Impact of Pharmacist-Led Antimicrobial Stewardship on Appropriate Antibiotic Prescribing in the Emergency Department: A Systematic Review and Meta-Analysis

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Study objective: The aim of this study was to evaluate the impact of pharmacist presence or pharmacist-led antimicrobial stewardship interventions on appropriate prescribing of antibiotics in the emergency department (ED).

Methods: Systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines were conducted. Studies describing the role of pharmacists and their association with antimicrobial stewardship in the ED were included. The comparator for pharmacist intervention was hours without a pharmacist present, preprotocol implementation, and nonpharmacist culture follow-up.

Results: In total, 24 studies (9,984 patients) were included in the qualitative synthesis, and 22 studies (5,791 patients) had data for the primary outcome and were included for the quantitative assessment (meta-analysis). Appropriate prescribing of antibiotics was more likely with pharmacist intervention (22 studies; odds ratio [OR], 3.47; 95% confidence interval [CI] 2.39 to 5.03), particularly among patients with pneumonia (5 studies; OR, 3.74; 95% CI 2.14 to 6.54) or urinary tract infection (4 studies; OR, 1.76; 95% CI 1.24 to 2.50). Time to culture review was similar with or without pharmacist intervention. Time to appropriate antibiotic was shorter with pharmacist intervention (mean difference, 18.9 hours; 95% CI 11.9 to 25.9; $P<.001$). Repeat ED visit for the same complaint was not significant (10 studies; OR, 0.65; 95% CI 0.39 to 1.10).

Conclusion: Pharmacist presence and pharmacist-led antimicrobial stewardship interventions appear to be effective for the appropriate prescribing of antibiotics in adult patients presenting to EDs with a variety of infectious syndromes. [Ann Emerg Med. 2022;79:374-387.]

Please see page 375 for the Editor's Capsule Summary of this article.

A **podcast** for this article is available at www.annemergmed.com.

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INTRODUCTION

Background

Up to 80% to 90% of all antibiotics administered to human beings are prescribed in an outpatient setting; approximately 30% of these antibiotics are inappropriate.[1,2] The emergency department (ED) is a major source of prescribing medications, with antibiotics being the second most common type of medication prescribed in 16% of all ED visits.[1,3,4] A 2017 systematic review of antimicrobial stewardship in the ED reported a benefit of patient and clinician education and guidelines or pathway implementation on improved delivery of care and decrease in antibiotic use. However, specific assessment of pharmacist involvement was not conducted.[5]

Antimicrobial stewardship programs that include pharmacists have demonstrated improvement in patient prescribing; however, a large-scale assessment of their role in the ED is lacking.[6-8] Clinical pharmacy practice in the ED has been demonstrated to improve patient outcomes in a variety of areas; however, the specific impact of pharmacists on ED stewardship is unknown.[9]

Goals of This Investigation

The primary objective of this systematic review and meta-analysis was to determine the impact of pharmacist presence or pharmacist-led antimicrobial stewardship interventions on appropriate prescribing of antibiotics in the ED. Secondary objectives included determining the

Editor's Capsule Summary

What is already known on this topic

Antibiotics are commonly prescribed to emergency department patients. Increasingly, EDs are becoming staffed with pharmacists who may be an important resource to improve antibiotic stewardship.

What question this study addressed

A systematic review and meta-analysis were conducted to evaluate the impact of pharmacist-led antimicrobial stewardship interventions on appropriate prescribing of antibiotics in the ED.

What this study adds to our knowledge

Analysis of 22 studies involving 5,791 patients found pharmacist intervention to be associated with a higher rate of appropriate antibiotic prescribing, particularly for patients with pneumonia. Studies were retrospective, observational, with a before-and-after design, and had a moderate risk of bias; there were no randomized trials.

How this is relevant to clinical practice

Pharmacist antimicrobial stewardship interventions appear to be effective. Randomized trials are needed.

impact of these interventions on time to culture review, time to appropriate antibiotics, and ED return rates.

MATERIALS AND METHODS

Study Design

The current study was a systematic review and meta-analysis. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology.[10]

Protocol and Registration

A protocol was written prior to the initiation of this review. This protocol was not registered in public databases. Primary and secondary outcomes and analyses were defined a priori.

Eligibility Criteria

Studies describing the role of pharmacists and their association with antimicrobial stewardship in the ED were included. Studies in which the intervention was entirely outside the ED setting or not focused on antibiotic stewardship were not included. Our population, intervention, comparison, and outcome elements were as follows:

1. Population: adult patients seen in ED settings requiring antibiotics.
2. Intervention: pharmacist-led stewardship interventions or pharmacist presence.
3. Comparison: standard of care prior to pharmacist intervention, hours when pharmacists were not present, or direct comparison of stewardship alternative intervention.
4. Outcome: primary—appropriate antibiotic selection; secondary—time to appropriate antibiotics and repeat visits to ED for the same complaint.

Pharmacist presence was defined as time with a pharmacist physically present in the ED. Aiding clinicians in antibiotic selection is a standard expectation of clinical pharmacists in nearly all settings, particularly the ED environment.

Search and Information Sources

A comprehensive search of several databases from 2000 to January 12, 2021, excluding animal studies, was conducted. The databases included Ovid MEDLINE and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, Ovid Embase, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, CINAHL (EBSCOhost), Web of Science, and Scopus.

The search strategy was designed and conducted by an experienced librarian with inputs from the study's principal investigator (K.K.). Controlled vocabulary supplemented with key words was used to search for studies related to pharmacists and antimicrobial stewardship in the ED setting. Terms included broad assessment of antibacterial and anti-infective terminology, emergency services in the hospital, and pharmacists. The search strategy is available in Appendix E1 (available at http://www.annemergmed.com/).

Study Selection

Two investigators (KK and EC) independently reviewed each title and abstract from the literature search to select potential articles. Abstracts were considered for full text review if they fulfilled all of the following criteria: population of the study included adults with infection in the ED setting, pharmacists were mentioned in the abstract or were authors, and there appeared to be a comparison group for the primary outcome.

