these treatments must meet certain criteria to be viable, including that they must have a wide spectrum of antimicrobial activity, not induce resistance, not have any cytotoxic properties that may interfere with wound healing, and not cause any adverse events that might cause greater patient suffering. These treatments must also be cost effective.

The adoption of AMS as a process within clinical centres, including in wound care, will be challenging. With this in mind, a 'grass roots' road map to support nurses and clinicians in developing AMS strategies would be a useful aid.

Conflict of interest

The authors declare no conflicts of interest.

Ethics statement

An ethics statement is not applicable.

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Author contribution

MGR, AAR and KO conceived the study design. MGR and AAR developed the review protocol and developed the search strategy and inclusion/exclusion criteria, conducted the review and synthesis of the literature. All authors provided critical revisions and feedback on the manuscript.

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