American Journal of Infection Control 52 (2024) 107–122

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

State of the Science Review

Clinical impact of antibiograms as an intervention to optimize antimicrobial prescribing and patient outcomes—A systematic review

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Key Words:
Antimicrobial resistance
Cumulative antimicrobial susceptibility test
Antimicrobial stewardship

Background: Antimicrobial stewardship (AMS) guidelines advocate for the use of antibiograms (cumulative antimicrobial susceptibility test data) as a tool to guide empirical antibiotic prescribing and inform local treatment guidelines. The objective of this review is to evaluate the effectiveness of antibiograms as an intervention to optimize antimicrobial prescribing and patient outcomes.

Methods: Embase, PubMed, CINAHL, and International Pharmacy Abstracts (IPA) databases were searched from inception until September 2022, to identify studies of antibiogram-related interventions in all health care settings. The National Institutes of Health Quality Assessment Tools were used to assess the methodological quality of the included studies.

Results: Of the 37 included studies, the majority of studies were conducted in the United States (n = 25) and in hospital settings (n = 27). All interventions were multifaceted and in 26 (70%) studies, facility-specific antibiograms could be considered as an integral component of the interventions. A positive impact on antibiotic consumption trends (17 studies), appropriateness of prescribing (16 studies), and cost of treatment (6 studies) was found, with minimal evidence for improvement in mortality, hospitalization, and resistance profiles. Due to the heterogeneity in study designs and outcomes, a meta-analysis was not performed.

Conclusions: AMS interventions including antibiograms may improve antibiotic use, appropriateness, and costs. Multifaceted interventions were often used, which precludes drawing conclusions about the effectiveness of antibiograms alone as an AMS tool.

BACKGROUND

Antimicrobial Resistance (AMR) is a significant problem as the increased quantity of antibiotic use and inappropriate antibiotic prescribing have increased the rate at which resistance is developing and spreading with limited development of new antibiotics.[1,2] Statistical modeling has estimated that 4·95 million deaths (3.62-6.57) were associated with bacterial AMR globally in 2019, which was the third leading cause of deaths, with only ischemic heart disease and stroke accounting for more deaths in the same year.[2] Ten million lives per year will be lost to AMR infections with an estimated global cost of $100 trillion US dollars by 2,050 if trends in antimicrobial resistance continue unabated.[3]

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Funding/support: This work has been funded by University of Queensland Research Training Program scholarship and Medical Research Future Fund 2017/MRF1152503.
Conflicts of interest: None to report.

https://doi.org/10.1016/j.ajic.2023.08.013

A primary principle of antimicrobial stewardship (AMS) programs is to establish effective empiric antibiotic recommendations for commonly encountered infections. Suboptimal empirical antibiotics may cause harm to patients, such as delay in effective therapy or treatment failure, and the use of unnecessarily broad-spectrum antibiotics can lead to antimicrobial resistance.[4,5] AMS guidelines advocate for the use of antibiograms to guide empirical prescribing and inform treatment guideline development.[6,7] An antibiogram comprises a table summarizing the percent of individual bacterial pathogens susceptible to different antibiotics for a specific setting and time period.[6,8] A variety of antibiograms exist ranging from the traditional to more sophisticated compilations such as weighted-incidence syndromic combined antibiogram.[9] Antibiograms can also be used to increase awareness of antibiotic resistance and track resistance patterns over time.[6,7]

Little is known about how effective antibiograms are as an intervention to optimize antibiotic use, and other related outcomes. This systematic review aims to synthesize findings from studies evaluating the clinical impact and effectiveness of antibiograms as an AMS tool, across all health care settings—including hospitals, primary care, and residential aged care (RACFs) or long-term care facilities (LTCFs).

METHODS

This systematic review is reported according to the preferred reporting items for systematic reviews and meta-analyses.[10] The protocol for study was published on PROSPERO (2021 CRD42021252262).[11] Due to the heterogeneity in study designs and outcomes, a meta-analysis was not performed.

Information sources and search strategy

A systematic literature search was conducted of five databases (PubMed, Embase, CINHAL, International Pharmaceutical Abstracts, and Scopus) for English language original research articles from inception until September 2022 (Supplementary 1—search strategy). We searched for articles that examined AMS interventions that used antibiograms in any health care setting with no limits of intervention types. Included articles were hand-searched for further relevant references using Scopus and Google Scholar. Covidence software was used for collaborative screening and Endnote 20 was used to manage the references.

Eligibility criteria

Original research articles reporting the effects of AMS interventions including antibiograms to improve antibiotic prescribing or other patient health outcomes in hospitals, primary care, and RACFs or LTCFs were eligible for inclusion. Studies were included if they reported intervention outcomes such as rates of antibiotic consumption, appropriate empirical antibiotic selection, hospitalization, cost-benefit ratios, mortality, resistance, or any other infection-related outcomes. Eligible study types included randomized controlled trials (RCT) and quasi-experimental studies such as controlled and uncontrolled before and after studies, interrupted time series, and observational studies. Cross-sectional and non-experimental studies, studies with non-human participants, and those which utilized antibiograms as only a surveillance tool were not eligible for inclusion.

Study selection

One author (DK) screened titles to exclude non-human studies. Two authors (DK, SC) independently reviewed the title and abstracts of citations returned from the search strategy, after the removal of duplicates, to identify potentially relevant citations for full-text review. An independent reviewer (NF) screened a random sample of > 5% (n = 240) of the excluded articles to ensure the reliability and integrity of the title screening process. The full text of all relevant citations was then reviewed independently by 2 authors (DK and NF/CF). Discrepancies between the 2 authors in the assessment of titles and abstracts and full-text articles were resolved through discussion and where necessary, through a third reviewer.

