Supplemental Online Content

Zay Ya K, Win PTN, Bielicki J, Lambiris M, Fink G. Association between antimicrobial stewardship programs and antibiotic use globally: a systematic review and meta-analysis. *JAMA Netw Open.* 2023;6(2):e2253806. doi:10.1001/jamanetworkopen.2022.53806

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Search String for the Systematic Review and Meta-analysis

Keywords in combination

"drug resistance, microbial"[MeSH Terms] OR Antibiotic resistance OR Antimicrobial Resistance OR Microbial Drug Resistance OR Antimicrobial Drug Resistance OR Multiple Drug Resistance OR Antibiotic Use OR Antibiotic Prescription OR Antibiotic Consumption

AND

Polic* OR Intervention* AND

Impact* OR Evaluate* OR Assess* OR Effect*

eTable 2. Inclusion and Exclusion Criteria for Article Screening

Inc	lucion	criteria
	เนรเบท	CILEIIA

- Studies in humans
- Reports on policy and interventions designed to reduce antibiotic use or antimicrobial resistance
- Primary studies
- Full text availability
- Report in English
- Studies within 1 Aug 2010 to 1 Aug 2020

Exclusion criteria

- Studies in animals
- > Reports not relating with AMR policies and interventions
- > Review, expert opinions, conference abstracts posters and newspaper articles
- Report in other language
- Study before 1 Aug 2010

Author	Study type	Selection	Study	Confounders	Blinding	Data	Withdrawal	Global
		bias	design			collection	and drop-	rating
						methods	outs	
Sloane et al	Controlled trial	S	S	S	м	S	S	м
Alvarez-Lerma	Prospective	S	м	w	М	S	м	м
et al	interventional							
	cohort							
Gonzales et tal	RCT	S	S	S	м	S	S	S
Cross et tal	Cluster-	M	м	w	м	s	м	м
	randomized							
Tedeschi et al	Quasi-	м	м	w	м	S	М	м
	experimental							
Aldeyab, M. A.	Retrospective	М	м	S	м	S	М	м
	interventional							
	cohort							
Brink et al	Prospective	S	м	S	м	S	М	S
	interventional							
	cohort							
Fortini et al	Retrospective	S	м	S	м	S	М	S
	interventional							
	cohort							
Rahbarimanes	Quasi-	S	м	м	w	S	S	м
h et al	experimental							
Pitiriga et al	Prospective	М	м	w	м	S	М	м
	interventional							
	cohort							
Ruiz et al	Prospective	S	м	S	w	S	М	м
	interventional							
	cohort							
Elligsen et al	Controlled trial	S	S	S	м	S	S	S
Dik, J. W. H et	Controlled trial	S	S	S	м	s	S	S
al								
Sikkens et al	Prospective	S	м	м	w	s	M	м
	interventional							
	cohort							
Di Pentima et	Prospective	S	м	м	w	S	M	м
al	interventional							
	cohort							
Strumann et al	Controlled trial	м	S	S	w	S	м	м
Wu, C. T et al	Cohort	S	M	S	w	S	S	м
Chang et al	RCT	S	S	S	M	S	S	S
-								
Wei, X et al	RCT	S	S	S	M	S	S	S
Gerber, J. S et al	RCT	S	S	s	м	S	S	S
Gong et al	Prospective	S	м	S	М	S	М	S
	interventional							
	cohort		1			1	1	

eTable 3. Quality Assessment of the 57 Studies Using the Effective Public Health Practice Project Quality Assessment Tool

M yon Duril at	Controlled trial	e	6	e	M	e	м	6
W. van Buul et	Controlled trial	S	S	S	м	S	м	S
al			<u> </u>			L		
Llor, C et al	Controlled trial	S	s	s	м	s	S	S
Llor C et a;l	Cohort	S	M	S	w	w	м	w
		-		-				
Little et al	RCT	S	S	S	S	S	S	S
	DOT		-					
McNulty et al	RCT	S	S	S	S	S	S	S
March-López	Quasi-	s	M	S	w	S	M	м
et al	experimental							
Newland et al	Controlled trial	м	s	S	м	м	M	S
Craft et al	Cohort	м	M	м	w	м	w	w
Khdour et al	Prospective	м	м	w	м	M	M	м
	interventional	1						
	cohort							
Talpaert et al	Quasi-	M	M	w	м	S	м	M
. aipaon ot ai	experimental							
Fleet et al	RCT	S	S	S	s	S	м	s
		-				-		
Stenehjem et	RCT	S	S	м	М	S	М	S
al								
Ouldali et al	Quasi-	м	М	м	м	S	Μ	S
	experimental							
Zhou, Y et al	Prospective	м	М	м	М	S	w	м
	interventional							
	cohort							
Abubakar et al	Prospective	S	м	м	w	S	М	М
	interventional							
	cohort							
Magedanz et	Cohort	м	м	w	w	М	М	w
al								
Singh et al	Prospective	S	м	м	w	м	М	М
	interventional							
	cohort							
Tavares et al	Prospective	S	м	м	м	м	М	S
	interventional							
	cohort							
Borde et al	Quasi-	S	м	м	w	м	М	М
	experimental							
Nitsch-Osuch	Cohort	S	м	w	w	М	м	w
et a;								
Lu, C et al	Prospective	м	м	м	w	м	М	м
	interventional							
	cohort							
Hürlimann et	RCT	S	S	S	м	S	М	S
al								
Le Corvoisier	RCT	м	S	S	s	S	S	S
et al								
Jenkins et al	Quasi-	S	м	м	м	S	w	м
	experimental							
Wei, X. et al	Cluster	s	s	s	м	S	S	s
	randomized							
	1	_	-	1	+	`	S	S
Kreitmeyr et al	Prospective	S	м	S	м	S	3	U
Kreitmeyr et al	Prospective interventional	S	м	5	м	5	5	Ū

