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Systematic Review

Mapping hospital antimicrobial stewardship programmes in the Gulf Cooperation Council states against international standards: a systematic review

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SUMMARY

Background: While there is evidence of implementation of antimicrobial stewardship programmes (ASPs) in the Gulf Cooperation Council (GCC) states, there has been limited benchmarking and mapping to international standards and frameworks.

Aim: To critically appraise and synthesize the evidence of ASP implementation in GCC hospitals with reference to the framework of the Centers for Disease Control and Prevention (CDC), identifying key facilitators and barriers.

Methods: A systematic review protocol was developed based on Preferred Reporting Items for Systematic Reviews and Meta-analyses for Protocols guidelines. Five electronic databases were searched for studies published in English from 2010 onwards. Study selection, quality assessment and data extraction were performed independently by two reviewers. A narrative synthesis was conducted with ASP interventions mapped to CDC core elements.

Findings: Seventeen studies were identified, most of which (N=11) were from Saudi Arabia. Mapping to the CDC framework identified key areas of strengths and weaknesses in reporting implementation. Studies more commonly reported core elements of pharmacy expertise, selected aspects of implementation actions, tracking, antibiotic use and resistance, and education. Little emphasis was placed on the reporting of leadership and accountability. Key implementation facilitators were physician and organization support, information systems and education, and barriers were dedicated staff, workload and funding.

Conclusion: There is a need to enhance the reporting of ASP implementation in GCC hospitals. The CDC framework should be used as a guide during the development, implementation and reporting of ASP interventions. Action is required to identify facilitators and overcome barriers, where possible.

Introduction

An antimicrobial stewardship programme (ASP) is defined by the World Health Organization (WHO) as 'An organizational or system-wide health-care strategy to promote appropriate use

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of antimicrobials through the implementation of evidence-based interventions [1]. To facilitate successful ASP implementation, several national and international collaborative groups have developed consensus-based interventions [2,3]. These interventions, grouped in toolkits, guidelines or frameworks, have been used in planning, developing, implementing and measuring the impact of ASPs [3] and in guiding audit [4]. Examples of grouped interventions include: 'Start Smart then Focus toolkit' in English hospitals [5], 'European Union Guidelines for the Prudent Use of Antimicrobials in Human Health' [6], and the 'WHO Practical Toolkit for ASP in Healthcare Facilities in Low and Middle Income Countries' [1].

One of the most widely cited grouped interventions is the framework produced by the Centers for Disease Control and Prevention (CDC) which groups interventions for hospital-based ASPs into seven core elements: hospital leadership; commitment; accountability; pharmacist expertise; actions; tracking; and reporting and education [7]. First published in 2014, the framework was updated in November 2019 to reflect new evidence and experiences gained in the preceding years (see Appendix I, online supplementary material) [8].

In the USA, the CDC Division of Healthcare Quality Promotion uses the framework to evaluate the level of ASP implementation across acute care hospitals, identifying and defining gaps to be addressed at national level [9,10]. The framework has also been used in several US studies as an analysis tool to identify gaps in ASP implementation in acute care hospitals [10—13]. In addition, it has been adopted in the development of consensus-based checklists for high- and low-to-middle income countries [3,4].

The Gulf Cooperation Council (GCC) is a political and economic alliance of six countries in the Arabian Peninsula — Bahrain, Kuwait, Oman, Qatar, Kingdom of Saudi Arabia (KSA) and United Arab Emirates (UAE). ASP implementation in GCC healthcare systems was largely driven by the increased antimicrobial resistance (AMR) burden and the identification of novel and rare resistance mechanisms [14—16]. Specific reasons for the development of resistance in GCC healthcare systems include: lack of ASP; high burden of broad-spectrum antimicrobial prescribing; outdated hospital architectural design; lack of robust infection control programmes; lack of trained staff; and lack of integrated computerized hospital systems and information technologists [15,17,18]. Recognition of the growing burden of AMR led to establishment of the GCC Centre for Infection Control in 2005. A decade later, the Centre published and disseminated the first GCC strategic plan for combating AMR, addressing several aspects (healthcare systems, agriculture and research) with the major strategic aim being to preserve antibiotics from increasing development of resistance [17]. This was a high-level plan which included general recommendations rather than specific actions to implement ASPs, and aimed to complement the global action plan issued by WHO [19]. The task of implementation was then passed on to each individual country. However, there is a paucity of data on the success or otherwise of actual implementation of the plan in each of the countries.

While a number of systematic reviews have summarized components of hospital-based ASPs [20—23], few have focused on specific countries or regions of the Middle East [24] or GCC states [25]. It is well recognized and documented that ASP implementation can vary greatly between geographical regions for different reasons, including diagnostic challenges, variation in knowledge and awareness, access to quality assured antibiotics, structure of healthcare facilities and equipment [26]. Geographically based systematic reviews are therefore important to capture and reflect cultural variations in practice and available resources [3].