Data extraction

Data extraction was undertaken by 1 reviewer (DK), with 25% randomly selected for verification by a second reviewer (SC). The predefined variables extracted included study characteristics (country, study design, health care setting), intervention details, and outcomes of interest. Indicators to evaluate antibiotic use included defined daily doses per 1,000/patient or resident days (DDD/1,000 days), days of antibiotic therapy per 1,000 patient or resident days (DOT/1,000 days), and percentage of patients prescribed or charted an antibiotic. Indicators of the appropriateness of antibiotics included the percentage of antibiotic prescriptions that were concordant with local treatment guideline or recommendations. All data on outcome measures specifying length of stay (LOS), mortality rates, resistance rates, costs of treatment, or any infection-related outcomes was extracted in any form or unit available. The type of infection or antimicrobial agent focus of the study was also extracted.

Intervention details included antibiogram type and its clinical application. If antibiograms were used in combination with other interventions, the details of these other interventions were also extracted. The Cochrane effective practice and Organization of care group's Taxonomy of Health System Interventions[12] was used as a guide to classify intervention components (Supplementary 2—Effective Practice and Organization of Care Taxonomy). Antibiograms were considered to have an integral role if the AMS intervention was not possible without the use of the antibiogram.

Methodological quality assessment

Risk of bias was assessed using validated checklists published by the US National Institutes of Health (NIH).[13] Internal validity of the studies was evaluated using these checklists. This tool specifies different checklists for different study designs. The guidance document provided by NIH recommends against using the checklists to 'score' in order to judge a study's quality. The checklist of questions for each of these study types is included in Supplementary 3- Table 3.

RESULTS

There were 37 studies included in this review. The preferred reporting items for systematic reviews and meta-analyses diagram (Fig 1) illustrate the process by which the studies were screened. A total of 11,889 studies were identified. After duplicates (4,129), non-English (758), and non-human (4,692) studies were removed, 2,310 studies were assessed for title and abstract, and 89 studies were fully assessed. Thirty-one studies were included from this process. An additional 5 studies were found from hand-searching reference lists and citations of included articles. The search was updated prior to data analysis which added an additional study.

Study design and setting

The study (author, year, study design, location, setting, and sample size) and intervention characteristics are presented in Table 1. The study designs included before and after (n = 27),[14–40]

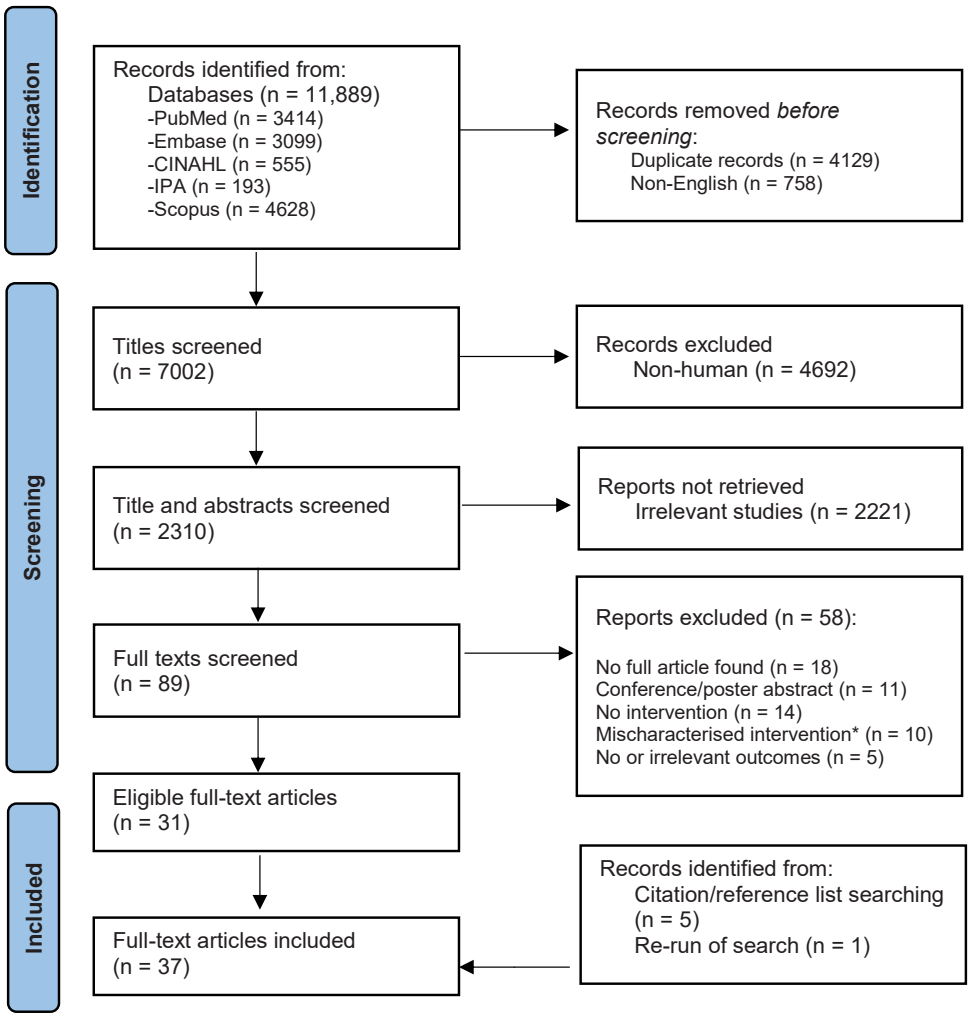

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses flowchart of screening results. *Mischaracterized intervention—included interventions that are not of interest as they describe individual and not cumulative antimicrobial susceptibility test results.

interrupted time series (n = 7),[41–47] crossover randomized controlled trial (n = 1),[48] and observational case/cohort studies (n = 2).[49,50] The majority of studies were conducted in the United States (n = 25),[17–21,23–25,29–32,35–38,40,42–49] followed by 5 studies in India,[14,16,27,34,41] 2 in Egypt,[22,39] 2 in Canada,[26,28] and 1 each in Thailand,[15] South Africa,[33] Australia, and New Zealand.[50] A total of 27 studies[14–16,18,21,22,26–30,33–42,44–46,48–50] were conducted in hospitals and associated outpatient clinics which included intensive care units, emergency departments, medical and surgical wards. Three studies were conducted in RACF or LTCF for aged residents.[20,24,32] Other settings included LTCF or medical centers for veterans[31,47] or specialist outpatient clinics.[17,19,23,25,43]

Quality appraisal

Specific NIH[13] Quality Assessment Tool for the relevant study types was used for quality appraisal of included studies. These findings are detailed in Supplementary 3–Table 4.

