

STUDY PROTOCOL

Official Title: Evaluating a Customised Antibiotic Duration Strategy in Acute Exacerbations of COPD: a Single-Centre, Open-Label, Randomised Non-Inferiority Trial of 7-Day Versus 14-Day Antibiotic Therapy

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Sponsor and trial site: Capital Development Authority (CDA) Hospital Islamabad, Pakistan

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Ethics approval: Institutional Review Board of CDA Hospital Islamabad (IRB-113-07-08-25)

Version history

Version	Date	Summary of changes
1.0	8 July 2026	Original protocol posted on ClinicalTrials.gov: multicentre design with randomisation stratified by site; target enrolment 558 (registry field 502); clinical success at Day 7, Day 14 and Day 30 described in different sections.
2.0	30th September 2026	Single-centre trial at CDA Hospital Islamabad; site stratification removed. Single primary outcome: clinical success at Day 30 (± 3 days) after randomisation; clinical success at Day 14 (± 2 days) is a secondary outcome. Operational definition of clinical success specified (including a ≥ 2 -point reduction in CAT score). Exclusion of patients whose antibiotics for the current exacerbation started >48 hours before randomisation; definition of study days added. Sample size recalculated: 252 per arm, 560 in total including 10% attrition. Statistical methods aligned with statistical analysis plan version 1.1. All changes were made before any participant was enrolled; recruitment is expected to begin in November 2026.

1. Background and rationale

Chronic obstructive pulmonary disease (COPD) ranks among the leading causes of death and disability worldwide. Much of its burden arises from acute exacerbations (AECOPD), episodes in which breathlessness, cough and sputum worsen enough to require a change in treatment and often admission to hospital.¹ Bacterial infection contributes to roughly half of these episodes,² and antibiotics lower the risk of treatment failure, particularly in patients with more severe exacerbations and purulent sputum. In hospitalised patients who are not critically ill, however, the size of the benefit is less certain.^{3,4}

Whether to prescribe an antibiotic and how long to continue it are two different questions. Meta-analyses of randomised trials have found courses of 5 days or fewer to be as effective as longer courses for exacerbations of chronic bronchitis and COPD,^{5,6} and both the Global Initiative for Chronic Obstructive Lung Disease (GOLD) and the American College of Physicians now recommend that treatment should normally last about 5 days.^{1,7} Most of this evidence comes from outpatients in high-income countries, and hospitalised patients continue to receive considerably longer courses in routine practice.⁸

Antimicrobial resistance (AMR) is a leading global cause of death,⁹ and antibiotic consumption in Pakistan is among the highest of all low- and middle-income countries.¹⁰ In a tertiary hospital in Islamabad, more than three-quarters of inpatient encounters involved an antibiotic, far above the level suggested by WHO prescribing indicators,¹¹ and resistance among common bacterial pathogens in Pakistan is widespread.¹² The country's national action plan on AMR calls for more rational antibiotic use,¹³ but there is still no national guidance on how long hospitalised patients with AECOPD should be treated. Decisions are left to individual prescribers and institutions, and courses of 14 days remain common. Every day of antibiotic exposure that brings no clinical benefit still carries a risk of adverse effects and adds selection pressure for resistance.^{14,15}

Biomarker-guided approaches, such as procalcitonin-guided treatment, can safely reduce antibiotic exposure in respiratory infections,¹⁶ but they depend on tests that are not routinely available or affordable in many hospitals in Pakistan. Shortening the planned duration of a course is a simpler alternative, and randomised trials in community-acquired pneumonia have shown that antibiotics can be stopped earlier in hospitalised adults without loss of effectiveness.^{17,18} There is growing support for tailoring the duration of treatment to the patient and the setting rather than defaulting to long fixed courses.¹⁹

A customised antibiotic duration strategy, in which the length of treatment is set deliberately rather than by habit, could avoid unnecessary antibiotic exposure without compromising patient outcomes. Local prescribers may regard an immediate move from 14 to 5 days as too large a step without local evidence. A 7-day course halves current exposure, and its duration threshold and supporting clinical materials were developed with prescribers through a structured consensus process. Evidence on the safety and effectiveness of such a strategy in hospitalised patients in Pakistan is lacking, and this trial is designed to provide it.