All designs, including prospective, retrospective, observational, cross-sectional, cohort, case-control, and case series, were considered for inclusion. All methods of

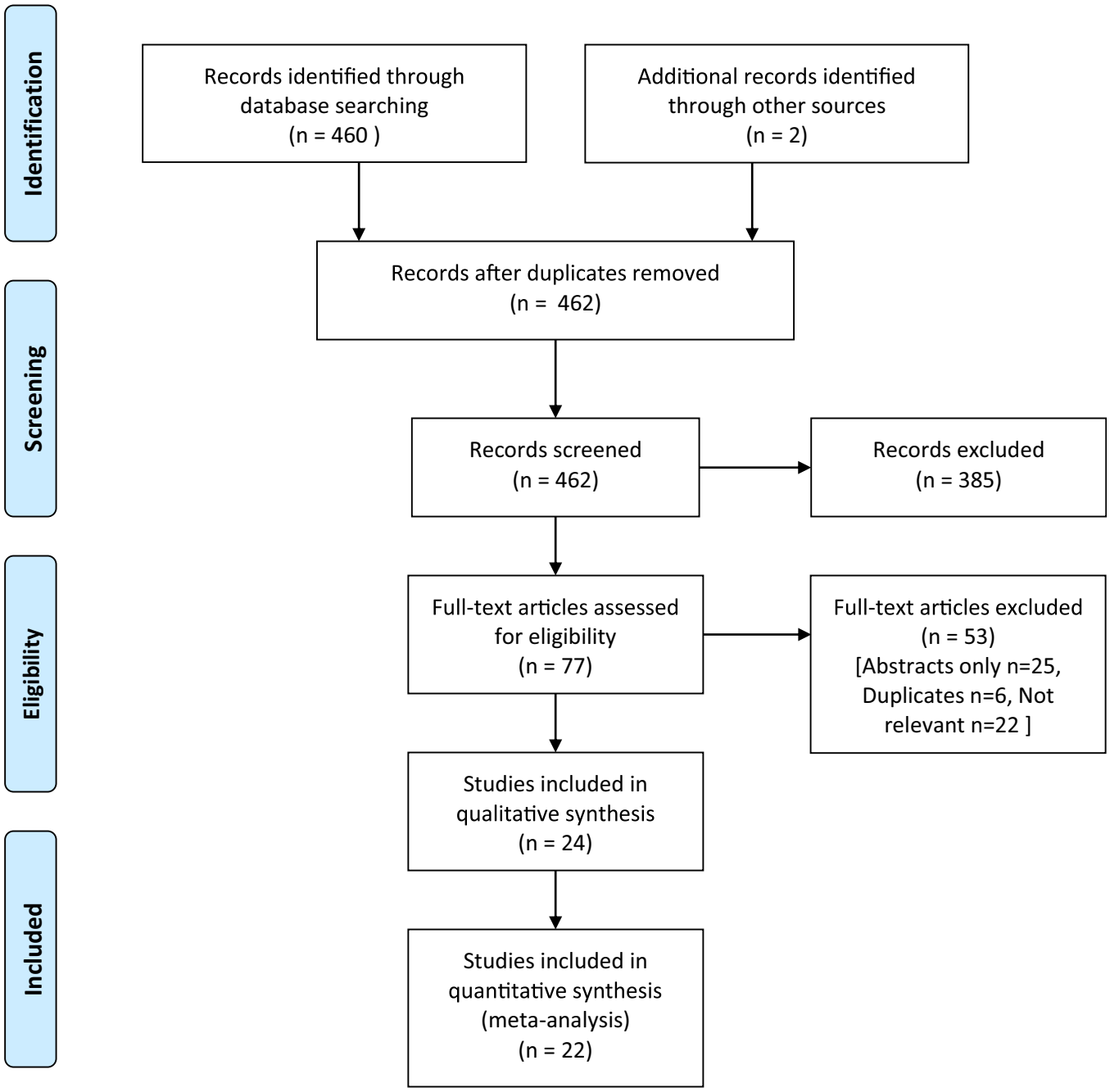

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

stewardship intervention were considered for inclusion. In full text assessment, we excluded abstract-only studies, duplicate studies, studies using the same patient population during the same time period of an already included study, single case reports, and studies that focused on pediatric population. We also excluded studies that may have had pharmacist authorship but did not report on a pharmacist-led stewardship intervention or practice. Articles that discussed stewardship in multiple settings were included if they separately reported patients and outcomes in the ED. The full text and references of each article were screened to identify other potentially relevant articles.

Data Collection

All selected abstracts were pulled for full text review. All full texts were reviewed in duplicate. Agreement for the inclusion of full text was κ=0.88 (95% confidence interval [CI] 0.77 to 0.99). Disagreements were resolved by consensus. For the included studies, 2 authors (KK and EC) independently abstracted data based on a prespecified

Table 1. Study data.

