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Point-of-care testing reduces antibiotic prescribing in acute exacerbations of chronic obstructive pulmonary disease: A systematic review and meta-analysis



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ABSTRACT

Background: Challenges in identifying the causes of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) have led to overuse of antibiotics. The advantages of point-of-care testing (POCT) may help to identify pathogens and use antibiotics more appropriately.

Methods: We conducted a systematic review to evaluate the effect of POCT to guide antibiotic prescriptions for AECOPD. Adhering to a protocol (CRD42024555847), we searched eligible studies. The outcomes included antibiotic-related and clinical outcomes. We evaluated the risk of bias and performed metaanalyses with subgroup based on the type and testing timing of POCT.

Results: A total of 18 studies evaluating 4346 AECOPD patients were included. Overall, POCT significantly reduced the number of AECOPD patients given antibiotic prescriptions by 16% (P < 0.001). Additionally, antibiotic treatment was reduced by 1.19 days (P = 0.04). There was no detrimental impact on clinical outcomes, such as the length of hospital stay (P = 0.19). Our results proved robust to sensitivity analyses. Conclusion: We offered reasonable evidence for using POCT to reduce antibiotic exposure for AECOPD without adversely affecting clinical outcomes. As diagnostic techniques become increasingly important in combating antimicrobial resistance, the use of POCT should be encouraged.

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Introduction

Chronic obstructive pulmonary disease (COPD) imposes a significant global health burden as the third leading cause of death

worldwide. In 2019, COPD was responsible for 3.23 million deaths globally [1]. Each year, approximately half of COPD patients experience one or more acute exacerbations [2], and 50%-80% of these patients receive antibiotic prescriptions-significantly higher than the average antibiotic exposure among individuals with other illnesses [3–5]. However, only about half of all acute exacerbations of COPD (AECOPD) cases are caused by infectious agents, with viruses being the leading cause [6]. Clinicians generally rely on patient symptoms alone to determine whether an AECOPD episode should be treated with antibiotics, but these symptoms can be associated

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with either bacterial or viral etiologies [7,8]. Healthcare professionals often prescribe antibiotics "to be on the safe side" due to concerns about an increased risk of adverse events, such as pneumonia or hospitalization, if antibiotics are withheld [9]. Such practices contribute to the irrational and excessive use of antibiotics, exacerbating the risks of antimicrobial resistance.

Point-of-care testing (POCT) is an effective and highly efficient method of identifying pathogens due to its rapid detection, affordability, and ease of use [10]. A point-of-care biomarker of inflammation such as procalcitonin (PCT) and C-reactive protein (CRP) can aid in diagnosing bacterial infections because these biomarkers increase rapidly during bacterial infections [11]. Other platforms like molecular POCT directly detect a comprehensive range of pathogens, which can potentially assist physicians in determining the cause of deterioration [12]. Such POCT could be very helpful in identifying bacterial cause of AECOPD, thereby encouraging judicious antibiotic use and combating antimicrobial resistance.

Several prior studies have examined the effect of POCT using CRP or PCT on antibiotic prescriptions in acute respiratory tract infections (ARIs) [13,14]. Smedemark et al. [9] found that the use of CRP POCT likely decreases the number of participants receiving antibiotic prescriptions. Mathioudakis et al. [15] drew the conclusion that PCT-based protocols reduce total antibiotic exposure. However, these reviews only looked at specific biomarkers without a specific focus on AECOPD.

To date, it is still not clear whether POCT benefits AECOPD patients in reducing antibiotic use and how. Therefore, our aim was to conduct a systematic review and meta-analysis to evaluate the effectiveness and safety of different POCTs in guiding antibiotic prescribing for the treatment of AECOPD.

Methods

Search strategy

This systematic review and meta-analysis was conducted with a Protocol Registered on the International Prospective Register of Systematic Reviews (PROSPERO), under the registration number CRD42024555847. This review was done following the Cochrane Handbook for Systematic Reviews of Interventions and the PRISMA 2020 guidelines.

Our systematic search strategy, detailed in Appendix 1, was meticulously designed to retrieve English-language studies involving human subjects in the Medline, Web of Science, Embase, Scopus, and Cochrane Library databases from their inception up to March 2024. The search encompassed a broad spectrum of Medical Subject Headings (MeSH) and text words, targeting three concepts: COPD, antibiotics, and POCT.

