Antimicrobial Stewardship Intervention Before and During The COVID-19 Pandemic in the Acute Care Settings: A Systematic Review

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Abstract

Introduction: Antibiotics are widely administered for various indications, leading to increased antimicrobial resistance (AMR) in acute care hospitals. Since the onset of the COVID-19 pandemic, Antimicrobial Stewardship (AMS) effective strategies should be used to maintain the rational use of antibiotics and decrease the threat of Antimicrobial Resistance (AMR).

Aim: To investigate the AMS intervention Pre-pandemic (PP) and During-the-pandemic (DP) from the literature.

Design and Setting: Systematic review of primary studies on AMS implementation in acute care settings.

Methods: Relevant studies published between 2000 and March 2021 were obtained from Medline (via PubMed), Embase, OVID, CINAHL, International Pharmaceutical Abstracts, Psych Info, Scopus, Web of Science, Cochrane Library, OpenGrey, and Google Scholar, using a comprehensive list of search terms. Public Health England (PHE) toolkit was agreed as a gold standard for the AMS intervention strategies. The methodological quality of included studies was assessed using the Critical Appraisal Skills Programme (CASP) Programme.

Results: There were 8763 articles retrieved from the databases. Out of these, 16 full-text articles met the inclusion criteria for the review. The AMS implementation was identified as AMS strategies, which include core and supplemental strategies and AMS measures PP and DP.

Conclusion: This Systematic review summarises AMS implementation strategies and measures. Appropriate interventions appeared to be effective in maintaining the proper use of antibiotics and decreasing the AMR threat, especially DP. Further studies to investigate AMS implementation presented in this systematic review are imperative.

Introduction:

Alexander Fleming mentioned the concept of antimicrobial resistance (AMR) during his Nobel Prize lecture [1]. Additionally, the rise in multi-drug resistant infections threatens global health through significant morbidity, mortality and global economic loss. Following the O'Neill review and findings in 2016, the number of deaths from AMR infections is estimated to reach 10 million annually due to the AMR crisis [2]. Antimicrobial Stewardship (AMS) is a coherent set of actions that promotes the effective use of antibiotics. It aims to maintain the optimal selection, dosage, route, and duration of antibiotic treatment [3]. Many AMS tools, interventions and activities (collectively termed "strategies") can be used to improve antimicrobial use and educate prescribers. Furthermore, improving antimicrobial use must be measured by identifying the measures to evaluate the outcomes of AMS implementation. AMR is a silent pandemic and one of the biggest threats to global health.

For this reason, Public Health England (PHE) has emphasised the need for AMS implementation to maintain the appropriate use of antibiotics [4]. It was estimated in Lancet's study in 2019 that more than 1.2 million people died worldwide from AMR [5]. The outbreak of infection caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; COVID-19) from Wuhan, China, in December 2019 escalated rapidly to become a global pandemic [6]. In June 2022, the global estimate for people who tested positive for COVID-19 was approximately 544 million. Additionally, the estimated number of total deaths is 6 million, 10% of the worldwide deaths of 60 million [7]. Recent evidence suggests that, as a consequence of the COVID-19 pandemic, increasing numbers of patients admitted to hospitals have been prescribed empirical antimicrobial therapy, which may not always be appropriate, potentially increasing the number of resistant infections globally [8, 9]. While consideration for AMR and AMS focused on supporting the selection of optimal empirical therapies and appropriate de-escalation or discontinuation of antimicrobials when bacterial co-infection is present or absent is essential [10]. Indeed, results from one published systematic review suggested that co-infection prevalence with resistant bacterial organisms was 24%. Sadly, of the 1959 unique isolates identified within the included studies, 569 (29%) were deemed resistant [11]. Additionally, another systematic review and meta-analysis found an overall high antimicrobial consumption among COVID-19 patients [12]. However, the AMS intervention during the COVID-19 pandemic within a systematic review has not been published to date. A critical knowledge gap exists regarding the AMS implementation strategies during the COVID-19 pandemic in acute care settings. This systematic review addressed the research question: "What are the AMS implementation strategies and measures?" The objectives were to (1) review AMS before and during the COVID-19 pandemic; (2) assess the acute care settings and geography; (3) document AMS strategies and measures if available, and (4) estimate the proportion of each strategy and measures reported in the literature.

Materials And Methods:

Study design and search strategy

The review protocol was registered on the PROSPERO database for systematic reviews: CRD42021242388 [14]. The scope of the review was defined by applying the acronym PICOS (Population, Intervention, Comparison, Outcome, Setting). After this, follow the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines for reporting. The PRISMA 2020 was drawn up and approved by the research team before the commencement of the systematic review [13]. The plan was employed as a guidance document to review relevant primary studies published between 2000 and 2021 systematically. It described the scope, intended purpose, and methodological and analytical approach to the review. Ethical approval was not required before the commencement of review as the use of patients' identifiable data was not intended.

Inclusion Criteria

Selected studies were assessed against the following inclusion criteria: (i) Studies written in the English language; (ii) Population of patients prescribed antibiotics aged 18 years and over; (iii) Studies describing the AMS intervention in acute care settings; (iv) Outcomes of AMS strategies, measures, metrics before and during the COVID-19 pandemic; (v) Primary studies (vi) Published between 2000 and 2021. The included study designs were observational (retrospective or prospective case-control, case series non-interventional, cross-sectional, cohort) and interventional (quasi-experimental, randomised controlled trials) studies (table 1).