Nasr *et al.* reported a systematic review of antimicrobial utilization and prescribing behaviours in a number of Middle Eastern countries [24]. Two studies reported that the use of proactive core interventions positively affected prescribing behaviours through audit and feedback. The remaining studies primarily described adherence of antimicrobial prescribing to local/national policies or international guidelines.

More recently, Alghamdi *et al.* reported a systematic review exploring the level of adoption of ASPs in GCC hospitals together with the facilitators, barriers and outcomes of adoption. Outcomes included reduction of: inappropriate antimicrobial prescribing; healthcare-associated infection; direct antimicrobial cost; length of stay; AMR; and broad-spectrum antimicrobial use. ASP adoption was found to be low and under-reported with a lack of a national AMR strategy in the countries included in this systematic review [25].

Neither of these systematic reviews considered ASP implementation with reference to the CDC framework. Mapping ASP implementation to international grouped interventions can assist in the identification of areas of deficiency and in evaluation of the magnitude of success of implementation. Consequently, this will highlight the required actions to improve the quality of service and ensure effective delivery of service by identifying required modifications of actions as well as facilitators and barriers.

This systematic review aimed to critically appraise and synthesize the evidence of ASP implementation in GCC hospitals with reference to the CDC framework, identifying key facilitators and barriers.

Methods

Protocol development

The Preferred Reporting Items for Systematic Reviews and Meta-analyses for Protocols (PRISMA-P) standards guided the development of the systematic review protocol, which was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (CRD42017079597) and is available online [27,28].

Search strategy

The search was conducted in Medline, Cumulative Index of Nursing and Allied Health Literature, International Pharmaceutical Abstracts, Web of Science and Cochrane databases. Search terms applied to all databases are listed in Appendix II (see online supplementary material). The reference lists of all identified papers were hand-searched to identify any further studies, and database alerts were created for notification of newly published studies during the timeline of the review. A random sample of 10% of titles, abstracts and full papers was reviewed independently (NH and AT or DS) to confirm reliability of the screening process.

Study inclusion criteria

Studies were included if they reported ASP implementation within acute care (short-term stay or urgent care) hospital settings in the GCC states. Studies could either report ASPs or any of the specific elements of ASPs, as defined in the core elements of the CDC guidelines [8]. Studies were descriptive with no comparator (other than pre- and post-implementation). Review outcomes were the description of implementation, facilitators and barriers. All primary research studies of any design (quantitative, qualitative or mixed), published in English from 2010 to January 2020, were included. A preliminary search of the peer-reviewed literature did not identify any studies reporting ASP implementation in the GCC prior to 2010, hence this was the search index date. Conference abstracts, proceedings and grey literature were excluded due to the lack of details to permit quality assessment and data extraction in such resources. Studies were excluded if they addressed primary care, nursing homes, outpatient or dental settings.

Quality assessment, data extraction and synthesis

Specific study quality assessment tools were adopted based on the study design from the National Heart, Lung and Blood Institute [29] and the Consolidated Criteria for Reporting Qualitative Research (COREQ) [30]. Quality assessment tools were applied by two independent reviewers (NH plus one of AT, DS or DP), with a third reviewer consulted in the case of disagreement. Quality assessment considered the potential for bias, with studies rated as good, fair or poor [31]. The COREQ checklist was used to evaluate qualitative studies in three domains: research team and reflexivity; study design; and data analysis and reporting [30].

Data extraction was undertaken independently by two reviewers (NH plus one of AT, DS or DP). Data extracted were: aim; setting; study design; dates of data collection; and sample description. Given the lack of homogeneity of the study designs, methods and outcome measures, the results were synthesized using a narrative approach as retrieved data cannot undergo statistical meta-analysis [32]. ASP interventions described were mapped to the seven core elements of the CDC framework [8], which has proven successful as an auditing tool in several US hospitals [10–13]. The core elements were categorized as infrastructure elements (leadership, accountability, pharmacist expertise) and implementation practices (actions, tracking, reporting and education), as described by Pollack *et al*. [10].

Results

Study screening

Eight hundred and ninety-six papers were identified, and the number was reduced to 483 following removal of duplicates. Screening of titles excluded a further 211 papers that were not in the included healthcare setting. Screening of the remaining 272 abstracts excluded a further 218 records that did not meet the objectives of this review. Full paper screening excluded an additional 37 papers (28 did not include a description of ASP implementation, four were not conducted in GCC states, four were abstracts and one was published prior to the search index date). Finally, 17 papers were included in this review: nine cohort studies; six before–after studies; one cross-sectional survey; and one qualitative study. The PRISMA flowchart shown in Figure 1 summarizes the screening and selection process.

