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Review
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Review

Impact of pharmacist-led services on antimicrobial stewardship programs: a meta-analysis on clinical outcomes

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Abstract

Purpose This meta-analysis aims to find out the impact of pharmacists on clinical outcomes of antimicrobial stewardship (AMS).

Method Articles were searched and analyzed based on quality assessed through the JSM quality assessment tool to filter articles with a low level of bias. Two thousand three hundred sixty articles were reviewed for initial screening and 28 articles were included for critical analysis. Statistical analysis used to risk ratio (RR) and standard mean differences calculated using Review manager 5.4. Confidence intervals (CI 95%) were calculated using the fixed-effect model. The I^2 statistic assessed heterogeneity. A random-effect model performed in the case of statistical heterogeneity, subgroup and sensitivity analyses. The primary outcome is mortality and inappropriateness, whereas the secondary outcome is cost, readmission, length of stay, consumption and duration of therapy.

Result A detailed review and analysis of 28 AMSs programs led by pharmacists showed low inappropriateness with pharmacist versus without pharmacist RR = 0.36 with 95% CI of (0.32 to 0.39) and mortality RR is 0.68 with 95% CI of 0.59 to 0.79. Secondary outcomes such as consumption, length of stay, duration of therapy and cost are standard mean difference of −1.61 with 95% CI (−1.72 to −1.50), −0.58 with 95% CI (−0.62 to −0.53), −0.95 with 95% CI (−1.01 to −0.89) and −0.99 with 95% CI (−1.12 to −0.86), respectively, whereas for 30 days readmission is RR = 0.81 with 95% CI (0.70 to 0.93).

Conclusion AMS with pharmacist effectively reduces mortality, inappropriateness, cost, length of stay, duration of treatment, consumption of antimicrobials and the return rate to hospital. So it is suggested pharmacists should lead or play a vital role in antimicrobial stewardship programs to get better outcomes.

Keywords: pharmacist; antimicrobial stewardship; appropriateness; mortality; antibiotics

Introduction

Antimicrobial stewardship programs (ASPs) around the globe help to reduce antimicrobial resistance (AMR). The complete definition of ASPs is as a set of coordinated interventions aimed at improving the appropriate use of antimicrobials in terms of regimen, dose, duration and route of administration, with the ultimate goal of limiting the damage resulting from antimicrobial overuse.[1, 2] The search term '(antimicrobial OR antibiotic) AND stewardship' first appeared on Pubmed in 1996, increasing year by year, such as 10 in 2005, over 50 per year in 2008 and over 100 per year in 2011.[3]

ASPs have various positive outcomes that attract the researchers and the whole medical team to develop and run the stewardship in their respective hospitals. Stewardship programs effectively reduce inappropriate antimicrobial use, improve patient outcomes and limit[4] the emergence of resistance. Higher burden of bacterial infection, health policy has traditionally emphasized resistance,[5] curtailing antibiotics and the spread of hospital-acquired difficile,[6] Clostridium and methicillin-resistant staphylococcus aureus.[7] In addition, it helps to reduce cost, length of stay, inappropriate prescribing, duration of treatment, antibiotic consumption, mortality and the return rate to the hospital.

The pharmacist plays a crucial role in healthcare setup and can be a game-changer in stewardship programs. Studies show that significant improvements were seen in guideline-concordant antibiotic selection 80.2%, dose 86.2% and duration of therapy 86.2% with the help of a pharmacist.[8] Another study concluded that an inexpensive program, in collaboration with infectious disease (ID) physician and pharmacist, may help in a more rational prescription of antimicrobial drugs, save cost and help to reduce the resistance.[9] Cost reduction with pharmacist-led antimicrobial stewardship (AMS) shows better results as average antibiotic costs per patient before and after stewardship decreased from $1265.81 to $592.08, a 53% savings.[10] This systemic review and meta-analysis aimed to evaluate the impact of pharmacists on clinical outcomes of AMS.

Methods

Our methodology adheres to the PRISMA guidelines (see PRISMA checklist: Appendix 1)

Data sources

AMSs were identified by searching: Pubmed, Embase and Elsevier. We included all stewardships, with English language restriction, published from 2012 to 2020. Keywords used were: 'antimicrobial stewardship,' 'antibacterial stewardship,' 'mortality,' 'appropriateness,' 'led by pharmacist,' 'pharmacist,' 'rational prescribing,' 'antifungal stewardship,' 'impact of pharmacist,' 'impact on cost,' 'outcomes of stewardship,' 'hospital readmission,' 'antibiotic consumption.' We restricted our search to primary literature, systematic reviews and meta-analyses and all other types of reviews were excluded. We manually searched the reference lists of systematic reviews were reviewed to identify potential studies.

The search strategy is illustrated in the search database and keywords supplementary file.

Study selection

We included primary literature on all types of ASPs (antibiotics, antifungal, antiviral) led by the pharmacist, whether retrospective, prospective or quasi-experimental studies included. Dichotomous results were extracted from the AMS program with pharmacists compared with the pre-antimicrobial stewardship (pre-AMS) program without pharmacist. The review articles, abstracts only without complete data, studies in language other than English, and stewardship programs other than antimicrobial were excluded.

Two investigators independently assessed eligibility (R.K.M. and M.J.A.). In case of discrepancy, a third observer adjudicated the eligibility (S.W.G. or S.M.G.). The extraction forms and the risk of bias assessments are attached as a supplementary file.

Quality assessment

Two authors (R.K.M. and M.J.A.) independently assessed trial quality. Internal validity was analyzed with the JSM quality assessment tool. Scale items numbered from 1 to 12. Quality parameters ranging from objectives to statistical analysis. Adding scores for each criterion together and divide by 12 will provide the *risk of bias rating (Low (75%–100%), Moderate (25%–75%) or High (0%–25%))*. These articles rated according to methodological quality: high, moderate or low.

Outcomes

Primary outcomes were 30 days mortality and inappropriate antimicrobial prescribing. Secondary outcomes were cost calculation, 30 days readmission (or return to the hospital within 30 days), duration of therapy in days, consumption of antimicrobials in defined daily dose (DDD) and length of stay in hospital in days.

Two reviewers (R.K.M. and M.J.A.) independently extracted the data for all the outcomes of interest.

Principal summary measures and statistical analyses by using Revman software version 5.4 (www.cc-ims.net/revman). The statistical analysis of the data was performed in RevMan software.

Evidence synthesis and analysis

We calculated risk ratios (RR) and standard mean differences with 95% confidence intervals (95% CI) for all studies using the fixed-effect model in the first approach. Heterogeneity was investigated with the I^2 statistic. It measures the proportion of overall variation attributable to between-study heterogeneity. I^2 values of 25%, >50% and >75 % refer, respectively, to a low, substantial and considerable degree of heterogeneity. In statistical heterogeneity, we tried to explain this with subgroup and sensitivity analyses than with funnel plot. Statistical significance was defined with an α threshold at 0.05.

Results and Findings

General characteristics

A total of 2360 articles were searched after removing duplication from Pubmed, two from Embase and Elsevier. Nine hundred one articles were excluded based on abstract and 1346 based on the title (Figure 1). One hundred ten were enrolled and studied thoroughly. Out of 110 23 included in the meta-analysis, 67 are excluded due to unavailability of complete data or outcome requirement and stewardship other than pharmacist with the physician. Twenty-three studies further reviewed and five included in the meta-analysis, so finally, 28 included (Table 1).[11–38]

Quality assessment

Quality assessment performed using JSM as a quality assessment tool for all of the studies run and included studies have a low or medium level of bias. Quality assessment details attached as supplementary

Table 1 Characteristics of studies included in this article.