Butt et al	Quasi-	S	М	S	w	S	S	S
	experimental							
Regev-Yochay	Cluster	S	S	S	М	S	S	S
et al	randomized							
Adhikari et al	Prospective	S	м	S	М	S	М	S
	interventional							
	cohort							
Onorato et al	Prospective	S	м	w	М	S	М	м
	interventional							
	cohort							
Al Bahar et al	Retrospective	S	М	М	м	S	М	S
	interventional							
	cohort							
Borde et al	Quasi-	S	S	S	S	S	S	S
	experimental							
Pate et al	Prospective	S	S	S	S	S	S	S
	interventional							
	cohort							
Abdallah et al	Retrospective	S	S	S	S	S	S	S
	interventional							
	cohort							
Sid Ahmed et	Prospective	S	S	S	S	S	S	S
al	interventional							
	cohort							
Al-Omari et al	Quasi-	S	S	S	S	S	S	S
	experimental							

In each component, a rating of strong, moderate, weak has to be assigned according to rating guidelines and dictionaries. For global rating of each paper, "Strong" rating was given when there are no weak ratings in all components, "Moderate" for one weak rating and "Weak" for two or weak ratings in one of assessment. Only articles with "Strong" and "Moderate" ratings were included in our analysis. We only included articles with high study quality that had strong or moderate ratings in at least 5 out of the 6 domains.

eTable 4. Characteristic of Included Studies in the Systematic Review and Meta-analysis

Authors	Year of	Study design	Country	Study	Study population	Interventions	Reduction in
	publication			settings			antibiotic
							consumption
Sloane et al	2020	Controlled	USA	community	nursing homes,	antimicrobial	Yes
		trial		Nursing	nursing staff and	stewardship	
				Homes	medical care	programmes	
					providers in nursing		
					homes		
Alvarez-Lerma et	2018	Prospective	Spain	ICU in	patients in the ICUs	antimicrobial	Yes
al		interventional		Acute-care	of a 400-bed acute-	stewardship	
		cohort		teaching	care teaching	programmes	
				hospital	hospital		
Gonzales et al	2013	RCT	USA	primary care	uncomplicated acute	electronic	Yes
				practices	bronchitis patients in	decision	
					primary care	support	
Tedeschi et al	2017	Quasi-	Italy	rehabilitation	patients with spinal-	antimicrobial	Yes
		experimental		hospital	cord injuries	stewardship	
						program	
Aldeyab, M. A.	2012	Retrospectiv	Northern	one hospital	patients with	hospital	Yes
		e	Ireland	within the	Clostridium difficile	antibiotic	
		interventional		Trust	infection	policy	
		cohort					
Brink et al	2016	Prospective	South	private	patients in private	antimicrobial	Yes
		interventional	Africa	hospitals	hospital	stewardship	
		cohort				programmes	
Fortini et al	2018	Retrospectiv	Italy	mid-sized	patients Internal	antimicrobial	Yes
		e	,	acute care	Medicine ward	stewardship	
		interventional		hospital		programmes	
		cohort				P 9	
Rahbarimanesh	2019	Quasi-	Iran	children's	paediatric patients	antimicrobial	Yes
et al	2010	experimental		hospital	pacalatile patiente	stewardship	
oru		oxponnontai		noopital		programmes	
Pitiriga et al	2018	Prospective	Greece	modern	Patients from	antimicrobial	No
r langa ot ar	2010	interventional		medicine	cardiac surgery,	stewardship	
		cohort		hospital	intensive care unit	programmes	
		oonon		noopital	(ICU), orthopaedic	programmee	
					surgery, oncology,		
					neurosurgery,		
					urology and acute		
					medical/surgical		
					care		
Ruiz et al	2018	Prospective	Spain	medical ICU	patients in ICU	antimicrobial	Yes
ו זעוב כו מו	2010	interventional	Spain	in a tertiary		stewardship	103
		cohort		hospital		programmes	
Ellisson et el	0040		Canada				Vee
Elligsen et al	2012	Controlled	Canada	single	medical and surgical	antimicrobial	Yes
		trial		tertiary care	patients as well as	stewardship	
				centre with 3	regional trauma	programmes	
				intensive	patients; cardiac		
				care units	and vascular		
					surgery patients;		
					and burn patients		
Dik, J. W. H et al	2015	Controlled	Netherland	university	patients in urology	antimicrobial	Yes
		trial		medical	ward	stewardship	
				centre		programmes	
				urology ward			