2. Objectives and hypotheses

The primary objective is to determine whether a 7-day antibiotic regimen is non-inferior to the conventional 14-day regimen in achieving clinical success at Day 30 after randomisation in adults hospitalised with AECOPD with suspected or confirmed bacterial infection.

The secondary objectives are to compare the two regimens with respect to clinical success at Day 14 after randomisation, time to symptom resolution, antibiotic-related adverse events, treatment failure, relapse,

rehospitalisation and all-cause mortality within 30 days, and total antibiotic consumption in adults hospitalised with AECOPD at a tertiary care hospital in Pakistan.

Let π_7 and π_{14} be the proportions of participants achieving clinical success at Day 30 in the 7-day and 14-day arms. The null hypothesis is that the 7-day regimen is inferior by at least the non-inferiority margin ($H_0: \pi_7 - \pi_{14} \leq -10$ percentage points). The alternative hypothesis is that the 7-day regimen is non-inferior ($H_1: \pi_7 - \pi_{14} > -10$ percentage points).

METHODS AND ANALYSIS

3. Trial design

This is a single-centre, prospective, parallel-group, open-label, randomised controlled non-inferiority trial in which adults with AECOPD are allocated 1:1 to a 7-day antibiotic course (experimental arm) or a 14-day course (active comparator arm). Outcome assessors and the trial statistician are blinded to allocation, following a prospective, randomised, open-label, blinded-endpoint (PROBE) design. The protocol is reported in line with the SPIRIT 2025 statement;²⁰ the completed checklist is provided as the SPIRIT 2025 checklist.

4. Setting

Participants are recruited from the inpatient wards of CDA Hospital Islamabad, a tertiary-level hospital and referral centre in Pakistan with facilities for diagnosing and managing AECOPD. CDA Hospital Islamabad is the sponsor and the sole trial site. The schedule of enrolment, interventions and assessments is shown in table 1, the flow of participants in figure 1 and the follow-up schedule in figure 2.

5. Eligibility criteria

Inclusion criteria. Patients are eligible if they meet all of the following:

1. adults aged 18 years or older;
2. physician-diagnosed COPD, confirmed by post-bronchodilator spirometry ($FEV_1/FVC < 0.70$) where available, or by documented previous spirometry consistent with COPD;
3. a current acute exacerbation of COPD for which the treating physician judges antibiotic therapy to be necessary, with at least two of the three cardinal symptoms (increased dyspnoea, increased sputum volume, increased sputum purulence);
4. able and willing to give written informed consent and to follow the study procedures and follow-up schedule.

Exclusion criteria. Patients are excluded if any of the following applies:

1. a documented infection that requires a defined, longer antibiotic course, such as pneumonia with complications, an exacerbation of bronchiectasis, lung abscess or empyema;
2. need for immediate admission to intensive care or for invasive mechanical ventilation at presentation;
3. severe immunosuppression, for example neutropenia, active malignancy under chemotherapy, organ transplantation or advanced HIV infection;

4. suspected or confirmed pulmonary tuberculosis, or another respiratory infection that needs a different antimicrobial approach;
5. pregnancy or breastfeeding;
6. previous enrolment in this trial, or current participation in another interventional trial in AECOPD;
7. systemic antibiotic treatment for the current exacerbation started more than 48 hours before randomisation.

6. Interventions

6.1 Trial arms

Participants in the experimental arm receive a 7-day antibiotic course and those in the active comparator arm a 14-day course. To keep the trial pragmatic and applicable to everyday practice, the treating physician chooses the agent according to institutional practice, the suspected cause, available microbiology results and patient factors, drawing on the same range of agents in both arms. Only the planned duration differs between arms. A switch from intravenous to oral therapy with the same or an equivalent agent is permitted and counts towards the allocated duration. The agent, dose, route, frequency, start and stop dates and any change are recorded on the case report form (CRF). Microbiological sampling, patient education, counselling and all other aspects of care are delivered in the same way in both arms, so that the randomised comparison concerns treatment duration alone.

6.2 Definition of study days

Day 0 is the day of randomisation, and every follow-up time point is counted from it, so the time points are the same in both arms. The allocated course is counted from the first dose of systemic antibiotic given for the current exacerbation, which must be no more than 48 hours before randomisation; doses given before randomisation count towards the allocated duration. The allocated course therefore ends no later than Day 7 in the experimental arm and no later than Day 14 in the comparator arm. The primary outcome is assessed at Day 30 (± 3 days), at least 13 days after the last possible dose in the 14-day arm, so both arms are assessed off treatment at the same time point.