Table 1: inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Participants	Studies targeting the public/patients' use of antibiotics. HCPs who responsible for prescribing, dispensing, or administering antibiotics (doctors, pharmacists).	Non-HCPs (patient family or community or nursing or long-term care patients).
Intervention	Studies describe an intervention to improve antibiotic prescribing or AMS or any other intervention as the use of the parenteral-to-oral switch, and the duration of IV and oral antibiotics.	Studies that do not describe an AMS intervention
Comparison	Comparison with a control group/a group that carried out usual care without an AMS intervention; comparison between two or more AMS interventions.	
Context	Interventions carried out in adult inpatient settings in acute care hospitals.	Interventions carried out in nursing homes, care homes or long-term healthcare facilities; community settings; paediatric setting/hospital; and animals/ veterinary practice.
Outcomes	Primary outcomes: reviewing the AMS implementation before and during the COVID-19 pandemic.	
	Secondary outcomes: other AMS measures, metrics, quality improvement before and during the COVID-19 pandemic.	
Study design	RCTs, non-randomized trials, CBA studies, interrupted time series designs, case-control studies and cohort studies, cross-sectional studies, qualitative studies.	Systematic reviews, meta-analysis, single case studies, case reports, and conference abstracts.

Exclusion Criteria

Any study that did not fulfil criteria for inclusion, studies unrelated to review objectives, abstract-only papers, non-human subject studies and systematic review studies.

Data Sources and Search Methods

An electronic search of International Pharmaceutical Abstracts, MEDLINE (via PubMed), CINAHL, Embase, PsychINFO, SCOPUS, Cochrane Library, Web of Science, Cochrane and Google Scholar [15], and references included articles were undertaken for relevant studies [16, 17] (table 2). Choices of databases to be searched were based on insights from the method's section-related reviews. All databases were searched from 2000 to March 2021. The AMS strategies and metrics identified within the MEDLINE database through the MeSH term "antimicrobial stewardship" was employed as search terms for AMS intervention. Antibiotic use before and during the COVID-19 pandemic was employed as the search term. Settings were specified as acute care settings, AND/OR were used to combine search terms. The "snowballing" strategy, going through the reference list of all included studies to obtain further relevant studies, was also employed.

Table 2: The systematic review of search strategies

Box 1 Search Strategy
1. Antimicrobial resistance OR antibiotic management OR acute care settings OR hospitals.
2. Antimicrobial stewardship OR antimicrobial utilisation OR antimicrobial use OR antimicrobial stewardship strategies OR antibiotic metrics OR antimicrobial stewardship intervention OR antimicrobial stewardship outcomes OR antibiotic use.
3. COVID19 OR coronavirus OR SARS CoV2 OR severe acute respiratory infection OR pandemic.
4. 1 AND 2 AND 3
5. Limit 18-65 to yr. = '2007-2021' = lang: 'English'

Study Selection and Validation Process

Following a literature search of the databases by one reviewer (RAE), studies were exported to Mendeley. Titles and abstracts were screened for relevance; duplicates were removed, followed by a screening of the complete articles for possible inclusion by one reviewer (RAE). Another reviewer (ZA) independently reviewed the titles, abstracts, and full studies, confirmed the relevance of studies in meeting the inclusion criteria and excluded studies deemed irrelevant. There was a complete agreement on the relevance of selected studies by RAE and ZA.

Data Collection:

Before performing the full review, a data extraction form was developed and tested through a pilot data extraction. The pilot extraction form was tested by co-authors (R.A.E., Z.A., and N.U.) on the first 60 articles extracted from PubMed and Embase databases. Additional suggestions and amendments to the search teams were made.

The studies included in the review were assessed for risk of bias using the Critical Appraisal Skills Programme (CASP), which has a set of eight critical appraisal tools which are designed to be used to assess the trustworthiness systematically, relevance and results of published papers designed for use with randomised controlled trials, cohort studies, case-control studies, and qualitative studies [18]. Articles were divided among the three authors (RAE, ZA, NU) equally and reviewed to ensure the quality assessment's accuracy, validity and reliability. After that, the three authors (RAE, NA and ZA) critically appraised all the included studies independently, and then the results were discussed. Articles were included if they fulfilled all the inclusion criteria (table 2).

Data extraction forms were created by the primary reviewer (RAE). It included the author's last name, year of study, country, study design, the AMS intervention strategies and outcome measures, and quality of study analysis. Three studies were initially piloted to test the form. RAE extracted the data into this form. Data obtained were grouped and summarised using narrative synthesis into two groups, each before the COVID-19 pandemic and another during the pandemic. Meta-analysis could not be performed because of the heterogeneity of the included studies. It is necessary to mention that the AMS strategies were categorised according to the Public Health England (PHE) toolkit for AMS implementation classification into core and supplement strategies [4].