Sikkens et al	2017	Prospective	Netherland	tertiary care	patients in 7 clinical	training and	Yes
Sikkelis et al	2017		Nethenand				165
		interventional		medical	departments	guidelines	
		cohort		centre and			
				general			
				teaching			
				hospital			
Di Pentima et al	2011	Prospective	USA	tertiary care	paediatric oncology	antimicrobial	Yes
		interventional		academic	patients and	stewardship	
		cohort		paediatric	patients who were	programmes	
				hospital	receiving stem cell		
					transplantations		
Strumann et al	2020	Controlled	Germany	primary care	URTI cases	training and	Yes
		trial		physicians in		guidelines	
				private			
				practices			
Wu, C. T et al	2017	Cohort	Taiwan	general	all patients admitted	antimicrobial	Yes
				hospital	to Nan Men General	stewardship	
					Hospital	programmes	
Chang et al	2020	RCT	China	primary care	patients in	computerized	Yes
Ŭ	-			institutions	community health	decision	
					service centres	support	
Wei, X et al	2017	RCT	China	primary care	paediatric	antimicrobial	Yes
Wei, X et al	2017		Onina	hospitals	outpatients	stewardship	103
				Tiospitais	outpatients	programmes	
Cartan I Catal	2012	DOT	USA	u a a diatoia	u a a diatuia		Vaa
Gerber, J. S et al	2013	RCT	USA	paediatric	paediatric	antimicrobial	Yes
				primary care	outpatients	stewardship	
		-		sites		programmes	
Gong et al	2016	Prospective	China	tertiary	paediatric	antimicrobial	Yes
		interventional		paediatric	outpatients	stewardship	
		cohort		hospital		programmes	
W. van Buul et al	2015	Controlled	Netherland	nursing	nursing homes	antimicrobial	No changes
		trial		homes and		stewardship	in antibiotic
				residential		programmes	use
				care facilities			
Llor, C et al	2011	Controlled	Spain	primary care	all cases of	antimicrobial	Yes
		trial		centres	pharyngitis	stewardship	
						programmes	
Little et al	2013	RCT	Six	primary-care	patients with LRTIs	internet-based	Yes
			European	practices		training	
			countries				
McNulty et al	2018	RCT	United	GP medical	patients in general	training and	Yes
-			Kingdom	practices	practices	guidelines	
March-López et	2020	Quasi-	Spain	primary	PHC patients	antimicrobial	Yes
		Quusi-	Spann	health care		stewardship	105
-		experimental			1	stewarusnip	
al		experimental				programmes	
al					poodiatria anti-anta	programmes	Vaa
-	2012	Controlled	USA	tertiary care	paediatric patients	antimicrobial	Yes
al			USA	tertiary care children's	paediatric patients	antimicrobial stewardship	Yes
al Newland et al	2012	Controlled trial		tertiary care children's hospital		antimicrobial stewardship programmes	
al		Controlled trial Prospective	Northern	tertiary care children's hospital tertiary	ICU and any	antimicrobial stewardship programmes antimicrobial	Yes
al Newland et al	2012	Controlled trial Prospective interventional		tertiary care children's hospital tertiary hospital	ICU and any antimicrobial drug	antimicrobial stewardship programmes antimicrobial stewardship	
al Newland et al	2012	Controlled trial Prospective	Northern	tertiary care children's hospital tertiary	ICU and any	antimicrobial stewardship programmes antimicrobial	
al Newland et al	2012	Controlled trial Prospective interventional	Northern	tertiary care children's hospital tertiary hospital	ICU and any antimicrobial drug	antimicrobial stewardship programmes antimicrobial stewardship	
al Newland et al	2012	Controlled trial Prospective interventional	Northern	tertiary care children's hospital tertiary hospital	ICU and any antimicrobial drug administered	antimicrobial stewardship programmes antimicrobial stewardship	
al Newland et al Khdour et al	2012 2018	Controlled trial Prospective interventional cohort	Northern Ireland	tertiary care children's hospital tertiary hospital including	ICU and any antimicrobial drug administered patients	antimicrobial stewardship programmes antimicrobial stewardship programmes	Yes