Selection criteria

We included randomized controlled trials (RCTs), cluster-RCTs, quasi-RCTs, and cohort studies examining the guiding effect of POCT in reducing antibiotic prescriptions for AECOPD patients, compared to usual care. Preprints, reviews, letters, editorials, protocols, conference abstracts, and trial registry records were excluded, as well as those with no full text available. We defined POCT as a diagnostic test conducted at or near the patient's care, where the result can lead to improved health outcomes in a fast turnaround time [16], without restrictions on any particular technology or method. Studies that merely mentioned test information but did not consider it as POCT were excluded. Our participant criteria encompassed patients diagnosed clinically with AECOPD, following Anthonisen criteria [17], of any condition duration or severity. However, patients with immunodeficiencies, chronic infections

requiring long-term antibiotic treatment, and individuals on immunosuppressant medications were excluded.

The articles identified were independently screened by two authors (XY Li and SY Qiu) using literature management software (https://www.rayyan.ai/), according to titles and abstracts, followed by eligibility assessment through full texts. Any discrepancies were resolved through discussion, and a third party (LP Yang) provided adjudication where consensus was not achieved.

Outcome measures

The antibiotic-related outcomes included: 1) antibiotic prescription rate, defined as the proportion of patients who were prescribed antibiotics; 2) duration of antibiotic treatment; 3) duration of intravenous antibiotics; and 4) cost of antibiotics per patient. The clinical outcomes included: 1) length of hospital stay; 2) composite adverse event rate, defined as a collection of negative events including antibiotic side effects, combined bacterial infections, worsening of signs and symptoms, and disease-specific complications; 3) ICU (intensive care unit) transfer rate; 4) exacerbation recurrence rate over the observation period; 5) mortality over the observation period; 6) all-cause readmission rate over the observation period; and 7) readmission rate due to exacerbation over the observation period.

We proposed the hypotheses that POCT-guided care could lead to a notable reduction in antibiotic exposure and associated costs while not jeopardizing the clinical treatment outcomes of the patient compared to usual care.

Data abstraction

Essential information was extracted from each eligible study, including author, year, country, country income, region, study design, study duration, sample size, healthcare setting, and age of participants. In addition, we collected intervention information such as the type, testing timing, and adherence to POCT guidance, together with observation period. Predefined outcomes were also recorded. If information could not be obtained, we did not impute missing data and only used studies with accessible data in the corresponding analysis process.

Two authors (XY Li and SY Qiu) independently extracted the information from eligible studies in a data extraction table, followed by cross-checking each other's work. A third party (LP Yang) would be involved to resolve any question if there were inconsistencies.

Risk of bias and quality of evidence

For RCTs, cluster-RCTs, and quasi-RCTs, we reached a risk-ofbias judgment based on the Cochrane Handbook [18], considering seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each domain was rated as low risk, high risk, or unclear. The blinding of outcome assessment was deemed not to affect the judgment of outcome measures by evaluators if there were no subjective indicators; otherwise, the risk of detection bias was recorded as high. Considering the impossibility to conceal the intervention from participants and care providers, trials were determined to be at low overall risk of bias if they had a low risk in at least five of the other six quality domains.

For cohort studies, the Newcastle–Ottawa Scale [19] was employed to assess the risk of bias, focusing on three dimensions of study quality: selection, comparability, and outcome. Each domain was scored on a scale from 1 to 3. A summed score was calculated, with a score of 7-9 indicating high quality, 4-6 indicating moderate quality, and a score of less than 4 indicating low quality.

Data analysis

Meta-analyses were used to estimate the outcome measures. Data were combined using random-effect models when heterogeneity was deemed significant, as determined by $I^2 > 50\%$ [18]; otherwise, fixed-effect models were used. Notable heterogeneity, as signified by $I^2 > 50\%$, was subjected to further investigation through subgroup analyses. These analyses were also aligned with prespecified categories based on the type and timing of POCT. Results were presented in the form of risk difference (RD) (95% CI) for dichotomous indicators and in the form of mean differences (MD) or standard mean differences (SMD) (95% CI) for continuous indicators. Mean and standard deviation (SD) were used to describe characteristics of included participants. When only median and IQR or range were reported, we estimated the mean and SD using the methods described by Luo et al. [20] and Wan et al. [21].

To assess how study quality might influence the outcomes, sensitivity analyses were conducted by including only studies with low risk of bias or high quality or restricting to studies with RCT design only. In addition, the effect size was changed to risk ratio for dichotomous data to strengthen statistical persuasion.