Author, Year Published	Study Design	Infection Type	Number of Infection Types (n)	Definition of Appropriate	Intervention	Comparator Group
Almulhim,[13] 2019	Pre/post cohort	UTI		Culture susceptibility	Pharmacist culture follow-up	Nurse practitioner lead culture follow-up
Baker,[14] 2012	Retrospective cohort	All positive cultures	Blood: 130, UTI: 103, SSTI: 49, STI: 12, CAP: 19, other: 24	IDSA guidelines and culture susceptibility	Pharmacist culture follow-up	NPPA culture follow-up
Campbell,[15] 2020	Pre/post cohort	Patients with penicillin allergy—all infections	UTI: 136, pulmonary: 103, SSTI: 72, IAI: 37, sinus: 5, blood: 2, bone: 1, other/unknown: 24	IDSA guidelines	Pharmacist lead allergy assessment	Preimplementation
Davis,[16] 2016	Retrospective cohort	UTI and SSTI	UTI: 51, SSTI: 8, blood: 17	Organism covered by selection	Pharmacist culture follow-up	RN follow-up
DeFrates,[36] 2013	Retrospective cohort	HCAP		IDSA guidelines	Pharmacist presence in ED	Patients during hours without pharmacists, same timeframe
DeWitt,[17] 2016	Retrospective cohort	All infections	Sepsis: 66, pulmonary: 49, UTI: 8, SSTI: 48, IAI: 35, CNS: 3, osteo: 1	Institutional guidelines	Pharmacist presence in ED	Patients during hours without pharmacists, same timeframe
Dumkow,[18] 2018	Retrospective cohort	Streptococcal pharyngitis		IDSA guidelines	Pharmacist lead algorithm	Previous standard of care
Dumkow,[19] 2014	Pre/post cohort	UTI or bacteremia	UTI: 307, blood: 14	Institutional guidelines and culture susceptibility	Pharmacist culture follow-up	Previous standard of care
Ellena,[20] 2020	Retrospective cohort	UTI		IDSA guideline and local susceptibility	Pharmacist presence	Prestewardship program
Faine,[21] 2017	Retrospective cohort	Pneumonia		IDSA guidelines	Pharmacist presence in ED	Patients during hours without pharmacists, same timeframe
Giruzzi,[22] 2020	Retrospective cohort	Any positive culture	UTI: 550, SSTI: 187, blood: 35, other: 18	IDSA guidelines and culture susceptibility	Pharmacist lead algorithm	MD/RN assessment
Harvey,[23] 2018	Retrospective cohort	Open fractures		EAST guidelines	Pharmacist presence in ED	Patients during hours without pharmacists, same timeframe
Hunt,[24] 2016	Pre/post cohort	All infections	Respiratory: 56, UTI: 23, SSTI: 15, IAI: 6	IDSA guidelines, culture susceptibility, dosing	Pharmacist lead antibiotic algorithm	Preverification
Ibarra,[25] 2020	Retrospective cohort	Patients given vancomycin	Respiratory: 20, blood: 25, bone: 3, CNS: 13	IDSA and ASHP guideline dosing	Pharmacist lead education	Preintervention
James,[26] 2019	Pre/post cohort	UTI		IDSA guidelines	Pharmacist lead education and algorithm	Preintervention
Kulwicki,[27] 2019	Retrospective cohort	CAP and IAI	CAP: 160, IAI: 160	IDSA guidelines and local susceptibilities	Pharmacist presence in ED	Patients during hours without pharmacists, same timeframe
Miller,[28] 2014	Retrospective cohort	Any positive culture	UTI: 80 STI: 42, SSTI: 6, throat: 17, blood: 1, stool: 2	IDSA guidelines and local dosing recommendations	Pharmacist culture follow-up	RN culture review
Moussavi,[29] 2016	Retrospective cohort	Sepsis, severe sepsis, or septic shock	CAP:100 IAI: 36 UTI: 70, CNS: 4, SSTI: 14, blood: 11, other: 13	Syndrome recommendations from Sandford Guide	Pharmacist presence in ED	Patients during hours without pharmacists, same timeframe
Olson,[30] 2020	Retrospective cohort	UTI or STI	UTI: 188, STI: 95	NA	Pharmacist culture follow-up	RN culture review
Randolph,[31] 2011	Retrospective cohort	Any positive culture		NA	Pharmacist culture follow-up	MD culture review
Santiago,[32] 2016	Retrospective cohort	Given antibiotics in ED	UTI: 87, SSTI: 41	Intervention made when needed, independent assessment of 2 reviewers K 0.9314	Pharmacist culture follow-up	RN culture review
Shealy,[33] 2020	Pre/post cohort	UTI or STI	UTI: 82, STI: 39, blood: 6	National and local guidelines	Pharmacist culture follow-up	Clinical admin culture review
Stoll,[34] 2020	Pre/post cohort	CAP, UTI, or SSTI	UTI: 202, CAP: 122, SSTI: 154	IDSA guidelines and algorithm compliance	Pharmacist lead algorithm	Preimplementation
Zimmerman,[35] 2019	Pre/post cohort	CAP		IDSA guidelines and algorithm compliance	Pharmacist lead algorithm	Preimplementation

Table 1. Continued.

Pharmacist, No.	Appropriate Antibiotics, No. (%)	Comparator, No.	Appropriate Antibiotics, No. (%)	Time to Review, Days (Median, IQR) (Mean, SD)	Time to Patient Contact, Days (Median, IQR) (Mean, SD)	Time to Appropriate Antibiotic, Hours (Median, IQR) (Mean, SD)	Repeat ED Visit	Mortality
55	28 (50.9)	102	44 (43.1)	NA	NA	NA	NA	NA
61	61 (100)	69	66 (95.7)	Pharmacist: 2, 0-4 Comparator: 3, 1-15	Pharmacist: 2, 0-4 Comparator: 3, 1-9	NA	NA	NA
125	72 (57.6)	255	114 (44.7)	NA	NA	NA	NA	NA
30	24 (80)	42	21 (50)	NA	Pharmacist: (3.5, 1.2) Comparator: (3.4, 1.9)	NA	NA	NA
81	40 (49.4)	70	18 (25.7)	NA	NA	Pharmacist: (11.37, 17.9) Comparator: (15.56, 19.37)	NA	Pharmacist: 6 Comparator: 11
105	100 (95.2)	105	78 (74.3)	NA	NA	Pharmacist: (60, 58) Comparator: (60, 55)	NA	NA
108	88 (81.5)	100	9 (9)	NA	NA	NA	Pharmacist: 6 Comparator: 2	NA
197	143 (72.6)	124	78 (62.9)	NA	NA	NA	Pharmacist: 12 Comparator: 12	NA
51	42 (82.4)	57	34 (59.7)	NA	NA	NA	Pharmacist: 1 Comparator:3	NA
103	60 (58.3)	303	116 (38.3)	NA	NA	NA	NA	Pharmacist: 2 Comparator: 11
392	382 (97.5)	398	354 (88.9)	Pharmacist: 0.32, 0.076-1.12 Comparator: 9.83, 2.34-13.21	NA	Pharmacist: 47.8, 8.2-81.8 Comparator: 162.96, 26.2-225.1	Pharmacist: 36 Comparator: 43	NA
67	54 (80.6)	79	37 (46.8)	NA	NA	NA	NA	NA
64	59 (92.2)	64	42 (65.6)	NA	NA	Pharmacist: (8.1, 8.6) Comparator: (15.2, 22.8)	NA	NA
31	11 (35.5)	30	2 (6.7)	NA	NA	NA	NA	NA
134	103 (76.9)	134	81 (60.5)	NA	NA	NA	NA	NA
185	144 (77.8)	135	82 (60.7)	NA	NA	NA	NA	NA
75	64 (85.3)	73	39 (53.4)	NA	NA	NA	NA	NA
92	89 (96.7)	94	76 (80.9)	NA	NA	Pharmacist: 0.64, 0.35-0.98 Comparator: 1, 0.6-1.7		Pharmacist: 19 Comparator: 23
139	NA	144	NA	NA	Pharmacist: 0.38, 0.1-0.91 Comparator: 1.1, 0.9-2.1	NA	Pharmacist: 1 Comparator: 9	NA
2361	NA	2278	NA	NA	NA	NA	Pharmacist: 165 Comparator: 432	NA
25	24 (96)	30	16 (53.3)	Pharmacist: 3, 1-6.3 Comparator: 2, 0.3-5.5	NA	Pharmacist: 6.6, 3.5-8.1 Comparator:8.1, 4.1-9.1	Pharmacist: 9 Comparator: 10	NA
63	33 (52.4)	64	49 (76.6)	NA	NA	NA	Pharmacist: 0 Comparator: 5	NA
353	308 (87.3)	325	148 (45.5)	NA	NA	NA	Pharmacist: 54 Comparator: 71	NA
330	175 (53)	411	99 (24.1)	NA	NA	NA	Pharmacist: 36 Comparator: 30	NA