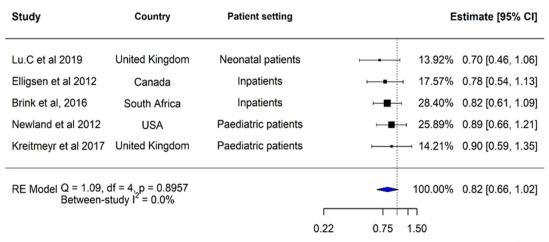
Fleet et al	2014	RCT	United	nursing	nursing homes	antimicrobial	Yes
			Kingdom	homes		stewardship	
						programmes	
Stenehjem et al	2018	RCT	USA	critical	patients in 15 small	antimicrobial	No
				access	hospitals	stewardship	
				hospitals		programmes	
				with			
				paediatric			
				units and			
				ICU			
Ouldali et al	2017	Quasi-	France	paediatric	ARTI	treatment	Yes
	2011	experimental	1 runoo	patients with	/	guidelines	100
		oxponnontar		ARTI		guidelinee	
				diagnosis			
Zhou, Y et al	2015	Prospective	China	department	patients with clean	antimicrobial	Yes
	2015	interventional	China		operation	stewardship	Tes
				of Urology	operation		
	0010	cohort				programmes	
Abubakar et al	2019	Prospective	Nigeria	obstetrics	women who had	antimicrobial	Yes
		interventional		and	elective and	stewardship	
		cohort		gynaecology	emergency obstetric	programmes	
				settings	and gynaecologic		
					surgeries		
Singh et al	2019	Prospective	India	academic	patients in surgical,	antimicrobial	Yes
		interventional		large	medical units and	stewardship	
		cohort		hospital	critical care	programmes	
Tavares et al	2018	Prospective	Portugal	university	patients in tertiary	antimicrobial	Yes
		interventional		hospital	care	stewardship	
		cohort			public teaching	programmes	
					hospital		
Borde et al	2015	Quasi-	Germany	university	non-trauma	antimicrobial	Yes
		experimental		hospital	emergency patients	stewardship	
				centre		programmes	
Lu, C et al	2019	Prospective	China	neonatal	infants who received	antimicrobial	Yes
		interventional		ICU	antibiotics during	stewardship	
		cohort			their hospital stay	programmes	
Hürlimann et al	2015	RCT	Switzerland	primary care	upper RTIs, lower	treatment	Yes
				physicians	RTIs	guidelines	
Le Corvoisier et	2013	RCT	France	GPs with a	patients treated by	interactive	Yes
al	2010		Tranco	practice in	GPs	workshop and	100
				three		educational	
				counties		seminar	
Jenkins et al	2015	Quasi	USA	public safety	inpatients		Yes
Jenkins et al	2015	Quasi-	USA		inpatients	antimicrobial	res
		experimental		net hospital		stewardship	
	00.10					programmes	
Wei, X. et al	2019	Cluster	China	primary care	children with URTIs	interactive	Yes
		randomized		facilities in		workshop and	
				rural		educational	
				counties		seminar	
Kreitmeyr et al	2017	Prospective	Germany	academic	paediatric patients	antimicrobial	Yes
		interventional		children's		stewardship	
		cohort		hospital		programmes	
Butt et al	2019	Quasi-	Pakistan	tertiary care	patients with	pharmacist's	Yes
		experimental		hospital	clean/clean	educational	
					contaminated	intervention	
					surgeries from three		
					different surgery		
					wards, general,		
				1			1

					orthopaedic and		
					gynaecology		
Bagay Vaabay	2011	Cluster	Israel	primon (ooro	children in a	antimicrobial	Yes
Regev-Yochay	2011	-	Israel	primary care			res
et al		randomized		paediatric	community setting	stewardship	
				solo		programmes	
				practices			
Adhikari et al	2018	Prospective	Australia	medical-	patients in tertiary	antimicrobial	Yes
		interventional		surgical	referral hospital	stewardship	
		cohort		tertiary	level-6 ICU	programmes	
				Australian			
				adult ICU			
Onorato et al	2020	Prospective	Italy	ICUs of an	patients in ICU	antimicrobial	Yes
		interventional		acute-care		stewardship	
		cohort		teaching		programmes	
				hospital.			
Al Bahar et al	2020	Retrospectiv	United	teaching	patients in a tertiary	computerised	Yes
		e	Kingdom	hospital	care hospital	decision	
		interventional				support	
		cohort					
Borde et al	2014	Quasi-	Germany	academic	patients in a tertiary	antimicrobial	Yes
		experimental		teaching	care hospital	stewardship	
				hospital and		programmes	
				tertiary care			
				referral			
				centre			
Pate	2012	Prospective	USA	long-term	patients in long-term	antimicrobial	Yes
		interventional		acute care	acute care hospital	stewardship	
		cohort		hospital		programmes	
Abdallah	2017	Retrospectiv	Saudi	tertiary care	patients in adult ICU	antimicrobial	Yes
		e	Arabia	centre		stewardship	
		interventional		particularly		programmes	
		cohort		spinal and			
				neurosurger			
				y			
Sid Ahmed	2020	Prospective	Qatar	acute care	patient in an acute	antimicrobial	Yes
		interventional		hospital	care hospital	stewardship	
		cohort				programmes	
Al-Omari	2020	Quasi-	Saudi	tertiary	adult inpatients	antimicrobial	Yes
	2020	experimental	Arabia	private		stewardship	
		experimental	, 1000	hospitals		programmes	
	l			nospitais		programmes	