Meta-analyses were performed using Review Manager 5.4, with statistical significance being set at a *P*-value threshold of less than 0.05.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Characteristics of the included studies

Among 8760 search results returned from databases, 174 proceeded to full-text screening. Ultimately, 18 studies (see references list in Appendix 2) evaluating 4346 AECOPD patients met the inclusion criteria (Figure 1). Characteristics of each study are in the Appendix 3. Eleven studies recruited only patients with AECOPD, while six studies recruited patients with lower respiratory tract infections (LRTIs), and one study recruited patients with ARIs in general but included well-characterized subsets of patients with AECOPD. Most included studies were RCTs (n = 13), while five were cohort studies (Table 1). Seventeen studies reported the age of participants: An average of 66.59 (SD = 2.09) years in the POCT group compared to 66.46 (SD = 3.77) years in the usual care.

The type of POCT intervention was distributed as follows: 12 studies used PCT, 3 studies used CRP, 1 study used neutrophillymphocyte ratio (NLR), and 2 studies used molecular POCT. The



Figure 1. PRISMA flow diagram.

Table 1

Characteristics of included studies.

	St	udies $(n = 18)$
	n	Proportion (%)
Study design, n (%)		
RCT	13	72.22
Cohort study	5	27.78
Country income ^a , n (%)		
High income	16	88.89
Upper middle income	2	11.11
Region, n (%)		
East Asia and Pacific	1	5.56
Europe and Central Asia	13	72.22
North America	4	22.22
Healthcare setting, n (%)		
Hospital	16	88.89
Primary care	2	11.11
Disease classification, n (%)		
COPD	11	61.11
LRTI including COPD	6	33.33
ARI including COPD	1	5.56
Type of POCT, n (%)		
PCT	12	66.67
CRP	3	16.67
NLR	1	5.56
Molecular POCT	2	11.11
Testing of POCT, n (%)		
<5 min	3	16.67
5 min to 2 h	8	44.44
>2 h	4	22.22
Unknown	3	16.67
Observation period, n (%)		
<30 days	7	38.89
1 month to 1 year	7	38.89
Unknown	4	22.22

^a Country income is classified by World Bank's country classification system.

testing timing of POCT in 3 studies was less than 5 min, 8 studies between 5 min to 2 h, and 4 studies more than 2 h (Table 1).

POCT was used to direct the initiation of antibiotic treatment in 6 studies, discontinuation in 2 studies, and both initiation and discontinuation in 10 studies. Antibiotics were encouraged for PCT levels >0.25 μ g/L and discouraged for levels <0.25 μ g/L in all 12 studies using PCT. However, there was no consistent cut-off point for CRP-POCT: Two studies used CRP levels higher than 50 mg/L and 100 mg/L, respectively, for initiation of antibiotics, while another study suggested that antibiotics may be beneficial for CRP levels between 20 and 40 mg/L and are likely to be beneficial above 40 mg/L. The only NLR study advised antibiotic prescriptions when NLR \geq 4, and no algorithm was reported for Molecular POCT studies. Adherence to POCT guidance was reported in only 3 PCT studies, which differed significantly, ranging from 49.2% to 61.29%.

Risk of bias assessment

The overall risk of bias of RCTs was low (Appendices 4 and 5): Seven were deemed to have low risk of bias. The blinding of outcome assessment was not conducted in 3 studies, indicating a high risk of detection bias. Additionally, selection bias was unclear in 6 studies.

All 5 cohort studies were identified with a score of 7-9, indicating high quality (Appendix 6).

Changes in antibiotic prescribing

Overall, we observed a significant reduction in antibiotic exposure in the POCT group. Thirteen studies, including 3260 participants, reported antibiotic prescription rates. The pooled result showed that POCT was associated with a likely reduction of 16% in antibiotic prescriptions for patients with AECOPD (RD –0.16, 95% CI –0.22 to –0.10; $l^2 = 75\%$). Meta-analysis excluding the 3 non-RCT studies generated a consistent result (RD –0.16, 95% CI –0.23 to –0.08; $l^2 = 79\%$) (Appendix 7). PCT guidance led to a 22% decrease in antibiotic prescriptions (RD –0.22, 95% CI –0.32 to –0.12; $l^2 = 76\%$), making it the largest contributor among all types of POCT. Meanwhile, CRP-guided management showed a 15% reduction (RD –0.15, 95% CI –0.22 to –0.08; $l^2 = 44\%$). A single study involving NLR-guided antibiotic use also demonstrated a lower antibiotic prescription rate (RD –0.14, 95% CI –0.21 to –0.07).

However, there was no significant difference between the molecular POCT group and usual care (RD -0.03, 95% Cl -0.15 to 0.08; $l^2 = 70\%$) (Figure 2, Table 2).