Additionally, the AMS metrics or measures were categorised according to the practical guide for AMS implementation, the NICE guidelines, and the WHO criteria [19]. The comprehensive classification was applied for AMS intervention strategies and measures based on the PHE guidelines and WHO criteria. Another author (ABA) independently extracts the data in the data extraction form. AM identified the final set of included and relevant studies. ABA read the full text of each article and extracted data in the data extraction form. Discrepancies in the extracted data were documented and resolved by discussion or adjudication with a third author (ZA).

The following data were extracted for all included articles:

- location of study (specific hospital department or hospital-wide);
- country of study;
- year of study (before or during the COVID-19 pandemic);
- method(s) of data collection;
- antimicrobial stewardship strategies, measures, outcomes, and quality improvements;
- Quality of study.

Results:

The Ams Implementation Lead

This study also determined the healthcare professionals' (HCPs) role in AMS implementation. Of the 16 studies, only three mentioned the pharmacists' role as a lead for AMS implementation PP [20, 21, 26]. The pharmacists' lead role decreased from 22–17% DP. Microbiology lead for AMS represented 45% and 50% of the studies BP and DP, and the infection control AMS lead stayed the same in 33% of the studies, BP and DP (Fig. 3).

- After the search records, title, abstract, and full-text screening, 16 articles met the inclusion criteria for the review (Tables 3, 4).

Table 3
Characteristics of Included Studies Pre-pandemic.

Study	Country	Study type	AMS strategies	AMS Measures/Metrics	Study Quality
Chung (2013)	Singapore	Prospective cohort	Prospective audit and feedback, clinical Decision support systems (CDSS), formulary restriction, drug pre-authorization, prescriber education, patient education, clinical guidelines, point of care tests, microbiology laboratory susceptibility reporting, and antibiotic review (48–72 hrs) for bacterial culture results.	The defined daily doses (DDD) or days of therapy (DOT), reduce the length of hospital stay, 14-d reinfection rate and infection-related re-admissions, mortality related to antimicrobial-resistant pathogens, and other antibiotic use measures: timeliness, correct antibiotic choice and duration of therapy.	**
Mehta (2014)	United States	Randomized clinical trial	The change from prior authorisation to prospective audit with feedback was associated with a significant increase both in the use of the affected antimicrobials and in the overall use of all antimicrobial agents.	Quality improvement projects, such as parenteral-to-oral switch projects, and appropriate use of restricted antibiotics. Quality indicators, such as empirical systemic antibiotics prescribed according to the national guideline, switched antibiotic therapy from a parenteral-to-oral switch within 48–72 hours based on the clinical condition and when oral treatment is adequate, empirical antibiotic therapy should be changed to pathogen-directed therapy if culture results become available, and renal dose adjustment.	***
Ababneh (2020)	Jordan	Cross-sectional study	Antibiotic review in the electronic charts, and hospitals' electronic healthcare system (iSoft) for each patient to obtain information regarding age, gender, hospital ward, antimicrobials (agents, dose, route, duration, starting/ending dates), and the total number of admissions.	DDDs and DOTs	**
Moriyama (2021)	Japan	Cross-sectional study	Prospective audit and feedback protocol, preauthorization procedures, notification protocols, antibiotic guidelines, and antibiotic review when using broad-spectrum antimicrobials within 7 days.	The numbers for hospitals that had intervention procedures within 7 days and 28 days.	***
Panditrao (2021)	India	Randomized clinical trial	Antibiotic timeout, antibiotic review, and education	DDD, LOS, DOT, and care bundle approach for prevention of hospital-acquired infections (HAIs).	***
Thakkar (2021)	India	Prospective cohort study	Generation of antibiogram, education, antibiotic policies and guidelines, antibiotic review at 48–72 hours from the time of prescription, and multidisciplinary AMS committee.	DOT, Colistin susceptibility rates compared to the previous years, assess the compliance to AMS recommendations.	**
Trivedi (2013)	United States	Cross sectional study	AMS core strategies, such as formulary restriction, antibiotic review, automatic stop orders, preauthorization, and prospective review with feedback. AMS supplemental strategies, such as education, dose optimisation, dose adjustments, guidelines and clinical pathways, parenteral-to-oral switch, streamlining, de-escalation, and antimicrobial order forms.	Outcomes measured included antimicrobial resistance patterns (39%), antimicrobial utilization (36%), antimicrobial costs (35%), Clostridium difficile infection rates (32%), adverse effects (22%), 17% reported monitoring DDD and 13% reported monitoring DOT. For a positive trend in outcomes data since the initiation of the ASP, including improved antimicrobial use (74%), decreased antimicrobial costs (63%), and improved antimicrobial susceptibility patterns (47%), and 38% used computer software to interface with electronic records facilitated ASP.	***
Spernovasilis (2021)	Greece	Cross sectional study	Prospective audit and feedback strategy, case-based education of treating doctors, provide unsolicited in-person ("handshake") consultation within 72 hours, and antibiotic review	Hospital resistance data, hospital guidelines for the MDROs, AMS Education and training, and AMS mobile applications.	***