#	Year & place	Title	Design	Variable	Conclusion
1	2012 USA	Pharmacist-managed antimicrobial stewardship program for patients discharged from the emergency department.	Retrospective	Inappropriateness	An emergency medicine clinical pharmacist-managed antimicrobial stewardship program significantly reduced time to the culture that affects the appropriate prescribing.
2	2012 USA	Antimicrobial stewardship pharmacist interventions for coagulase-negative *Staphylococci* positive blood cultures using rapid polymerase chain reaction.	Quasi-experimental	Cost, length of stay, duration of treatment	Timely blood culture affects the cost of treatment with the length of stay and duration of therapy.
3	2013 USA	Evaluating the impact of a pharmacist's absence from an antimicrobial stewardship team.	Retrospective	Inappropriateness	Inappropriate prescribing increases with the absence of a pharmacist.
4	2015 USA	Antimicrobial stewardship programs: comparison of a program with infectious diseases pharmacist support to a program with a geographic pharmacist staffing model.	Retrospective	Inappropriateness, length of stay	Pharmacist, through stewardship, responsible for better antibiotic prescribing measures and conversion from parenteral to oral therapy.
5	2015 Thailand	Design and analysis of a pharmacist-enhanced antimicrobial stewardship program in Thailand.	Prospective	Inappropriateness, length of stay mortality, duration of treatment	The study suggests better outcomes with Infectious disease Clinical Pharmacist training and incorporation of pharmacist in the stewardship.
6	2016 USA	Urine culture guided antibiotic interventions: a pharmacist driven antimicrobial stewardship effort in the emergency department.	Prospective	Consumption	Pharmacist intervention in discontinuing antibiotics for urine cultures reduced unnecessary antibiotic exposure, thus helped in the reduction of antimicrobial consumption.
7	2017 Canada	Transition from a dedicated to a non-dedicated, ward-based pharmacist antimicrobial stewardship program model in a non-academic hospital and its impact on length of stay of patients admitted with pneumonia: a prospective observational study.	Prospective	Length of stay, consumption	This study shows that an antimicrobial stewardship intervention reduced the length of stay in patients with Community Acquired Pneumonia by about 0.5 days regardless of the pharmacist model.
8	2017 Pakistan	Impact of pharmacist-led antibiotic stewardship program in a Pediatric Intensive Care unit of low/middle-income country.	Prospective	Cost, consumption, mortality, inappropriateness	The study shows the impact of pharmacist on cost, consumption, mortality and inappropriate antimicrobial prescribing.
9	2017 China	Pharmacist-driven antimicrobial stewardship in intensive care units in East China: a multicenter prospective cohort study.	Prospective	Mortality, length of stay, duration of therapy	Pharmacist-driven antimicrobial stewardship in an intensive care unit decreased patient mortality.
10	2018 Japan	Evaluation of treatment outcomes of patients with MRSA bacteremia following antimicrobial stewardship programs with pharmacist intervention.	Prospective	Length of stay, duration of therapy, mortality, inappropriateness	The use of an appropriate bundle, established by an Antibiotic Stewardship team with pharmacist intervention, can affect the treatment of Methicillin-resistant Staphylococcus aureus-B and impact other outcomes significantly.
11	2018 USA (OH)	A pharmacist-driven antimicrobial stewardship intervention targeting cytomegalovirus viremia in ambulatory solid organtransplant recipients.	Retrospective quasi-experimental	Duration of therapy and mortality	Findings suggest a vital role for pharmacist in Human *cytomegalovirus* surveillance and treatment optimization in the ambulatory organ transplant recipient.
12	2018 USA	The clinical and financial impact of a pharmacist-driven penicillin skin testing program on antimicrobial stewardship practices.	Prospective	Cost	Pharmacist-driven Penicillin Skin testing optimizes antimicrobial therapy and has a positive impact on the costs of patient treatment.
13	2019 USA	Pharmacist-led antimicrobial stewardship program in an urgent care setting.	Retrospective	Inappropriateness, readmission	A pharmacist-led urgent care ASP was associated with a reduction in inappropriate prescribing and readmission.
14	2019 Canada	Evaluation of a pharmacist-led antimicrobial stewardship service in a pediatric emergency department.	Retrospective	Inappropriateness, readmission	Although this pharmacist-led AMS program did not affect the readmission, it may have led to much better result on inappropriate prescribing.

Table 1 Continued

#	Year & place	Title	Design	Variable	Conclusion
15	2019 Nigeria	Impact of pharmacist-led antibiotic stewardship interventions on compliance with surgical antibiotic prophylaxis in obstetric and gynecologic surgeries in Nigeria.	Prospective	Cost	The pharmacist interventions in the stewardship team improve compliance with surgical antibiotic prophylaxis and reduce antibiotic utilization and cost.
16	2019 Canada	Factors predicting vancomycin therapy outcomes in hemodialysis outpatients and the role of the nephrology stewardship pharmacist.	Retrospective	Mortality	The suggested vancomycin pre-hemodialysis concentration in the guidelines did not predict the treatment outcomes.
17	2019 USA	Evaluation of antibiotic utilization in an emergency department after implementation of an antimicrobial stewardship pharmacist culture review service.	Retrospective	Inappropriateness, readmission	ASP pharmacist evaluation of positive cultures in the ED has a positive impact on reducing the time to appropriate therapy.
18	2019 Japan	Support for fungal infection treatment mediated by pharmacist-led antifungal stewardship activities.	Retrospective	Consumption, mortality, inappropriateness and cost	These results suggest that pharmacist-led antifungal stewardship positively impacts outcome measures like cost, consumption and mortality.
19	2019 Spain	Pharmacist recommendations for Carbapenem de-escalation in urinary tract infection within an antimicrobial stewardship program.	Prospective	Length of stay, mortality, duration of therapy, inappropriateness and readmission.	Carbapenem de-escalation under pharmacist recommendation proves a positive intervention that can help to reduce mortality, inappropriateness and readmission.
20	2020 USA	Impact of pharmacist-driven antiretroviral stewardship and transitions of care interventions on persons with human immunodeficiency virus.	Retrospective	Inappropriateness, readmission	It is concluded that prescribing practices and readmissions in hospital affected by pharmacist-led Antiretroviral Stewardship stewardship and Transitions of Care program.
21	2020 Ethiopia	Half of prescribed antibiotics are not needed: a pharmacist-led antimicrobial stewardship intervention and clinical outcomes in a referral hospital in Ethiopia.	Prospective	Length of stay, duration of therapy, consumption and mortality	A pharmacist-led AMS intervention focused on the time of antibiotic treatment, consumption and mortality.
22	2020 USA	Impact of mandatory infectious diseases consultation and real-time antimicrobial stewardship pharmacist intervention on Staphylococcus aureus bacteremia bundle adherence.	Retrospective	Mortality, readmission, inappropriateness, length of stay	The addition of AMS pharmacist review to mandatory infectious disease consultation impacts the outcome measures of stewardship.
23	2020 China	Impact of a multifaceted pharmacist-led intervention on antimicrobial stewardship in a gastroenterology ward: a 24 segmented regression analysis.	Retrospective	Length of stay	Pre-intervention and post-intervention of multifaceted pharmacist-led AMS show a positive impact on the outcomes of stewardship on the length of stay.
24	2020 USA	Clinical impact of pharmacist-directed antimicrobial stewardship guidance following blood culture rapid diagnostic testing.	Quasi-experimental	Readmission, length of stay and mortality	Rapid identification of bacteremia combined with a pharmacist's recommendations shows a positive impact on the length of stay.
25	2020 USA	Outpatient antimicrobial stewardship: optimizing patient care via pharmacist-led microbiology review.	Prospective	Duration of therapy, mortality, readmission	Microbiology review and positive intervention impact on the patient care. Effect on decreasing treatment failure rate and effects on mortality
26	2020 South Africa	A pharmacist-led prospective antibiotic stewardship intervention improves compliance to community acquired pneumonia guidelines in 39 public and private hospitals across South Africa.	Prospective	Mortality	Pharmacist in public and private facilities of South Africa shows a positive impact on the outcomes of stewardship.
27	2020 USA	Implementing outpatient antimicrobial stewardship in a primary care office through ambulatory care pharmacist-led audit and feedback.	Retrospective	Inappropriate duration of therapy	An ambulatory care pharmacist-led ASP intervention within a primary care office incorporating audit and feedback improved antibiotic prescribing practice for upper respiratory tract infections and Urinary Tract Infections, including duration of therapy.
28	2020 Italy	Role of the hospital pharmacist in an Italian antimicrobial stewardship programme.	Prospective	Cost	The interventions of the antibiotic stewardship pharmacist led to an improvement in cost and care of the patient.