eTable 5. Summary of ASP Components Identified in the Included Studies

ASP component	component description
Training and Guidelines	 Training on antibiotic use in formal and informal settings, messaging through posters, flyers, newsletters, or electronic communication to health care providers/service providers, e.g. training on antibiotic use, internet-based training Educating prescribers, pharmacists, and nurses about adverse reactions from antibiotics, antibiotic resistance, and optimal prescribing e.g. interactive workshop and educational seminar Developing or updating guideline and protocol about appropriate antibiotic use e.g. develop community-acquired pneumonia guidelines for hospitalists.
Decision support tools	Decision support through electronic or paper-based strategies for antibiotic use e.g. electronic-based treatment algorithm or a poster with a clinical algorithm
Antibiotic restriction	 Restricting antibiotic use by interventions, such as preauthorization, requires prescribers to gain approval before using certain antibiotics. e.g. preauthorization through an electronic order entry system or ID physician.
Prospective audit and feedback	 An external review of antibiotic therapy by antibiotic experts (usually physicians and/or pharmacists), e.g. case-by-case review of patients prescribed antibiotics by an infectious diseases (ID) physician.
Tracking	 Monitoring and evaluation of antibiotic prescribing and other vital outcomes (antibiotic prescribing and outcome tracking systems) and reporting prescription practices, infection and resistance patterns, e.g. monitoring <i>C. difficile</i> infection and resistance patterns.
Pharmacy-based Interventions	 The engagement of pharmacists in ASPs to improve antibiotic use. The pharmacist's role in ASPs is to document antibiotic indications, dosage adjustment, and duplicative antibiotic therapy alerts and to monitor antibiotic-related drug interactions and adverse effects e.g. clinical pharmacist provides a notification to switch antibiotic therapy.
Microbiology-based interventions	Antimicrobial susceptibility testing results to show antibiotics that are in line with hospital/clinical treatment guidelines or ASPs and to help providers in clinical decision making with microbiology report e.g. antibiotic culture and sensitivity test report.

eFigure 1. Change in Total Antibiotic Consumption after ASPs (DDD or DOT per 100 Patient-Days)



Change in overall antibiotic consumption after ASP(axis in log scale)

Figure 1 shows the average change in antibiotic consumption post- compared to pre-intervention. RR:rate ratio. The rate ratio (RR) of antibiotic consumption was obtained by dividing the post-intervention consumption rate measured in DDD or DOT per 100 PD by the pre-intervention consumption rate. A rate ratio below the value of 1 indicates that ASPs are associated with a reduction of (1-RR)% in antibiotic consumption. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets. No significant reduction in consumption was measured among studies that reported consumption pooled across antibiotics (RR=0.82, 95% CI [0.66 to 1.02]; 5 estimates).

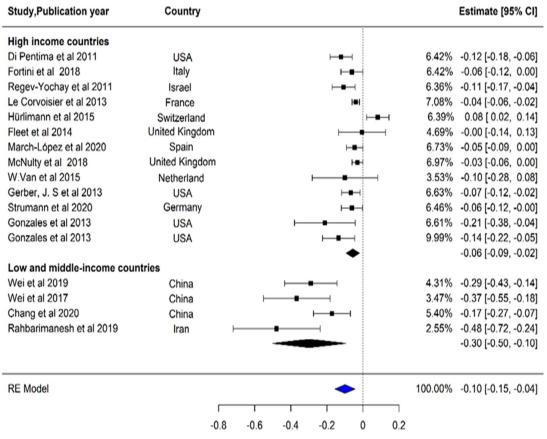
eFigure 2. Subgroup Analyses (Antibiotic Prescriptions)

A Forest plot of included studies stratified by patient settings (Antibiotic prescriptions)

Study,Publication year	Country			Estimate [95% CI]
Pediatric patients				
Wei et al 2019	China	⊢− →	4.31%	-0.29 [-0.43, -0.14]
Wei et al 2017	China	—	3.47%	-0.37 [-0.55, -0.18]
Rahbarimanesh et al 2019	Iran	⊢	2.55%	-0.48 [-0.72, -0.24]
Di Pentima et al 2011	USA	⊢− -1	6.42%	-0.12 [-0.18, -0.06]
Regev-Yochay et al 2011	Israel	⊢■⊣	6.36%	-0.11 [-0.17, -0.04]
Gerber, J. S et al 2013	USA	⊢■⊣	6.63%	-0.07 [-0.12, -0.02]
				-0.21 [-0.36, -0.05]
Outpatients				
Le Corvoisier et al 2013	France	Ħ	7.08%	-0.04 [-0.06, -0.02]
Hürlimann et al 2015	Switzerland	⊢∎⊣	6.39%	0.08 [0.02, 0.14]
March-López et al 2020	Spain	⊦⊷⊣	6.73%	-0.05 [-0.09, 0.00]
McNulty et al 2018	United Kingdom	I -	6.97%	-0.03 [-0.06, 0.00]
Strumann et al 2020	Germany	⊢− -(6.46%	-0.06 [-0.12, -0.00]
Gonzales et al 2013	USA	⊢ i	6.61%	-0.21 [-0.38, -0.04]
Gonzales et al 2013	USA	⊢	9.99%	-0.14 [-0.22, -0.05]
		•		-0.04 [-0.11, 0.03]
Inpatients/Nursing Home				
Chang et al 2020	China	⊢ ∎→1 │	5.40%	-0.17 [-0.27, -0.07]
Fortini et al 2018	Italy	⊢∎⊣	6.42%	-0.06 [-0.12, 0.00]
Fleet et al 2014	United Kingdom	⊢	4.69%	-0.00 [-0.14, 0.13]
W.Van et al 2015	Netherland	ⅠⅠ 1	3.53%	-0.10 [-0.28, 0.08]
		-		-0.08 [-0.20, 0.03]
RE Model		•	100.00%	-0.10 [-0.15, -0.04
		-0.8 -0.6 -0.4 -0.2 0 0.2		
		Subgroup analysis for patient settings		