ASHP, American Society of Health-System Pharmacists; *CAP,* Community-acquired pneumonia; *CNS,* central nervous system; *EAST,* Eastern Association for the surgery of Trauma; *HCAP,* health care–associated pneumonia; *IAI,* intra-abdominal infection; *IDSA,* Infectious Disease Society of America; *IQR,* interquartile range; *MD*, medical doctor; *NA*, not applicable; *NPPA*, nurse practitioner and physician's assistant; *RN*, registered nurse; *SSTI,* skin and soft tissue infection; *STI,* sexually transmitted infection; *UTI,* urinary tract infection.

data collection form. This included the author, year, trial design, comparator group, stewardship intervention, population, primary outcome, secondary outcomes, and study details. We also retrieved data on appropriate versus inappropriate antibiotic use as defined by each study, time to intervention or appropriate antibiotic selection, and patient return to ED for the same complaint. The definition of appropriate or inappropriate antibiotic selection was determined within each study that reported this outcome, as appropriate for the infection type under consideration. In some studies, the consideration for appropriateness included stopping or not prescribing antibiotics, for example, in pharyngitis with negative streptococcal test or stopping antibiotics if the urine culture was negative.

Risk of Bias of Individual Studies

Risk of bias was assessed in duplicate for each study using the National Institutes of Health study quality assessment tools for the appropriate study design type, which rates designs as poor, fair, or good, and the Newcastle-Ottawa scale for observational studies, which rates risk as high, moderate, or low.[11,12] Disagreements were resolved by the third investigator (FB). Publication bias was assessed with funnel plot inspection.

Risk of Bias Across Studies

The certainty in the evidence available for each outcome was evaluated in duplicate using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methods. The GRADE approach involves the consideration of 5 domains that may decrease the certainty in the evidence (risk of bias, inconsistency, indirectness, imprecision, and publication bias) and 3 domains that may increase the certainty (large effect, dose response, and plausible confounding).

Summary Measures

The summary effect of pharmacist involvement in ED stewardship efforts on appropriate versus inappropriate antibiotic selection was determined using a random effects model with Mantel-Haenszel analysis. Odds ratios (ORs) and 95% CIs were calculated and displayed with forest plots. Subgroup analyses were planned a priori and were based on the intervention type (pharmacist presence in ED, pharmacist-led culture review, or pharmacist-directed algorithm and educational interventions) and infection type (pneumonia, urinary tract infection, and skin and soft tissue infection). Secondary endpoint assessments were determined using a random effects model with Mantel-Haenszel analysis. Heterogeneity was assessed with the I^2 statistic. We chose to use random effects models due to the significant variability that we expected to observe in the study populations. We collected medians (interquartile ranges) and means (SDs) as reported in each manuscript; for the meta-analysis, the variables were converted to mean, following the Cochrane manual methods. Statistical analyses were performed using RevMan Review Manager (version 5.4; The Nordic Cochrane Centre, The Cochrane Collaboration).

RESULTS

Study Selection

The initial literature search found 460 titles and abstracts of potential relevance. After screening and full text review, 24 studies were included, comprising 9,984 patients. Figure 1 depicts the PRISMA flow diagram. Appendix E2 (available at http://www.annemergmed.com/) depicts the funnel plot to assess for publication bias among the selected articles.

Study Characteristics

A total of 24 studies were included for qualitative assessment. These are summarized in Table 1.[13-35] Most studies were retrospective observational cohorts, including 7 before/after assessments. There were no randomized controlled trials. A total of 22 studies had data for the primary outcome and were included for the quantitative assessment (meta-analysis) comprising 5,062 patients. Interventions included pharmacist-led culture review in 7 studies, pharmacist presence in 7 studies, pharmacist-directed clinical algorithms and clinician education in 7 studies, and prospective antibiotic review in 1 study. All types of infections were included in 10 studies, pneumonia in 5 studies, urinary tract infection in 8 studies, sexually transmitted infection in 2 studies, skin and soft tissue infection in 2 studies, and streptococcal pharyngitis in 1 study. One study included only patients in sepsis or septic shock. The majority of studies with multiple infection types did not distinguish outcomes based on infection type.

The comparator for the pharmacist intervention was hours without a pharmacist present in 6 studies, preprotocol implementation in 9 studies, and nurse/advanced practice clinician/physician culture follow-up in 9 studies.

Risk of Bias

On the National Institutes of Health study quality assessment, 1 study was scored as poor quality, 18 as fair

quality, and 5 as good quality.[11] The majority of studies did not assess confounding variables for the primary outcome, which lowered the overall quality of the studies. The Newcastle-Ottawa risk of bias assessment was overall rated as low risk of bias in 3 studies, moderate in 18 studies, and high in 3 studies.[12] Summary of the quality of individual studies is displayed in Table 2.

Table 2. Risk of bias.

Study Author	NIH Quality Grade	Newcastle-Ottawa Risk of Bias[12]
Almulhim[13]	Fair	Moderate
Baker[14]	Fair	Moderate
Campbell[15]	Fair	High
Davis[16]	Poor	High
DeFrates[36]	Fair	Moderate
DeWitt[17]	Good	Low
Dumkow[18]	Fair	Moderate
Dumkow[19]	Good	Moderate
Ellena[20]	Good	Moderate
Faine[21]	Good	Low
Giruzzi[22]	Fair	Moderate
Harvey[23]	Fair	Moderate
Hunt[24]	Fair	Moderate
Ibarra[25]	Fair	Moderate
James[26]	Fair	Moderate
Kulwicki[27]	Fair	Low
Miller[28]	Fair	Moderate
Moussavi[29]	Fair	Moderate
Olson[30]	Fair	Moderate
Randolph[31]	Fair	High
Santiago[32]	Fair	Moderate
Shealy[33]	Fair	Moderate
Stoll[34]	Fair	Moderate
Zimmerman[35]	Good	Moderate

NIH, National Institutes of Health.