Table 2 Quality assessment of included studies using JSM tool

Sr. no.	Study name	Scale items												
		1	2	3	4	5	6	7	8	9	10	11	12	Score
1	Abubakar *et al.* 2019	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N	L
2	Apisarnthanarak *et al.* 2015	Y	Y	Y	Y	CD	Y	Y	N	CD	Y	Y	N	L
3	Arensman *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	CD	Y	Y	N	L
4	Baker *et al.* 2012	Y	Y	Y	Y	CD	Y	Y	N	Y	Y	Y	N	L
5	van den Bergh *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Y	CD	L
6	Bessesen *et al.* 2015	Y	Y	Y	Y	N	Y	Y	NR	Y	Y	N	CD	M
7	Brizzi *et al.* 2020	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	CD	L
8	Burns *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	CD	Y	Y	N	L
9	Cappelletty and Jacobs 2013	Y	CD	Y	Y	CD	Y	Y	NR	CD	Y	Y	N	M
10	DiDiodato and McArthur 2017	Y	Y	Y	Y	CD	Y	Y	Y	Y	Y	Y	N	L
11	Sadyrbaeva-Dolgova *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	CD	Y	Y	Y	L
12	Fay *et al.* 2019	Y	Y	Y	Y	Y	Y	Y	NR	NR	Y	Y	CD	L
13	Gebretekle *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	NR	Y	CD	N	M
14	Giruzzi *et al.* 2019	Y	Y	Y	Y	Y	Y	Y	NR	NR	Y	CD	Y	L
15	Haque *et al.* 2018	Y	Y	Y	Y	CD	Y	Y	N	NR	Y	N	Y	M
16	Harmon *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	CD	Y	CD	Y	L
17	Li *et al.* 2017	Y	Y	Y	Y	Y	Y	Y	Y	CD	Y	Y	CD	L
18	MacMillan *et al.* 2019	Y	Y	Y	Y	Y	Y	Y	CD	NR	Y	Y	Y	L
19	Mahrous *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	CD	Y	CD	Y	L
20	Nekidy *et al.* 2019	Y	Y	Y	Y	NR	Y	Y	Y	NR	Y	CD	N	M
21	Ohashi *et al.* 2018	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	NR	Y	L
22	Polidori *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	NR	Y	N	Y	L
23	Samura *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	N	NR	Y	NR	Y	L
24	Wang *et al.* 2018	Y	Y	Y	Y	Y	Y	Y	NR	NR	Y	N	Y	L
25	Wattengel *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	CD	CD	Y	NR	Y	L
26	Wong *et al.* 2012	Y	Y	Y	Y	N	Y	Y	CD	NR	Y	NR	N	M
27	Du *et al.* 2020	Y	Y	Y	Y	Y	Y	Y	NR	NR	Y	CD	Y	L
28	Zhang *et al.* 2017	Y	Y	Y	Y	Y	Y	Y	CD	CD	Y	NR	Y	L

Y, yes; N, no; NR, not reported; CD, cannot determine; M, moderate; L, low.

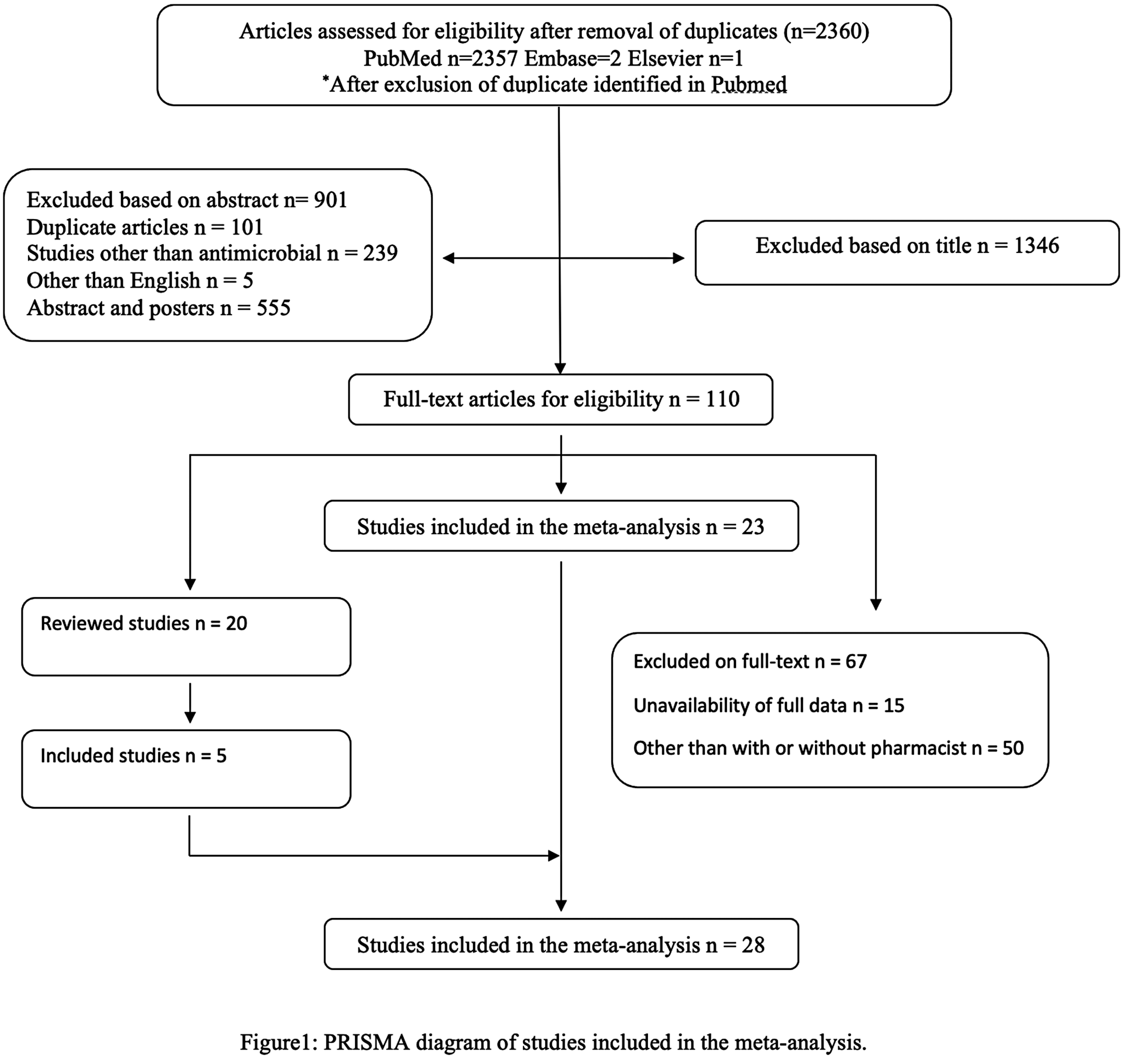

Figure 1 PRISMA diagram of studies included in the meta-analysis.

documents with all elements. Articles assessed in detail with purpose, methodology, results and discussions (Table 2).