Study	Country	Study type	AMS strategies	AMS Measures/Metrics	Study Quality
Weston (2012)	United States	Cross sectional study	Antibiotic restriction, by using new restriction methods, such as front-end back end, automatic stop orders, ID consult required, verbal approval required. Antibiotic guidelines and clinical pathways, antimicrobial order forms, streamlining or de-escalation, dose optimization, parenteral-to-oral switch, and closed formulary.	A structured educational program entitled, 'Building Stewardship': A Team Approach Enhancing Antibiotic Stewardship. The program focuses on the importance of ASPs, strategies for implementation, and operational issues, including an understanding of pharmacodynamics, business models, and electronic surveillance. New educational techniques, such as newsletter, email, grand rounds conferences.	***
Kallen (2017)	Netherlands	Randomized clinical trial	The extraction and feedback on antibiotic use data provide feedback on validated quality indicators (QIs) for appropriate antibiotic use (PPS-QI, and performance of a PPS to provide feedback measurement.	LOS, DOT, and the percentage of patients admitted to the ICU was lower after the intervention (4.8%, N = 201 patients).	***

Table 4
Characteristics of Included Studies During the Pandemic.

Study	Country	Study type	AMS strategies	AMS Measures/Metrics	Study Quality
Guisado-Gil (2020)	Spain	Quasi-experimental before-after study of interrupted time-series	Multidisciplinary teams to attend COVID-19 patients, differentiation of a “clean area” for SARS-CoV-2 uninfected patients and a “contaminated area” for patients diagnosed with COVID-19, periodical training sessions on the use of personal protective equipment, daily online meetings about local pandemic evolution and patient management, and development of local clinical guidelines for the treatment of SARS-CoV-2 infection, in which it is specifically recommended not to prescribe empirical antibiotics unless there is clinical suspicion of a bacterial infection.	The weekly antimicrobial use increased in the non-COVID-19 wards as well as the COVID-19 ward, with the latter increase being statistically significant (+ 45.0% weekly change; p = 0.006), the death rate on day + 14 due to MDR bacterial BSI was 0.07 cases per 1000 OBD, DDD per 1000 occupied bed days (OBD), and the causal agents of hospital-acquired BSI recorded weekly: Escherichia coli, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa, and Staphylococcus aureus.	***
Guerra (2021)	United States	Prospective cohort study	Prior authorization, prospective audit with feedback	The primary outcome was the development of hospital-acquired infection (HAI). For each HAI episode, causative microorganism and susceptibility patterns were recorded. The secondary outcomes included death during hospitalisation and LOS.	**
Williams (2021)	United Kingdom	Retrospective observational study	Procalcitonin (PCT) measurement for any patient requiring admission to a hospital with COVID-19 and the inclusion of PCT in an electronic ‘COVID order set’ also promoted its measurement, and the PCT assay was undertaken within 48 h of collection of the first positive SARS-CoV-2 sample.	Patients in the negative PCT group received significantly fewer DDDs of antibiotics compared with patients in the positive PCT group (median DDD 3.0 vs 6.8; P < 0.001).	***
Ashiru-Oredope (2021)	United Kingdom	Cross sectional study	Audit (Start Smart then Focus (SSTF) studies, and the use of the CURB65 scoring, education and training, multidisciplinary AMS team and updated antimicrobial guidelines National Institute for Health and Care Excellence (NICE).	The use of Clostridioides difficile infection (CDI) number of cases, parenteral-to-oral switch. Novel biomarkers, such as Procalcitonin Test was used for differentiating viral and bacterial infections, Antibiotic Kit Review (ARK). The technology was increasingly used as a tool to facilitate AMS, e.g., virtual meetings, Point Prevalence Surveys (PPS), and the use of Key Performance Indicators (KPIs), such as the AMR local indicators - produced by the UKHSA.	***
Surat (2021)	Germany	Retrospective cohort analysis	AMS multidisciplinary committee and regular ward rounds, the formulary restriction, the antibiotic resistogram profiles, the implementation and electronic access to antimicrobial prescribing guidelines, and mobile applications.	Surveillance data on antimicrobial resistance, and antibiotic consumption rate measured by the recommended daily doses (DDDs) per 100 patient days for the hospital, overall reduction in the total days on antibiotic therapy (DOT) from a mean of 6.1 days to 4.8 days.	
Tamma (2021)	United States	Cross sectional study	Implementation webinars of AMS, antibiotic guidelines, antibiotic time-out, clinical rounds, and antibiotic user guides, identify antibiotic safety and adverse events, antibiotic review, use innovative strategy of the four moments of antibiotic decision-making framework including: make the diagnosis, cultures, and empiric therapy, stop, narrow, change to oral antibiotics and duration.	The Team Antibiotic Review Forms (TARF) participating per month in the units and submit results on the Program website, A hospital-wide gap analysis was done in the start of the program, and antibiotic use decreased from 861 to 845 DOT per 1000 PD.	

AMS Strategies Pre- and During the Pandemic

The AMS strategies have optimised antibiotic prescribing and reduced antibiotic use. In this review, a range of AMS intervention strategies has been classified according to the AMS implementation guidelines of the United States Infectious Disease Society of America (IDSA) and UK Public Health England toolkit into core and supplemental strategies [4, 27, 28].