Subgroup analyses showed a 15% reduction in antibiotic prescriptions (RD -0.15, 95% CI -0.22 to -0.08; $l^2 = 44\%$) among those undergoing POCT within 5 min and a 20% reduction (RD -0.20, 95% CI -0.31 to -0.09; $l^2 = 81\%$) among those undergoing POCT between 5 min to 2 h. However, there were no significant reductions (RD 0.02, 95% CI -0.06 to 0.11) observed among those undergoing POCT after 2 h compared to the controls (Figure 3, Table 2).

The duration of antibiotic treatment was assessed in 7 studies involving a total of 1703 patients. The POCT groups showed a significant reduction of 1.19 days in the duration of antibiotic treatment compared to usual care (MD –1.19, 95% CI –2.29 to –0.08; $I^2 = 83\%$) (Table 2, Appendix 8). Specifically, there was a notable decrease in the molecular POCT group, with a decrease of 1.90 days (MD –1.90, 95% CI –3.18 to –0.62).

Studies assessing the duration of intravenous antibiotics showed a reduction of 0.73 days in POCT groups compared to usual care (MD -0.73, 95% CI -1.17 to -0.30; $l^2 = 51\%$). One study reported intravenous antibiotic prescription rate, showing no significant reduction (RD -0.02, 95% CI -0.09 to 0.04).

Additionally, a significant reduction in the cost of antibiotics (SMD -0.44, 95% CI -0.65 to -0.23; $I^2 = 0\%$) was found in association with POCT intervention (Table 2).

Clinical outcomes

Overall, our findings indicate that the implementation of POCT did not significantly impact the clinical outcomes of patients when compared to usual care. The length of hospital stay was reported in 13 trials involving 2738 patients. The average lengths ranged from 2.9 to 13.7 days in POCT groups and from 4.1 to 10.8 days in the usual care groups. There was no statistically significant difference observed between the two groups (MD -0.38, 95% CI -0.95 to 0.19; $l^2 = 68\%$). Similar results were observed for PCT, CRP, and NLR POCT, whereas molecular POCT showed a noteworthy decrease in the length of hospital stay (MD -1.37, 95% CI -2.20 to -0.55; $l^2 = 0\%$). These results did not change by testing timing (Table 3, Appendix 9).

Studies assessing the rate of composite adverse events showed no significant difference between the POCT and control groups (RD -0.01, 95% CI -0.04 to 0.02; $l^2 = 0$ %). Similarly, no significant difference was found in the ICU transfer rate (RD 0, 95% CI -0.02 to 0.02; $l^2 = 0$ %). Rates of re-exacerbation over the observation period did not differ significantly between the POCT and usual care groups (RD 0.05, 95% CI -0.02 to 0.12; $l^2 = 0$ %). No significant differences in the rates of all-cause re-admission and re-admission due to exacerbation were found between POCT and usual care groups, with an RD of 0.01 (95% CI -0.02 to 0.04; $l^2 = 0$ %) and -0.03 (95% CI -0.07 to 0.02; $l^2 = 57$ %), respectively. No significant differences in mortality were found between POCT and usual care groups in both short-term (RD 0, 95% CI -0.02 to 0.02; $l^2 = 0$ %) and long-term (RD 0, 95% CI -0.03 to 0.02; $l^2 = 26$ %).