Quality assessment

The quality assessment of studies is summarized in Appendices III and IV (see online supplementary material). Five studies (29.4%) were rated 'good', 12 (70.6%) were rated 'fair' and none were rated 'poor'. Key study limitations for the qualitative study were the lack of detail on methodological underpinning, and measures to maximize researcher reflexivity and credibility [33].

The cohort and before–after studies were conducted in KSA (N=9), Qatar (N=3), UAE (N=2) and Kuwait (N=1), with no studies conducted in Bahrain or Oman. Hospitals were described as tertiary (N=11), community (N=3) and quaternary (N=1), with data collected from the entire hospital(s) (N=9), or exclusively from surgical units (N=3), intensive care units (N=2) or specific hospital departments (surgical, obstetrics and gynaecology, medical, critical care, medical intensive care, surgical intensive care unit) (N=1). Data collection periods in the studies ranged from 6 months to 3 years. One study from Saudi Arabia, Mecca, included Hajj time (annual Islamic pilgrimage) in one of the phases of data collection as this mass gathering significantly increases the risk for development of AMR [34].

The cross-sectional study included a total of 184 health professionals practising in six large hospitals in KSA [35]. The qualitative study was also conducted in KSA, comprising 22 interviews with hospital practitioners, managers and Saudi health authority representatives [33]. Hospitals in the cross-sectional survey and qualitative study were described as tertiary. Data extraction of the 17 studies is given in Appendix V (see online supplementary material).

Data synthesis

Data were synthesized according to the aims of the review with ASP interventions mapped to CDC core elements, and facilitators and barriers to implementation.

Mapping of ASP interventions to CDC core elements

The mapping of the ASP interventions to the CDC core elements is summarized in Table I.

Infrastructure elements

Only one study reported hospital commitment and leadership support (Core Element 1), described in terms of financial resources, integrated information technology, clinical decision support systems, an identified ASP point of contact and dedicated ASP time for staff [36]. While the involvement of infectious disease (ID) physicians in ASP activities was described in six studies [34,36–40], only two referred to physician leadership with respect to accountability for programme management and outcomes (Core Element 2) [38,40]. Pharmacist expertise (Core Element 3) was described in nine studies, five