Figure 2a shows the stratified results for the average change in the proportion of patients receiving an antibiotic prescription in the post-intervention compared to the pre-intervention period. This was calculated as the proportion of all patients that received an antibiotic prescription post-intervention minus the same proportion measured in the pre-intervention period. For randomised controlled trials, pre-intervention differences in the proportion of prescriptions between treatment and control groups were subtracted from post-intervention differences. A negative effect size indicates that ASPs are associated with a reduction in antibiotic prescriptions of magnitude equal to the value of the effect size itself. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets.

B: Forest plot of included studies stratified by income classification (Antibiotic prescriptions)



Subgroup analysis for income clasiification

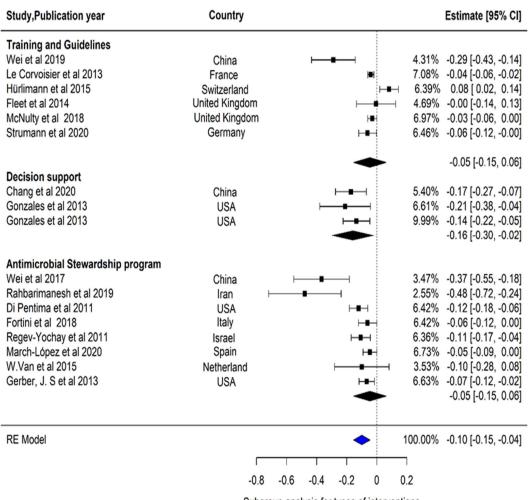
Figure 2b shows the stratified results for the average change in the proportion of patients receiving an antibiotic prescription in the post-intervention compared to the pre-intervention period. This was calculated as the proportion of all patients that received an antibiotic prescription post-intervention minus the same proportion measured in the pre-intervention period. For randomised controlled trials, pre-intervention differences in the proportion of prescriptions between treatment and control groups were subtracted from post-intervention differences. A negative effect size indicates that ASPs are associated with a reduction in antibiotic prescriptions of magnitude equal to the value of the effect size itself. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets.

C: Forest plot of included studies stratified by study settings (Antibiotic prescriptions)

Study,Publication year	Country							Estimate [95% CI]
Public hospital								
Wei et al 2017	China	F	-				3.47%	-0.37 [-0.55, -0.18]
Chang et al 2020	China				+		5.40%	-0.17 [-0.27, -0.07]
Fortini et al 2018	Italy				•		6.42%	-0.06 [-0.12, 0.00]
		-						-0.18 [-0.54, 0.18]
Outpatients/primary care pr	actices							
Wei et al 2019	China		—				4.31%	-0.29 [-0.43, -0.14]
Le Corvoisier et al 2013	France				HHI I		7.08%	-0.04 [-0.06, -0.02]
Hürlimann et al 2015	Switzerland				- H	•	6.39%	0.08 [0.02, 0.14]
Fleet et al 2014	United Kingdom			⊢		-	4.69%	-0.00 [-0.14, 0.13]
March-López et al 2020	Spain						6.73%	-0.05 [-0.09, 0.00]
McNulty et al 2018	United Kingdom				H=-i		6.97%	-0.03 [-0.06, 0.00]
W.Van et al 2015	Netherland						3.53%	-0.10 [-0.28, 0.08]
Strumann et al 2020	Germany			F	•		6.46%	-0.06 [-0.12, -0.00]
Gonzales et al 2013	USA		⊢	-	-		6.61%	-0.21 [-0.38, -0.04]
Gonzales et al 2013	USA				-		9.99%	-0.14 [-0.22, -0.05]
				-	•			-0.06 [-0.13, 0.01]
Pediatric hospital								
Rahbarimanesh et al 2019	Iran	—	•	_			2.55%	-0.48 [-0.72, -0.24]
Di Pentima et al 2011	USA			—	-		6.42%	-0.12 [-0.18, -0.06]
Regev-Yochay et al 2011	Israel				-		6.36%	-0.11 [-0.17, -0.04]
Gerber, J. S et al 2013	USA			H	•		6.63%	-0.07 [-0.12, -0.02]
			-		-			-0.15 [-0.36, 0.05]
RE Model					>		100.00%	-0.10 [-0.15, -0.04]
	-							
	-0.8	-0.6	-0.4	-0.2	0	0.2		
	-0.0			s for study	-			