For the AMS core strategies, the prospective audit and feedback was the most implemented AMS strategy, as it is found in 8 of the 16 studies. During the COVID-19 pandemic, the prospective audit & feedback strategy was used in only 2 studies [19, 29]. The multidisciplinary team was the second most common AMS strategy; 50% of studies applied PP (Table 3), and three implemented interdisciplinary teams DP [17, 18, 30] (Table 4). The formulary restriction was the third common strategy used PP as it was applied in 5 of 16 studies. Though only two studies applied DP [18, 30]. The prior authorisation AMS strategy was the fourth strategy most used before the COVID-19 pandemic, and only one study used this strategy DP [29].

Regarding the AMS supplemental strategies, AMS education was the most common strategy for the supplemental strategies, as 6 of 16 studies applied this strategy. AMS education strategy was used in 3 of 16 studies DP [19, 30, 31]. The clinical decision support strategy was the second most common supplemental strategy, it was used in two studies DP [16, 18]. The clinical practice guidelines and streamlining/escalation were the third most used AMS strategies DP. Antibiotic review strategy was reported in three studies PP [23, 32, 21]. Descriptive statistics were used to describe the variability and proportion of the AMS implementation strategies reported in all the included studies.

Most quantitative studies were retrospective. Only three studies were prospective [1, 27, 31]. Most of the studies were interventional, whereas three studies were randomised-controlled trials [33, 19, 34], one study had a before-and-after design [31], another study was observational [16], and two studies were cross-sectional [17, 19] (Tables 3, 4).

AMS Measures Pre- and During the Pandemic

In both PP and DP, most of the sixteen studies included in this research report AMS measures in terms of Daily Defined Dose (DDD) and/or Day of Therapy (DOT) [23, 32, 33] (Table 5).

Pre-pandemic, the following measures were used. The AMS outcome measures of DDD and DOT were used in eight studies. The parenteral-to-oral switch measure was the fourth most common AMS measure, as only three studies applied it [20, 21, 26]. Of the 16 studies. At the same time, the Length of Stay measure (LOS) was found in only one study [20]. Interestingly.

During the pandemic, the following measures were used. Four studies used DOT [16, 18, 19, 30], and five studies used DDD [16, 17, 18, 19, 31]. The Clostridium Difficile Infection (CDI) measure was used in only three [16, 17, 30]. Significantly, the use of specific measures, for example, the Procalcitonin Test (PCT), was found in only one study but showed a promising outcome [16]. Interestingly, one study showed that the use of Key Performance Indicators (KPIs), such as the AMR local indicators - produced by The UK Health Security Agency (UKHSA) and the WHO watch of narrow-spectrum antibiotics in NHS hospitals in the UK, was very helpful during the pandemic [19].

Discussion:

In this systematic review, data from all the included studies were analysed from over 64,000 patients prescribed antibiotics PP and DP between January 2000 and March 2021 in acute care settings. It aimed to investigate the AMS strategies and measures PP and DP [34]. Potential overuse and irrational antimicrobial prescribing have become a complex conundrum for healthcare [35]. This can impact patient safety, progressive AMR, and an incremental economic burden on the healthcare system [12]. The leading cause of respiratory tract infections, mainly upper respiratory tract infections (URTI), are viruses [36]. According to the WHO's statement, 71% of URTIs are usually treated with antimicrobials [37]. Interestingly, findings from Chung et al. (2013) study reported a lack of strong scientific evidence for most antimicrobial stewardship interventions, which has led to confusion and disagreement about their effectiveness. Both experts and professional bodies continue to reiterate the need for more effective AMS research [1].

Although COVID-19 is a viral disease, prescribing antimicrobials has become a more common practice since the onset of the pandemic [38]. This high antimicrobial consumption in COVID-19 patients was initiated after early reports from China revealed that 50% of patients died from secondary bacterial infection [39]. There was a variation in the AMS implementation strategies and measures among different studies, which can be attributed to several factors. For instance, the core AMS implementation strategies, such as prospective audit & feedback, formulary restriction and multidisciplinary team, were the most common strategies used by PP and DP, as they have been implemented in 70% of the studies PP. Then they decreased to 23% DP [19, 29] (Table 5).

Meanwhile, the AMS supplemental strategies, such as clinical decision support, clinical practice guidelines and education, were the most used, as they were applied in 33% of the included studies PP. Then they decreased to 17% DP [16, 18]. This means that the AMS strategies that require organisational collaboration or hospital-wide implementation were more effective than the AMS strategies on the individual level during a crisis or emergency, such as the COVID-19 pandemic.

Significantly, AMS education using active learning activities was a helpful AMS core strategy PP. For example, in Weston et al. study (2012), it was reported that the use of the AMS educational program entitled 'Building Stewardship: A Team Approach Enhancing Antibiotic Stewardship in Acute Care Hospitals' offered by the Agency for Healthcare Research and Quality (AHRQ) safety program was highly effective, as it focused on the importance of Antimicrobial Stewardship Programs (ASPs), strategies for implementation, and operational issues, including an understanding of pharmacodynamics, business models, and electronic surveillance [40]. Notably, the national study that mandated the presence of ASPs in the state of California has revealed successful outcomes in this arena [21]. Additionally, the educational program in Massachusetts also had a significant effect on the implementation of ASPs and the improvement of existing programs [40]. During the COVID-19 pandemic, there was a critical need for structured ASP education to deal effectively with this crisis as AMS education decreased by 50% DP [26, 28, 41].