6.3 Choice of comparator

The 14-day comparator reflects entrenched usual practice at the trial hospital; it is not an internationally endorsed standard, since GOLD recommends 5 days.¹ The question is whether halving current exposure preserves clinical benefit without an unacceptable loss of effectiveness, for which an active-controlled non-inferiority design is appropriate. The comparator should therefore be read as local usual care rather than as a guideline standard.

6.4 Development of the intervention

Before the trial, the 7-day duration threshold and supporting clinical materials were agreed through a Delphi consensus process.²¹ In January 2026, approximately 30 experts, comprising prescribers, pharmacists and academics from the trial hospital and reference hospitals, took part in three structured rounds to agree the components of the intervention and the supporting materials. Items that had not reached at least 80% agreement by the end of the third round were discarded. This preparatory work shaped the intervention but is not a co-intervention: it involved no trial participants and does not differ between arms.

6.5 Microbiological sampling and susceptibility testing

Blood and sputum samples for culture and antibiotic susceptibility testing are collected from participants in both arms at baseline, before or at the start of treatment. Isolates are tested by the Kirby–Bauer disc-diffusion method in an accredited laboratory:^{22,23} a 0.5 McFarland inoculum is spread on Mueller–Hinton agar, antibiotic discs are applied, plates are incubated at 35°C for 16–18 hours, and zones of inhibition are read against current standardised breakpoints, with quality-control strains in every run. Results are usually available within 48 hours. They may prompt a clinically indicated change of agent in either arm, but they do not change the allocated duration. A change of agent guided by susceptibility results in a participant who is clinically stable is not counted as treatment failure.

6.6 Routine care and contact

Participants in both arms receive the same scheduled ward reviews and telephone contacts. Participants discharged before the end of their allocated course are contacted by telephone to confirm that the course has been completed as prescribed, and all participants are followed up by clinic visit or telephone at Day 30.

6.7 Discontinuation, modification and withdrawal

The allocated course may be stopped or modified because of a serious adverse drug reaction, allergy, intolerance, clinical deterioration, the need to escalate antimicrobial treatment, withdrawal of consent, or any other reason judged necessary by the treating physician or principal investigator. The allocated intervention is discontinued in the event of a serious adverse reaction, treatment failure with the allocated antibiotic, a major protocol deviation or withdrawal of consent. The reasons are documented in full. Participants whose intervention is discontinued remain in follow-up so that their data contribute to the intention-to-treat analysis, unless they withdraw consent for further contact.

6.8 Adherence and concomitant care

Adherence to the allocated duration is supported through counselling, documentation of the stop date in the medical record and clear communication with patients and treating teams. For inpatients, adherence is checked against medication administration charts. For participants discharged before completing their course, it is assessed through prescription review, self-report, pill counts where feasible and follow-up contact. All standard treatments for AECOPD, including bronchodilators, systemic corticosteroids, oxygen and non-invasive ventilation, are permitted. Any non-protocol antibiotic, change of antibiotic class, escalation of treatment or extension beyond the allocated duration is recorded and taken into account in the analysis.

7. Outcomes

Clinical success is assessed at two time points, both counted from randomisation and identical in both arms: at Day 30 (± 3 days) as the primary outcome and at Day 14 (± 2 days) as a secondary outcome. Each is analysed as a single between-arm comparison, and only the Day 30 comparison is confirmatory. Assessments at Day 3–5 and Day 7 are used for monitoring, adherence and safety and are not outcome comparisons. All outcomes are summarised in table 2.

7.1 Primary outcome

The primary outcome is clinical success at Day 30 (± 3 days) after randomisation. It is a binary outcome. A participant is classified as a clinical success only if all of the following criteria are met at the Day 30

assessment: (a) the exacerbation-related signs and symptoms present at baseline (dyspnoea, sputum volume and sputum purulence) have resolved or substantially improved, as judged by the blinded outcome assessor using predefined criteria, together with a reduction of at least 2 points from baseline in the COPD Assessment Test (CAT)²⁴ score, the minimal clinically important difference;²⁵ (b) no additional or alternative systemic antibiotic has been given for a respiratory indication after the allocated course, and the course has not been extended because of lack of improvement; (c) there has been no hospital readmission or emergency department visit for AECOPD; and (d) the participant is alive. Participants who do not meet all four criteria are classified as clinical failures. The outcome is reported as the number and proportion of participants with clinical success in each arm and compared between arms as the risk difference (7-day minus 14-day). Day 30 is the same assessment point in both arms and falls after both allocated courses have been completed, so the comparison reflects the full consequence of stopping treatment earlier, including any relapse after the shorter course.