Figure 2c shows the stratified results for the average change in the proportion of patients receiving an antibiotic prescription in the post-intervention compared to the pre-intervention period. This was calculated as the proportion of all patients that received an antibiotic prescription post-intervention minus the same proportion measured in the pre-intervention period. For randomised controlled trials, pre-intervention differences in the proportion of prescriptions between treatment and control groups were subtracted from post-intervention differences. A negative effect size indicates that ASPs are associated with a reduction in antibiotic prescriptions of magnitude equal to the value of the effect size itself. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets.

D: Forest plot of included studies stratified by intervention types (Antibiotic prescriptions)



Subgroup analysis for types of interventions

Figure 2d shows the stratified results for the average change in the proportion of patients receiving an antibiotic prescription in the post-intervention compared to the pre-intervention period. This was calculated as the proportion of all patients that received an antibiotic prescription post-intervention minus the same proportion measured in the pre-intervention period. For randomised controlled trials, pre-intervention differences in the proportion of prescriptions between treatment and control groups were subtracted from post-intervention differences. A negative effect size indicates that ASPs are associated with a reduction in antibiotic prescriptions of magnitude equal to the value of the effect size itself. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets.(Antimicrobial Stewardship program= multi-component ASPs)

eFigure 3. Subgroup Analyses (Consumption in DDD per 100 Patient-Days)

A. Forest plot of included studies stratified by patient settings (Antibiotic consumption in DDD per 100 patient days)

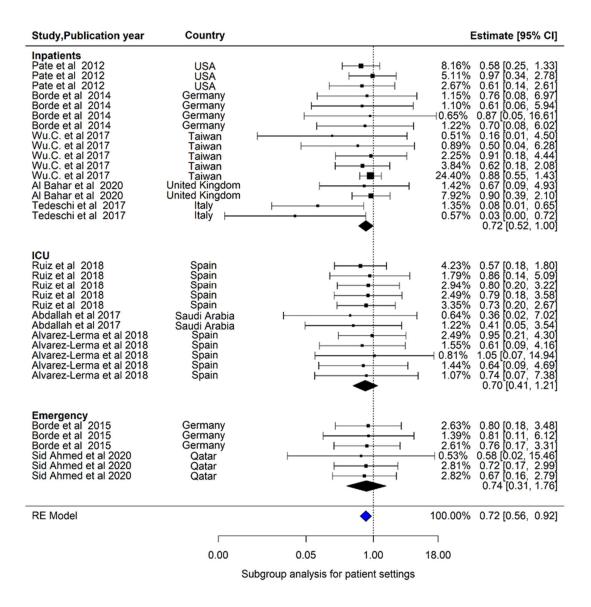


Figure 3a shows the stratified results for the average change in antibiotic consumption post- compared to preintervention. RR:rate ratio. The rate ratio (RR) of antibiotic consumption was obtained by dividing the postintervention consumption rate measured in DDD per 100 PD by the pre-intervention consumption rate. A rate ratio below the value of 1 indicates that ASPs are associated with a reduction of (1-RR) % in antibiotic consumption. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets. (ICU= Patients in intensive care unit, Emergency = Patients in acute care hospital). B. Forest plot of included studies stratified by antibiotic restriction as per individual protocol settings (Antibiotic consumption in DDD per 100 patient days)

Study,Publication year	Country		Estimate [95% CI]
Restricted Pate et al 2012 Borde et al 2014 Borde et al 2015 Borde et al 2015 Borde et al 2015 Borde et al 2015 Borde et al 2018 Ruiz et al 2018 Ruiz et al 2017 Wu.C. et al 2017 Wu.C. et al 2017 Wu.C. et al 2017 Wu.C. et al 2017 Al-Omari et al 2020 Al-Bahar et al 2020 Al-Bahar et al 2020 Sid Ahmed et al 2020 Sid Ahmed et al 2020 Abdallah et al 2020 Pitiriga et al 2018 Pitiriga et al 2018 Pitiriga et al 2018	Carbapenems Macrolides Fluoroquinolones Carbapenems Cephalosporins Macrolides Fluoroquinolones Cephalosporins Daptomycin Linezolid Carbapenems Carbapenems Tigecycline Fluoroquinolones Cephalosporins Carbapenems Fluoropetides Linezolid Cephalosporins Carbapenems Fluoroquinolones Fluoroquinolones Carbapenems		$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Non-restricted Pate et al 2012 Pate et al 2012 Borde et al 2014 Borde et al 2014 Borde et al 2015 Ruiz et al 2018 Ruiz et al 2018 Ruiz et al 2018 Ruiz et al 2018 Ruiz et al 2018 Wu.C. et al 2017 Wu.C. et al 2017 Wu.C. et al 2017 Wu.C. et al 2017 Abahar et al 2020 Abdallah et al 2020 Abdallah et al 2017 Alvarez-Lerma et al 2018 Alvarez-Lerma et al 2018	Fluoroquinolones Echinocandins Cephalosporins Penicillins Penicillins Macrolides Fluoroquinolones Cephalosporins Antifungals Penicillins & BLI Macrolides Penicillins & BLI Penicillins & BLI Linezolid Carbapenems Coljstin Fluoroquinolones Azoles Glycopeptides Macrolides Cephalosporins Penicillins & BLI Penicillins & BLI		$\begin{array}{cccccccccccccccccccccccccccccccccccc$
RE Model		•	100.00% 0.79 [0.66, 0.94]
	ſ	· · · · · · · · · · · · · · · · · · ·	
	0.00	0.05 1.00 20. Subgroup analysis for antibiotic restriction	00