Using clinical practice guidelines, DP was essential to decreasing AMR [41, 28, 25]. In addition, adherence to the local, national, and international guideline recommendations is vital to prevent over- and inappropriate prescribing of antimicrobials. For example, the study of Ashiru-Oredope (2021) suggested the importance of the updated antimicrobial guidelines National Institute for Health and Care Excellence (NICE), as well as international guidelines from the World Health Organization (WHO) and International Pharmaceutical Federation (FIP), were highly effective DP [28]. The local or organisational clinical practice guidelines should be adapted based on the local antibiograms and resistogram in order to maintain the relevance of the antimicrobial guidelines, as recommended by Surat et al. (2021) study, which will decrease the inappropriate use of antibiotics and decrease the AMR [25]. Additionally, the management of clinical pathways, such as pneumonia and respiratory tract infections in COVID-19 patients, should be updated [28].

During the pandemic, the use of technology in the clinical decision support system was very interesting, as it provided an innovative and simple way for the AMS implementation. For example, it enhanced electronic access to antimicrobial prescribing guidelines. Additionally, its use in the novel metrics, such as the PCT in an electronic 'COVID order set', facilitated AMS measures and surveillance [29]. The use of integrated computerised systems was still effective in reducing AMR. Interestingly, the use of new technology ideas such as mobile applications in updating the antimicrobial guidelines was effective, such as the Commonwealth Partnerships for Antimicrobial Stewardship (CwPAMS) App [28], antibiotic order forms, prescribing and availability of guidelines on smartphones [29, 25]. The use of technology was effectively considered in the AMS measures, such as KPIs, and the use of novel PCT lab tests significantly improved antibiotic prescribing and enhanced the proper communication of hospital-wide DP [29].

As mentioned in the result section, it must be measured by identifying the measures that can be used to evaluate the outcome of AMS implementation to improve antibiotic use and AMS intervention. These measures or metrics can be used for many purposes, such as quality assurance, improvement, comparisons, and benchmarking. Before 2019, there were no reliable means for measuring antimicrobial usage. The WHO promoted measurable tools, such as the defined daily dose (DDD) and Day of Therapy (DOT), to allow comparisons for antimicrobial usage among hospitals and countries [37, 42]. In the included studies, the DDD and DOT are the most common AMS measures, as it was used in 53% of PP and 28% of DP. Significantly, Ashiru-Oredope et al. (2021) study promoted the use of KPIs, such as the AMR local indicators - produced by the UKHSA among the National Health Service (NHS) hospitals in England, and it showed a significant outcome in AMS and provided a comparative measure for the antibiotic prescribing among different periods DP [28, 43].

During the pandemic, some measures were of limited use, such as re-admission, antimicrobial utilisation, surveillance reports, and parenteral-to-oral switch. Hence, it is difficult to determine which of these measures are effective, and further investigation is required. Additionally, some measures only used PP, such as the LOS and cost [31, 21]; however, there is insufficient information in the literature regarding their use in pandemics DP (Table 5).

This review has also identified how HCPs were involved in leading AMS in acute care settings, where their work had potentially influenced the AMS implementation in acute care settings. Both microbiology and infection control practitioners represented around 70% of leading AMS, either PP or DP. The infection control champion practitioner has a vital role in Point Prevalence Surveys (PPS), implementation of the infection prevention and control (IPC) bundles, and preventive measures, such as hand hygiene and other *personal protective equipment* (PPE) measures [28]. On the other hand, the microbiology roles in an antibiotic review (48–72 Hours), antibiogram, antimicrobial resistance reports (resistogram), novel lab test measures such as PCT, and multidrug resistance incidence were highly effective DP [25]. Although pharmacists are antibiotic experts, they were underutilised in leading AMS, as the pharmacist AMS champion was represented in only 22% PP and 17%. Pharmacists have a thorough knowledge of medications, and their emerging role in medication safety is crucial in AMS implementation. In Weston et al. (2012) study, pharmacists led AMS implementation; the hospitals reported a positive outcome after initiation of ASP education; pharmacists were able to perform the "low-hanging fruit" outcomes to facilitate ASP intervention. In addition, they were dedicated to applying AMS supplemented strategies, such as antimicrobial review and antibiotic restriction [40]. Pharmacists also have an essential role in the interdisciplinary rounds (IDR) [44], which enable them to review patients prescribed antibiotics using the electronic medical record, in addition to monitoring the antibiotics used, culture results, and therapy duration. The involvement of pharmacists in the multidisciplinary meetings and leading AMS was so helpful [45]. Pharmacists working in collaboration with other health care professionals have an essential role in the global mandate of AMS implementation.

Limitations of the Systematic Review

Searching only published databases could have resulted in missing some potentially relevant but unpublished studies from the review. Secondly, limiting studies to being published in the English language could have resulted in missing essential studies published in other languages.

Limitations of the Evidence

To the knowledge of the authors, this is the first systematic review to assess the AMS implementation of PP and DP. However, there are insufficient studies using the AMS strategies and measures. Authors did their best to compare the AMS strategies and measures, but variation in their use affected the comparability of findings across studies.