7.2 Secondary outcomes

1. clinical success at Day 14 (± 2 days) after randomisation, defined as for the primary outcome;
2. time to resolution of exacerbation symptoms (days);
3. incidence of antibiotic-related adverse events and serious adverse events;
4. treatment failure by Day 30, defined as the need for additional or alternative systemic antibiotics because of clinical deterioration or lack of improvement, escalation to non-invasive or invasive ventilation or intensive care after Day 3, or death;
5. relapse by Day 30, defined as a new or worsening exacerbation requiring systemic antibiotics or corticosteroids after initial clinical improvement;
6. rehospitalisation for any cause and for AECOPD within 30 days;
7. all-cause mortality within 30 days;
8. total antibiotic consumption per participant, in defined daily doses (DDD).²⁶

Each secondary outcome is analysed and reported separately. Secondary outcomes are not combined into a composite and are not used to support a claim of non-inferiority.

8. Participant timeline

Potentially eligible patients are screened against the predefined criteria. Once eligibility is confirmed and written consent obtained, baseline demographic and clinical data are recorded, the participant is randomised and the allocated course begins or continues. Assessments take place at baseline (Day 0), during treatment (Day 3–5), at Day 7, at Day 14 and at Day 30; all are counted from randomisation and are identical in both arms. Clinical success is assessed as a secondary outcome at Day 14 and as the primary outcome at Day 30 (table 1, figures 1 and 2).

Table 1 Schedule of enrolment, interventions and assessments

Timepoint	Screening (-t ₁ to 0)	Randomisation (Day 0)	During treatment (Day 3–5)	Day 7 (end of 7-day course)	Day 14 ± 2 (end of 14- day course)	Day 30 ± 3 (follow-up)
Enrolment						
Eligibility screening	X					
Written informed consent	X					

Timepoint	Screening (-t ₁ to 0)	Randomisation (Day 0)	During treatment (Day 3–5)	Day 7 (end of 7-day course)	Day 14 ±2 (end of 14- day course)	Day 30 ±3 (follow-up)
Baseline demographic and clinical data	X					
Blood and sputum cultures	X					
Randomisation (1:1)		X				
Interventions						
Experimental arm: antibiotics for 7 days		Start	→	Stop		
Active comparator arm: antibiotics for 14 days		Start	→	→	Stop	
Assessments						
Clinical signs and symptoms; CAT	X		X	X	X	X
Treatment adherence and protocol compliance			X	X	X	
Antibiotic-related adverse events			X	X	X	X
Treatment failure / additional antibiotics			X	X	X	X
Relapse, rehospitalisation or death					X	X
Secondary outcome: clinical success at Day 14 (both arms)					X	
Primary outcome: clinical success						X

X indicates a scheduled time point. CAT, COPD Assessment Test. All time points are counted from randomisation (Day 0) and are identical in both arms. Day 30 (±3 days) is the primary outcome time point; clinical success at Day 14 (±2 days) is a secondary outcome. Assessments at Day 3–5 and Day 7 are for monitoring, adherence and safety.

Table 2 Trial outcomes and planned analyses

Outcome	Time point	Type	Analysis	Role
Clinical success	Day 30 (±3)	Binary	Risk difference with two-sided 95% Miettinen–Nurminen CI; ITT and PP; margin –10 percentage points	Primary
Clinical success	Day 14 (±2)	Binary	Risk difference, 95% CI	Secondary
Time to resolution of exacerbation symptoms	Up to Day 30	Time to event	Kaplan–Meier, log-rank; Cox hazard ratio	Secondary
Antibiotic-related AEs and SAEs	Up to Day 30	Binary	Risk difference, 95% CI (safety population)	Secondary
Treatment failure	Up to Day 30	Binary	Risk difference, 95% CI	Secondary
Relapse	Up to Day 30	Binary	Risk difference, 95% CI	Secondary
Rehospitalisation (any cause; AECOPD)	Within 30 days	Binary	Risk difference, 95% CI	Secondary
All-cause mortality	Within 30 days	Binary	Descriptive (counts and percentages)	Secondary
Total antibiotic consumption (DDD)	Up to Day 30	Continuous	Median difference (Hodges–Lehmann), 95% CI	Secondary

AE, adverse event; DDD, defined daily doses; ITT, intention-to-treat; PP, per-protocol; SAE, serious adverse event.