Overall, the studies in this review would be considered at high risk of bias as 92% were uncontrolled prepost design. Of these, seven studies[41–47] used an interrupted time series (ITS) design to detect whether an intervention has had an effect significantly greater than the underlying trend.

When assessed for internal validity using the NIH checklist, most studies (86%) had an adequate response to the quality domains (ie, positive response to at least 5 checklist points). Only five of these studies[25,28,29,46,50] had positive responses to 9 or more domains.

Study outcomes

Table 2 includes outcome details and how the antibiogram was utilized for all included studies.

Overall, 22 studies[15,16,18,20,21,23,25,28–30,32,35–37,39–43,45–47] measured volume of antibiotic use or patterns of prescribing and 20 studies[14–16,18,20–24,26–28,31,35,38,41,43–45,49] reported appropriateness of antibiotic use. Other reported outcomes included mortality (n = 10),[14,16,18,37–40,48,50] resistance rate (n = 9),[15,22,25,29,33,36,40,42,48] costs of treatment (n = 7),[14,15,18,22,30,39,48] hospitalization or length of stay (n = 9)[18,21,29,35–39,48] and infection-related outcomes, including *C difficile* rates (n = 13).[17,19,25,29,30,32,34,38,41,43,44,47,48]

Antibiograms were considered an integral component of the AMS interventions in 26 studies.[17–33,36,37,42–45,47–49] A sub-analysis of these studies was conducted indicated that all 26 studies used multifaceted interventions in association with facility-specific antibiograms. In 20 of the 26 studies, antibiograms were used to guide empirical antibiotic prescribing and develop treatment guidelines.[20–24,26,28–33,36,37,42–45,48,49] Often educational strategies, local

Table 1
Study and intervention characteristics of included studies

Author, year	Country	Study-design	Health care setting (and number)	Sample size	AMS interventions in addition to antibiograms (EPOC taxonomy)	Antibiogram isolate numbers
Agarwal, 2021[41]	India	ITS	Hospital[1]	2,292 prescriptions	Local consensus processes, Clinical Practice Guidelines, Reminders, Educational strategies	NR
Ahmed, 2018[14]	India	Before-After	Hospital[1]	200 patients	Educational strategies, Audit and Feedback, Reminders, Local consensus processes, Use of information and communication technology	*E coli*—9
Apisarnthanarak, 2006[15]	Thailand	Before-After	Hospital[1]	7,135 prescriptions	Educational strategies, Audit and Feedback, Reminders, Local consensus processes, AMS teams	NR
Banerjee, 2020[16]	India	Before-After	Hospital[1]	NR	Audit and Feedback, AMS teams	NR
Baracco, 2014[17]	USA	Before-After	Outpatient clinic[1]	512 patients	Local consensus processes, Clinical Practice Guidelines, Reminders	*E coli*–1,000
Black, 2022[42]	USA	ITS	Hospital[2]	NR	Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Boggan, 2012[49]	USA	Case-study survey	Hospital/ outpatient clinic[1]	75 prescribers	Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Box, 2019[18]	USA	Before-After	Hospital[1]	1,051 patients	Local consensus processes, Reminders	NR
Concepcion, 2019[19]	USA	Before-After	Outpatient clinic[9]	1,578 biopsies	Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Durham, 2020[20]	USA	Before-After	LTCF (Aged care)[1]	300 patients	Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR
Ebied, 2022[21]	USA	Before-After	Hospital[1]	180 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
El-Sokkary, 2020[22]	Egypt	Before-After	Hospital[1]	240 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	199
Eudaley, 2019[23]	USA	Before-After	Outpatient clinic[1]	198 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR
Fitzpatrick, 2021[50]	Australia/ New Zealand	Cohort (retrospective observational study)	Hospital (173)	799, 901 patients	AMS teams	NR
Funaro, 2021[43]	USA	ITS[2]	Outpatient clinic[2]	4,724 patients	Educational strategies, Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Furuno, 2014[24]	USA	Before-After	LTCF (Aged care)[1]	839 charts	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Gregg, 2018[25]	USA	Before-After	Outpatient clinic[1]	1,245 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	3,329
Halpape, 2014[26]	Canada	Before-After	Hospital[1]	34 patients	Educational strategies, Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR
Khan, 2006[34]	India	Before-After	Hospital[1]	278 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	168
Krishnamoorthy, 2022[27]	India	Before-After	Hospital[1]	NR	Educational strategies, AMS teams	NR
Landry, 2014[28]	Canada	Before-After	Hospital/ outpatient clinic[1]	172 patients	Educational strategies Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Liang, 2016[29]	USA	Before-After	Hospital[1]	87 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	67
Libertin, 2017[30]	USA	Before-After	Hospital[1]	NR	Educational strategies, Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR

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Table 1 (*continued*)