Comparison with Existing Literature

A few reviews have assessed the AMS in hospitalised patients. However, none of the reviewers has focused on the core and supplemental AMS strategies, nor the AMS measures in Secondary care and acute care settings PP and DP as explored in this present systematic review.

Implications for Research and Practice

Few studies identified the AMS measures, the use of AMS indicators and quality improvement projects which are relevant to this systematic review. Therefore, further studies are required to provide measurable indicators for assessing AMS implementation. It will also enable the planning and evaluation of suitable AMS interventions. Secondly, further research is required to develop methods for standardised measurements for AMS implementation that will allow greater comparability of AMS outcomes and measures across studies. Lastly, there was evidence that antibiotic use is best achieved with organisational collaboration, especially during an emergency or pandemic. All HCPs have an effective role to play in this.

Summary and recommendations

This systematic literature review showed promising outcomes in selecting the appropriate AMS intervention strategies. However, the ongoing global crisis of AMR must not be neglected. The present systematic review included studies showing the AMS strategies and measures used PP and DP in acute care settings. There are so many lessons learnt from the COVID-19 pandemic. Each hospital should use relevant AMS strategies and measures during a crisis or emergency. This will ensure effective AMS implementation and decrease the AMR threat. Urgent actions are required to provide better preparedness for future pandemics. Advocacy for AMS must continue in the post-pandemic era to assure the safety of patient care. Results from studies in AMS implementation need to be robust to provide a basis for clinical decision-making and policymakers. Therefore guidance development is needed for AMS implementation, as summarised in the following recommendations:

1. Reliability of the AMS implementation strategies can be country-specific, such as the UKHSA national indicators. Appropriate tools must be used in each country to achieve reliable outcomes.
2. Presently, though DDD and DOT are the most common AMS measures, other measures are used PP and DP. There is thus a need to standardise systems as this will allow better comparison of outcomes and planning of effective AMS interventions.
3. Appropriate use of antibiotics and use of the proper AMS strategy result in the reduction of AMR and achieve the action plan goal, such as the UK government released a 5 Year AMR Strategy 2013–2018 in 2013 and a five-year National Action Plan 2014–2019 in 2019, with ambitions to reduce UK antimicrobial use in humans by 15% by 2024.
4. Collaboration among health care professionals in planning and implementing the AMS interventions is required for optimal results of decreasing AMR.
5. Novel AMS measures, such as PCT and the proper use of technology, provide a promising effect on AMS.
6. Collaborative AMS implementation, such as multidisciplinary team, AMS education, and country-level KPIs, showed promising outcomes rather than individual AMS strategies, such as antibiotic review and de-escalation, especially during an emergency or pandemic.
7. During a crisis, or emergency, such as the COVID-19 pandemic, antibiotics appeared to be over-used in hospitalised people. There should be an action plan for AMS to be prepared for any further or future emergencies.

Declarations:

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data supporting the conclusions of this article are included within the article and a list of references.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RAE participated in protocol development, literature searching, data extraction, data analysis and manuscript preparation; NU participated in protocol development and data analysis and independently reviewed the quality of studies and manuscript preparation. ZA participated in protocol development, literature searching, and data extraction, independently reviewed the quality of studies, selection, and driving ideas, and provided subject-specific comments to update the manuscript. ABA conducted the data extraction for the included studies independently.

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Table 5:

Table 5 is available in the Supplemental Files section.