Inappropriateness

Fourteen out of twenty-eight AMSs led by a pharmacist in the last 8 years discusses the appropriate antibiotic therapy. We have found all 14 studies show the positive outcome of reducing inappropriate antimicrobial prescribing, as shown in Figure 2. The risk of inappropriate prescribing of antimicrobials is less in AMS with pharmacist than pre-AMS without pharmacist. Total inappropriateness in AMS with the pharmacist is 423/3560, whereas in pre-AMS without pharmacist is 1492/4421. Pooled RR = 0.36 with 95% CI = (0.32 to 0.39). The test with the overall effect is 21.27 ($P < 0.00001$). Heterogeneity calculated at about $I^2 = 91\%$. A funnel plot was used to reduce the bias, as shown in supplementary Figure 2s. Inappropriateness reduced to $I^2 = 39\%$.

Mortality

Thirteen out of 28 studies have reported the impact of stewardship-led pharmacist on mortality among the patients. Figure 2 shows that mortality rates are less in AMS led by pharmacist than to pre-AMS without pharmacist. Three out of 13 studies are not favouring AMS with the pharmacist in case of mortality risk. The pooled effect is 325 patients death out of total 3027 reported in group pre-AMS without pharmacist compared with AMS with the pharmacist is 292 patient deaths reported out of 3402. RR is 0.68 with 95% CI of (0.59 to 0.79; Figure 3). The overall effect is 5.07 with ($P < 0.0001$), heterogeneity is 67%. Heterogeneity is reduced to 41% with subgroup analysis and publication bias with the help of a funnel plot, as shown in Figure 3s.

Impact on cost

AMS can help to reduce the cost of treatment as we have evaluated the cost reduction in AMS with pharmacist versus pre-AMS without pharmacist. The standard mean difference was calculated using Review manager 5.4 and results show a positive impact of pharmacist in cost reduction as shown in Figure 4. Six out of 28 articles calculated the cost difference and found a positive effect of pharmacist −0.99 95% CI (−1.12 to −0.86) with over effect Z = 14.87 ($P < 0.00001$), but with higher heterogeneity $I^2 = 98\%$. Heterogeneity reduced to 0% with the help of the funnel plot, as shown in Figure 4s.

Study or Subgroup	AMS with Pharmacist Events	AMS with Pharmacist Total	Pre-AMS without Pharmacis Events	Pre-AMS without Pharmacis Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Baker 2012	0	80	6	132	0.4%	0.13 [0.01, 2.21]	2012
Cappelletty 2013	12	119	45	111	3.7%	0.25 [0.14, 0.45]	2013
Apisarnthanarak 2015	8	104	45	150	2.9%	0.26 [0.13, 0.52]	2015
Bessesen 2015	6	190	13	100	1.3%	0.24 [0.10, 0.62]	2015
Haque 2017	70	127	127	135	9.7%	0.59 [0.50, 0.69]	2017
Ohashi 2017	14	51	24	43	2.0%	0.49 [0.29, 0.83]	2017
Fay 2019	70	150	88	150	6.9%	0.80 [0.64, 0.99]	2019
Giruzzi 2019	32	392	57	398	4.4%	0.57 [0.38, 0.86]	2019
MacMillan 2019	46	952	68	975	5.3%	0.69 [0.48, 1.00]	2019
Samura 2019	0	18	4	14	0.4%	0.09 [0.01, 1.50]	2019
Brizzi 2020	8	68	16	60	1.3%	0.44 [0.20, 0.96]	2020
Arensman 2020	1	121	17	371	0.7%	0.18 [0.02, 1.34]	2020
Burns 2020	146	1107	963	1700	59.6%	0.23 [0.20, 0.27]	2020
Dolgova 2020	10	81	19	82	1.5%	0.53 [0.26, 1.07]	2020
Total (95% CI)		**3560**		**4421**	**100.0%**	**0.36 [0.32, 0.39]**	
Total events	423		1492				

Heterogeneity: Chi² = 141.73, df = 13 (P < 0.00001); I² = 91%
Test for overall effect: Z = 21.07 (P < 0.00001)

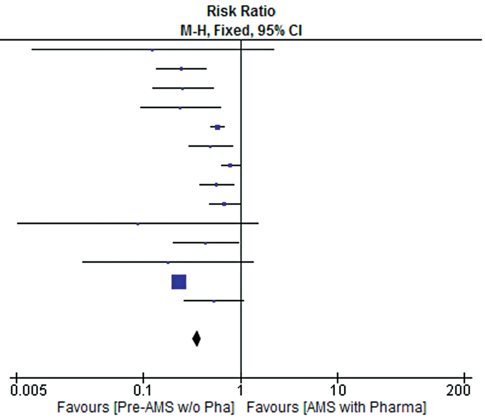

Figure 2 It shows the 14 AMS results for inappropriate antimicrobial prescribing.

Study or Subgroup	AMS with Pharmacist Events	AMS with Pharmacist Total	Pre-AMS without Pharmacis Events	Pre-AMS without Pharmacis Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Apisarnthanarak 2015	38	320	10	150	3.8%	1.78 [0.91, 3.48]	2015
Ohashi 2017	14	51	25	43	7.5%	0.47 [0.28, 0.79]	2017
Zhongwang Li 2017	68	353	65	224	22.1%	0.66 [0.49, 0.89]	2017
Haque 2017	20	127	22	135	5.9%	0.97 [0.55, 1.68]	2017
Wang 2018	10	85	13	100	3.3%	0.90 [0.42, 1.96]	2018
Samura 2019	12	20	5	17	1.5%	2.04 [0.90, 4.63]	2019
Nekidy 2019	0	46	7	24	2.7%	0.04 [0.00, 0.60]	2019
Arensman 2020	6	121	16	371	2.2%	1.15 [0.46, 2.87]	2020
Bergh 2020	47	1217	55	1247	15.1%	0.88 [0.60, 1.28]	2020
Dolgova 2020	6	81	24	82	6.6%	0.25 [0.11, 0.59]	2020
Gebretekle 2020	49	707	59	402	20.9%	0.47 [0.33, 0.68]	2020
Mahrous 2020	14	148	30	164	7.9%	0.52 [0.29, 0.94]	2020
Wattengel 2020	1	148	1	46	0.4%	0.31 [0.02, 4.87]	2020
Total (95% CI)		**3424**		**3005**	**100.0%**	**0.68 [0.59, 0.79]**	
Total events	285		332				

Heterogeneity: Chi² = 36.47, df = 12 (P = 0.0003); I² = 67%
Test for overall effect: Z = 5.07 (P < 0.00001)

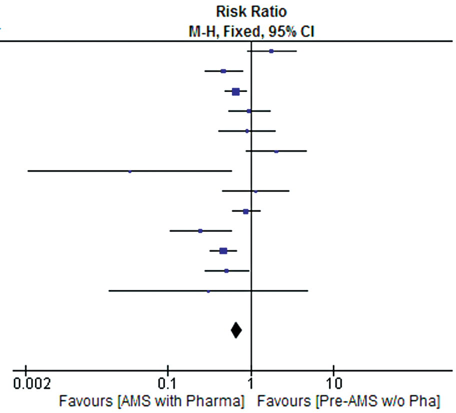

Figure 3 It shows the 13 articles AMS with pharmacist impact on mortality.

