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Title Page

Mapping hospital antimicrobial stewardship programs in the Gulf Cooperation Council States against international standards: A systematic review

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Antimicrobial stewardship in Gulf Cooperation Council – Systematic Review

Summary

Background

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

Aim

To critically appraise and synthesise the evidence of ASP implementation in GCC hospitals while comparing to the framework of the Centers for Disease Control and Prevention (CDC) and identifying key facilitators and barriers.

Methods

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

Findings

Seventeen studies were identified, mostly from Saudi Arabia (n=11). 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 organisation support, information systems and education with barriers being 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 ASP intervention development, implementation and reporting. Action is required to identify facilitators and overcome barriers, where possible.

Keywords:

Antimicrobial, Stewardship, Gulf Cooperation Council, Mapping, Centers for Disease Control and Prevention, Systematic review.

Introduction

An antimicrobial stewardship programme (ASP) is defined by World Health Organization (WHO) as *'An organizational or system-wide health-care strategy to promote appropriate use 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 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, reporting and education [7]. First published in 2014, the framework was recently updated in November 2019 reflecting new evidence and experiences gained in the preceding years (see Supplementary Appendix I) [8].

In the United States (US), the CDC Division of Healthcare Quality Promotion (DHQP) uses the framework to evaluate the level of ASP implementation across acute care hospitals, identifying and defining gaps to be addressed at a national level [9,10]. The framework has been also 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 resistance development 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 the establishment of the GCC Centre for Infection Control (GCC-IC) 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 resistance development [17]. This was a high-level plan which included general recommendations rather than specific actions to implement ASP and aimed to complement the global action plan issued by WHO [19]. The task of implementation was then passed on to each individual country. There is however a paucity of data on the success or otherwise of the actual implementation of the plan in each of the countries.

While a number of systematic reviews have summarised 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 across geographical regions for different reasons, including diagnostic challenges, variation in knowledge and awareness, and access to quality assured antibiotics and healthcare facilities structure 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 utilisation and prescribing behaviours in a number of Middle Eastern countries [24]. Two studies reported the use of proactive core interventions as positively affecting prescribing behaviours through audit and feedback. The remaining 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 underreported 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 identifying 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 synthesise 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-analysis 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 available online [27,28].

Search strategy

The search was conducted in Medline, Cumulative Index of Nursing and Allied Health Literature (CINAHL), International Pharmaceutical Abstracts (IPA), Web of Science and Cochrane databases. Search terms applied to all databases are in Supplementary Appendix II. The reference lists of all identified papers were hand-searched to establish any further studies and database alerts created to notify of newly published studies during the timeline of the review. A random sample of 10% of titles, abstracts and full papers were independently reviewed (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 ASP or any of the specific elements of ASP, as defined in the core elements of the CDC [8]. Studies were descriptive with no comparator (other than pre- post- implementation). Review outcomes were the description of implementation and 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 identified no studies reporting ASP implementation in the GCC prior to 2010 hence this was 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 addressing primary care, nursing homes, outpatient or dental setting.

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 (NHLBI) [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 consulted in the case of any disagreements. 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 of research team and reflexivity, study design and data analysis and reporting [30].

Data extraction was independently undertaken 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, results were synthesised using a narrative approach, since 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 categorised 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 reduced to 483 following removal of duplicates. Screening of titles excluded a further 211 that were not in the included healthcare setting. Screening of remaining 272 abstracts excluded a further 218 records that did not meet review objectives. Full paper screening excluded an additional 37 (28 had no description of ASP implementation, four not conducted in GCC, four abstracts and one was published prior to the search index data). The 17 papers comprised nine cohort studies, six before-after studies, one cross-sectional survey and one qualitative study. The PRISMA flowchart provided in Figure 1 summarises the screening and selection process.

Quality assessment

Study quality assessment is summarised in Supplementary Appendices III and IV. Five studies (29.4%) were rated 'good', 12 (70.6%) 'fair' and none 'poor' quality. Key study limitations for the qualitative study were the lack of detail on methodological underpinning, and measures to maximise 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 none from 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 (ICU) (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 since this mass gathering is significantly increasing the risk for development of AMR [34].

The cross-sectional study included a total of 184 health professionals practicing in six large hospitals from 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 Supplementary Appendix V.