Figures

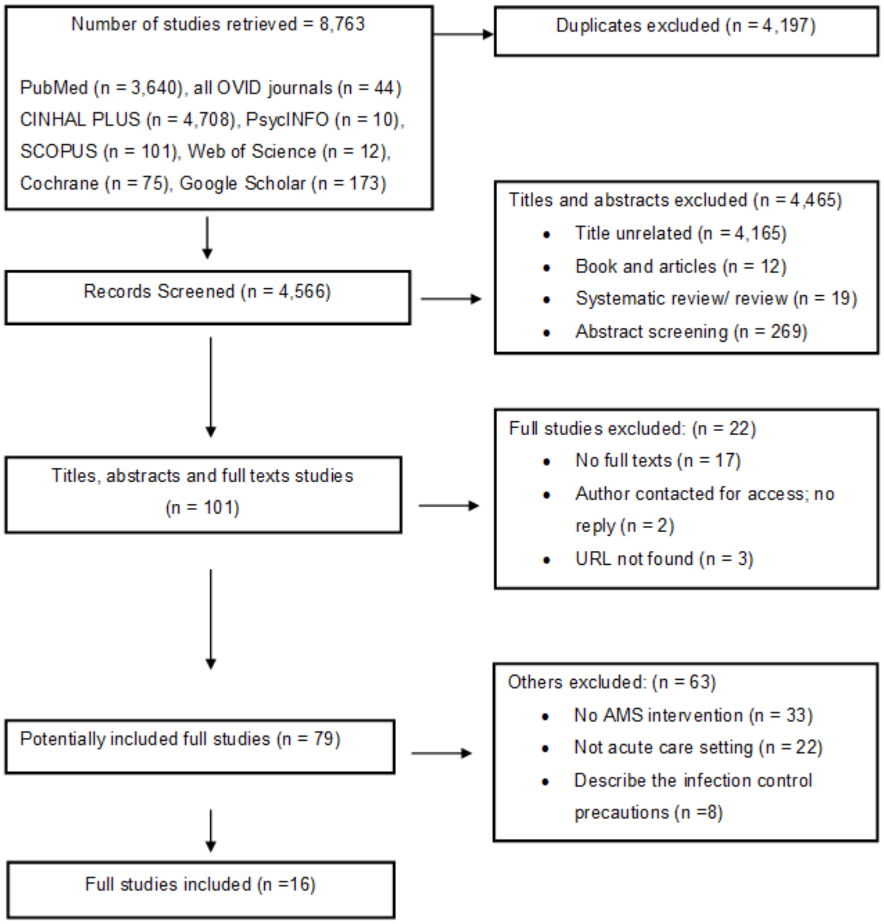

Figure 1

The PRISMA flow diagram for study selection

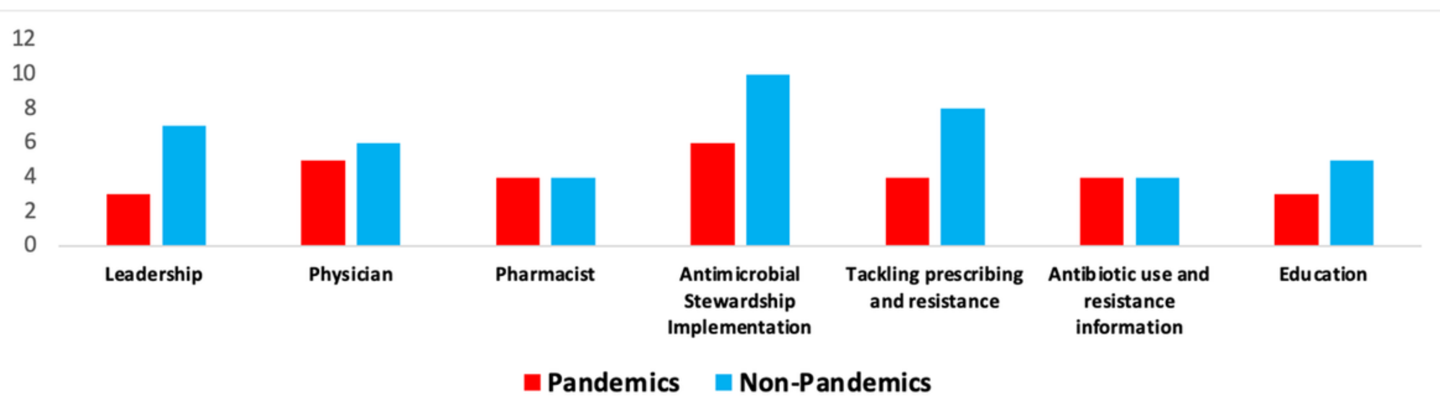

Figure 2

ECDC Elements for Successful Antimicrobial Stewardship

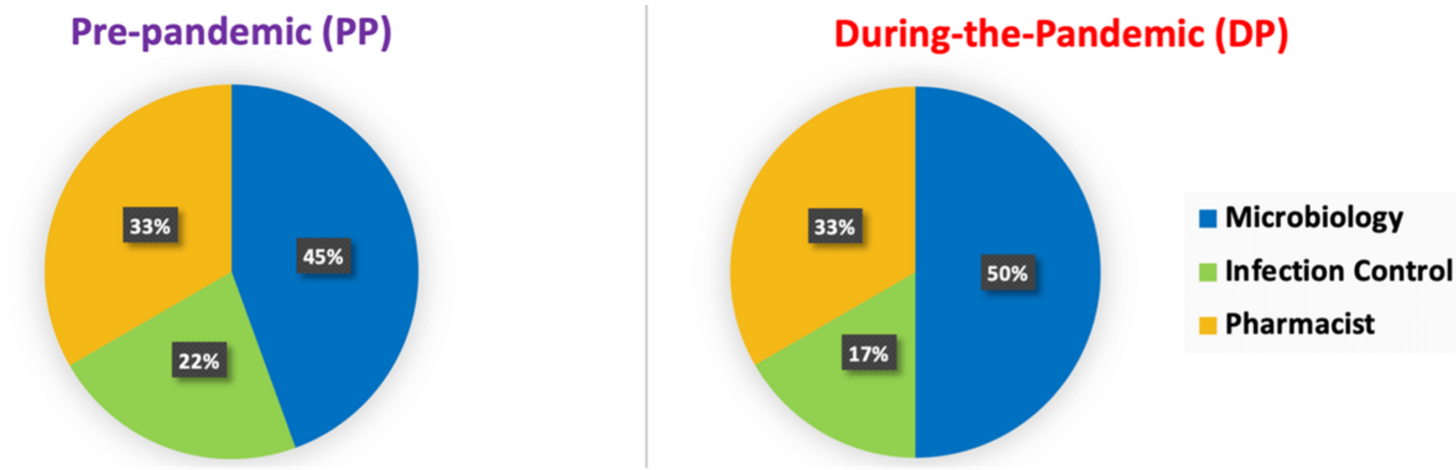

Figure 3

Healthcare Professionals (HCPs) roles in leading AMS implementation

Supplementary Files

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- Table5.docx