Study or Subgroup	AMS with Pharmacist Mean	AMS with Pharmacist SD	AMS with Pharmacist Total	No AMS no Pharmacist Mean	No AMS no Pharmacist SD	No AMS no Pharmacist Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Year
Wong 2012	20,635	2,987.13	22	28,973	4,012.11	31	3.4%	-2.27 [-2.97, -1.56]	2012
Haque 2017	3,098.66	1,063.23	127	7,375	1,491.86	135	12.2%	-3.28 [-3.65, -2.90]	2017
Harmon 2018	3,376.37	997.43	31	5,618.91	1,372.39	31	4.7%	-1.85 [-2.45, -1.25]	2018
Abubakar 2019	2,856	1,547.6	238	3,661.2	1,723.2	226	49.6%	-0.49 [-0.68, -0.31]	2019
Samura 2019	5,930.8	4,687	20	9,390.8	5,687.1	17	3.8%	-0.66 [-1.32, 0.01]	2019
Polidori 2020	3,014.26	2,013.61	116	4,587.68	3,112.68	134	26.3%	-0.59 [-0.84, -0.34]	2020
Total (95% CI)			**554**			**574**	**100.0%**	**-0.99 [-1.12, -0.86]**	

Heterogeneity: Chi² = 203.59, df = 5 (P < 0.00001); I² = 98%
Test for overall effect: Z = 14.87 (P < 0.00001)

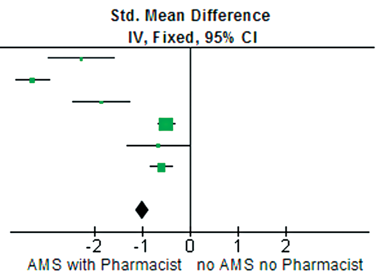

Figure 4 It shows the six articles AMS with pharmacist impact on mortality.

Length of stay

Twelve articles out of 28 were analyzed and found 1 article (Arensman *et al.* 2020) not in favor, but the rest all are in favor of AMS with the pharmacist. Length of stay calculated in the number of days using Review manager 5.4, standard mean difference calculated among AMS with the pharmacist compared with pre-AMS without pharmacist as shown in Figure 5. Standard mean difference value is −0.58 with 95% CI (−0.62 to −0.53). Overall Z = 25.03 (P < 0.0001). Heterogeneity I^2 = 98%. Heterogeneity reduced by subgroup analysis and a funnel plot drawn, as shown in Figure 5s.

Return rate within 30 days to a hospital

The impact of pharmacist with AMS calculated through Review manager 5.4 as a risk ratio. Eight articles out of 28 discuss the hospitalization within 30 days. Pool analysis shows 288 out of 2148 patients return to the hospital in 30 days in AMS with a pharmacist, while 368 out of 2341 patients return to the hospital in 30 days in pre-AMS without a pharmacist. The risk of return to the hospital within 30 days in AMS with the pharmacist is lesser than pre-AMS without a pharmacist. RR = 0.81 with 95% CI (0.70 to 0.93). Heterogeneity I^2 = 60%. Figure 6 shows the impact.

Duration of treatment

Eight articles out of 28 articles showed the impact of pharmacist on the duration of treatment. Impact of pharmacist calculated as the standard mean difference in duration of treatment is calculated through Review manager 5.4 and found significant results. Figure 7 shows that all eight studies show a positive impact of pharmacist on the duration of treatment, as the duration of treatment decreases in AMS with the pharmacist compared with pre-AMS without

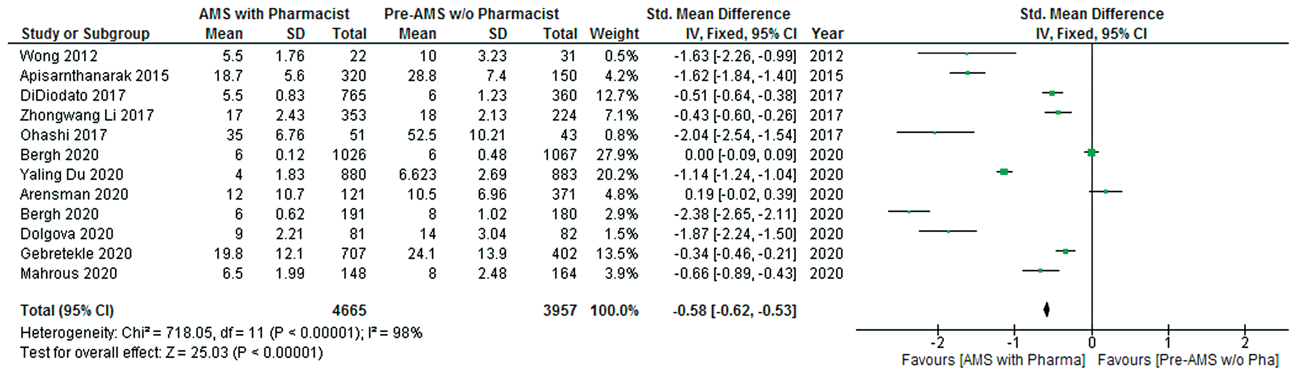

Figure 5 It shows the 12 articles AMS with pharmacist impact on the length of stay in hospital.

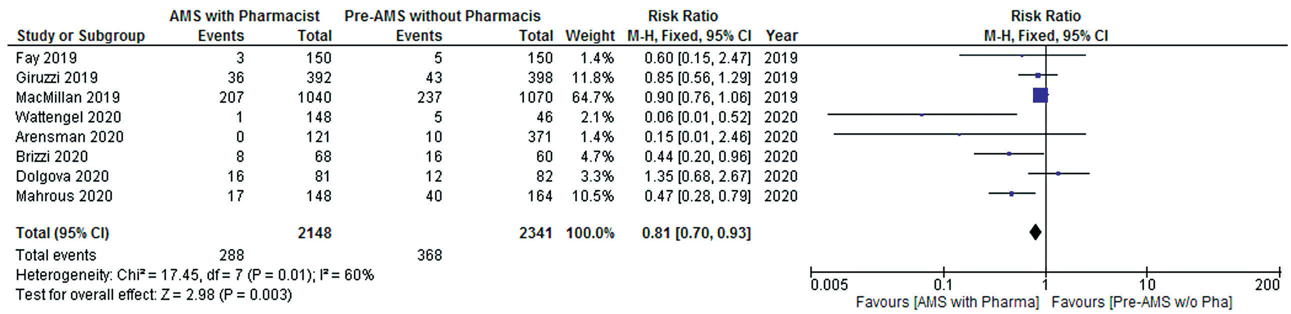

Figure 6 It shows the eight articles AMS with pharmacist impact on the patient's return to the hospital in 30 days.

pharmacist. Standard mean difference is −0.95, 95% CI (−1.01 to −0.89). Overall value effect Z = 32.15 (P < 0.0001) with the heterogeneity of 97%. High heterogeneity can be reduced with the biased publication that is corrected with subgroup analysis through funnel plot as shown in Figure 7s.