	POCT t	est	Usual c	are		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
1.1.1 PCT							
Christ-Crain M, 2004	11	29	27	31	4.4%	-0.49 [-0.70, -0.28]	
Corti C, 2016	36	62	43	58	5.7%	-0.16 [-0.33, 0.01]	
Huang DT, 2018	191	265	200	259	9.3%	-0.05 [-0.13, 0.02]	
Nguyen LJ, 2021	49	77	61	73	6.8%	-0.20 [-0.34, -0.06]	
Picart J, 2016	42	121	73	124	7.4%	-0.24 [-0.36, -0.12]	
Schuetz P, 2009	56	115	79	113	7.3%	-0.21 [-0.34, -0.09]	
Stolz D. 2007	41	102	76	106	7.1%	-0.32 [-0.44, -0.19]	
Subtotal (95% CI)		771		764	48.0%	-0.22 [-0.32, -0.12]	\bullet
Total events	426		559				
Heterogeneity: Tau ² =	0.01: Chi ² :	= 25.42	2. df = 6 (F	= 0.0	003): l ² = 7	76%	
Test for overall effect:	Z = 4.41 (P	P < 0.00	001)		,,		
			,				
1.1.2 CRP							
Butler CC, 2019	150	263	212	274	9.1%	-0.20 [-0.28, -0.13]	
Prins HJ, 2019	32	101	55	119	7.2%	-0.15 [-0.27, -0.02]	
Strykowski DF, 2015	210	282	105	125	9.0%	-0.10 [-0.18, -0.01]	
Subtotal (95% CI)		646		518	25.3%	-0.15 [-0.22, -0.08]	\bullet
Total events	392		372				
Heterogeneity: Tau ² =	0.00; Chi ² :	= 3.59,	df = 2 (P	= 0.17); I ² = 44%		
Test for overall effect:	Z = 4.10 (P	v < 0.00	001)				
1 1 3 Molecular POCI	r						
Propdick NLL 2017	75	01	75	02	0 00/	0.02[0.06_0.11]	
Shangahan D. 2010	75	01	10	100	0.0 /0		
Subtotal (95% CI)	00	90 179	90	100	0.0%	-0.09 [-0.19, 0.00]	
Total overte	155	175	172	131	17.570	-0.03 [-0.13, 0.00]	
Hotorogonoity: Tou ² -	100 0.00. Chi2.	- 2 20	173 df = 1 (D	- 0.07	12 - 60%		
Telefogeneily. Tau	0.00, CHE ·	-3.20,	ui – i (P	- 0.07), 1 09%		
rest for overall effect.	Z – 0.56 (P	- 0.57)				
1.1.4 NLR							
Kabil NK, 2023	83	96	95	95	9.4%	-0.14 [-0.21, -0.07]	
Subtotal (95% CI)	00	96	00	95	9.4%	-0.14 [-0.21, -0.07]	\bullet
Total events	83		95				
Heterogeneity: Not apr	olicable						
Test for overall effect:	Z = 3.77 (P	e = 0.00	002)				
T-4-1 (05% OI)		4000		4500	400.00	0.40 0.00 0.401	
Total (95% CI)	4050	1092	4.400	1208	100.0%	-0.10 [-0.22, -0.10]	▼
l otal events	1056		1199	-			
Heterogeneity: Tau ² =	0.01; Chi ²	= 48.35	o, df = 12	(P < 0.0	00001); l²	= 75%	-1 -0.5 0 0.5 1
Test for overall effect:	Z = 5.44 (P	° < 0.00	0001)				Favours [POCT test] Favours [Usual care]
Test for subaroup diffe	rences: Ch	$i^2 = 6.2$	25. df = 3	(P = 0.7)	10). $l^2 = 52$	2.0%	

Figure 2. Random-effects forest plot of the effect of POCT intervention on antibiotic prescribing rate by POCT type. df, degrees of freedom; M–H, Mantel–Haenszel method; Tau², variability in the underlying true effects.

|--|

Meta-analyses of overall effects of POCT on antibiotic-related outcomes.

	Studies (n)	Participants (n)	RD/MD/SMD (95% CI)	I² (%)	Р
Antibiotic prescription rate	13	3260	$-0.16(-0.22, -0.10)^{a}$	75	< 0.001
Intravenous antibiotic prescription rate	1	524	$-0.02(-0.09, 0.04)^{a}$	NA	0.50
Duration of antibiotic treatment					
Overall result	7	1703	$-1.19(-2.29, -0.08)^{b}$	83	0.04
Type of POCT					
PCT	6	1539	$-1.07(-2.35, 0.22)^{b}$	85	0.10
Molecular POCT	1	164	$-1.90(-3.18, -0.62)^{b}$	NA	0.004
Testing of POCT					
5 min to 2 h	6	1539	$-1.07(-2.35, 0.22)^{b}$	85	0.10
>2 h	1	164	$-1.90(-3.18, -0.62)^{b}$	NA	0.004
Duration of intravenous antibiotics	2	511	$-0.73(-1.17, -0.30)^{b}$	51	0.001
Cost of antibiotics	3	366	$-0.44(-0.65, -0.23)^{c}$	0	< 0.001

CI, confidence interval; MD, mean difference; NA, not available; NR, not reported; RD, risk difference; SMD, standardized mean difference.

^a Refers to RD.
 ^b Refers to MD.
 ^c Refers to SMD.