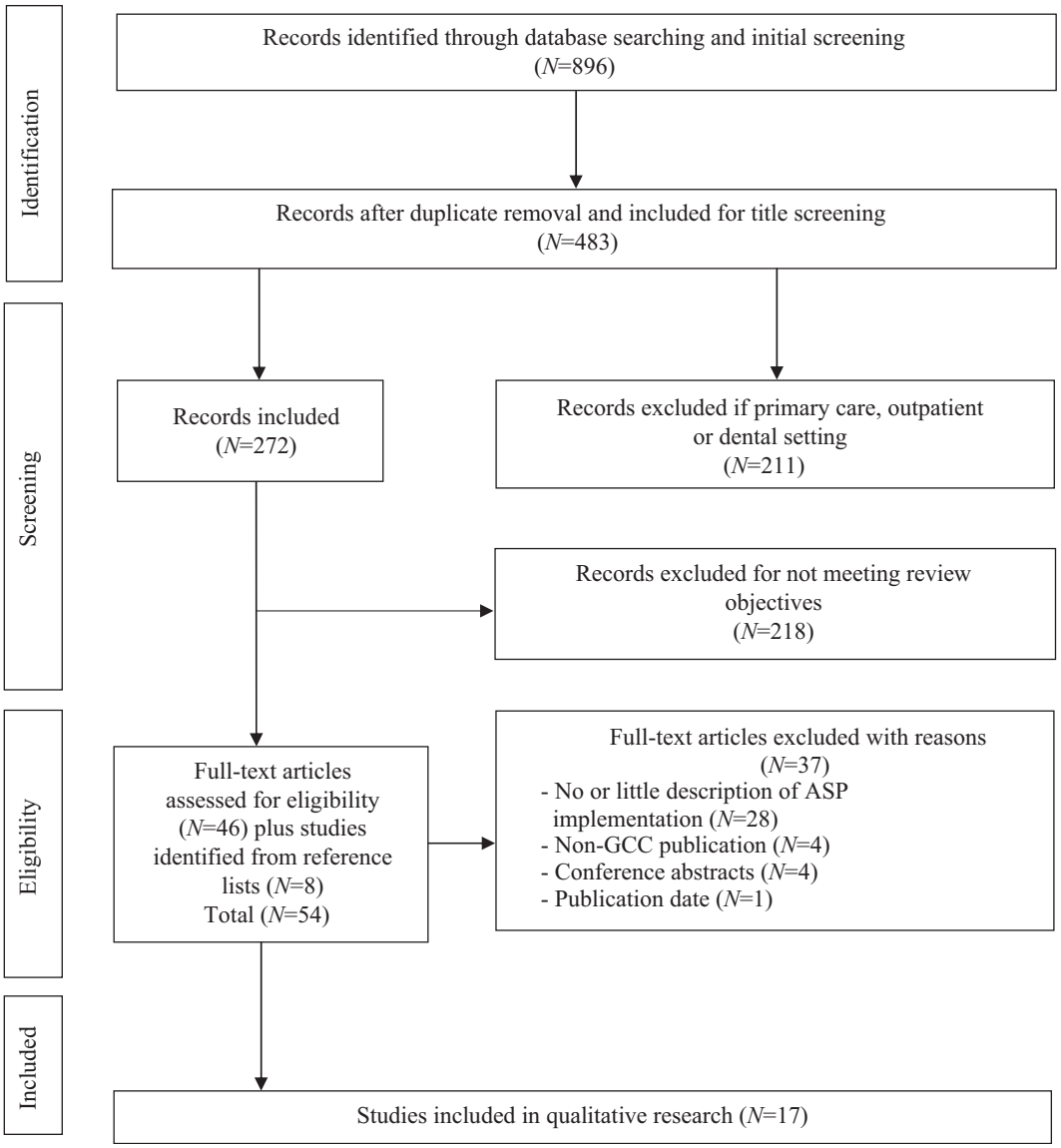

Figure 1. PRISMA flow chart for search and inclusion process. Adapted from Moher *et al.* [50].

of which reported dedicated full-time ASP pharmacists [34,36,37,41,42] and one had a pharmacist with special ID training [36]. The other studies only reported pharmacist involvement in monitoring antimicrobial consumption [39,43–45].

Implementation practices

All studies described practices related to Core Element 4 (actions), although the specific descriptions of the scope of practices varied. The majority of the studies reported locally developed guidelines based on antimicrobial culture and sensitivity testing, as recommended in the CDC framework [33,35–38,41,44,46–49]. Prospective audit and feedback were the most commonly reported practices [34,36–40,42–44,48], followed by pre-authorization [33,35,36,39,40,42,43].

Pharmacy-based interventions largely comprised documentation of indication for antibiotic use in patients' medical records, as described in 10 studies [34,36,37,39,40,43,44,47–49]. Only six studies reported optimizing antimicrobial dose [36–40,45], three of which also emphasized dose adjustment [37,39,40]. The remaining pharmacy-based interventions – namely time-sensitive automatic stop order, intravenous to oral switch, and duplicative therapy alerts – were minimally reported, and detection and prevention of antibiotic-related drug–drug interactions were not reported at all.

Provider-based interventions were seldom reported, with antibiotic 'timeouts' described in three studies [36,45,48]. None of the papers refer to assessing patients for penicillin allergy.

Microbiology-based interventions and infection-based interventions were scarcely reported, with only one study describing the effect of selective reporting of antimicrobial susceptibilities [41], and another study referred to comments in microbiology reports [42]. Notably, none of the studies reported any nursing-based interventions.

Core Element 5 (tracking) is classified as antibiotic use measures, and outcome measures and process measures for quality improvement. The majority of studies reported at least

Table I
Mapping of studies (N=17) against Centers for Disease Control and Prevention core elements [8]

	Dib *et al.*, 2009 [37]	Aly *et al.*, 2012 [46]	Al-Tawfiq, 2013 [38]	Amer *et al.*, 2013 [39]	Al-Somai *et al.*, 2014 [34]	Al-Tawfiq *et al.*, 2015 [41]	El Hassan *et al.*, 2015 [47]	Tobaiqy *et al.*, 2015 [40]	Alawi and Darwesh, 2016 [43]	Garcell *et al.*, 2016 [48]	Abdallah *et al.*, 2017 [42]	Garcell *et al.*, 2017 [49]	Garcell *et al.*, 2017 [44]	Momattin *et al.*, 2018 [45]	Baraka *et al.*, 2019 [35]	Alghamdi *et al.*, 2019 [33]	El-Lababidi *et al.*, 2019 [36]	Total
Infrastructure elements (leadership, accountability and pharmacy expertise)																		
Core Element 1: Hospital leadership commitment																	√	1
Core Element 2: Accountability for programme management and outcome			√					√										2
Core Element 3: Pharmacy expertise	√			√	√	√			√		√		√	√			√	9
Implementation practices (actions, tracking, reporting and education)																		
Core Element 4: Actions that implement interventions that report antibiotic use																		
A. High-priority interventions																		
Prospective audit and feedback	√		√	√	√			√	√	√	√		√				√	10
Pre-authorization				√				√	√		√				√	√	√	7
Facility-specific treatment guidelines	√	√	√			√	√			√		√	√		√	√	√	11
B. Actions focusing on the most common indications for hospital antibiotic use (common infection-based interventions)																		
Urinary tract infections																		0
Community-acquired pneumonia										√				√				2
Skin and soft tissue infection																		0
C. Actions focusing on less common indications for hospital antibiotic use (less common infection-based interventions)																		
Sepsis																		0
Meticillin-resistant *Staphylococcus aureus*	√																√	2
Clostridioides difficile				√		√											√	3
Culture-proven invasive infection																		0
Review of planned outpatient parenteral antibiotic therapy																		0
D. Provider-based intervention																		
Antibiotic 'timeout'										√				√			√	3