Consumption of antimicrobials

Articles with consumption calculated in days of therapy (DOT) per 1000 days only included. Five studies out of 28 show a positive impact of pharmacist with AMS as compared with the pre-AMS without pharmacist. Consumption of antimicrobials calculated through Review manager 5.4 and assessed with a standard mean difference and found that standard mean difference of −1.61 with 95% CI (−1.72 to −1.50). Overall effect Z = 29.37 (P < 0.00001). Heterogeneity is very high 100%, as consumption of antimicrobial can vary from treatment to treatment. But the overall effect is in favor of AMS with the pharmacist, as shown in Figure 8.

Discussion

The inappropriateness of antibiotics practice is the main reason behind resistance, cost, mortality and length of stay. Stewardship programmes run to reduce inappropriate antibiotic prescribing. In our previous systematic review, we have discussed many antibiotic prescribing patterns in outpatient in the Gulf region.[39] There is a need to reduce inappropriateness through AMS and pharmacist can play a vital role in stewardship programs. One study shows that antibiotic change occurred in ≤2 hours in more patients in the pharmacist intervention group (28% versus 10.5%, P = 0.0002) with the help of rapid testing.[40] This meta-analysis fully supports that pharmacist-led AMSs can help to reduce the inappropriate prescribing of antimicrobials.

Mortality can reduce with help of AMS. If we compare mortality in AMS with pharmacist versus pre-AMS without pharmacist, we can understand that pharmacists have a positive impact on reducing mortality. Three out of 13 studies in this meta-analysis shows that the mortality rate is not significant.[11, 13, 21] The insignificance can vary because of the style of research, antimicrobials, sample size and infection related. The author, in one study, has explained the mortality rate as considering the high mortality rate is associated with Gram-positive bacteremia and potential ethical conflict of withholding rapid identification, so the author has decided to follow a specific design to reduce the patient harm.[40] But overall, 10 studies are in favor of AMS pharmacist and the overall effect is significant.

Cost reduction is one of the best tools to find the efficacy of any sort of stewardship. AMS led by a pharmacist can have a positive impact on cost. Six out of six studies shows the positive effect of pharmacist on price. Still, the heterogeneity level is very high, and heterogeneity can be explained due to different research in different countries with the other type of stewardship. The cost of treatment also varies from region to region. Cost reduction explained by one study of up to 69% in stewardship with the pharmacist.[9] Whereas in another study, pharmacist helps reduce the prophylaxis treatment of *Respiratory Syncytial Virus* by following exact inclusion and exclusion criteria followed by the American Academy of Pediatrics (AAP) and reduced to cost \$191,034 on palivizumab during the 2013–2014 academic year versus \$29,983 2014–2015.[41]

Length of stay in hospital can reduce with reasonable measures and ASPs, so it is an outcome. AMS with the pharmacist can help to reduce the length of stay of the patient in the hospital. One study out of 12 is not in favor of AMS with the pharmacist. Length of stay is significant in 11 studies and 1 shows insignificant results. High heterogeneity as the length of stay may vary with the type of infection or type of study. As the author mentioned, complicated bacteremia

Study or Subgroup	AMS with Pharmacist Mean	SD	Total	Pre-AMS w/o Pharmacist Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Year
Wong 2012	2.25	0.91	22	4.07	1.23	31	0.8%	-1.62 [-2.25, -0.98]	2012
Apisarnthanarak 2015	8.9	7	320	17.5	20	150	8.5%	-0.68 [-0.88, -0.48]	2015
Zhongwang Li 2017	4	2.14	353	5	3.23	224	11.8%	-0.38 [-0.55, -0.21]	2017
Ohashi 2017	14	3.23	51	17	4.23	43	1.9%	-0.80 [-1.22, -0.38]	2017
Wang 2018	25.5	3.03	85	28.9	4.69	100	3.7%	-0.84 [-1.15, -0.54]	2018
Dolgova 2020	4	0.91	81	6	1.23	82	2.5%	-1.84 [-2.21, -1.47]	2020
Gebretekle 2020	8.7	6.9	707	12.8	11.7	402	22.0%	-0.46 [-0.58, -0.33]	2020
Burns 2020	7	0.98	1107	10	2.81	1700	48.7%	-1.32 [-1.40, -1.24]	2020
Total (95% CI)			**2726**			**2732**	**100.0%**	**-0.95 [-1.01, -0.89]**	

Heterogeneity: $Chi^2 = 214.92$, df = 7 (P < 0.00001); $I^2 = 97\%$
Test for overall effect: Z = 32.15 (P < 0.00001)

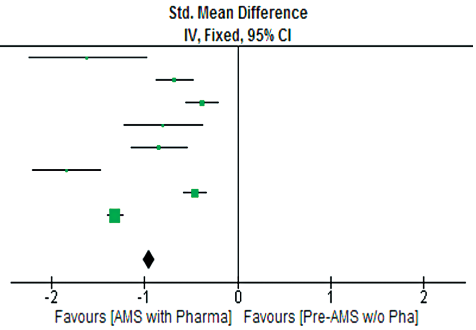

Figure 7 It shows the eight articles AMS with pharmacist impact on the duration of treatment.

Study or Subgroup	AMS with Pharmacist Mean	SD	Total	Pre-AMS w/o Pharmacist Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI	Year
Zhang 2016	304	39.23	136	426	63.16	136	12.2%	-2.31 [-2.62, -2.01]	2016
DiDiodato 2017	9	5.25	765	12.12	7.98	360	71.8%	-0.50 [-0.63, -0.37]	2017
Haque 2017	1,323	33.23	127	3,477	74.23	135	0.1%	-36.97 [-40.17, -33.77]	2017
Samura 2019	3.4	0.38	20	6	1.03	17	1.1%	-3.39 [-4.43, -2.35]	2019
Gebretekle 2020	754	99.8	707	1,549	175.2	402	14.9%	-6.01 [-6.29, -5.73]	2020
Total (95% CI)			**1755**			**1050**	**100.0%**	**-1.61 [-1.72, -1.50]**	

Heterogeneity: $Chi^2 = 1751.50$, df = 4 (P < 0.00001); $I^2 = 100\%$
Test for overall effect: Z = 29.37 (P < 0.00001)

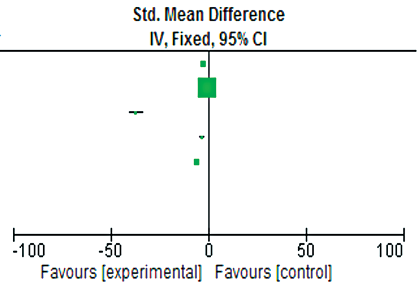

Figure 8 It shows the five articles AMS with pharmacist impact on consumption of antimicrobials.

and metastatic sites of infection may require more extended hospital stay to obtain source control.[11] The same type of results explained as patients with uncomplicated bacteremia in their study of a successful AMS intervention for Staphylococcus aureus bacteremia.[42]

Hospitalization within 30 days is an essential outcome of ASPs, as it shows the complete recovery of the patient from the infection, without relapse and reinfection. One study out of eight shows that the return rate to the hospital within the last 30 days increases in AMS with pharmacist, while all other show that return rate decreases. This study,[30] carbapenem de-escalation with the help of a pharmacist showed no association with readmission, however another study reported negative cultures in patients with nosocomial pneumonia with pharmacist interventions.[43] Heterogeneity was already low, near 60%. But the overall result shows that readmission or hospital return rate decreases in ASPs led by pharmacists.

