Supplementary Material

Rapid Diagnostic Test Value and Implementation in Antimicrobial Stewardship Across Low-to-Middle and High-Income Countries: A Mixed-Methods Review

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Grading the quality of the evidence in the literature review

Methods

The quality of the evidence for key outcomes reported in the targeted literature review was considered using criteria based on Grading of Recommendations, Assessment, Development, and Evaluations methodology. To establish the initial level of confidence, evidence from randomised controlled trials started at high quality, and evidence from observational studies at low quality.

The confidence in the evidence was downgraded if:

(1) The patients studied were different from those in the research question

(2) Confounding factors were unaccounted for

(3) The interventions studied were different to the real intervention

(4) Evidence was missing.

The confidence in the evidence would have been upgraded if:

(1) The evidence had had a very large magnitude of effect

(2) Sample sizes had been powered.

An overall quality rating was applied by outcome, or body of outcomes where appropriate, by taking the most common quality of evidence.

Table S1 Targeted literature review search string

Search no.	Search string
PubMed	
1	antimicrobial stewardship[MeSH Terms]
2	(("Antimicrobial stewardship") OR ("antimicrobial program*") OR (stewardship) OR (program*))
3	“immunisation program*” OR “immunization program*”
4	#1 OR #2 NOT #3
5	("Rapid diagnostic test") OR ("rapid diagnostic") OR ("rapid test") OR (“rapid antigen”) OR (“rapid assay”) OR (“RDT”)
6	point-of-care testing[MeSH Terms]
7	#6 OR #5
8	#7 AND #4

Table S2 Targeted literature review PICOS inclusion and exclusion criteria

	Inclusion criteria	**Exclusion criteria**
Population	Any hospital/long-term care facility patients with any infection	Non-humans
Intervention	Any 'rapid' diagnostic test used within any ASP/AMS initiative	No report of ASP
Comparator	No use or suboptimal use of RDT	
Outcome	Clinical and economic value of RDTs	
Study type	Randomised controlled trials, clinical trials Therapy recommendations, eg. treatment guidelines, best practice articles, consensus recommendations Reviews Observational studies including real world Cross-sectional studies Surveys Delphi panels Economic models e.g., cost-effectiveness, budget impact models	Secondary reports such as editorials, comments and letters Case reports (i.e., single patient) Case studies Case series Technical validation studies of RDTs where no implementation is described

AMS antimicrobial stewardship, *ASP* antimicrobial stewardship programme, *PICOS* population, intervention, comparator, outcome, and study type, *RDT* rapid diagnostic test

Table S3 Hospital RDT implementation checklist

Implementation stage	***Action required***	***ASP team***	***Microbiology laboratory personnel***	***Infectious disease clinicians and pharmacists***	***Other department clinicians and pharmacists***
Pre-implementation	Ensure AMR and RDT awareness amongst hospital providers	X			
	Ensure competence of microbiology laboratory personnel	X	X		
	Consider the prevalent or problematic organism(s) in the hospital	X	X	X	
	Evaluate the sensitivity and specificity of candidate RDT(s)	X	X		
	Evaluate the cost of the RDT(s)	X	X		
	Consider environmental and ethical aspects of candidate RDT(s)	X	X		
	Identify funding sources for the required RDT	X	X		
	Identify individuals in the local-unit and hospital level involved in decision-making to adopt the RDT	X			
	Build business case for the	X	X		

	implementation of the required RDT					
Implementation	Ensure relevant support programmes are in place	X				
	Adjust or design local protocols and algorithms that incorporate RDT use	X	X	X		
	Conduct thought experiments to identify potential barriers or bottlenecks	X	X			
	Set realistic expectations for RDT turnaround times	X	X			
	Identify location for use of RDT (e.g., point of care vs. laboratory)	X	X			
	Ensure smooth transport and storage of the RDT		X			
	Identify who will conduct the test	X	X			
	Assess distance from the diagnosticians	X		X		X
	Prevent reproducibility and contamination issues with specimen		X			
	Ensure efficient sample transport and anticipate logistical issues		X			
	Establish expected communication channels and	X		X		