Data synthesis

Data were synthesised according to the review aims 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 summarised in Table I.

Infrastructure elements

Only one study reported hospital commitment and leadership support (core element one), described in terms of financial resources, integrated information technology (IT), clinical decision support systems, an identified ASP point of contact and dedicated ASP time for staff [36]. While ID physician involvement 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 two) [38,40]. Pharmacist expertise (core element three) was described in nine studies, five of which reported dedicated full-time ASP pharmacists [34,36,37,41,42] and one had a pharmacist with special infectious diseases 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 four (Actions), although the specific descriptions of the scope of practices varied. The majority of the studies reported

252 locally developed guidelines based on antimicrobial culture and sensitivity testing, as
253 recommended in the CDC framework [33,35-38,41,44,46-49]. Prospective audit and
254 feedback were the most commonly reported practices [34,36-40,42-44,48] followed by
255 pre-authorization [33,35,36,39,40,42,43].
256
257 Pharmacy-based interventions largely comprised documentation of indication for
258 antibiotic use in patients' medical records as described in ten studies
259 [34,36,37,39,40,43,44,47-49]. Only six studies reported optimising antimicrobial dose
260 [36-40,45], three of which additionally emphasized dose adjustment [37,39,40]. The
261 remaining pharmacy-based interventions namely time sensitive automatic stop order, IV
262 to oral switch and duplicative therapy alerts, were minimally reported while detection
263 and prevention of antibiotic related drug-drug interactions were not reported at all.
264
265 Provider-based interventions were seldom reported, with antibiotic 'timeouts' described
266 in three studies [36,45,48]. None of the papers refer to assessing patients for penicillin
267 allergy.
268
269 Microbiology-based interventions and infection-based interventions were scarcely
270 reported, with only one study describing the effect of selective reporting of antimicrobial
271 susceptibilities [41] and another referred to comments in microbiology reports [42].
272 Notably, none of the studies reported any nursing-based interventions.
273
274 The fifth core element (Tracking) is classified as antibiotic use measures, and outcome
275 measures and process measures for quality improvement. The majority of studies
276 reported at least one of the CDC tracking measures. Eight studies monitored antibiotic
277 use, by reporting defined daily doses (DDD) [34,39,41,42,44,45,48] or days of therapy
278 (DoT) [36,45]. Alawi et al monitored number of units of restricted antibiotics pre and
279 post implementation [43]. All these studies have shown a statistically significant decline
280 in antimicrobial consumption with optimising antibiotic use.

The specific outcome measures described in CDC core element five (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 statistically significant decline in infection rate by multidrug resistant organisms [36,41-43] and three described statistically significant reduction in *Clostridioides 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, being described in seven studies. Increased adherence and compliance to local hospital guidelines was observed over study duration in five studies [36,37,44,48,49], while the remaining two reported low compliance rate [46,47]. Other additional process measures as specified in the CDC framework, on monitoring antibiotic timeout and IV to oral switch [36] as well as performing medication use evaluation [34] were minimally reported.

Reported outcomes (not part of CDC framework) were: faster rate of transfer from ICU to regular ward with 4-5 days of follow up [39] and infectious disease consultation with beneficial impact on antimicrobial utilization [36,38].

The sixth core element, 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]. Only in two studies, an antibiogram was distributed to prescribers [36,41].

Eight studies described the seventh core element, education of prescribers and health

care 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 majority of the studies (n=14), the scope and detail of description varied widely. These were described in terms of regional and national levels, hospital organisation, culture and environment. Education and training were the most commonly reported facilitator followed by pharmacist, microbiology and infection control personnel involvement. There appeared to be less focus on investigating barriers; when reported, a lack of higher managerial support was most frequent (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 organisational 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 infectious diseases 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 ASP personnel contribution was highlighted in ten 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 diverse backgrounds and a range of experiences [49]. Information technology support has been reported as a solution supporting 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 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 organisation support, information systems and education with barriers being dedicated staff, workload and funding.