	POCT t	est	Usual c	are		Risk Difference	Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.2.1 <5min							
Butler CC, 2019	150	263	212	274	9.1%	-0.20 [-0.28, -0.13]	
Prins HJ, 2019	32	101	55	119	7.2%	-0.15 [-0.27, -0.02]	
Strykowski DF, 2015	210	282	105	125	9.0%	-0.10 [-0.18, -0.01]	
Subtotal (95% CI)		646		518	25.3%	-0.15 [-0.22, -0.08]	▼
Total events	392		372				
Heterogeneity: $Tau^2 = 0$	0.00; Chi ² :	= 3.59,	df = 2 (P	= 0.17)	; I ² = 44%		
Test for overall effect: Z	2 = 4.10 (P	° < 0.00	001)				
1 2 2 Emin 2h							
Christ Croin M 2004	4.4	20	07	04	4 40/	0 40 [0 70 0 20]	
Contist-Crain M, 2004	26	29	27	51	4.4%	-0.49 [-0.70, -0.28]	
Corti C, 2016	101	265	40	250	0.20/		_ _
Sobustz B 2000	191	205	200	112	9.3%	-0.05[-0.13, 0.02]	
Schuelz P, 2009 Shangahan D, 2010	90	115	79	100	7.3%		
Shengchen D, 2019	41	102	90	100	7 10/		
Subtotal (95% CI)	41	671	70	675	1.1% 12 3%	-0.32 [-0.44, -0.19]	
Total events	415	0/1	523	0/5	42.570	-0.20 [-0.01, -0.03]	•
Heterogeneity: $Tau^2 = 0$	- 10 0.01: Chi² :	= 25.68	df = 5 (F)		001)· I² = 8	1%	
Test for overall effect: 7	' = 3.53 (P	= 20.00	5, ui – 5 (F 104)	- 0.00	<i>J</i> 01 <i>)</i> , 1 – C	1170	
	. – 0.00 (i	- 0.00	,04)				
1.2.3 >2h							
Brendish NJ, 2017	75	81	75	83	8.8%	0.02 [-0.06, 0.11]	- <u>+</u>
Subtotal (95% CI)		81		83	8.8%	0.02 [-0.06, 0.11]	•
Total events	75		75				
Heterogeneity: Not app	licable						
Test for overall effect: Z	2 = 0.51 (P	? = 0.61)				
1.2.4 NR							
Kabil NK, 2023	83	96	95	95	9.4%	-0.14 [-0.21, -0.07]	
Nguyen LJ, 2021	49	77	61	73	6.8%	-0.20 [-0.34, -0.06]	
Picart J, 2016	42	121	73	124	7.4%	-0.24 [-0.36, -0.12]	
Subtotal (95% CI)		294		292	23.6%	-0.18 [-0.26, -0.10]	▼
Total events	174		229				
Heterogeneity: Tau ² = 0	0.00; Chi² =	= 3.40,	df = 2 (P	= 0.18)	; I² = 41%		
Test for overall effect: Z	2 = 4.43 (P	° < 0.00	0001)				
Total (95% CI)		1692		1568	100.0%	-0.16 [-0.22, -0.10]	◆
Total events	1056		1199	00.0.0	. 6 Augustalis		
Heterogeneity: $Tau^2 = 0$).01: Chi² :	= 48.35	5. df = 12 (P<0.0)0001): I ² :	= 75%	
Test for overall effect: 7	(= 5.44 (P	< 0.00	0001)				-1 -0.5 0 0.5 1
Test for subgroup differ	Test for subgroup differences: Chi ² = 15.52 df = 3 (P = 0.001) l ² = 80.7% Favours [POCT test] Favours [Usual care]						

Figure 3. Random-effects forest plot of the effect of POCT intervention on antibiotic prescribing rate by POCT timing. df, degrees of freedom; M–H, Mantel–Haenszel method; Tau², variability in the underlying true effects.

Sensitivity analysis

We conducted sensitivity analyses by restricting included studies to the 7 RCTs with low risk of bias and the 5 cohort studies of high quality. The analyses confirmed all of the findings, including the effects of POCT in reducing antibiotic prescription rates (RD -0.14, 95% CI -0.20 to -0.07; $I^2 = 67\%$), and shortening the duration of antibiotic treatment (MD -1.66, 95% CI -2.93 to -0.38; $I^2 = 79\%$) (Appendices 10, 11, 13), without jeopardizing the clinical outcomes (Appendices 12 and 13). Additionally, the analyses using risk ratios for dichotomous data did not change the direction of the results either (Appendix 14).

Discussion

In this systematic review and meta-analysis, we found POCT significantly reduced antibiotic exposure in AECOPD patients by decreasing prescription rates and treatment durations. It also enabled early discontinuation of antibiotics when patients had already been prescribed antibiotics before obtaining POCT results, leading to shorter treatment durations. Clinical outcomes like hospital stay, re-exacerbation rate, and mortality were not negatively affected by reduced antibiotic use. These benefits were consistent across POCT types and remained in sensitivity analyses.