Author, year	Country	Study-design	Health care setting (and number)	Sample size	AMS interventions in addition to antibiograms (EPOC taxonomy)	Antibiogram isolate numbers
Nys, 2022[44]	USA	ITS	Hospital[3]	8,742 patients	Educational strategies, Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Patros, 2018[31]	USA	Before-After	LTCF (not for aged care)[1]	112 patients	Educational strategies	1,121
Rahme, 2016[32]	USA	Before-After	LTCF (Aged care)[1]	NR	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	80 *E coli* 29 *Proteus species*
Ridgway, 2021[48]	USA	Cross-over RCT	Hospital[4]	6,849 patients	Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR
Savage-Reid, 2020[33]	South Africa	Before-After	Hospital[1]	NR	Local consensus processes, Clinical Practice Guidelines, Reminders	674
Shoff, 2020[45]	USA	ITS	Hospital/ outpatient clinic[1]	5,517 prescriptions	Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Stoll, 2021[35]	USA	Before-After	Hospital/ outpatient clinic[1]	678 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Stratton, 1993[36]	USA	Before-After	Hospital[6]	NR	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Sullivan, 2020[46]	USA	ITS	Hospital[1]	1,070 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders	NR
Swearingen, 2016[37]	USA	Before-After	Hospital[1]	153 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR
Toth, 2010[38]	USA	Before-After	Hospital[1]	160 patients 442 antibiotic orders	Educational strategies, Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders, AMS teams	NR
Vissichelli, 2022[47]	USA	ITS	LTCF (not for aged care)[1]	NR	Local consensus processes	5,103
Wassef, 2020[39]	Egypt	Before-After	Hospital[1]	312 patients	Educational strategies, Local consensus processes, Clinical Practice Guidelines, AMS teams	NR
Wong-Beringer, 2009[40]	USA	Before-After	Hospital[1]	NR	Educational strategies, Audit and Feedback, Local consensus processes, Clinical Practice Guidelines, Reminders	NR

EPOC, effective practice and organization of care group's Taxonomy of Health System Interventions (Supplementary 2—EPOC Taxonomy)[12] ; *ITS*, interrupted time series; *LTCF*, long-term care facility; *NR*, not reported; *RCT*, randomized controlled trial; *USA*, United States of America.

Table 2
Type of antibiogram, role in AMS intervention, and details of outcome measures reported for all included studies

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Agarwal, 2021[41]	Location-specific	No	To review yearly antibiotic policy	↓32% total AUR ↓29% vancomycin *P* < .01	↑ proportion of newborns who never received antibiotics (22%-37%) *P* < .045 ↑ proportion of appropriate antibiotic stoppage in absence of positive culture (16%-54%) *P* < .001	NA	NA	NA	NA	No difference in enterocolitis (NS)
Ahmed, 2018[14]	Traditional	No	Unclear	NA	↑ overall (25% vs 46%) *P* = .002 ↑antibiotic de-escalation (21% vs 36%) *P* = .019	Rate 28% vs 33% *P* = .44	NA	↓24 207.5 versus 16 517.5 Rupees per patient *P* = .013	NA	NA
Apisarnthanarak, 2006[15]	NR	No	Unclear	↓ 57.0 versus 49.8 DDDs/ 1,000 patient-days ↓ 640 versus 400 prescriptions/1,000 admissions ↓24% antibiotic prescribing rate *P* < .001	↓ inappropriate use (42% vs 20%) *P* < .001	NA	NA	↓US$84,450 vs $52,219 *P* < .001	↓ incidence of MRSA 48% vs 33.5%; ESBL-*E Coli* 33% vs 21%, ESBL-*K Pneumoniae* 30% vs 20%, 3rd gen Cephalosporin resistant *A.baumanii* 27% vs 19% *P* < 0.001	NA
Banerjee, 2020[16]	NR	No	Unclear	Cumulative usage trend of clindamycin/ metronidazole per 100PD 10.8 versus 2.2 (NS)	Shift toward more effective antibiotics as per antibiogram (NS)	No impact on all- cause mortality rate (NS)	NA	NA	NA	NA
Baracco, 2014[17]	Traditional	Yes	To alter prophylactic antibiotic recommendation	NA	NA	NA	NA	NA	NA	Procedure associated sepsis (5.4% vs 1.0%) (NS)
Black, 2022[42]	Syndromic	Yes	To guide empirical prescribing/ develop guidelines	Ciprofloxacin mean monthly 26.9-15.8 DOT/1,000 PD *P* = .43 ↓Levofloxacin mean monthly 14.1 versus 8.4 DOT/1,000 PD *P* = .035 ↑overall all antibiotic use 604.1 versus 646.7 *P* = .001	NA	NA	NA	NA	No difference in *E coli* and *P aeruginosa* susceptibility to ciprofloxacin 85% versus 84% (NS)	NA

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Boggan, 2012[49]	Location-specific	Yes	To guide empirical prescribing/ develop guidelines	NA	Infants- ↑ effective antibiotic choice 68.6% (no antibiogram) to 82.2% (overall antibiogram) to 92.5% (Pediatric specific antibiogram) $P = .08$, $P < .01$ Adolescent- ↑ effective antibiotic choice 32.4-57.4-79.4% $P < .01$, $P = .01$	NA	NA	NA	NA	NA
Box, 2019[18]	NR	Yes	To identify target microorganisms	↓AP antibiotic consumption (0.4 vs 0.2 DOT/ PD $P < .0001$ ↑non-AP antibiotic consumption (0.6 vs 0.8 DOT/PD) $P < .0001$	↓Incidence of patients who received empiric AP (67.6% vs 61.7%) $P = .02$	Rate 7.0% vs 5.2% $P = .21$	Median LOS = 5 days versus 5 days. $P = .85$ Median ICU LOS = 3 days vs 2 days. $P = .12$	Total median direct variable costs ($7125 vs $7472) $P = .25$ ↓median direct variable pharmacy costs ($285 vs $206) $P < .001$ ↓median total antibiotic costs ($25 vs $21) $P = .04$	NA	NA
Concepcion, 2019[19]	NR	Yes	To alter prophylactic antibiotic recommendation	NA	NA	NA	NA	NA	NA	↓infection related complications (3.1% vs 1.4%) $P = .031$
Durham, 2020[20]	NR	Yes	To guide empirical prescribing/ develop guidelines	↓TMP/SMX (32% vs 8%), ciprofloxacin (14% vs 1%), amoxicillin (13% vs 0%), levofloxacin (9% vs 0%), amoxicillin/ clavulanate (5% vs 1%) ↑cefpodoxime (9% vs 46%), ceftriaxone (8% vs 10%), nitrofurantoin (4% vs 30%) $P < .001$	↑ 22% vs 88% $P < .001$	NA	NA	NA	NA	NA