Strengths and limitations

There are several strengths to this review. The protocol was developed according to the standards of PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) [27], registered in the PROSPERO database [28], and the systematic review reported according to PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) criteria [50]. One key strength is the approach to synthesis of information on ASP implementation using the CDC framework which will facilitate international comparison. There are some weaknesses hence the review findings should be interpreted with caution. Restricting the search to English language excluding those written in Arabic may have limited retrieval of potentially relevant studies. However, English is the preferred language of most professional organisations in the GCC states. While there was rationale in restricting the review to studies conducted in the GCC states, this may reduce the potential generalisability 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 facilitates 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 carefully selected [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 (JCI), 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 intervention 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 CDC framework is adopted at a US national level. Of note, the compliance of GCC studies with CDC core elements has increased in the recent years especially with the release of the AMR strategic plan for GCC-IC [17] and inclusion of ASP in JCI accreditation standards [57], which reflects the increased importance of ASP 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], and 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 one) described in only one study [36] and accountability for program management (core element two) in another two studies [38,40]. It is evident that positive collaboration amongst 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 multidisciplinary comprising physicians, pharmacists, nurses, microbiologists [1,5,6,8], including infectious disease (ID) physicians, ID trained pharmacists and infection prevention and control specialist 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 [64,65,66], consideration should be given to optimising 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 included studies [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 local context, could enhance ASP

implementation effectiveness and efficiency with consequences for resources and outcomes [71]. Furthermore, facilitating education (core element seven) 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 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 categorised tracking (core element five) into: antimicrobial consumption; outcome measures and processes measures [8]. However, according to this systematic review, the current focus in GCC is on implementation phase evaluation with 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 with only a few 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 to the CDC framework in GCC states. Further consideration should also be given to the 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 utilise implementation frameworks.

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 rigor infrastructure framework (leadership support, accountability and pharmacist expertise) is required to enhance efficacy, governance and ensure sustainability of implementation interventions (actions, tracking, reporting and education). Attention should be paid to the CDC framework during ASP intervention development, implementation and reporting. Action is required to identify facilitators and overcome barriers, where possible.

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Conflict of interest statement

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Tables:

Table I: Mapping of studies (n=17) against CDC 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 one: Hospital leadership commitment																	√	**1**
Core element two: Accountability for programme management and outcome			√					√										**2**
Core element three: Pharmacy expertise	√			√	√	√			√		√		√	√			√	**9**
Implementation practices (Actions, Tracking, Reporting and Education)																		
Core element four: Actions that implement interventions that report antibiotic use																		
A. High priority interventions																		
Prospective audit and feedback	√		√	√	√			√	√	√	√		√				√	**10**
Pre-authorisation				√				√	√		√				√	√	√	**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**

	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
Meticillin resistant *Staphylococcus aureus*	√																√	**2**
Clostridioides difficile				√		√											√	**3**
Culture proven invasive infection																		**0**
Review of planned outpatient parenteral antibiotic therapy (OPAT)																		**0**
D. Provider-based intervention																		
Antibiotic time out										√				√			√	**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**

	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
Comments in microbiology reports											√							**1**
G. Nursing-based interventions																		
Optimizing antimicrobial cultures																		**0**
IV to oral transitions																		**0**
promote antibiotic review "time out"																		**0**
Core element five: Tracking																		
A. Antibiotic use measures																		
Consumption data reported as days of therapy (DoT) or defined daily doses (DDD)				√	√	√				√	√		√	√			√	**8**
B. Outcome measures																		
Clostridioides difficile infection				√		√											√	**3**
Antibiotic resistance patterns						√			√		√						√	**4**
Financial impact in terms of cost reduction				√					√								√	**3**
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																		

	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
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 six: Reporting on antibiotic use and resistance	√			√	√	√			√	√		√	√				√	**9**
Core element seven: Education	√			√		√				√		√	√	√			√	**8**

Abbreviations: IV, Intravenous.

Table II: Facilitators to 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 organisational 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		√		√											√	√	√	**5**

		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
	IT system																		
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**

Abbreviations: ASP, Antimicrobial stewardship programme; IT, Information technology.

Table III: Barriers to 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 organisational 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 information																√		**1**

		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
	technology																		
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**

Abbreviations: AMR, Antimicrobial resistance; ASP, Antimicrobial stewardship programme; ID, Infectious diseases; IT, Information technology.