AECOPD has diverse causes, including bacteria and viruses, often prompting antibiotic therapy. Approximately 70% of AECOPD cases are caused by infections, with pathogenic respiratory viruses accounting for roughly half of these infections [22]. While antibiotics benefit AECOPD patients by potentially shortening recovery, reducing relapses, treatment failure, hospitalization duration, and extending time to next exacerbation, unnecessary antibiotic use contributes to antimicrobial resistance [23]. Therefore, reducing antibiotic use with safety is a global imperative. POCT plays a crucial role by rapidly identifying AECOPD causes and guiding rational use of antibiotics.

Our results are consistent with a number of similar studies on this topic. Mathioudakis et al. [15] found PCT-based protocol reduced antibiotic prescriptions and total antibiotic exposure in AE-COPD patients without adverse effects on clinical outcomes. Simi-

Table 3

Meta-analyses of c	overall effects	of POCT on	clinical outcomes	s.
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	Studies (n)	Participants (n)	RD/MD (95% CI)	I ² (%)	Р
Length of hospital stay		,			
Overall result	13	2738	$-0.38(-0.95, 0.19)^{b}$	68	019
Type of POCT	10	2,50	0.50(0.655, 0.15)	00	0110
PCT	9	1957	$-0.36(-1.12, 0.41)^{b}$	68	0.36
CRP	1	220	$0.60(-0.32, 1.52)^{b}$	NA	0.20
Molecular POCT	2	370	$-1.37(-2.20, -0.55)^{b}$	0	0.001
NLR	1	191	$0.20(-0.45, 0.85)^{b}$	NA	0.55
Testing of POCT					
<5 min	1	220	0.60 (-0.32, 1.52) ^b	NA	0.20
5 min to 2 h	7	1651	$-0.33 (-1.22, 0.56)^{b}$	74	0.47
>2 h	3	431	$-1.30 (-2.70, 0.10)^{b}$	64	0.07
Unknown	2	436	0.13 (-0.46, 0.72) ^c	0	0.67
Composite adverse event rate	9	2397	$-0.01(-0.04, 0.02)^{a}$	0	0.51
ICU transfer rate	4	643	$0(-0.02, 0.02)^{a}$	0	0.96
Exacerbation recurrence rate	4	596	$0.05(-0.02, 0.12)^{a}$	0	0.14
1 month to 1 year	4	596	$0.05(-0.02, 0.12)^{a}$	0	0.14
All-cause readmission rate	10	2531	$0.01(-0.02, 0.04)^{a}$	0	0.57
<30 days	4	930	0(-0.05, 0.05) ^a	13	0.87
1 month to 1 year	5	1356	$0.01(-0.03, 0.04)^{a}$	0	0.64
Unknown	1	245	$0.05(-0.05, 0.16)^{a}$	NA	0.31
Readmission due to exacerbation rate	4	794	$-0.03(-0.07, 0.02)^{a}$	57	0.29
<30 days	2	311	$-0.08(-0.17, 0)^{a}$	39	0.05
1 month to 1 year	2	483	$0.01(-0.04, 0.07)^{a}$	36	0.66
Mortality	11	2756	$0(-0.02, 0.02)^{a}$	0	0.95
<30 days	4	938	$0(-0.02, 0.02)^{a}$	0	0.82
1 month to 1 year	6	1573	$0(-0.03, 0.02)^{a}$	26	0.76
Unknown	1	245	$0.01(-0.05, 0.07)^{a}$	NA	0.74

CI, confidence interval; MD, mean difference; NA, not available; NR, not reported; RD, risk difference.

^a Refers to RD.

^b Refers to MD.

^c Refers to SMD.

larly, Li et al. [24] also reported fewer antibiotic prescriptions with PCT, demonstrating comparable efficacy and safety to standard antibiotic therapy for AECOPD. However, there was limited research on the use of CRP to guide antibiotic in AECOPD patients. While CRP-POCT has shown significant reductions in antibiotic prescribing for LRTIs, its impact on AECOPD remains uncertain. Notably, Butler et al. [25], conducted a multicenter, randomized, controlled trial involving primary care clinic patients with AECOPD, concluding that CRP-guided antibiotic prescribing led to lower antibiotic use without evidence of harm.

Our subgroup analysis of POCT testing timing showed reduced antibiotic prescriptions in groups receiving results under 5 min and 5 min to 2 h, suggesting quicker results lead to lower prescribing rates. We also find no negative effects on clinical outcomes and minimal heterogeneity. Despite limited data, we noted lower antibiotic costs in the POCT group but did not analyze costeffectiveness due to data constraints. A prolonged hospital stay is the primary contributor to high patient care costs; however, we did not find a reduction in hospital stays associated with POCT. Therefore, the overall cost-effectiveness of POCT remains uncertain despite its potential to reduce inappropriate antibiotic prescriptions [26]. This underscores the need for future cost-effectiveness studies on POCT interventions.