Synthesis of Results

Meta-analysis of the 22 studies with an assessment of appropriate versus inappropriate antibiotics resulted in a pooled OR of 3.47 (95% CI 2.39 to 5.03) for appropriate antibiotic chosen during pharmacist intervention (Figure 2). In the studies that provided infectious syndrome–specific results, appropriate antibiotic selection was more likely with pharmacist present in the ED in patients with pneumonia (5 studies; OR, 3.74; 95% CI 2.14 to 6.54) or urinary tract infection (4 studies; OR, 1.76; 95% CI 1.24 to 2.50) (Figure 3). Skin and soft tissue and intra-abdominal infections lacked condition-specific data, and we were unable to conduct meta-analysis.

Subgroup analysis based on intervention type is displayed in Figure 4. Interventions included pharmacist presence in the ED for appropriate antibiotic selection (OR, 3.13; 95% CI 2.27 to 4.32), pharmacist-led culture review (OR, 2.22; 95% CI 0.98 to 5.04), and pharmacist-directed algorithm and educational interventions (OR, 5.23; 95% CI 2.68 to 10.23).

Secondary Endpoints

Time to culture review, time to patient contact, and time to appropriate antibiotic are displayed in Figure 5. Neither time to culture review nor patient contact appeared to differ between pharmacist intervention and comparator group. Time to appropriate antibiotic was shorter with pharmacist intervention (mean difference, 18.86 hours; 95% CI 11.87 to 25.85). Repeat ED visit for the same complaint was assessed in 10 studies with a pooled OR of 0.65 (95% CI 0.39 to 1.10) (Appendix E3 [available at http://www.annemergmed.com/]).

GRADE

The certainty on the estimates of each outcome was evaluated with GRADE (Table 3). The GRADE assessment resulted in very low to moderate range of estimates, depending on the outcome. For the main outcome of overall assessment of pharmacist-led interventions, the benefit observed had low level of certainty secondary to high risk of bias, high inconsistency (as measured by the visual inspection of the forest plots and $I^2 \geq 75\%$), and risk of publication bias. There were no concerns for indirectness, as all included studies were in the ED setting. Among the interventions, pharmacist presence in the ED was the one with the best certainty and had a strong association of benefit.

LIMITATIONS

All studies included in this meta-analysis are retrospective cohort studies with most having a moderate risk of bias. The definitions of appropriate antibiotic varied across the study and disease types, although broadly they were defined with the use of local and national guidelines for infection type. A few studies included a multivariable regression to assess the primary outcome, and most studies had no adjusted estimates; however, adjustments were more likely among the studies that observed a statistically significant impact of pharmacist stewardship intervention. We had high statistical heterogeneity across the studies as measured by I^2, possibly due to the wide variety of infection and intervention types that we included. Also, pharmacist presence is difficult to blind as an intervention,

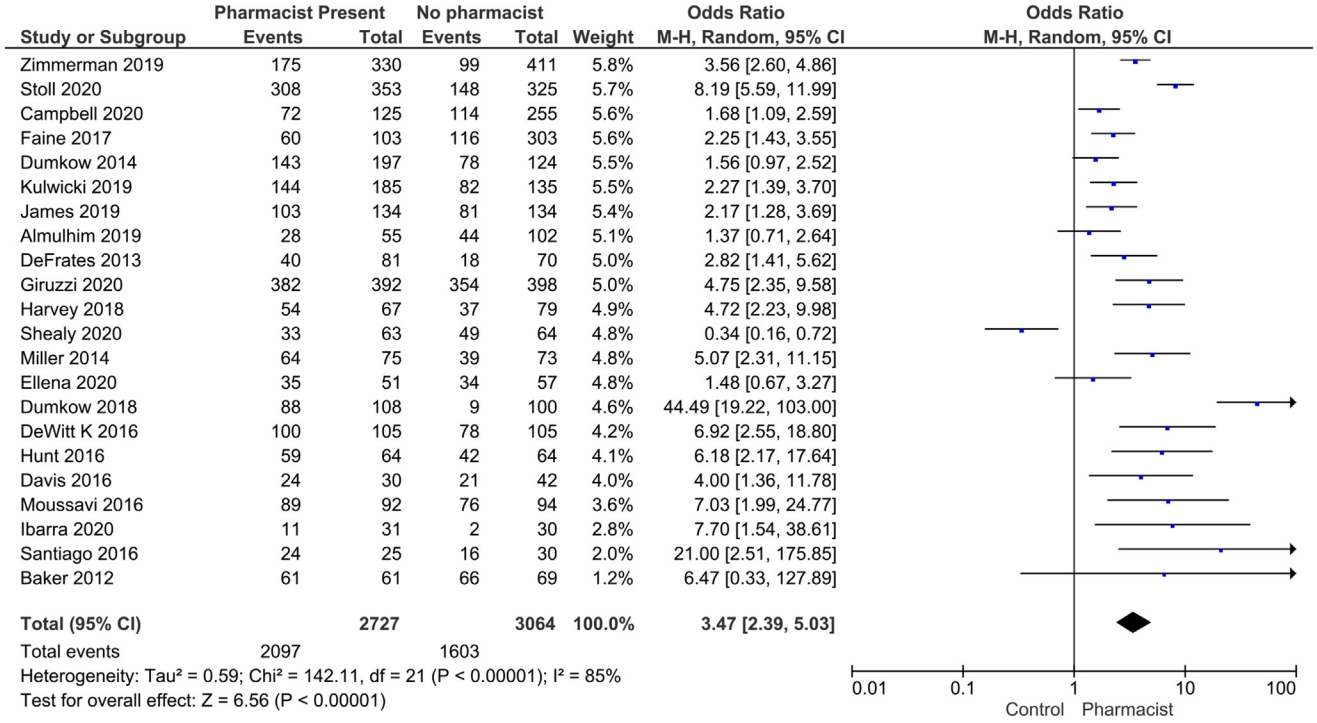

Figure 2. Meta-analysis of appropriate antibiotic selection with pharmacist intervention. *M-H*, Mantel-Haenszel.