Duration of treatment in days also used to measure the outcome of the ASP. Consumption should be controlled or reduced to reduce the cost of treatment. The overall effect of a cost reduction will be significant. Eight articles discussed the course of treatment, and all eight reports show the favour for AMS with the pharmacist. Another study shows how pharmacist intervention treatment recommendations provided by ASP pharmacists included selecting antimicrobial agent, dosing, formulation and duration of therapy.[44] Many infections treated for 10 or 14 days will respond to shorter antibiotic courses, including most uncomplicated skin/soft tissue infections, pneumonia and urinary tract infections.[45]

Consumption of antibiotics calculated in DDD or DOT. One article found with DDD per 100 days and five reports with DOT per 1000 days are searched and analyzed. Consumption for meta-analysis we use five articles of DOT per 1000 days. Consumption of antimicrobials has an impact on cost and considered an outcome of stewardship. Stewardship led by pharmacist shows a positive reduction in consumption of antimicrobials. Heterogeneity is 100% because of difference in treatment, type of study and type of infection. A study conducted in Brazil shows that comparing stage 1 and 3, there was a significant reduction of 25% in antimicrobial consumption after implementation of ASP.[9]

Other factors that can indirectly impact AMS are the insurance policy, hospital policy and guidelines and infection control policies that may hurt our outcomes. These are the significant limitations that can change the clinical effects of AMS and address before starting the study.

Conclusion

This evidence synthesis meta-analysis concluded that AMSs led by pharmacist shows significant reduction and improvement of clinical outcomes. Furthermore, the pharmacist-led AMS program not only reduces mortality or inappropriateness of antimicrobial prescribing but also helps in the reduction of treatment cost, duration of treatment as well as the decrease in consumption of antimicrobials.

Supplementary Material

Supplementary data are available at *Journal of Pharmaceutical Health Services Research* online.

Authors contribution

R.K.M.: data extraction, content design and interpretation. S.W.G.: Principal investigator, data curation, data analysis and methodology. M.W.S.: data collection, validation and analysis. P.V.: data collection, draft writing, review and editing. M.J.M.A.A.: data collection, draft writing, review and editing.

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Data Availability Statement

All the data is provided in the manuscript including supplementary file. The raw data can be provided upon request to corresponding author.

Conflict of Interest

I, Dr. Syed Wasif Gillani, declare as a corresponding author that the paper has not been submitted or accepted for publication elsewhere has not been presented at a conference or has not been included on a preprint server; there is no potential conflicts of interest by any means financial or moral. All contributors agreed to submit this paper for publication.

References

1. Barlam TF, Cosgrove SE, Abbo LM *et al*. Executive summary: implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016; 62: 1197–202. http://doi.org/10.1093/cid/ciw217
2. Davey P, Sneddon J, Nathwani D. Overview of strategies for overcoming the challenge of antimicrobial resistance. *Expert Rev Clin Pharmacol*. 2010; 3: 667–86. http://doi.org/10.1586/ecp.10.46
3. Dyar OJ, Huttner B, Schouten J *et al*.; ESGAP (ESCMID Study Group for Antimicrobial stewardshiP). What is antimicrobial stewardship? *Clin Microbiol Infect*. 2017; 23: 793–8. http://doi.org/10.1016/j.cmi.2017.08.026
4. Davey P, Marwick CA, Scott CL *et al*. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev*. 2017; 2: CD003543. http://doi.org/10.1002/14651858.CD003543.pub4
5. PHE. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Report.No Title [Internet]. 2017. https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report (23 March 2021, date last accessed).
6. Duerden BI. Contribution of a government target to controlling Clostridium difficile in the NHS in England. *Anaerobe*. 2011; 17: 175–9. http://doi.org/10.1016/j.anaerobe.2010.12.004
7. Duerden B, Fry C, Johnson AP *et al*. The control of methicillin-resistant Staphylococcus aureus blood stream infections in England. *Open Forum Infect Dis*. 2015; 2: ofv035. http://doi.org/10.1093/ofid/ofv035
8. Westerhof LR, Dumkow LE, Hanrahan TL *et al*. Outcomes of an ambulatory care pharmacist-led antimicrobial stewardship program within a family medicine resident clinic. *Infect Control Hosp Epidemiol*. 2021; 42: 715–21. http://doi.org/10.1017/ice.2020.1275
9. Magedanz L, Silliprandi EM, dos Santos RP. Impact of the pharmacist on a multidisciplinary team in an antimicrobial stewardship program: a quasi-experimental study. *Int J Clin Pharm*. 2012; 34: 290–4. http://doi.org/10.1007/s11096-012-9621-7
10. Chen JR, Tarver SA, Alvarez KS *et al*. Improving aztreonam stewardship and cost through a penicillin allergy testing clinical guideline. *Open Forum Infect Dis*. 2018; 5: ofy106. http://doi.org/10.1093/ofid/ofy106
11. Arensman K, Dela-Pena J, Miller JL *et al*. Impact of mandatory infectious diseases consultation and real-time Antimicrobial Stewardship Pharmacist Intervention on Staphylococcus aureus bacteremia bundle adherence. *Open Forum Infect Dis*. 2020; 7: ofaa184. http://doi.org/10.1093/ofid/ofaa184
12. Polidori P, Leonardi Vinci D, Adami S *et al*. Role of the hospital pharmacist in an Italian antimicrobial stewardship programme. *Eur J Hosp Pharm [Internet]*. 2020 Sep 8. https://ejhp.bmj.com/lookup/doi/10.1136/ejhpharm-2020–002242
13. Apisarnthanarak A, Lapcharoen P, Vanichkul P *et al*. Design and analysis of a pharmacist-enhanced antimicrobial stewardship program in Thailand. *Am J Infect Control*. 2015; 43: 956–9. http://doi.org/10.1016/j.ajic.2015.05.011
14. Du Y, Li J, Wang X *et al*. Impact of a multifaceted pharmacist-led intervention on antimicrobial stewardship in a gastroenterology ward: a segmented regression analysis. *Front Pharmacol*. 2020; 11: 1–8. http://doi.org/10.3389/fphar.2020.00442
15. Wang N, Athans V, Neuner E *et al*. A pharmacist-driven antimicrobial stewardship intervention targeting cytomegalovirus viremia in ambulatory solid organ transplant recipients. *Transpl Infect Dis*. 2018; 20: e12991. http://doi.org/10.1111/tid.12991
16. Wattengel BA, Sellick JA, Mergenhagen KA. Outpatient antimicrobial stewardship: optimizing patient care via pharmacist led microbiology review. *Am J Infect Control*. 2020; 48: 189–93. http://doi.org/10.1016/j.ajic.2019.07.018
17. Wong JR, Bauer KA, Mangino JE *et al*. Intervenciones del farmacéutico responsable a la administración antimicrobiana para hemocultivos positivos de estafilococos coagulasa negativos usando la rápida reacción en cadena de la polimerasa. *Ann Pharmacother*. 2012; 46: 1484–90.
18. El Nekidy WS, El-Masri MM, Ghazi IM *et al*. Factors predicting vancomycin therapy outcomes in hemodialysis outpatients and the role of the nephrology stewardship pharmacist. *Hemodial Int*. 2019; 23: 449–57. http://doi.org/10.1111/hdi.12775
19. Ohashi K, Matsuoka T, Shinoda Y *et al*. Evaluation of treatment outcomes of patients with MRSA bacteremia following antimicrobial stewardship programs with pharmacist intervention. *Int J Clin Pract*. 2018; 72: e13065. http://doi.org/10.1111/ijcp.13065
20. Mahrous AJ, Thabit AK, Elarabi S *et al*. Clinical impact of pharmacist-directed antimicrobial stewardship guidance following blood culture rapid diagnostic testing. *J Hosp Infect*. 2020; 106: 436–46. http://doi.org/10.1016/j.jhin.2020.09.010
21. Samura M, Hirose N, Kurata T *et al*. Support for fungal infection treatment mediated by pharmacist-led antifungal stewardship activities. *J Infect Chemother*. 2020; 26: 272–9. http://doi.org/10.1016/j.jiac.2019.09.016
22. Haque A, Hussain K, Ibrahim R *et al*. Impact of pharmacist-led antibiotic stewardship program in a PICU of low/middle-income country. *BMJ Open Qual*. 2018; 7: e000180. http://doi.org/10.1136/bmjoq-2017-000180
23. Harmon S, Richardson T, Simons H *et al*. The clinical and financial impact of a pharmacist-driven penicillin skin testing program on antimicrobial stewardship practices. *Hosp Pharm*. 2020; 55: 58–63. http://doi.org/10.1177/0018578718817917
24. MacMillan KM, MacInnis M, Fitzpatrick E *et al*. Evaluation of a pharmacist-led antimicrobial stewardship service in a pediatric emergency department. *Int J Clin Pharm*. 2019; 41: 1592–8. http://doi.org/10.1007/s11096-019-00924-1
25. DiDiodato G, McAthur L. Transition from a dedicated to a non-dedicated, ward-based pharmacist antimicrobial stewardship programme model in a non-academic hospital and its impact on length of stay of patients admitted with pneumonia: a prospective observational study. *BMJ Open Qual*. 2017; 6: e000060. http://doi.org/10.1136/bmjoq-2017-000060
26. Giruzzi ME, Tawwater JC, Grelle JL. Evaluation of antibiotic utilization in an emergency department after implementation of an antimicrobial stewardship pharmacist culture review service. *Hosp Pharm*. 2020; 55: 261–7. http://doi.org/10.1177/0018578719844171
27. Fay LN, Wolf LM, Brandt KL *et al*. Pharmacist-led antimicrobial stewardship program in an urgent care setting. *Am J Health Syst Pharm*. 2019; 76: 175–81. http://doi.org/10.1093/ajhp/zxy023
28. Gebretekle GB, Haile Mariam D, Abebe Taye W *et al*. Half of prescribed antibiotics are not needed: a pharmacist-led antimicrobial stewardship intervention and clinical outcomes in a referral hospital in Ethiopia. *Front Public Health*. 2020; 8: 109. http://doi.org/10.3389/fpubh.2020.00109
29. Bessesen MT, Ma A, Clegg D *et al*. Antimicrobial stewardship programs: comparison of a program with infectious diseases pharmacist support to a program with a geographic pharmacist staffing model. *Hosp Pharm*. 2015; 50: 477–83. http://doi.org/10.1310/hpj5006-477
30. Sadyrbaeva-Dolgova S, Aznarte-Padial P, Jimenez-Morales A *et al*. Pharmacist recommendations for carbapenem de-escalation in urinary tract infection within an antimicrobial stewardship program. *J Infect Public Health*. 2020; 13: 558–63. http://doi.org/10.1016/j.jiph.2019.09.014