Assessing penicillin allergy																0
E. Pharmacy-based interventions																
Documentation of indication	√		√	√		√	√	√	√		√	√			√	10
Automatic IV to oral switch									√				√		√	3
Dose adjustment	√		√				√									3
Dose optimization	√	√	√				√						√		√	6
Duplicative therapy alerts															√	1
Time-sensitive automatic stop order									√	√		√			√	4
Detection and prevention of antibiotic-related drug −drug interaction																0
F. Microbiology-based interventions																
Selective reporting of antimicrobial susceptibility testing results					√											1
Comments in microbiology reports										√						1
G. Nursing-based interventions																
Optimizing antimicrobial cultures																0
IV to oral transitions																0
Promote antibiotic review 'timeout'																0
Core Element 5: Tracking																
A. Antibiotic use measures																
Consumption data reported as days of therapy or defined daily doses			√	√	√				√	√		√	√		√	8
B. Outcome measures																
Clostridioides difficile infection			√		√										√	3
Antibiotic resistance patterns					√			√		√					√	4
Financial impact in terms of cost reduction			√					√							√	3

(*continued on next page*)

Table I (*continued*)

	Dib *et al.*, 2009 [37]	Aly *et al.*, 2012 [46]	Al-Tawfiq, 2013 [38]	Amer *et al.*, 2013 [39]	Al-Somai *et al.*, 2014 [34]	Al-Tawfiq *et al.*, 2015 [41]	El Hassan *et al.*, 2015 [47]	Tobaiqy *et al.*, 2015 [40]	Alawi and Darwesh, 2016 [43]	Garcell *et al.*, 2016 [48]	Abdallah *et al.*, 2017 [42]	Garcell *et al.*, 2017 [49]	Garcell *et al.*, 2017 [44]	Momattin *et al.*, 2018 [45]	Baraka *et al.*, 2019 [35]	Alghamdi *et al.*, 2019 [33]	El-Lababidi *et al.*, 2019 [36]	Total
C. Process measures for quality improvement focusing on specific interventions implemented in the hospital																		
Priority process measures																		
Tracking prospective audit and feedback																		0
Monitoring pre-authorization																		0
Monitoring adherence to facility-specific treatment guidelines	√	√					√			√		√	√				√	7
Additional process measures																		
Monitor antibiotic 'timeouts'																	√	1
Performing medication use evaluation					√													1
Monitor IV to oral switch,																	√	1
Monitor unnecessary duplicates in therapy																		0
Monitor discharge on correct antibiotic																		0
Core Element 6: Reporting on antibiotic use and resistance	√			√	√	√			√	√		√	√				√	9
Core Element 7: Education	√			√		√				√		√	√	√			√	8

IV, intravenous.

one of the CDC tracking measures. Eight studies monitored antibiotic use by reporting defined daily doses (DDDs) [34,39,41,42,44,45,48] or days of therapy (DoT) [36,45]. Alawi *et al*. monitored the number of units of restricted antibiotics pre- and post-implementation [43]. All of these studies showed a significant decline in antimicrobial consumption with optimizing antibiotic use.

The specific outcome measures described in Core Element 5 (financial impact, antimicrobial resistance or *Clostridioides difficile* infection) were all minimally reported. Studies addressing financial impact have shown variable reduction in antimicrobial expenditure from pre-intervention or initial phase of intervention [36,39,43]. Four studies reported a significant decline in infection rate by multi-drug-resistant organisms [36,41–43], and three studies described a significant reduction in the *C. difficile*-associated disease rate [36,39,41].

Among the different process measures for quality improvement (high priority and additional measures), monitoring adherence to local facility-specific guidelines was the most commonly reported measure, described in seven studies. Increased adherence and compliance with local hospital guidelines was observed over the duration of the study in five studies [36,37,44,48,49], while the remaining two studies reported low compliance rates [46,47]. Other additional process measures as specified in the CDC framework, on monitoring antibiotic timeout and intravenous to oral switch [36] as well as the evaluation of medication use [34], were minimally reported.

Reported outcomes (not part of the CDC framework) were: faster rate of transfer from intensive care unit to regular ward with 4–5 days of follow-up [39]; and ID consultation with beneficial impact on antimicrobial utilization [36,38].