Figure 3b shows the stratified results for the average change in antibiotic consumption post- compared to preintervention. RR:rate ratio. The rate ratio (RR) of antibiotic consumption was obtained by dividing the postintervention consumption rate measured in DDD per 100 PD by the pre-intervention consumption rate. A rate ratio below the value of 1 indicates that ASPs are associated with a reduction of (1-RR) % in antibiotic consumption. Numbers quoted in percentage terms are the weights assigned to each effect size by the three-level random effects model. 95% confidence intervals are included in brackets. Non-restricted= No restriction on antibiotic as per individual protocol). eFigure 4. Meta-analysis Summary (Antibiotic Consumption in DDD per 100 Patient-Days)

Antibiotic classes	RR (95% CI)	Favors ASPs Not favors ASPs
Penicillins & BLI	0.61 (0.24,1.59)	·
Penicillins	0.94 (0.62,1.45)	· · · · · · · · · · · · · · · · · · ·
Macrolides	0.74 (0.20,2.68)	
Fluoroquinolones	0.58 (0.30,1.11)	······
Cephalosporins	0.85 (0.53,1.38)	
Carbapenems	0.69 (0.38,1.25)	·
	0	.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0 Rate ratio (95% CI)
anel B		
AWaRe antibiotic classifi	cation RR (95% CI)	Favors ASPs Not favors ASPs
Access	0.90 (0.65,1.25	· ·
Watch	0.72 (0.56,0.92	
Reserve	0.77 (0.43,1.41	
		0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8 2.0
		D ((050) OI)
		Rate ratio (95% CI)
anel C		Rate ratio (95% CI)
anel C Antibiotic restriction	RR (95% CI)	_
	RR (95% CI) 0.75 (0.57,0.98)	_
Antibiotic restriction		_
Antibiotic restriction Restricted	0.75 (0.57,0.98)	_
Antibiotic restriction Restricted	0.75 (0.57,0.98)	Favors ASPs Not favors ASPs
Antibiotic restriction Restricted	0.75 (0.57,0.98)	Favors ASPs Not favors ASPs
Antibiotic restriction Restricted Non-Restricted	0.75 (0.57,0.98)	Favors ASPs Not favors ASPs
Antibiotic restriction Restricted Non-Restricted	0.75 (0.57,0.98) 0.82 (0.64,1.04)	Favors ASPs Not favors ASPs 0.6 0.8 1.0 1.2 Rate ratio (95% CI)
Antibiotic restriction Restricted Non-Restricted	0.75 (0.57,0.98) 0.82 (0.64,1.04) RR (95% CI)	Favors ASPs Not favors ASPs 0.6 0.8 1.0 1.2 Rate ratio (95% CI)
Antibiotic restriction Restricted Non-Restricted	0.75 (0.57,0.98) 0.82 (0.64,1.04) RR (95% CI) 0.72 (0.52,1.00)	Favors ASPs Not favors ASPs 0.6 0.8 1.0 1.2 Rate ratio (95% CI)
Antibiotic restriction Restricted Non-Restricted	0.75 (0.57,0.98) 0.82 (0.64,1.04) RR (95% Cl) 0.72 (0.52,1.00) 0.70 (0.41,1.21)	Favors ASPs Not favors ASPs 0.6 0.8 1.0 1.2 Rate ratio (95% CI)

Figure 4 5 summarizes stratified results for the change in antibiotic consumption after ASPs in post- to the preintervention period. RR:rate ratio. The rate ratio (RR) of antibiotic consumption was obtained by dividing the postintervention consumption rate measured in DDD per 100 PD by the pre-intervention consumption rate. A rate ratio below the value of 1 indicates that ASPs are associated with a reduction of (1-RR) % in antibiotic consumption. Error bars represents 95% CI and the size of each square represents the pooled effect size. Panel A: Stratified result by antibiotic classes, Panel B: Stratified result by AWaRe WHO antibiotic classification, Panel C: Stratified result by antibiotic restriction, Panel D: Stratified result by patient settings