Figures:

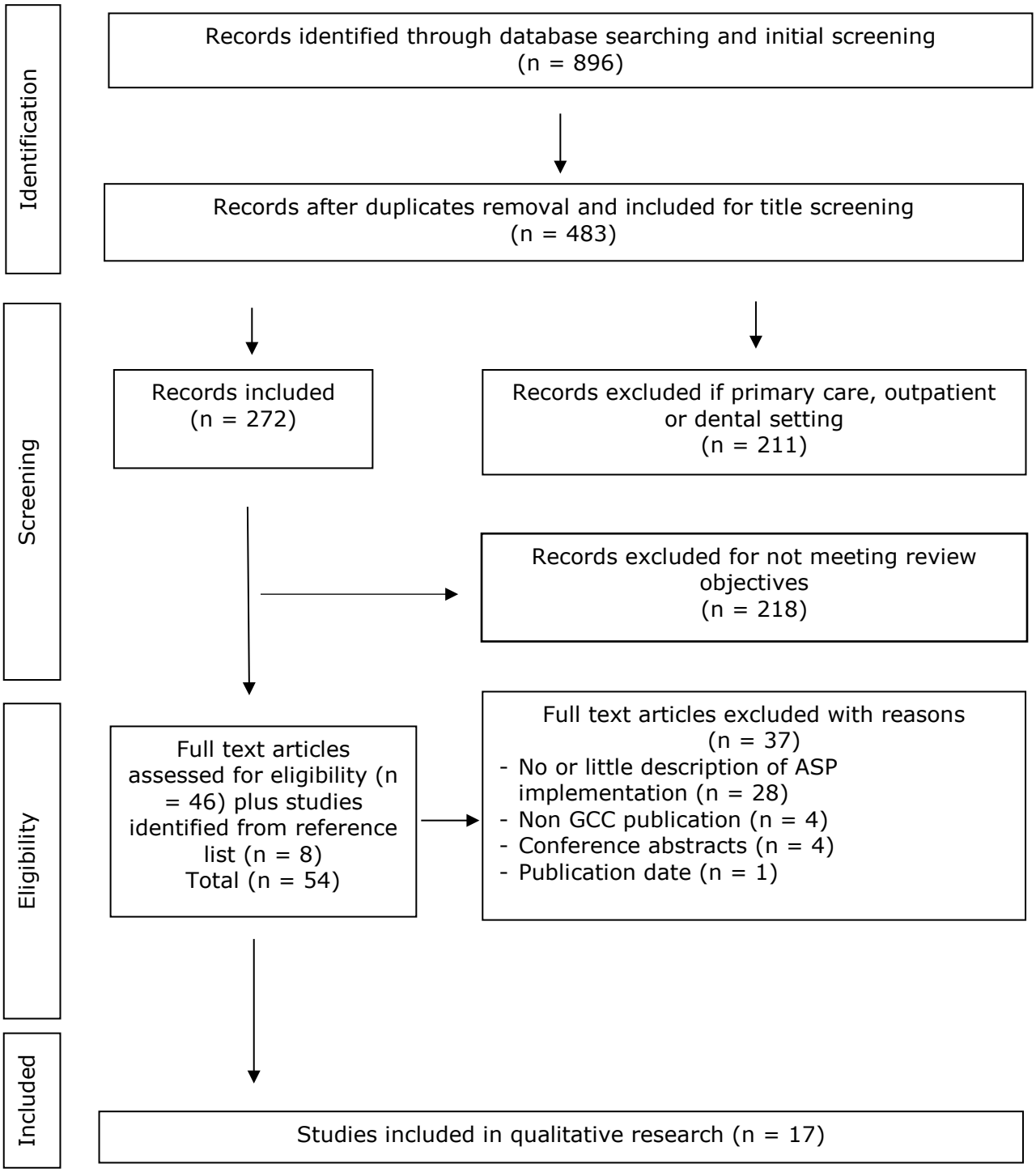

Figure 1: PRISMA flow chart for search and inclusion process. Adapted from Moher *et al* [50].

Supplementary Appendices:

Supplementary Appendix I. Summarised definitions of the CDC core elements for Hospital ASP [8].