Core Element 6 (personal communication with staff to improve antibiotic use and resistance) was reported in nine studies [34,36,37,39,41,43,44,48,49], four of which described circulating facility-specific reports on antibiotic use to prescribers [39,44,48,49]. In two studies, an antibiogram was distributed to prescribers [36,41].

Eight studies described Core Element 7 (education of prescribers and healthcare workers), comprising small group meetings, verbal and personal communications, and e-mail reminders [36,37,39,41,44,45,48,49].

Facilitators and barriers to implementation

While facilitators and barriers to implementation were reported in the majority of studies (N=14), the scope and detail of description varied widely. These were described in terms of regional and national levels, hospital organizational level, and hospital culture and environment. Education and training were the most commonly reported facilitators, followed by the involvement of pharmacist, microbiology and infection control personnel. There appeared to be less focus on investigating barriers; when reported, a lack of higher managerial support was most common (see Tables II and III).

While one study from Saudi Arabia reported that regional and national legislation facilitated implementation in Saudi Arabia, the lack of enforcement of the legislation and lack of surveillance were reported as barriers [33].

In terms of hospital organizational facilitators, five studies reported higher managerial support [33,35,36,39,49] through addressing several issues such as: policy enforcement [33]; lack of ASP-dedicated staff, including the lack of ID physicians and clinical pharmacists; workload associated with ASP audits; lack of novel diagnostics and insufficient funding [39]; and mandating infection prevention and medication safety educational activities [49].

For human resources, the importance of the contribution of ASP personnel was highlighted in 10 studies [34–39,41,46,47,49]. Lack of personnel dedicated to ASP activities was reported as a major barrier to effective ASP implementation [33,35,39,43], notably increased workload associated with audits [35,39,43] and high turnover of physicians [43].

For information resources, education and training of healthcare professionals was the most commonly reported facilitator through various forms of education, hospital policies and guidelines [33,35,37,39,41,43,46,47,49]. Lack of education and training on local hospital guidelines was considered a major barrier [33,35,37,46,49], especially in newly established settings with staff with diverse backgrounds and a range of experiences [49]. Information technology support has been reported as a solution to support the implementation of hospital policies and guidelines [33,35,36,39,46].

For hospital functionality, several studies addressed the diagnostic and prescribing challenges faced by physicians leading to potential unnecessary antibiotic prescribing [33,41,43,46]. Diagnostic challenges took the form of inaccurate diagnosis, imprecise recognition of conditions warranting antibiotics, inconsistent availability of antibiotics [43], lack of microbiological testing and suboptimal triage systems [41]. Novel diagnostic systems such as procalcitonin biomarker [46] and enhancing the availability of antimicrobial susceptibility testing were potential solutions to diagnostic and prescribing barriers [35,36,39,41,42].

The effect of hospital culture and environment was addressed in several studies. Factors such as resistance to changing prescribing habits [43,46], fear of liability risk [46], lack of confidence [35] and poor communication among teams [33] were identified. Lack of adherence to guidelines was suggested to be due to lack of awareness of the existence of such policies [33,35].

Discussion

Statement of key findings

The reporting of ASP implementation aligned to the CDC framework was variable and generally incomplete. The most commonly reported core elements were: pharmacy expertise; aspects of implementation actions; reporting on antibiotic use and resistance; and education. Seldom reported core elements were: hospital leadership commitment; accountability for programme management and outcome; and tracking. Key implementation facilitators were physician and organization support, information systems and education, and barriers were dedicated staff, workload and funding.

Strengths and limitations

There are several strengths to this review. The protocol was developed according to the PRISMA-P standards [27],

Table II
Facilitators to antimicrobial stewardship programme (ASP) implementation reported in included studies (N=17)

		Dib *et al.*, 2009 [37]	Aly *et al.*, 2012 [46]	Al-Tawfiq, 2013 [38]	Amer *et al.*, 2013 [39]	Al-Somai *et al.*, 2014 [34]	Al-Tawfiq *et al.*, 2015 [41]	El Hassan *et al.*, 2015 [47]	Tobaiqy *et al.*, 2015 [40]	Alawi and Darwesh, 2016 [43]	Garcell *et al.*, 2016 [48]	Abdallah *et al.*, 2017 [42]	Garcell *et al.*, 2017 [49]	Garcell *et al.*, 2017 [44]	Momattin *et al.*, 2018 [45]	Baraka *et al.*, 2019 [35]	Alghamdi *et al.*, 2019 [33]	El-Lababidi *et al.*, 2019 [36]	Total
Facilitators																			
A. Regional and national level																			
Regional and national legislation																	√		1
B. Hospital organizational level																			
Higher managerial support					√								√			√	√	√	5
Human resources	Pharmacist feedback	√			√	√	√	√								√		√	7
	Microbiology and infection control personnel involvement	√	√	√	√		√						√					√	7
Information resources	Formulary management									√						√	√		3
	Institutional policy and guidelines		√					√				√	√					√	5
	Supplemental online ASP resources															√			1
	Education and training for healthcare professionals	√	√		√		√	√		√			√			√	√		9
	Education and training for undergraduate medical students and at an early stage of medical training						√			√									2
	Integrating clinical decision support system in hospital IT system		√		√											√	√	√	5