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Ebied, 2022[21]	NR	Yes	To guide prescription order set revision	rate of antibiotic continued from ED to admission (62.1% vs 59.4%) *P* = .99	↑74.4% vs 78.9% *P* = .6 When order set used: ↑in admitted patients (50% vs 88.2%) *P* = .0382 ↑in total patient (50% vs 81.8%) *P* = .037	NA	LOS 4.93 vs 4.32 *P* = .61	NA	NA	NA
El-Sokkary, 2020[22]	Location-specific	Yes	To guide empirical prescribing/ develop guidelines	NA	↓ unindicated antibiotic prophylaxis (27.4% vs 5.8%) *P* = .04 ↑empirical prescribing according to the site of infection (64.4% vs 82.7%) *P* = .025	NA	NA	↓median (Egyptian pound 4042 vs 2341) *P* = .04	↓MDR/XDR (68% vs 46%) *P* = .001	NA
Eudaley, 2019[23]	Syndromic	Yes	To guide empirical prescribing/ develop guidelines	↓ FQ use (42% vs 15%) *P* < .001 ↓by 20% TMP/SMX *P* = .003 ↑by 31% Nitrofurantoin *P* = .005	↑ by 32% guideline directed duration of therapy *P* = .005	NA	NA	NA	NA	NA
Fitzpatrick, 2021[50]	Location-specific	No	Unclear	NA	NA	↓ risk of in-hospital mortality (OR 0.95 (99% CI 0.92-0.99) *P* = .001	NA	NA	NA	NA
Funaro, 2021[43]	Syndromic	Yes	To guide empirical prescribing/ develop guidelines	↓ by 52% FQ use (NS)	↑ by 22% guideline concordance initially but ↓ by 0.5% every 2 weeks afterward 95% CI 12%-32%	NA	NA	NA	NA	↓ by 21% UTI diagnosis (IIR = 0.79) 95% CI (0.67-0.93)
Furuno, 2014[24]	Traditional	Yes	To guide empirical prescribing/ develop guidelines	NA	32% vs 45% *P* = .32	NA	NA	NA	NA	NA
Gregg, 2018[25]	Syndromic	Yes	To alter prophylactic antibiotic recommendation	↓ prophylactic antibiotic use (94.8% vs 69.8%) *P* < .01	NA	NA	NA	NA	resistance to FQ (63.2% vs 31.3%) *P* = .09	UTIs post procedure (3.0% vs 2.6%) *P* = .69

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Halpape, 2014[26]	NR	Yes	To guide empirical prescribing/ develop guidelines	NA	↑proportion of adherence with best practice (10% vs 38%) *P* = .043	NA	NA	NA	NA	NA
Khan, 2006[34]	Syndromic	No	To identify resistance patterns	NA	NA	NA	NA	NA	NA	Infection rate (9.45% vs 0%) (NS)
Krishnamoorthy, 2022[27]	NR	Yes	For education purposes	NA	76% of prescriptions were adherent/ 24% not adherent to the antibiogram guidelines (NS)	NA	NA	NA	NA	NA
Landry, 2014[28]	NR	Yes	To guide empirical prescribing/ develop guidelines	Change in overall antibiotic selection OR 0.25 95% CI 0.11-0.58; *P* < .001 ciprofloxacin (32% vs 11%) (NS) nitrofurantoin (30%-50%) (NS)	↑ adherence to best practice (41% vs 66% OR 2.81) 95% CI 1.51-5.25; *P* < .001	NA	NA	NA	NA	NA
Liang, 2016[29]	Traditional	Yes	To guide empirical prescribing/ develop guidelines	↓ FQ (3.7 vs 1.4 DOT) *P* < .001 FQ mean days (SD) (421.5 (± 32.6) vs 338 (± 71.3)) *P* = .08 Patients receiving double coverage (33% vs 31%) *P* = .57 ↓Double coverage mean days (SD) (3.4 (± 3.2) versus 1.3 (± 1.2)) *P* < .001	NA	NA	LOS 9.5 (± 6.1) vs 7.4 (± 4.8) *P* = .22	NA	No difference *P* = .57	clinical success (37% vs 48%) *P* = .18
Libertin, 2017[30]	NR	Yes	To guide empirical prescribing/ develop guidelines and identify target antimicrobial agents	↓ by 10% (126.7 vs 115 DDDs/1,000 PD) *P* < .001	NA	NA	NA	↓by $8.49 total targeted antimicrobial costs ($16.93 vs $8.44 per PD) 95% CI $7.80-$9.18; *P* < .001	NA	↓by 2 cases of *C.difficile* (3.35 vs 1.35 cases/ 1,000 OBDs) 95% CI 0.62-3.39; *P* < .001