	determine results reporting process				
	Communicate RDT use to patients			X	X
Post-implementation	Document clinical and economic outcomes associated with RDT	X		X	X
	Define metrics of success and monitor KPIs at the institutional level	X			
	Maintain availability of RDT		X		
	Plan for supply chain failure (e.g., reagents, repairs)		X		
	Ongoing communication of RDT availability	X	X	X	
	Conduct quality improvement studies or audits	X	X		

AMR antimicrobial resistance, *ASP* antimicrobial stewardship programme, *KPI* key performance indicator, *RDT* rapid diagnostic test

Table S4 Quality of evidence: Mortality

Study	Confidence	Quality of evidence	Reason for downgrade/upgrade
Eby et al. 2018 [1]	Low	Low	-
Huang et al. 2013 [2]	Low	Low[a]	-
Mahrous et al. 2020 [3]	Low	Low[a]	-
Nagel et al. 2014 [4]	Low	Very low	No attempt to adjust for potential differences between cohorts, and no mention of sample size
Patel et al. 2017 [5]	Low	Very low[a]	Noted differences in characteristics between groups which may have influenced mortality
Walker et al. 2016 [6]	Low	Low[a]	-
Banerjee et al. 2021 [7]	High	Moderate	Insufficiently powered, and noted differences in baseline characteristics
Banerjee et al. 2015 [8]	High	High	-
Hogan et al. 2020 [9]	Low	Very low	Not statistically powered for mortality
Murri et al. 2018 [10]	Low	Very low[a]	Study group 1 was slightly underpowered and had no adjustment for potentially confounding factors, which can be seen in the baseline characteristics
Robinson et al. 2021 [11]	Low	Low	-

Evidence overall rated: Low

[a]Data showed statistical significance.

Table S5 Quality of evidence: Improved AMS metrics

Study	Confidence	Quality of evidence	Reason for downgrade/upgrade
Huang et al. 2013 [2]	Low	Low[a]	-
Nagel et al. 2014 [4]	Low	Very low[a]	No attempt to adjust for potential differences between cohorts, and no mention of sample size
Ehren et al. 2020 [12]	Low	Low[a]	-
Gawrys et al. 2020 [13]	Low	Low[a]	-
Perez et al. 2014 [14]	Low	Low	-
Kim et al. 2022 [15]	High	Moderate[a]	Subgroups may not be adequately powered, and there was no adjustment for multiple comparisons
Kunz Coyne et al. 2021 [16]	Low	Very low[a]	Differences between groups
Messacar et al. 2017 [17]	Low	Low[a]	
Perez et al. 2013 [18]	Low	Low	
Porter et al. 2019 [19]	Low	Low[a]	
Neuner et al. 2016 [20]	Low	Very low	Potential confounding, and imbalances in baseline characteristics
Rivard et al. 2017 [21]	Low	Low[a]	
Bookstaver et al. 2017 [22]	Low	Low[a]	
Bannerjee et al. 2015 [7]	High	High	
Hogan et al. 2020 [9]	Low	Low	

Evidence overall rated: Low

[a]Data showed statistical significance.