Financial resources	Adequate budget		√						1
Hospital functionality	Introduction of novel diagnostics	√							1
	Availability of antimicrobial susceptibility testing		√	√		√	√	√	5
C. Hospital culture and environment									
Key antibiotic prescribers' support					√			√	2
Peer-to-peer communication			√	√					2

IT, information technology.

registered in the PROSPERO database [28], and the systematic review was reported according to PRISMA criteria [50]. One key strength is the approach to synthesis of information on ASP implementation using the CDC framework, which will facilitate international comparison. However, there are some weaknesses, so the review findings should be interpreted with caution. Restricting the search to studies published in English, and excluding those written in Arabic, may have limited the retrieval of potentially relevant studies. However, English is the preferred language of most professional organizations in the GCC states. While there was rationale in restricting the review to studies conducted in the GCC states, this may have reduced the potential generalizability and transferability to other countries in the Middle East and beyond. Of note, the majority of the studies included were from KSA.

Interpretation of key findings

Mapping studies to standardized quality criteria identified that most were of fair quality, often with small sample sizes, hence emphasizing the need for higher quality, larger, more robust studies with greater consideration of validity and reliability.

Implementation research in the healthcare sector focuses on a full and complete description of the implementation processes, allowing for consideration of contextual factors that affect delivery of the intervention and provide a link between what can be theoretically achieved and real-life practice [51]. For successful implementation, researchers are encouraged to focus on factors such as process of implementation, context, influencing factors and evaluation [52] which facilitate improvement, accountability and long-term sustainability [53]. Furthermore, complete description of the intervention, together with details about real-world setting conditions, will enable understanding of what was actually implemented, thus aiding replication [53,54].

Implementation frameworks ideally provide focus on the nature of the interventions and the implementation processes, thus facilitating interpretation of implementation outcomes [51]. Given that these frameworks target specific components, they must be selected with care [52]. This systematic review used the CDC framework to provide a complete description of ASP interventions and implementation, with elements relevant to infrastructure, practices and monitoring [8]. Furthermore, the CDC framework has been adopted by Joint Commission International, the most widely sought accreditation body across GCC hospitals [55,56], as an ASP standard for hospital accreditation [8,57], which is an added strength and further adds to the relevance of the results in the GCC context. While most studies in this review had key limitations when mapped to this framework, it should be borne in mind that these may reflect deficiencies in study reporting, and not necessarily weaknesses in ASP interventions and implementation. Compliance with the framework was found to be variable outwith GCC studies [58,59], reaching almost 100% in US studies [10–13] where the CDC framework is adopted at a US national level. Of note, the compliance of GCC studies with the CDC core elements has increased in recent years, especially with the release of the AMR strategic plan for the GCC Centre for Infection Control [17] and inclusion of ASPs in the Joint Commission International accreditation standards [57], which

Table III
Barriers to antimicrobial stewardship programme (ASP) implementation reported in included studies (N=17)

		Dib *et al.*, 2009 [37]	Aly *et al.*, 2012 [46]	Al-Tawfiq, 2013 [38]	Amer *et al.*, 2013 [39]	Al-Somai *et al.*, 2014 [34]	Al-Tawfiq *et al.*, 2015 [41]	El Hassan *et al.*, 2015 [47]	Tobaiqy *et al.*, 2015 [40]	Alawi and Darwesh, 2016 [43]	Garcell *et al.*, 2016 [48]	Abdallah *et al.*, 2017 [42]	Garcell *et al.*, 2017 [49]	Garcell *et al.*, 2017 [44]	Momattin *et al.*, 2018 [45]	Baraka *et al.*, 2019 [35]	Alghamdi *et al.*, 2019 [33]	El-Lababidi *et al.*, 2019 [36]	Total
Barriers																			
A. Regional and national level																			
Lack of enforcement of national legislations																	√		1
Lack of AMR and antibiotic consumption national surveillance systems																	√		1
B. Hospital organizational level																			
Lack of higher managerial support			√		√					√			√			√	√		6
Human resources	Lack of dedicated ASP personnel					√					√						√	√	4
	Shortage of ID physicians																	√	1
	Shortage of microbiologist																	√	1
	Lack of clinical pharmacist																	√	1
	Physicians' high turnover										√								1
	Physicians' high workload and limited time					√					√						√		3
Information resources	Lack of internal policy and guidelines										√						√		2
	Lack of education and training on local hospital guidelines		√	√										√			√	√	5