31. Zhang X, Rowan N, Pflugeisen BM *et al*. Urine culture guided antibiotic interventions: a pharmacist driven antimicrobial stewardship effort in the ED. *Am J Emerg Med*. 2017; 35: 594–8. http://doi.org/10.1016/j.ajem.2016.12.036
32. Brizzi MB, Burgos RM, Chiampas TD *et al*. Impact of pharmacist-driven antiretroviral stewardship and transitions of care interventions on persons with human immunodeficiency virus. *Open Forum Infect Dis*. 2020; 7: ofaa073. http://doi.org/10.1093/ofid/ofaa073
33. Burns KW, Johnson KM, Pham SN *et al*. Implementing outpatient antimicrobial stewardship in a primary care office through ambulatory care pharmacist-led audit and feedback. *J Am Pharm Assoc*. 2020; 60: e246–51. http://doi.org/10.1016/j.japh.2020.08.003
34. Cappelletty D, Jacobs D. Evaluating the impact of a pharmacist's absence from an antimicrobial stewardship team. *Am J Health Syst Pharm*. 2013; 70: 1065–9. http://doi.org/10.2146/ajhp120482
35. Baker SN, Acquisto NM, Ashley ED *et al*. Pharmacist-managed antimicrobial stewardship program for patients discharged from the emergency department. *J Pharm Pract*. 2012; 25: 190–4. http://doi.org/10.1177/0897190011420160
36. van den Bergh D, Messina AP, Goff DA *et al*.; South African Antibiotic Stewardship Programme Pharmacist Community-acquired Pneumonia Study Alliance. A pharmacist-led prospective antibiotic stewardship intervention improves compliance to community-acquired pneumonia guidelines in 39 public and private hospitals across South Africa. *Int J Antimicrob Agents*. 2020; 56: 106189. http://doi.org/10.1016/j.ijantimicag.2020.106189
37. Li Z, Cheng B, Zhang K *et al*. Pharmacist-driven antimicrobial stewardship in intensive care units in East China: a multicenter prospective cohort study. *Am J Infect Control*. 2017; 45: 983–9. http://doi.org/10.1016/j.ajic.2017.02.021
38. Abubakar U, Syed Sulaiman SA, Adesiyun AG. Impact of pharmacist-led antibiotic stewardship interventions on compliance with surgical antibiotic prophylaxis in obstetric and gynecologic surgeries in Nigeria. *PLoS One*. 2019; 14: e0213395. http://doi.org/10.1371/journal.pone.0213395
39. Mahmood RK, Gillani SW, Saeed MW *et al*. Systematic review: study of the prescribing pattern of antibiotics in outpatients and emergency departments in the Gulf Region. *Front Pharmacol*. 2020; 11: 585051. http://doi.org/10.3389/fphar.2020.585051
40. Heyerly A, Jones R, Bokhart G *et al*. Implementation of a pharmacist-directed antimicrobial stewardship protocol utilizing rapid diagnostic testing. *Hosp Pharm*. 2016; 51: 815–22. http://doi.org/10.1310/hpj5110-815
41. Rostas SE, McPherson C. Pharmacist-driven respiratory syncytial virus prophylaxis stewardship service in a neonatal intensive care unit. *Am J Health Syst Pharm*. 2016; 73: 2089–94. http://doi.org/10.2146/ajhp150989
42. Remtulla S, Zurek K, Cervera C *et al*. Impact of an unsolicited, standardized form-based antimicrobial stewardship intervention to improve guideline adherence in the management of Staphylococcus aureus Bacteremia. *Open Forum Infect Dis*. 2019; 6: ofz098. http://doi.org/10.1093/ofid/ofz098
43. Schlueter M, James C, Dominguez A *et al*. Practice patterns for antibiotic de-escalation in culture-negative healthcare-associated pneumonia. *Infection*. 2010; 38: 357–62. http://doi.org/10.1007/s15010-010-0042-z
44. Sapozhnikov J, Huang A, Revolinski S *et al*. Impact of an antimicrobial stewardship program pharmacist during microbiology rounds. *Am J Clin Pathol*. 2021; 155: 455–60. http://doi.org/10.1093/ajcp/aqaa132
45. Spellberg B, Rice LB. Duration of antibiotic therapy: shorter is better. *Ann Intern Med [Internet]*. 2019 Aug 6; 171: 210. Available from: https://annals.org/aim/fullarticle/2737827/duration-antibiotic-therapy-shorter-better