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Nys, 2022[44]	Syndromic	Yes	To guide empirical prescribing/ develop guidelines	NA	↑ by 15% initial guideline concordance (Phase1 vs preintervention IRR 1.15) 95% CI, 1.03-1.29; *P* = .02 ↑in guideline-concordant prescriptions was seen with every 2-week interval during phase 2 (IRR, 1.03) 95% CI, 1.01-1.04); *P* < .01	NA	NA	NA	NA	No change in UTI diagnosis (NS)
Patros, 2018[31]	Traditional	Yes	To guide empirical prescribing/ develop guidelines	NA	↑ 47.9% vs 71.8% *P* = .015	NA	NA	NA	NA	NA
Rahme, 2016[32]	Syndromic	Yes	To guide empirical prescribing/ develop guidelines	↓Ciprofloxacin (7.08 ± 2.49 vs 4.34 ± 1.98) *P* = .02 Levofloxacin (6.16 ± 2.46 vs 6.72 ± 2.41) *P* = .65 Moxifloxacin (0.34 ± 0.31 vs 0.32 ± 0.38) *P* = .93 total antibiotic use (82.33 ± 12.23 vs 72.71 ± 6.80) *P* = .06	NA	NA	NA	NA	NA	UTI (1.71 ± 0.21 vs 1.61 ± .24) *P* = .28 RTI (1.35 ± 0.47 vs 1.27 ± .44) *P* = .67 SSTI (0.92 ± 0.19 vs 1.04 ± 0.33) *P* = .27 *C difficile* rates (0.094 ± 0.09 vs 0.076 ± 0.59) *P* = .58
Ridgway, 2021[48]	WISCA	Yes	To guide empirical prescribing/ develop guidelines	NA	NA	overall 30-day mortality (5.37% vs 5.49%) *P* = .87 ↓CAP associated mortality (aOR = 0.582; 95% CI,.396, .854); *P* = .0204	overall LOS (4.54 (4.42) vs 4.50 (4.39)) *P* = .68 ↓cellulitis LOS (coefficient estimate = 0.53) 95% CI, −.97, −.09; P = .0186 30-day hospital re-admission (10.38% vs 10.58%) *P* = .82	No change ($546.75 vs $548.72) *P* = .89	MDR organism (1.6% vs 1.47%) *P* = .56	*C difficile* rates (4.56% vs 4.67%) *P* = .87

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Savage-Reid, 2020[33]	NR	Yes	To guide empirical prescribing/ develop guidelines	NA	NA	NA	NA	NA	Organism prevalence: Increased ↑ *Streptococci* by 2.7%. *P* = .0199 ↑*Candida auris* by 1.7%. *P* = .0031 *A baumannii* by 4.6%. *P* = .0508 ↓*P aeruginosa* by 4.4%. *P* = .0196 Resistance profile: ↓MDR *A baumannii* by 28.9% *P* = .0001 ↓MDR *P aeruginosa* by 60.4% *P* = .0001 ↑carbapenem-resistant *Enterobacterales* by 6.5% *P* = .007	NA
Shoff, 2020[45]	Syndromic	Yes	To guide empirical prescribing/ develop guidelines	↓monthly FQ prescriptions (median 45.0% vs 32%) *P* < .001 ↑ prescriptions for B-lactams (median of 14.0% vs 24.5%) *P* < .001	antibiotic concordant with microbiological results (79% vs 77%) *P* = .65	NA	NA	NA	NA	NA
Stoll, 2021[35]	Location-specific	No	To provide resistance data	↓ FQ prescribing rate (12.3% vs 2.3%) *P* < .00001	↑ guideline adherent (11.7% vs 61.5%) *P* < .00001 ↑ appropriate agent (45.5% vs 87.3%) *P* < .00001 ↑ appropriate dose (77.2% vs 91.5%) *P* < .00001 ↑appropriate duration (39.1% vs 71.1%) *P* < .01	NA	30-day re-admission to ED (21% vs 15.3%) *P* = .36 30-day inpatient admission (4.9% vs 3.4%) *P* = .32	NA	NA	NA

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Stratton, 1993[36]	Location-specific	Yes	To guide empirical prescribing/ develop guidelines	AP use in medical ICU except tobramycin and ciprofloxacin which ↑ 3-fold (NS)	NA	NA	LOS by wards: by 11.7% in Medical ↑ by 4.1% in surgical ↑ by 3.9% in neurosurgical ↑ by 4.7% in pediatric ↑ by 1.4% in neonatal ↑ by 5.3% in burns (NS)	NA	↑MRSA in medical, surgical, neurosurgical ICUs ↑susceptibility of *P aeruginosa* in medical ICU (NS)	NA
Sullivan, 2020[46]	Location-specific	No	Unclear	↓ monthly FQ DOT/100 ED visits (18.4, 17.8, 16.5, 19.8, 16.8 vs 8.7, 7.9, 8.0, 6.3, 6.0) 95% CI (8.45-12.31); *P* = .0009	NA	NA	NA	NA	NA	NA
Swearingen, 2016[37]	Traditional	Yes	To recommend alternative antibiotics to reduce aztreonam use	↓median aztreonam DOT (4.0 vs 2.0) *P* = .0001 ↓median DOT/1,000 PD (14.5 vs 9.3) *P* = .0001 ↓median DOT/1,000 PD 1-year post intervention (18.5 vs 6.5) *P* = .0001	NA	In-hospital mortality (16.7% vs 23.8%) *P* = .28	LOS 8 vs 9 days *P* = .98	NA	NA	NA
Toth, 2010[38]	NR	No	Education about antibiogram	NA	↑rate of appropriate de-escalation (72% vs 90%) *P* = .01 ↑documented indication (95% vs 100%) *P* = .12 appropriate empirical therapy (69% vs 81%) *P* = .06 ↑compliance with all quality indicators (16% vs 54%) *P* < .001	No difference in mortality (NS)	No change in LOS (NS)	NA	NA	*C difficile* rates (10% vs 5%) *P* = .23

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Table 2 (*continued*)