Table S6 Quality of evidence: Decreased length of stay

Study	Confidence	Quality of evidence	Reason for downgrade/upgrade
Huang et al. 2013 [2]	Low	Low[a]	-
Mahrous et al. 2020 [3]	Low	Low[a]	-
Pliakos et al. 2018 [23]	Unsuitable study design for assessment	Unsuitable study design for assessment	-
Murri et al. 2018 [10]	Low	Very low[a]	Study group 1 slightly underpowered and there was no adjustment for potentially confounding factors, which can be seen in the baseline characteristics
Perez et al. 2014 [14]	Low	Low[a]	-
Kunz Coyne et al. 2021 [16]	Low	Very low[a]	Differences between groups
Perez et al. 2013 [18]	Low	Low	
Rivard et al. 2017 [21]	Low	Low[a]	
O'Donnell et al. 2022 [24]	Moderate	Moderate[a]	
Walsh et al. 2021 [25]	Low	Low[a]	
Gray et al. 2018 [26]	Low	Very low[a]	Significant differences in clinical characteristics between study groups
Pardo et al. 2016 [27]	Low	Low[a]	
Cavalieri et al. 2019 [28]	Low	Low[a]	
Batwala et al. 2011 [29]	Moderate	Moderate	

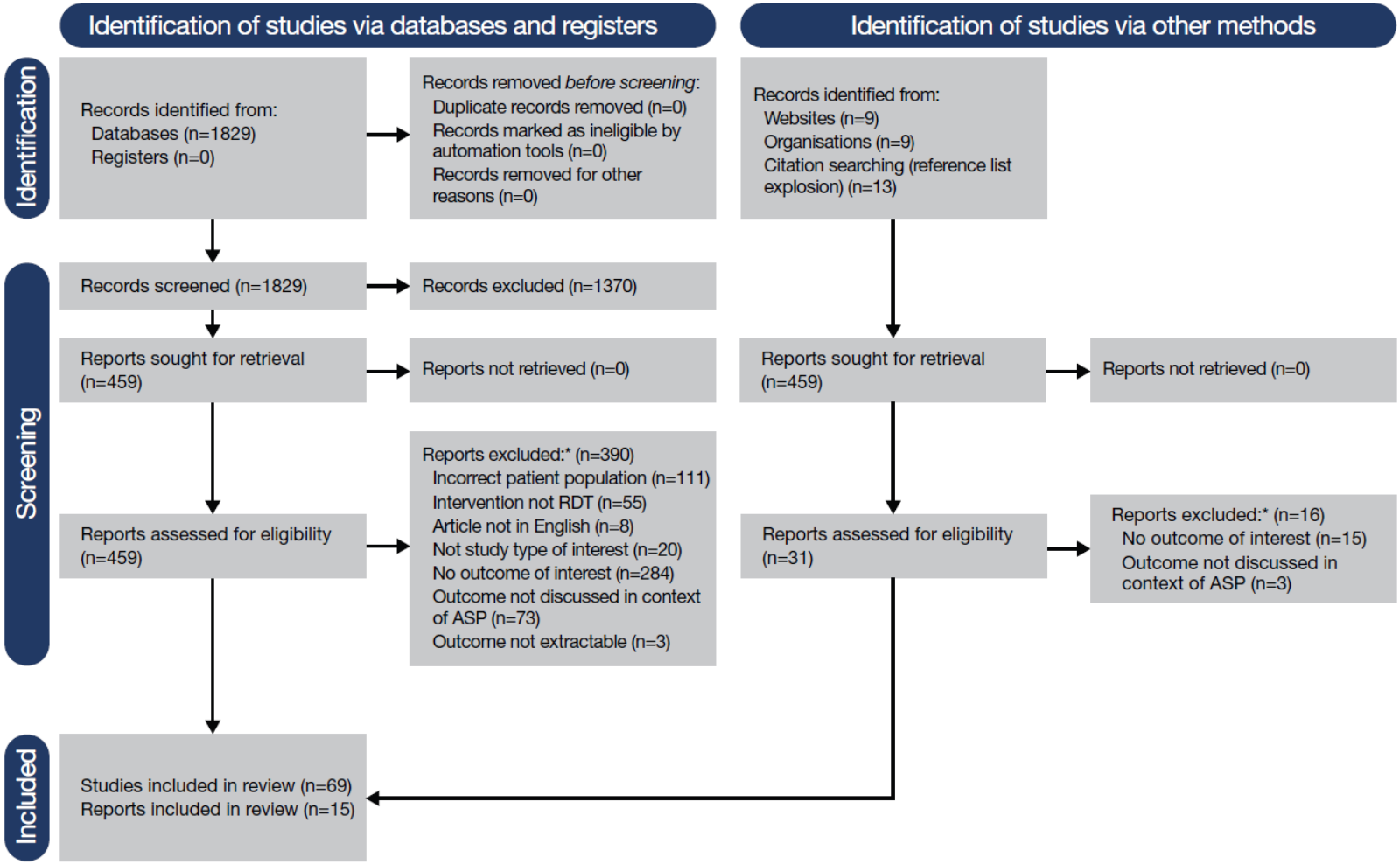
Evidence overall rated: Low

[a]Data showed statistical significance.

Table S7 Quality of evidence: cost-effectiveness

Study	Confidence	Quality of evidence	Reason for downgrade/upgrade