Core element	Definition
Hospital leadership commitment	Leadership support in the form of human, financial and information technology resources.
Accountability	The multidisciplinary team leader and co-leader is a physician and a pharmacist. The two of them are the core of the team and responsible for management and outcomes.
Pharmacist expertise	A pharmacist (co-leader), ideally with infectious diseases expertise.
Actions	Implementing at least one of the recommended actions.
Tracking	By monitoring antibiotic prescribing trends and pattern of resistance.
Reporting	Regular reports on antibiotic use and resistance patterns to health care professionals.
Education	Education of prescribers is crucial to change prescribing habits and also as a motivating tool.

Supplementary Appendix II: Search string applied to databases

anti-bacterial (MeSH) OR anti-infective (MeSH) OR antimicrob* (AB, TI) OR anti-microbial (AB, TI) OR antibio* (AB, TI) OR anti-biotic (AB, TI) OR antiinfect* (MeSH) OR infection* (AB, TI) OR antibacterial* (AB, TI)	**AND**	stewardship* (AB, TI) OR prescrib* (AB, TI) OR polic* (AB, TI) OR practic* (AB, TI) OR use (AB, TI) OR program* (AB, TI) OR manage* (AB, TI) OR intervent* (AB, TI) OR surgical prophylaxis (AB, TI) OR consum* (AB, TI) OR pattern* (AB, TI) OR trend*(AB, TI) OR optimi* (AB, TI) OR therap*(AB, TI) OR implement* (AB, TI) OR educat* (AB, TI) OR inform* (AB, TI) OR audit* (AB, TI) OR feedback* (AB, TI) OR disseminat* (AB, TI) OR guid* (AB, TI) OR quality assurance (AB, TI) OR utilization review (AB, TI) OR quality indicator* (AB, TI) OR formular* (AB, TI) OR pathway* (AB, TI) OR streamlin* (AB, TI) OR decision* (AB, TI) OR rational* (AB, TI) OR improper* (AB, TI) OR unnecessary* (AB, TI) OR resist* (AB, TI) OR over-use* (AB, TI) OR overus* (AB, TI) OR improv* (AB, TI) OR inform* campaign (AB, TI) OR educat* campaign (AB, TI) OR manag* (AB, TI) OR intraven* to oral switch (AB, TI)	**AND**	gulf cooperation council (AB, TI) OR gulf* (AB, TI) OR GCC OR Middle East* (MeSH) OR Bahrain (AB, TI) OR Kuwait (AB, TI) OR Oman (AB, TI) OR Qatar (AB, TI) OR Saudi (AB, TI) OR KSA (AB, TI) OR United Arab Emirates (AB, TI) OR Emirate* (AB, TI) OR UAE (AB, TI)

Abbreviations: AB, Abstract; MeSH, Medical Subject Headings; TI, Title.

Supplementary Appendix III. Quality assessment of the cohort (n=9) and cross-sectional (n=1) studies

Criteria	Aly *et al.*, 2012 [46]	Al-Tawfiq, 2013 [38]	El Hassan et al., 2015 [47]	Tobaiqy *et al.*, 2015 [40]	Alawi and Darwesh, 2016 [43]	Garcell *et al.*, 2016 [48]	Garcell, Arias *et al.*, 2017 [49]	Garcell *et al.*, 2017 [44]	El-Lababidi *et al.*, 2019 [36]	Baraka MA *et al.*, 2019 [35]
Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes	No	CD	Yes	Yes	No	Yes
Was the participation rate of eligible persons at least 50%?	NA	Yes	CD	Yes	NA	NA	CD	NA	CD	Yes
Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study pre-specified and applied uniformly to all participants?	CD	Yes	Yes	Yes	CD	CD	Yes	Yes	Yes	No
Was a sample size justification, power description, or variance and effect estimates provided?	CD	No	CD	No	NA	No	No	NA	No	Yes
For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	NA	Yes	NA	Yes	No	NA	Yes	No	NA	NA
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	Yes	NA	No	NA	Yes	Yes	Yes	Yes	NA
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	NA	Yes	NA	NA	NA	NA	NA	NA	Yes	NA

Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	NA	Yes	Yes	CD	Yes	No	No	Yes
Was the exposure(s) assessed more than once over time?	NA	NA	NA	NA	Yes	Yes	Yes	Yes	NA	NA
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcome assessors blinded to the exposure status of participants?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Was loss to follow-up after baseline 20% or less?	NA	NA	NA	NA	NA	NA	CD	NA	NA	CD
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	CD	No	No	No	No	NA	No	No	No	NA
Overall Quality rating	Fair	Fair	Fair	Good	Fair	Fair	Fair	Fair	Good	Good