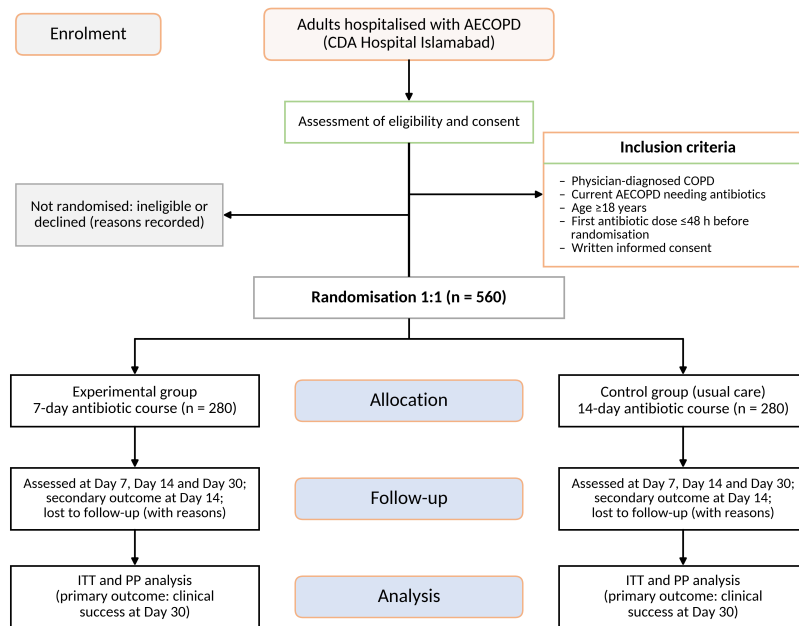


Figure 1. Planned flow of participants through the trial. ITT, intention-to-treat; PP, per-protocol.

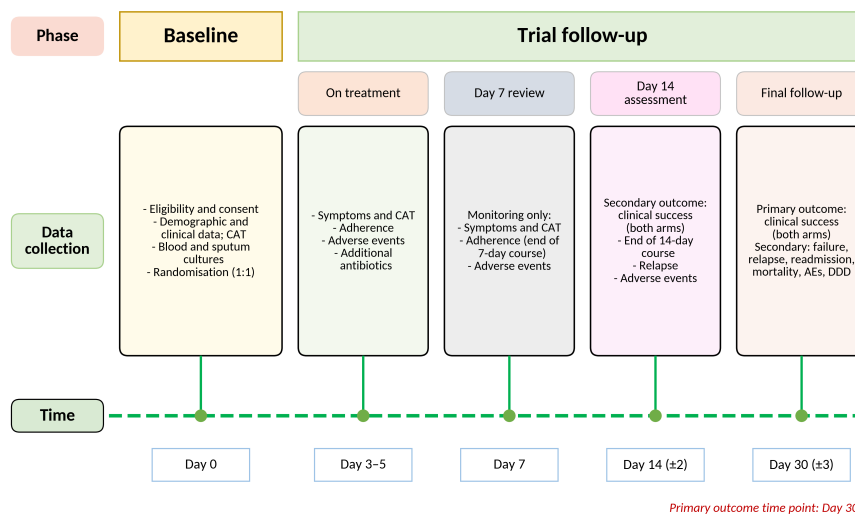


Figure 2 Schedule of assessments and outcome time points. AEs, adverse events; CAT, COPD Assessment Test; DDD, defined daily doses.