Author, year	Type of antibiogram used	Antibiogram integral component of intervention?	How the antibiogram was used	Outcomes assessed						
				Antibiotic use	Appropriateness	Mortality	Hospitalization/ LOS	Costs	Resistance	Infection related outcomes
Vissichelli, 2022[47]	NR	Yes	To develop cascade reporting algorithms	↓ mean monthly meropenem (52.96 vs 40.42) $P = .005$ ↓ mean monthly piperacillin/ tazobactam (132.56 vs 113.8) $P = .002$ ↑ cefepime (6.98 vs 19.01) $P = .001$ ↓ciprofloxacin by 2.16 DOT/1,000 days present/month $P < .001$	NA	NA	NA	NA	NA	No change in *C difficile* rates (NS)
Wassef, 2020[39]	Location-specific	No	Unclear	↓ by 25.2% prophylactic antimicrobials prescribed (25.2% vs 10%) $P = .002$ ↓ length of therapy (1,502 days—mean 9.82 days vs 1318 days mean 7.75days) $P = .001$	NA	mortality (31.1% vs 24.8%) $P = .20$	↓ LOS mean (10.66 (± 6) versus 9.16 (± 5) $P = .047$	↓ by 19.66% (Egyptian pound 68164.94 vs 54764.96) $P = .01$	NA	NA
Wong-Beringer, 2009[40]	NR	No	To provide resistance data	↓ by 30% empiric FQ prescribing (NS)	NA	↓ 2-fold mortality associated with *P aeruginosa* infections (NS)	NA	NA	↑ by 10% susceptibility for all AP agents against *P aeruginosa* (NS)	NA

AP, antipseudomonal; *AUR*, antibiotic usage rate; *CI*, confidence interval; *DDDs*, defined daily doses; *DOT*, day of therapy; *ED*, emergency department; *FQ*, fluoroquinolones; *ICU*, intensive care unit; *IRR*, incidence rate ratio; *LOS*, length of stay; *MDR*, multidrug-resistant; *NA*, not assessed; *NR*, not reported; *NS*, no statistical analysis reported; *OBD*, occupied bed days; *OR*, odds ratio; *PD*, patient-days; *RTI*, respiratory tract infection; *SD*, standard deviation; *SSTI*, skin and soft tissue infection; *TMP/SMX*, Trimethoprim/sulfamethoxazole; *UTI*, urinary tract infections; *WISCA*, weighted-incidence syndromic combined antibiogram; *XDR*, extensively-drug resistant.

consensus processes, clinical practice guidelines, and reminders were used together with the antibiogram to develop or inform empirical treatment guidelines, algorithms, or decision support tools (n = 14).[21–26,28–30,32,36,37,43,44]

Five studies used traditional antibiograms.[17,24,29,31,37] Seven studies used syndromic antibiograms[23,25,32,42–45] and 1 study used weighted incidence syndromic antibiograms.[48] Three studies[22,36,49] which did not clarify the use of traditional or syndromic antibiograms, specifically mentioned the location of origin of the antibiograms (ie, location-specific).

Overview of intervention effectiveness

Antibiotic use and prescribing patterns

The volume of antibiotics used was reported as an outcome in 22 studies.[15,16,18,20,21,23,25,28–30,32,35–37,39–43,45–47] Statistically significant improvements in prescribing patterns were found in 17 studies.[15,18,20,23,25,28–30,32,35,37,39,41,42,45–47] Of these 17 studies, 12 studies[18,20,23,25,28–30,32,37,42,45,47] utilized antibiograms as an integral component. Eight out of these 12 studies[18,23,28,29,32,42,45,47] found a reduction in broad-spectrum antipseudomonal antibiotics, mostly fluoroquinolone use, and this outcome was reported as DOT or DDDs/1,000 patient days or percentage or rate of prescribing or charting. Three studies indicated a trend toward increased use of narrower-spectrum antibiotics such as nitrofurantoin.[18,20,23] This outcome was not assessed in the RCT.[48]

Appropriateness of antibiotic prescribing

Outcome measures reporting the appropriateness of antibiotic prescribing included guideline-concordant prescribing, rates of empirical antibiotic prescribing, or choice of empirical antibiotics. This was reported as an outcome measure in 20 studies[14–16,18,20–24,26–28,31,35,38,41,43–45,49] and in 16 of these,[14,15,18,20–23,26,28,31,35,38,41,43,44,49] there was a statistically significant improvement in the appropriateness of antibiotic use. Eleven of the 16 studies[18,20–23,26,28,31,43,44,49] utilized antibiogram as an integral component of AMS interventions. This outcome was not assessed in the RCT.[48]

Hospitalization and length of stay

Hospital admission (30-day re-admission/inpatient admission) was reported in 2 studies[35,48] and LOS was reported in 8 studies.[18,21,29,36–39,48] Statistically significant reduction in LOS was only shown for Wassef et al[39] with a decrease in mean days of 1.5 ($P = .047$). LOS was a primary outcome in only 1 study which was a randomized crossover trial[48] which did not find a statistically significant difference.

Mortality

Mortality was not reported as a primary outcome in any included studies. Of all the studies that reported mortality as a secondary outcome measure, Fitzpatrick et al[50] found that patients admitted to intensive care units that used intensive care unit-specific antibiograms had a lower risk of in-hospital mortality (OR 0.95 [99% CI 0.92–0.99], $P = 0.001$). No other interventional studies found any statistically significant change in overall mortality rates; however, when stratified by infection type, the randomized crossover trial[48] did find statistically significant reduction in CAP associated mortality (adjusted OR 0.582 [95% CI 0.396, 0.854] $P = .0204$).

Costs associated with antimicrobial use

Cost effectiveness outcomes were reported in seven studies[14,15,18,22,30,39,48] and reduced costs associated with antibiotic use were shown in all but 1 study which was the randomized crossover trial.[48] Of the studies that used antibiogram as an integral component, Box et al[18] and El-Sokkary et al[22] found statistically significant reduced median total antibiotic costs ($4 and 1,701 Egyptian pounds, respectively) while Libertin et al[30] found a reduction of $8.49 antimicrobial costs per patient day (95% CI $7.80-$9.18; $P < .001$).