Abbreviations: CD, cannot determine; NA, not applicable

Supplementary Appendix IV. Quality assessment of the before-after (pre-Post) studies (n=6)

Criteria	Dib *et al.*, 2009 [37]	Amer et al., 2013 [39]	Al-Somai et al., 2014 [34]	Al-Tawfiq et al., 2015 [41]	Abdallah et al., 2017 [42]	Momattin et al., 2018 [45]
Was the study question or objective clearly stated?	Yes	Yes	Yes	Yes	Yes	No
Were eligibility/selection criteria for the study population pre-specified and clearly described?	Yes	Yes	Yes	Yes	Yes	Yes
Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest?	Yes	Yes	Yes	Yes	CD	CD
Were all eligible participants that met the prespecified entry criteria enrolled?	Yes	Yes	Yes	No	No	CD
Was the sample size sufficiently large to provide confidence in the findings?	No	CD	CD	CD	No	CD
Was the test/service/intervention clearly described and delivered consistently across the study population?	Yes	Yes	Yes	Yes	Yes	CD
Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?	Yes	Yes	Yes	Yes	No	Yes
Were the people assessing the outcomes blinded to the participants' exposures/interventions?	NA	No	NA	NA	No	No
Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?	NA	Yes	NA	NA	CD	NA
Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?	Yes	Yes	Yes	Yes	Yes	Yes

Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)?	No	No	No	No	NA	Yes
If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.) did the statistical analysis take into account the use of individual-level data to determine effects at the group level?	No	NA	No	No	No	NA
Overall quality rating	Fair	Fair	Fair	Good	Fair	Fair

Abbreviations: CD, cannot determine; NA, not applicable

Supplementary Appendix V: Characteristics of studies included in the systematic review (n=17).

Authors, year	Country	Aim(s) as stated by the study authors	Study design	Setting	Sample (type of hospital, wards and patient)	Data collection period
Dib *et al*., 2009 [37]	Saudi Arabia	Evaluate appropriateness of vancomycin use	Retrospective before-after study	One tertiary governmental hospital	All patients admitted who were prescribed vancomycin (n=74 before, 34 after)	Specific dates for data collection not reported; intervention implemented 2008, point prevalence at least 6 months post-intervention
Aly *et al*., 2012 [46]	Kuwait	Measure physicians' adherence to local hospital antibiotic policy guidelines	Retrospective cohort	Nine government, four tertiary and five specialized hospitals	Patients discharged in 2007 (n=2300)	July – December 2008
Al-Tawfiq, 2013 [38]	Saudi Arabia,	Evaluate the role of the ID consultations in reducing inappropriate antibiotic usage	Prospective cohort	One government tertiary hospital	Adult patients requiring an ID consultation (n=1444)	January 2006 – December 2009
Amer *et al*., 2013 [39]	Saudi Arabia	Compare prescribing appropriateness of empirical antibiotic therapy before and after ASP implementation	Prospective before-after study	One government tertiary hospital	Patients ≥18 years admitted to medical ICU (n=139; 49 control, 24 active, 66 excluded)	July – December 2009 (control); March 2011 (inception of intervention, end date not stated)
Al-Somai *et al*., 2014 [34]	Saudi Arabia	Measure impact of CP and ID consultant interventions on use of caspofungin, imipenem, meropenem	Prospective before-after study	One government tertiary hospital	receiving caspofungin, meropenem or imipenem regardless of condition, age, sex or ward (559 orders, 357 patients)	March 2011 – August 2012
Al-Tawfiq *et al*., 2015 [41]	Saudi Arabia	Examine effect of selective reporting of selected broad-spectrum agents against pathogens with high resistance rates	Prospective before-after study	One government tertiary hospital	Cultures susceptible to GNB: *Enterobacter aerogenes* (n=104 in 2009, 75 in 2010); *Proteus mirabilis* (n=168 in 2009, 116 in 2010); *Pseudomonas aeruginosa* (n=481 in 2009, 414 in 2010)	December 2009 – May 2010 (pre-intervention); June – December 2010 (post-intervention)