9. Sample size

The sample size was calculated for the primary non-inferiority comparison of clinical success at Day 30. We assumed a clinical success proportion of 80% in both arms, a non-inferiority margin (δ) of 10 percentage points, a one-sided type I error rate of 0.025 and 80% power, and used the normal approximation for the difference between two independent proportions:²⁷

$$n = (Z_{1-\alpha} + Z_{1-\beta})^2 \times [pC(1 - pC) + pT(1 - pT)] / [\delta - (pT - pC)]^2$$

where pC and pT are the expected success proportions in the 14-day and 7-day arms. With $pC = pT = 0.80$ and $\delta = 0.10$, $n = (1.960 + 0.842)^2 \times 0.32 / 0.10^2 = 251.2$, rounded up to 252 participants per arm (504 in

total). Allowing for 10% attrition (252/0.90), the target enrolment is 560 participants (280 per arm). Assuming no true difference between the arms is conservative. The calculation relates only to the single primary comparison at Day 30; no other outcome or time point contributed to it, and no adjustment for multiplicity is required. The same target applies to the intention-to-treat and per-protocol populations; the per-protocol result carries particular weight in a non-inferiority trial.

10. Recruitment and retention

Eligible patients are recruited consecutively as they present to CDA Hospital Islamabad. Screening logs record the numbers assessed, enrolled, excluded and withdrawn, with reasons. Retention is encouraged by explaining the follow-up requirements at enrolment, timing study assessments to coincide with routine clinical contacts and sending reminder calls or messages where feasible. Reasons for withdrawal or incomplete follow-up are documented, and participants who stop the intervention continue to be followed for the intention-to-treat analysis wherever consent allows.

11. Assignment of interventions and blinding

11.1 Sequence generation

An independent statistician who has no role in recruitment or clinical care prepares a computer-generated allocation sequence with a 1:1 ratio, using randomly permuted blocks of variable size that are not disclosed to the investigators.

11.2 Allocation concealment and implementation

Allocation is concealed through a password-protected, web-based randomisation system. If the web-based system is unavailable, sequentially numbered, opaque, sealed envelopes prepared by the independent statistician are used instead. The sequence remains hidden from enrolling staff until the moment of allocation. The investigator or trained research staff enrol participants and obtain the allocation immediately after consent and the baseline assessment.

11.3 Blinding

Because the two arms differ in treatment length, participants and treating clinicians cannot be blinded and the trial is open-label. To limit ascertainment and analysis bias, outcome assessors and the trial statistician are blinded to allocation. As no participant is blinded, emergency unblinding procedures are not needed. Outcome assessors are research staff who are not involved in the participant's clinical care, and participants are asked not to disclose their treatment duration at outcome assessments.

12. Data collection and management

A trained multidisciplinary team of pharmacists, medical officers and nurses, blinded to allocation where feasible, collects data on standardised CRFs. Baseline data include age, sex, smoking history, COPD history and severity, comorbidities, previous exacerbations, presenting symptoms, vital signs, relevant laboratory and radiological findings, the indication for antibiotics and treatment details. Follow-up data include adherence, symptom progression, adverse events, additional antibiotic use, relapse, rehospitalisation and death. Educational materials on appropriate antibiotic use are given to patients and prescribers in the same way in both arms. Data are entered into a secure, access-controlled database in

which participants are identified only by a study number, and quality is maintained through staff training, range and consistency checks and periodic central monitoring.

All participant information is handled confidentially in line with institutional and ethical requirements. Direct identifiers are stored separately from coded study data, and no participant will be identifiable in any publication.

13. Statistical methods

All analyses follow the prespecified statistical analysis plan (statistical analysis plan version 1.1) and are carried out by a statistician blinded to allocation.

13.1 Analysis populations

The intention-to-treat (ITT) population includes all randomised participants, analysed in the arm to which they were allocated regardless of treatment received, protocol deviations or early withdrawal. The per-protocol (PP) population includes randomised participants who received an antibiotic course consistent with their allocated duration (± 2 days), had no major protocol deviation affecting assessment of the primary outcome, and have primary outcome data at Day 30. The safety population includes all randomised participants who received at least one dose of study antibiotic, analysed according to the treatment actually received.

13.2 Primary analysis

The difference between arms in the proportion achieving clinical success at Day 30 (7-day minus 14-day) will be estimated with its two-sided 95% CI calculated by the Miettinen–Nurminen method.²⁸ Non-inferiority of the 7-day regimen will be concluded only if the lower limit of the 95% CI lies above -10 percentage points in both the ITT and PP populations; if the two populations disagree, non-inferiority will not be claimed and the discrepancy will be reported and explored. This is the single confirmatory hypothesis of the trial: it concerns one outcome at one time point, is tested at a one-sided α of 0.025 and requires no adjustment for multiplicity. A binomial generalised linear model with an identity link, adjusted for age, sex, baseline CAT score and number of exacerbations in the previous year, will be fitted as a supportive analysis.