	Lack of ASP information resources									√		1
	Lack of health IT										√	1
Financial resources	Limited funding			√						√		2
Hospital functionality	Microbiology-related barriers				√						√	2
	Diagnostic challenges	√			√		√					3
C. Hospital culture and environment												
Lack of confidence									√			1
Poor communication among teams										√		1
Fear of liability risk		√										1
Lack of support from senior to junior staff		√										1
Physicians' resistance to changing their prescribing habits		√				√						2
Lack of adherence to guidelines		√			√				√	√		4

AMR, antimicrobial resistance; ID, infectious diseases; IT, information technology.

reflects the increased importance of ASPs in confronting the increasing risk of AMR.

A collaborative approach engaging all key stakeholder groups in intervention development and implementation is more likely to result in successful outcomes generally [51], as well as those specifically related to ASP implementation [1,8,10,60]. One limitation of the studies in this systematic review was the lack of input from regulatory authorities, which was cited as a barrier to ASP implementation. Indeed, there were reports of only two GCC states having a national action plan to combat AMR [61,62], as promoted by WHO, to provide a framework of actions required in the battle against AMR [19]. This limitation was also reported as a finding of two other systematic reviews conducted in the Middle East [24,25]. Further evidence of a less well established ASP infrastructure as defined by CDC [8] is noted, with hospital leadership support (Core Element 1) only described in one study [36], and accountability for programme management (Core Element 2) described in another two studies [38,40]. It is evident that positive collaboration between key stakeholders at different levels can identify barriers to implementation and promote an iterative approach to improvement [51].

According to the WHO ASP toolkit [1], the ASP team should be multi-disciplinary comprising physicians, pharmacists, nurses and microbiologists [1,5,6,8], including ID physicians, ID-trained pharmacists and infection prevention and control specialists where available [1]. This systematic review identified potential barriers to ASP implementation with reported shortages of ID physicians and limited contributions from pharmacists, infection control preventionists, microbiologists and nurses [33,35,39,43]. Given the global shortage of healthcare professionals [63] and the difficulties of establishing an ASP team [64–66], consideration should be given to optimizing the contribution of existing professionals through role extension [67] and professional development [36,68].

Smart clinical decision support systems can leverage ASP implementation, especially when linked to antimicrobial resistance surveillance tools and antibiotic prescribing guidelines [69]. This was identified as a facilitator in the studies included in this review [33,35,36,39,46], and similar observations were reported in other non-GCC studies [69,70]. Embedding such smart clinical decision support systems linked to validated antimicrobial prescribing guidelines, to ensure appropriateness to the local context, could enhance the effectiveness and efficiency of ASP implementation with consequences for resources and outcomes [71]. Furthermore, facilitating education (Core Element 7) as well as training is crucial in terms of changing practice habits, especially in a diversity of backgrounds as present in GCC hospitals. It is recommended that GCC hospitals should include ASP education in hospital seminars, ward rounds and annual meetings [72].

Central to the continuum of implementation research is ongoing evaluation, allowing pre-implementation insights into intervention suitability, monitoring change in practice during implementation, and observing post-implementation impact and consequences [51,52,73]. CDC categorized tracking (Core Element 5) into antimicrobial consumption, outcome measures and process measures [8]. However, according to this systematic review, the current focus in GCC states is on evaluation of the implementation phase, with the majority of included studies reporting antimicrobial consumption [34,36,39,41,42,44,45,48] and adherence to facility-specific treatment guidelines [36,37,44,46–49] as the indicators of successful ASP implementation, and only a few studies reporting other tracking measures. There is a need to focus on exploring and maintaining positive outcomes in the long term after overcoming implementation challenges [74]. As ASP implementation continues to evolve and mature in GCC states, more focus should be placed on analysis of post-implementation long-term effects and determinants of sustainability.

Further research

There is a need for enhanced reporting of ASP implementation aligned with the CDC framework in GCC states. Further consideration should also be given to application of implementation theory to provide focus on facilitators and barriers to implementation. To facilitate identification and understanding of constructs that govern translation of research findings into real practice within the healthcare sector in GCC states, there is a need for rigorous qualitative in-depth research that utilizes implementation frameworks.

In conclusion, there appears to be a need to enhance the reporting of ASP implementation in GCC hospitals. Notably, ASP infrastructure is found to be insufficient and heterogenous. A rigorous infrastructure framework (leadership support, accountability and pharmacist expertise) is required to enhance efficacy and governance, and ensure the sustainability of implementation interventions (actions, tracking, reporting and education). Attention should be paid to the CDC framework during the development, implementation and reporting of ASP interventions. Action is required to identify facilitators and overcome barriers, where possible.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2020.09.004.

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