Resistance patterns

Changes in resistance or susceptibility patterns were reported in nine studies[15,22,25,29,33,36,40,42,48]. Three of these studies[15,22,33] found statistically significant improvements in susceptibility patterns. Of the 7 studies[22,25,29,33,36,42,48] that utilized antibiograms integrally, El-Sokkary[22] found the reduction of multi-drug/extensively-drug resistant microorganism by 22% ($P = .001$). Savage-Reid et al[33] found the reduced prevalence of *P aeruginosa* (by 4.4%; $P = .02$) and a statistically significant reduction MDR *A baumannii* by 28.9% ($P = .0001$) and MDR *P aeruginosa* by 60.4% ($P = .0001$); however, increased carbapenem-resistant *Enterobacterales* by 6.5% was noted ($P = .007$). No statistically significant improvements in resistance patterns were found in the randomized crossover trial.[48]

Infection related outcomes

C difficile rates were reported in 5 studies,[30,32,38,47,48] however, only Libertin et al[30] found a statistically significant reduction by two cases (3.35 vs 1.35) per 1,000 occupied bed days (95% CI 0.62-3.39; $P < .001$). No statistically significant reduction in *C difficile* rates was noted in the randomized crossover trial.[48]

Other infection related outcomes were reported in 9 studies.[17,19,25,29,32,34,41,43,44] Concepcion et al[19] found a 53% reduction in infection-related complications following the change in prophylactic antibiotic choice ($P = .031$), which was based on the antibiogram data. Funaro et al[43] found a reduced incidence of urinary tract infections diagnosis by 21% following the introduction of a decision support tool based on antibiogram data (IR 0.79; 95% CI, 0.67-0.93).

DISCUSSION

Main findings

This systematic review identified 37 studies evaluating the effectiveness of AMS interventions including antibiograms in hospital, primary, and aged care settings. Findings suggest that there is evidence for the use of antibiograms as part of AMS interventions to improve prescribing patterns and appropriateness of antibiotics. There was a positive impact on antibiotic consumption trends (17 studies), appropriateness of prescribing (16 studies), and cost of treatment (6 studies), with limited or minimal evidence for improvement in infection-related outcomes, mortality, hospitalization, and resistance profiles. The majority of included studies were of uncontrolled prepost design with only 1 study incorporating randomization.

AMS interventions are often multimodal and often simultaneously implemented. This makes evaluating impact of any one specific strategy difficult and hence benefits of each intervention on its own may remain unclear. All included studies, utilized facility, or unit-specific antibiograms, however, the details of how each antibiogram was developed, or the number of isolates included, was not well documented, hence it is unknown if the antibiograms were concordant with Clinical Laboratory Standards Institute guidelines.[6] This limits the ability to compare the nature of antibiograms used in the different studies and therefore the validity of the antibiograms used remains unclear.

Antibiograms are proposed to improve empirical antibiotic choices hence we would not expect any change in overall volumes of antibiotic use. Rather, we would expect to see a change in the pattern of antibiotics used. This was indicated from the findings of this

review as there was an overall trend of reduced antipseudomonal antibiotics and some evidence of increased use of narrow-spectrum antibiotics.

The scarcity of evidence about the impact on resistance, mortality or hospitalization may be because studies are not large enough to detect changes in rates of these outcomes that are generally not the primary outcomes of any studies. Importantly, included studies did not report any statistically significant worse clinical outcomes associated with the intervention.

Strengths and limitations

This systematic review includes the evaluation of multiple outcome measures to comprehensively explore the effectiveness of AMS interventions that included antibiograms. Other than antibiotic prescribing patterns and appropriateness, less reported patient-related health outcomes such as mortality, hospitalization, resistance patterns, cost-related factors, and infection-related outcomes were also included.

There was significant variation in the methods for assessing the appropriateness of antibiotic use, volume of antibiotics, type, and details of antibiograms, sample sizes of studies, and any associated statistical analysis. These factors may limit the comparability and generalizability of these results across different health care settings. The scarcity of good quality studies is a significant finding in this study. The majority of studies including antibiograms as an intervention were uncontrolled before and after studies which has an inherent risk of bias. It would be worth noting that the majority of ITS studies using antibiograms integrally indicated improvements in consumption and appropriateness of antibiotic use,[42–45,47] which suggests that the intervention may have had an effect significantly greater than the underlying trend.

Future research

There is a clear lack of studies evaluating antibiogram utility as an AMS tool in countries other than the United States, and in health care settings other than hospitals. Evaluation of antibiograms in other health care settings such as LTCFs for older adults and primary care should be considered for further research.

Other potential research opportunities include exploring the most effective accompanying AMS interventions to obtain the maximal benefit of antibiogram use. As highlighted in this review, antibiograms are rarely used as standalone AMS interventions.

CONCLUSIONS

Studies which used antibiograms as an integral component of AMS interventions suggest improved antibiotic prescribing patterns, appropriateness, and costs. There was limited evidence for improvement of any other outcomes such as mortality, hospitalization, resistance patterns, or infection-related outcomes such as *C difficile* rates. Further studies with rigorous design are recommended to evaluate the effectiveness of antibiograms in other less studied health care settings such as aged care where antibiotic use remains high.

AUTHOR CONTRIBUTIONS

D.K. conducted the Systematic Review, designed the paper, analyzed the data, and wrote the review. **N.F., S.C., and C.F.** assisted in conducting and validating review. **N.F., S.C., C.F., L.G. and D.P.** revised the manuscript. All authors approved the final version.

APPENDIX A. SUPPORTING INFORMATION

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ajic.2023.08.013.

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