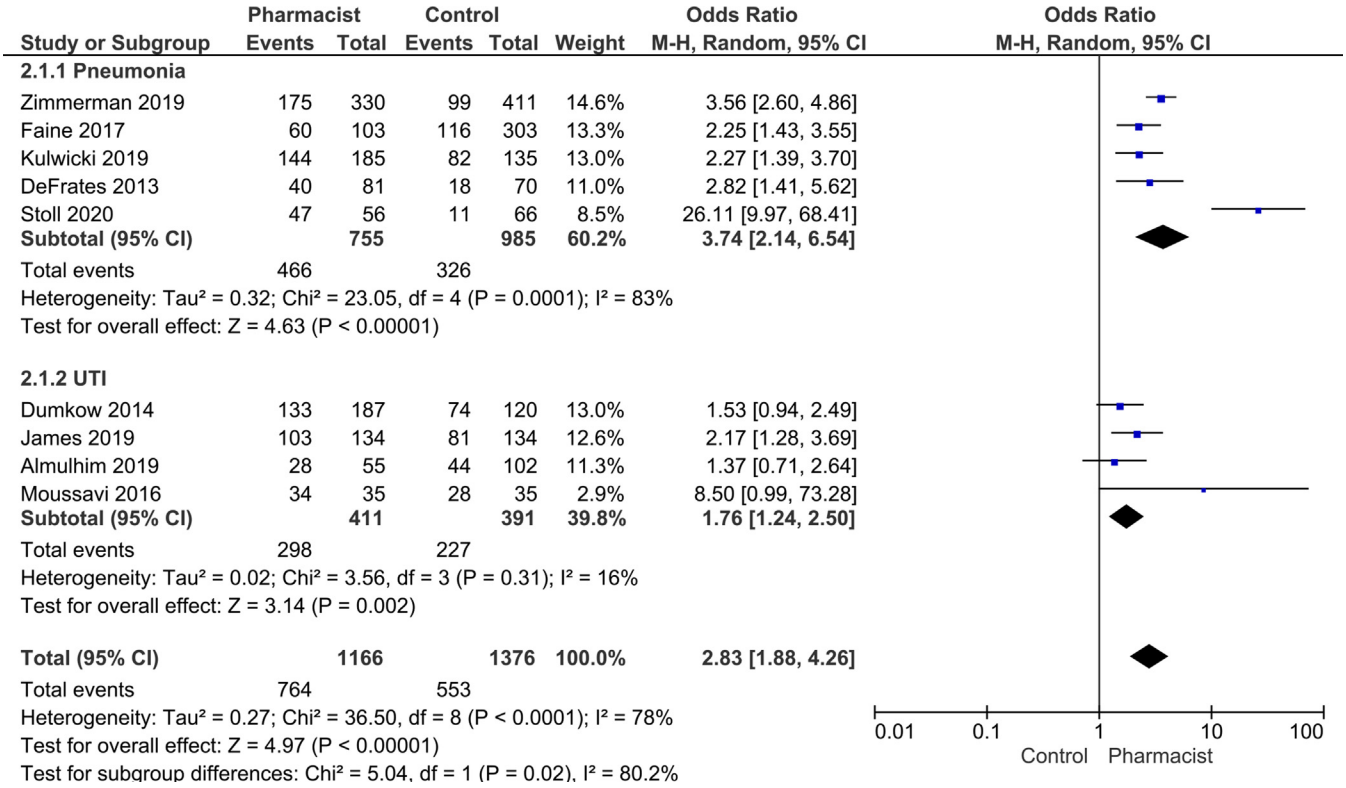

Figure 3. Meta-analysis of appropriate antibiotic with pharmacist intervention by infectious syndrome. *M-H*, Mantel-Haenszel.

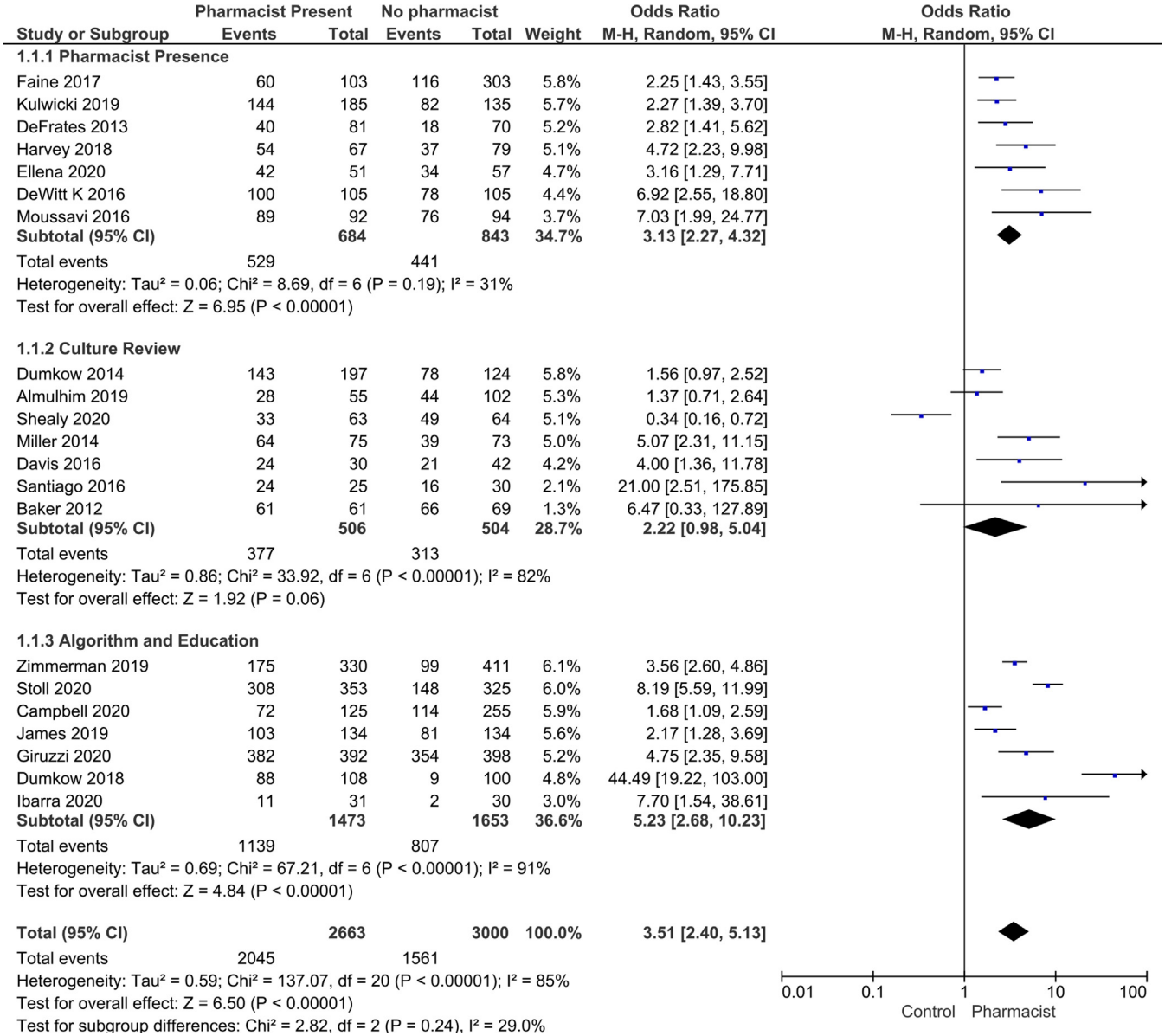

Figure 4. Meta-analysis of appropriate antibiotic selection by intervention type. *M-H*, Mantel-Haenszel.

thus this might account for clinical heterogeneity and potentially Hawthorne effect. Despite the heterogeneity, we decided that it was adequate to pool for a meta-analysis because the studies were in similar clinical settings (ED environment) and included interventions toward antibiotic stewardship.