13.3 Secondary analyses

Baseline characteristics will be summarised by arm as frequencies and percentages or as means with standard deviations or medians with interquartile ranges, without formal testing of baseline balance. Clinical success at Day 14, treatment failure, relapse and rehospitalisation will be compared using risk differences with 95% CIs; relative risks will also be reported. Time to resolution of exacerbation symptoms will be described with Kaplan–Meier curves and compared with the log-rank test, and a hazard ratio with 95% CI will be obtained from a Cox proportional hazards model. Antibiotic-related adverse events and serious adverse events will be summarised in the safety population and compared using risk differences with 95% CIs. Because deaths are expected to be few, all-cause mortality will be reported descriptively. Total antibiotic consumption will be summarised as median (IQR) and compared with the Mann–Whitney U test, with the Hodges–Lehmann median difference and its 95% CI. A prespecified adjusted analysis of secondary binary outcomes using modified Poisson regression²⁹ will account for the baseline covariates listed above. Secondary outcomes are exploratory, will be reported with 95% CIs without adjustment for multiplicity, and will not be used to support a claim of non-inferiority.

13.4 Missing data

Active follow-up will be used to keep missing data to a minimum. In the primary ITT analysis, participants without a Day 30 clinical success assessment will be classified as treatment failures. A complete-case analysis will be performed as a sensitivity analysis, and if more than 5% of primary outcome data are missing, multiple imputation by chained equations under a missing-at-random assumption will also be undertaken. Participants without an observed event in time-to-event analyses will be censored at their last known status. Protocol deviations, extensions of treatment, early discontinuation, crossover and non-protocol antibiotic use will be recorded and summarised by arm, and the flow of participants will be reported in a CONSORT diagram.

13.5 Interim analyses

No formal interim analysis of efficacy is planned. Accumulating safety data will be reviewed periodically by the data monitoring committee.

14. Monitoring and safety

The principal investigator and trial management team oversee the conduct of the trial, with particular attention to participant safety, protocol adherence, recruitment and data quality. Given that the trial compares antibiotic durations, an independent data monitoring committee has been established to review safety data and advise on whether the trial should continue. Institutional or regulatory authorities may audit the trial independently of the investigators, in line with institutional policy and national regulations.

All adverse events and serious adverse events are recorded and assessed for severity and for their relationship to antibiotic treatment, with particular attention to allergic reactions, gastrointestinal intolerance and clinical deterioration requiring escalation of care or hospitalisation. Serious adverse events are reported to the relevant ethics committees and institutional authorities within the timelines required locally.

15. Ethics and dissemination

15.1 Ethical approval

The protocol has been approved by the Institutional Review Board of Peking University Health Science Center (PUIRB-YS2025262) and by the Institutional Review Board of CDA Hospital Islamabad, the sponsor and trial site (IRB-113-07-08-25). Protocol version 2.0 was approved on [insert date]. The trial is conducted in accordance with the Declaration of Helsinki.

15.2 Consent

Before any study-specific procedure, the investigator or trained research staff obtain written informed consent after giving verbal and written information on the purpose of the trial, the two treatment durations, risks and benefits, confidentiality and the right to withdraw at any time without any effect on routine care. Cultural considerations, including the involvement of family members where appropriate and the participation of women, are respected, but the participant's own consent is always required for enrolment.

15.3 Protocol amendments

Any important change to the protocol, including changes to eligibility, outcomes, procedures or analysis, will be submitted to the ethics committees, communicated to investigators, updated on ClinicalTrials.gov

(NCT07708337) and reported in trial publications. Changes from version 1.0 are summarised in the version history at the start of this document.

15.4 Patient and public involvement

Patients and the public were not involved in designing this protocol. They will be involved during the conduct and dissemination of the trial, including feedback from participants on the acceptability of shorter antibiotic courses and the preparation of a lay summary of the findings.

15.5 Data access and sharing

Access to the de-identified trial dataset is restricted to the principal investigator, designated co-investigators and authorised statisticians. De-identified data will be made available on reasonable request after publication, subject to institutional and ethical approval.

15.6 Dissemination

The findings will be published in peer-reviewed journals and presented at scientific meetings whatever their direction or statistical significance, and will be shared with clinicians, hospital pharmacy and therapeutics committees and policymakers. Authorship will follow the ICMJE criteria.

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