Pliakos et al. 2018 [23]	Unsuitable study design for assessment	Unsuitable study design for assessment	-
Patel et al. 2017 [5]	Low	Low	-
Perez et al. 2014 [14]	Low	Low	-
Perez et al. 2013 [18]	Low	Low	-
Batwala et al. 2011 [29]	Moderate	Moderate	-
Sango et al. 2013 [30]	Low	Low	-
Lockwood et al. 2016 [31]	Low	Low	-
MacVane et al. 2016a [32]	Low	Low	-
Box et al. 2015 [33]	Low	Low	-
MacVane et al. 2016b [34]	Low	Low	-
Evidence overall rated: Low			

Fig. S1 Targeted literature review PRISMA flow diagram

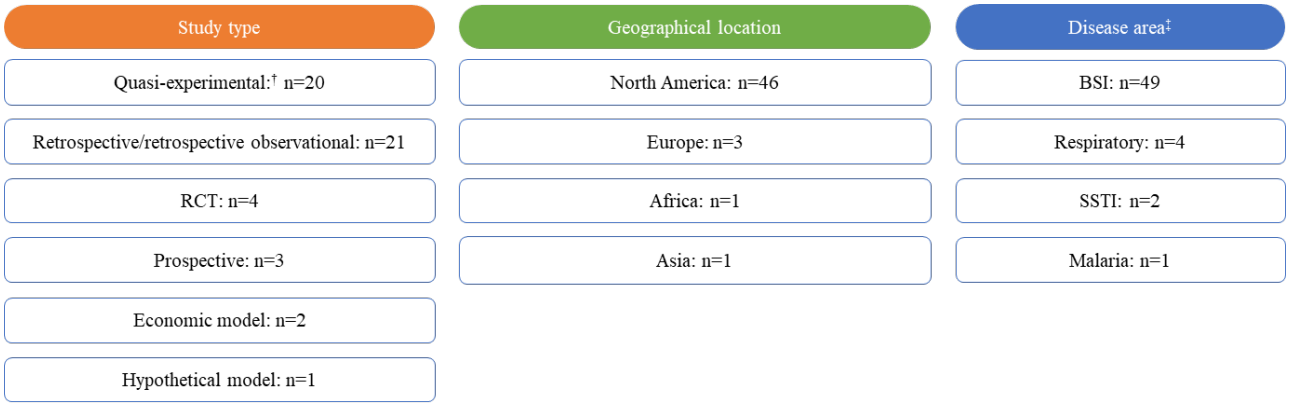


ASP antimicrobial stewardship programme, *RDT* rapid diagnostic test

*May have been excluded for more than one reason.

Adapted from: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Fig. S2 Study characteristics and inclusion criteria of primary research literature included in the targeted literature review



AMS antimicrobial stewardship, *BSI* bloodstream infection, *RCT* randomised controlled trial, *RDT* rapid diagnostic test, *SSTI* skin and soft tissue infection

†Included a pre-intervention period and a post-intervention period

‡Papers may report on more than one disease

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