DISCUSSION

We observed a positive impact of pharmacist-led interventions on stewardship and selection of appropriate antibiotics in adult patients presenting to EDs with a variety of infectious syndromes such as pneumonia and urinary tract infection. Interventions such as pharmacist presence in the ED and pharmacist-directed algorithm and educational interventions appear to be beneficial. Furthermore, pharmacist presence was associated with shorter time to appropriate antibiotic initiation.

We did not observe differences in time to culture review between pharmacists and other health care clinicians. The culture review process is centered on patients who are discharged home and does not involve the immediate care in the ED because cultures are not available at the time of empiric antibiotic administration. Antibiotic stewardship in the ED is complex, particularly when compared with other settings secondary to the variety of illness and atypical presentations. The range of stewardship activities in ED settings necessitates both an inpatient and outpatient focus.

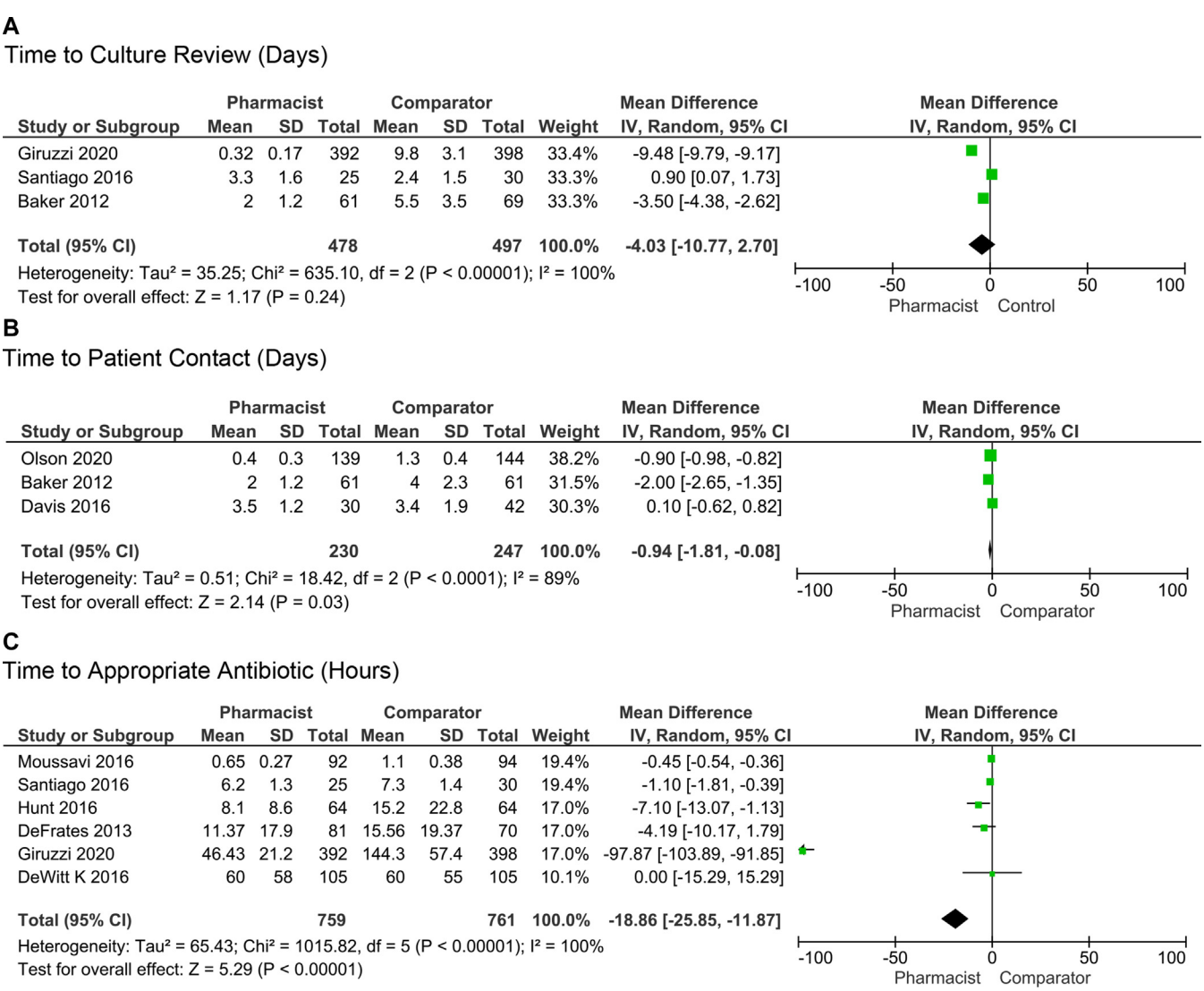

Figure 5. Time to culture review, patient contact, and appropriate antibiotics. A, Time to culture review (days). B, Time to patient contact (days). C, Time to appropriate antibiotic (hours). *IV*, inverse variance.

In this review, we included time to culture review and patient contact from patients discharged from the ED with antibiotic prescriptions. Owing to the nature of time required for bacteria to grow in culture, communication from the laboratory to the relevant ED personnel, and building in response time into the clinician workflow, we did not anticipate specific pharmacist-related benefit to this intervention. Having a dedicated person reviewing cultures makes the communication with the patient more reliable, and it is a step forward in antibiotic stewardship.