Clinicians generally view POCT positively for managing LRTIs, recognizing its ability to enhance diagnostic accuracy. This can help better manage patient expectations and demands for antibiotics. Most patients find the incorporation of POCT into routine care acceptable [27]. However, scaling up POCT testing still presents challenges. Concerns about adherence variability, ranging from 49.2% to 61.29% in our study, have been noted. POCT results are often considered supplementary, with ultimate antibiotic decisions still resting with clinicians, who take multiple factors into account. The rapid results provided by POCT help reduce diagnostic uncertainty, increasing clinicians' confidence in making decisions to reduce antibiotic prescriptions [28,29].

POCT can make a significant contribution to antibiotic stewardship in patients with AECOPD. The effectiveness of POCT-guided antibiotic strategies is likely to improve with the support of guidelines, training, and incentives [30]. Therefore, policymakers and healthcare managers play a crucial role in promoting and implementing POCT measures [31].

To our knowledge, this systematic review and meta-analysis represents the largest sample size and encompasses the most comprehensive types of POCT for AECOPD patients. We innovatively compared different types of POCT to identify the most effective to reduce antibiotic exposure and explored the impact of testing timing, distinguishing between rapid and longer turnaround times. However, the study has several limitations. The included studies were limited to those published in English. Although we identified a small number of studies published in other languages, their inclusion is unlikely to alter the findings.

Unfortunately, information regarding spirometric tests was not always available in the publications. Five studies did not report spirometric testing, 12 studies confirmed its use, and in one study, spirometry testing data was unavailable for 10% of participants. However, all included studies stated that they followed standard diagnostic procedures and criteria.

Regarding the inclusion of patients under the age of 40, 12 studies did not specify this information, while one study explicitly included such patients, and five studies explicitly excluded them. Although many of the included studies did not explicitly state whether individuals under 40 were included, most reported the median (e.g., 70.1 [68.7, 71.5] years) or mean age of participants, suggesting a low likelihood of including individuals under 40.

Furthermore, the relatively small number of included studies limited the scope for detailed subgroup analyses. Additionally, heterogeneity persisted within subgroups, particularly for outcomes related to antibiotic use. Nevertheless, both fixed-effect and random-effect models yielded similar results, suggesting probably tiny impact on overall findings.

Currently researches on molecular POCT and NLR-guided protocols were limited, despite their potential to reduce antibiotic exposure [32]. Although the molecular POCT showed no significant difference in antibiotic prescription rates, there was a notable reduction of 1.90 days in the duration of antibiotic exposure. Patient profile, care setting, and timing of POCT may have influenced its effects. For example, in two studies on molecular POCT involving hospitalized patients who had already received antibiotics before testing, no significant changes in antibiotic prescription rates were expected. However, POCT was anticipated to shorten the duration of antibiotic exposure. Meanwhile, the use of molecular POCT in ambulatory care settings faces challenges due to infrastructure requirements, high cost, high complexity, and low adherence [33]. Current research on molecular POCT remains limited, it is difficult for us to conduct additional analysis. Future studies should be conducted to provide more comprehensive evidence.

POCT is valuable in primary care and remote areas with limited lab facilities, enhancing weak healthcare systems and access to timely services by offering quick test results for immediate treatment and streamlined care. Unfortunately, most current research has focused on high- and middle-income countries and inpatient settings. Further study is needed on its impact in resource-limited settings and specific effects on primary care and ICU patients.

Despite these limitations, our findings provide compelling evidence supporting the use of POCT to guide antibiotic therapy for AECOPD without adverse effects on clinical outcomes. As efforts to enhance diagnostic techniques continue to combat antimicrobial resistance [34], our study contributes valuable evidence supporting expanded use of POCT in the future.

Author contributions

LPY, XYL, and SYQ designed the study and analysis. CJL, MZZ, XYY, HHX, RNW, SFY, JKZ, SQC, JC, GL, CCB, and LPY have substantial contributions to acquisition of funding, data materials, interpretation of data, and results. LPY, XYL, and SYQ verified, analyzed the data, and drafted the article; CJL, LPY, CCB, and SFY revised it critically for important intellectual content. LPY and CCB supervised this work. LPY, XYL, and SYQ were responsible for the decision to submit the manuscript, and all authors contributed to final approval of the paper.

Ethical approval

Ethical approval does not apply to this article.

Sequence information

Not applicable.

Data sharing

The datasets analyzed during the current study are all publicly available. The materials and datasets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2025.107889.

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