Authors, year	Country	Aim(s) as stated by the study authors	Study design	Setting	Sample (type of hospital, wards and patient)	Data collection period
Tobaiqy *et al*., 2015 [40]	Saudi Arabia	Investigate tigecycline prescription and patient outcomes in Saudi Arabia	Retrospective cohort	Three government tertiary hospitals	All 37 patients prescribed tigecycline	January 2013 – May 2014
El Hassan *et al*., 2015 [47]	UAE	Assess surgeons' adherence to SAP guidelines and evaluate antibiotic selection, first-dose timing, dosage interval and treatment duration	Retrospective cohort	One governmental tertiary hospital	Clean or clean-contaminated surgeries (n=250)	2012
Alawi and Darwesh, 2016 [43]	Saudi Arabia	Analyse and evaluate safety and cost-effectiveness of a gradually implemented ASP	Prospective cohort	One government tertiary hospital	Admissions to six hospital departments (surgical, obstetrics and gynaecology, medical, critical care, medical intensive care, surgical intensive care unit), number of patients not stated.	April 2012 – December 2013
Garcell *et al*., 2016 [48]	Qatar	Evaluate antibiotic consumption trend	Prospective cohort	One community hospital	281 admissions in 2012; 1278 in 2013; 3052 in 2014; 3741 in 2015	2012- 2015
Garcell *et al*., 2017 [44]	Qatar	Determine effect of focused ASP in compliance with antibiotic prophylaxis, and consumption in appendectomies	Prospective cohort	One community hospital	All appendectomy patients (n=603)	January 2013 – December 2015
Garcell *et al*., 2017 [49]	Qatar	Describe compliance with antibiotic prophylaxis in selected surgical procedures	Retrospective cohort	One community hospital	Gynaecology, obstetrics, plastic surgery, trauma, and general surgical procedures, medium complexity ones, open and laparoscopic procedures excluding transplant surgery (n=2386 procedures)	January 2013 – June 2016
Abdallah *et al*., 2017 [42]	Saudi Arabia	Compare antimicrobial susceptibility pattern of *P. aeruginosa* before and after carbapenem restriction	Retrospective before-after study	One tertiary governmental hospital	Adult patients in ICU prescribed carbapenem (August 2016, 819 cultures; December 2016, 947 cultures)	May – June 2016 pre-implementation); August – December 2016 (post implementation)

Authors, year	Country	Aim(s) as stated by the study authors	Study design	Setting	Sample (type of hospital, wards and patient)	Data collection period
Momattin *et al*., 2018 [45]	Saudi Arabia	Compare DDD, DOT, DDD per 100 bed-days, and adjusted DDD according to CMI	Retrospective before-after study	One tertiary governmental hospital	Adult patients (>15 years, n not stated)	2011 (baseline); 2013 – 2015
El-Lababidi *et al*., 2019 [36]	UAE	Report on the outcomes of an advanced ASP	Single-centre quasi-experimental cohort	A recently activated quaternary care hospital	Total discharges 1790 in 2015, 5365 in 2016 and 7181 in 2017	July 2015 – December 2017
Baraka *et al*., 2019 [35]	Saudi Arabia	Investigate practitioners' perceptions regarding ASP implementation and identify challenges and facilitators to execution	Cross-sectional study	Six large hospitals (four governmental and two private)	Physicians, pharmacists or nurses practicing in the hospitals (n=184)	Specific dates for data collection not reported
Alghamdi *et al*., 2019 [33]	Saudi Arabia	Explore ASPs team members' perspectives regarding the factors influencing the adoption and implementation of these programmes in Saudi hospitals	Qualitative study	Three MOH governmental hospitals	Total of 22 interviews (Physicians, nurses, pharmacists, infection control practitioners, infectious disease consultant, microbiologist, and hospital managers and representatives from the Saudi MOH departments of Infection Control and Pharmaceutical Care)	January – February 2017

Abbreviations: ASP, Antimicrobial stewardship programme; CP, clinical pharmacist; DDD, Defined daily dose; DOT, Days of therapy; ID, infectious disease; IV, Intravenous; *P. aeruginosa*, *Pseudomonas aeruginosa*; SAP, Surgical antimicrobial prophylaxis.