Greater interest has been taken in optimizing ED antimicrobial stewardship in recent years, as this environment is responsible for a significant proportion of inappropriate antibiotic prescription.[8,36-38] This issue carries across patient severity and admission or discharge status. Clinical pharmacy presence has been growing in ED settings around the world, and ED organizations formally recognized the important role that pharmacists play.[6,39] The Infectious Disease Society of America has acknowledged the role of emergency pharmacists in antimicrobial stewardship in the ED setting, and there is an upcoming confirmation of specialty status by the Board of Pharmaceutical Specialties.[6,9] Clinical pharmacy is present in a variety of settings, evidenced by a 2016 national survey in which 59.6% of respondents practiced in community settings and 36.1% practiced in academic medical centers.[40]

Although many small single-center studies exist that demonstrate a positive effect, to our knowledge, our study is the first to assess an overall comparison for antibiotic appropriateness. In 2017, Losier et al[5] conducted a

Table 3. GRADE assessment: pharmacist compared with usual care/no pharmacist for appropriate antibiotic selection in ED patients.

Certainty Assessment							No. of Patients		Effect		
No. of Studies	Study Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Pharmacist	Usual Care/No Pharmacist	Relative (95% CI)	Absolute (95% CI)	Certainty
Appropriate antibiotic selection (overall)											
22	Observational studies	Serious*	Serious†	Not serious	Not serious	Publication bias strongly suspected strong association all plausible residual confounding would reduce the demonstrated effect dose response gradient‡	2,097/2,727 (76.9%)	1,603/3,064 (52.3%)	OR 3.47 (2.39-5.03)	235 more per 1,000 (from 151 more to 296 more)	⊕⊕◯◯ Low
Pharmacist presence											
7	Observational studies	Serious *	Not serious	Not serious	Not serious	Publication bias strongly suspected strong association all plausible residual confounding would reduce the demonstrated effect dose response gradient‡	529/684 (77.3%)	441/843 (52.3%)	OR 3.13 (2.27-4.32)	251 more per 1,000 (from 190 more to 303 more)	⊕⊕⊕◯ Moderate
Culture review											
7	Observational studies	Serious *	Serious†	Not serious	Serious§	Publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect‡	377/515 (73.2%)	313/504 (62.1%)	OR 1.89 (0.88-4.06)	135 more per 1,000 (from 31 fewer to 248 more)	⊕◯◯◯ Very low
Algorithm and education											
7	Observational studies	Serious *	Serious†	Not serious	Not serious	Publication bias strongly suspected strong association all plausible residual confounding would reduce the demonstrated effect dose response gradient‡	878/1,175 (74.7%)	670/1,394 (48.1%)	OR 6.13 (2.85-13.18)	370 more per 1,000 (from 244 more to 444 more)	⊕⊕◯◯ Low
Pneumonia											
5	Observational studies	Serious *	Serious†	Not serious	Not serious	Publication bias strongly suspected strong association all plausible residual confounding would reduce the demonstrated effect‡	466/755 (61.7%)	326/985 (33.1%)	OR 3.74 (2.14-6.54)	318 more per 1,000 (from 183 more to 433 more)	⊕◯◯◯ Very low

Urinary tract infection												
4	Observational studies	Serious *	Serious†	Not serious	Not serious	Publication bias strongly suspected all plausible residual confounding would reduce the demonstrated effect‡	298/411 (72.5%)	227/391 (58.1%)	OR 1.76 (1.24-2.50)	128 more per 1,000 (from 51 more to 195 more)	⊕◯◯◯ Very low	

*Most studies had moderate or high risk of bias. Very few studies had adjustments for potential confounders.
†Through visual inspection of the forest plots and a predefined cutoff of $I^2 \geq 75\%$.
‡Publication bias: we suspected that studies with negative results will be less likely to be published.
§We evaluated the width of the CI. If the CI of the effect estimate crossed 1, we downgraded for imprecision.

systematic review of antimicrobial stewardship interventions in the ED and reported an association between antimicrobial stewardship intervention and improved patient care. The authors reported high risk of bias in the available literature.

We identified several mechanisms for pharmacists to be involved in stewardship efforts in the ED: pharmacist-led culture review and follow-up, pharmacist-driven creation of algorithms and implementation, and pharmacist presence in the ED. The majority of pharmacist presence in EDs in the United States is less than 24 hours of continuous coverage.[6] We demonstrated that, in these types of EDs, patients have improved antimicrobial selection in the time when a pharmacist is present compared with when there is no pharmacist. This potentially provides evidence for expansion of pharmacy clinical services and hours. Pharmacist practice involves direct interfacing with clinicians in the area, and we suspect that the shorter time to antibiotics is related to pharmacists aiding clinicians in antibiotic decisionmaking.

Despite the limitations and bias of the included studies secondary to study design, we demonstrated a positive impact of pharmacist stewardship on appropriate selection of antimicrobials. Epidemiologists have recommended against relying solely on study design or numeric quality scores when performing quality assessments and recommended to separate risk of bias from other constructs such as applicability and precision and evaluating the risk of bias per outcome.[41] Through the GRADE assessment, we estimated overall low quality of evidence, meaning that our certainty in the estimates is limited. This means that we must be cautious in the interpretation of the results, as the GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the quantity of specific interest, and future studies might find the interventions to be less helpful. Pharmacist presence in the ED was the intervention with best confidence in the estimates.

Future directions for research in this area should emphasize a randomized controlled approach to increase the quality of evidence as opposed to nonrandomized and before and after intervention studies. Additional mechanisms of stewardship that have been demonstrated to be successful for inpatient stewardship should be studied in the ED setting, for example, audit and feedback.

In conclusion, pharmacist presence and pharmacist-led antimicrobial stewardship interventions appear to be effective in appropriate prescribing of antibiotics in adult patients presenting to EDs with a variety of infectious syndromes. The majority of included studies had a moderate risk of bias.

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IMAGES IN EMERGENCY MEDICINE

(continued from p. 353)

DIAGNOSIS:

Type A aortic intramural hematoma occluding the right coronary artery. Following the return of spontaneous circulation, a computed tomography with angiography scan demonstrated decreased contrast enhancement of the right coronary artery caused by an aortic intramural hematoma (Figure 2). She underwent immediate surgical repair and was discharged neurologically intact 21 days later.

Intramural hematoma is a life-threatening aortic disease. Like the aortic dissection, an intramural hematoma can be divided into Stanford type A (involving the ascending aorta) and B (isolated involvement of the aortic arch or descending aorta). Type A intramural hematoma is typically complicated by hemopericardium or acute aortic regurgitation. However, approximately 3.3% wound involve coronary arteries, mimicking the presence of ST-segment elevation myocardial infarction, leading to unnecessary cardiac catheterization and heparinization.[1] Transesophageal echocardiography may be used to demonstrate this diagnosis during cardiac arrest and resuscitation.[2,3]

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