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Pharma Research

An International Peer Reviewed, Indexed Journal

10.62655/s-epub.2022.v14.i01.pp73-82

COST ANALYSIS OF ANTIBIOTIC TREATMENT IN COMMUNITY-ACQUIRED PNEUMONIA

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Article info

Received date:11-07-2021
Accepted date:06-11-2021
Published date:04-02-2022
ISSN;0975-8216

Keywords:

Community-acquired pneumonia, Antibiotic cost, Pharmacoeconomics, Antimicrobial stewardship, Treatment duration

Abstract

Community-acquired pneumonia is a common infection that uses a large share of hospital resources, and the antibiotic itself is only a small part of the expense. This narrative review brings together published evidence on what antibiotic treatment of the condition costs and what drives those costs, including the setting of care, severity, regimen choice, route and duration of therapy, and the downstream effect of resistance. It reports no new data. The literature consistently shows that hospital admission, not drug price, dominates expenditure, and that shorter courses, early oral switch and guideline-concordant therapy can lower spending without worse outcomes. Comparison between studies is limited by differing cost perspectives, currencies and designs, and few analyses capture resistance.

1. INTRODUCTION

Community-acquired pneumonia (CAP) is an infection of the lung parenchyma contracted outside hospital, or within the first two days of admission. It remains one of the commonest reasons for adults to seek emergency care and one of the leading infectious causes of death worldwide [1, 2, 3]. In Europe the number of adults treated for the condition each year is very large, and admission rates climb steeply after the age of 65 [4, 5]. In the United States it accounts for a substantial share of medical admissions, with *Streptococcus pneumoniae* still the bacterial pathogen most often identified [6, 7]. Behind every one of these episodes sits a prescribing decision, usually made before the causative organism is known. The burden of the disease is therefore clinical and financial at the same time, and the two are tied together more

tightly than the drug acquisition price suggests.

Treatment guidelines agree on the broad shape of care: judge severity, start empirical antibiotics promptly, and narrow therapy when a pathogen or a clear response emerges [8, 9, 10]. They say much less about money. A drug that costs little per dose can be expensive if it prolongs the stay, fails and prompts retreatment, or selects resistant organisms. A dearer drug can be economical if it shortens admission or allows discharge from the emergency department. Cost analysis tries to put these trade-offs on a single scale, using methods set out in standard texts and reporting checklists [11, 12, 13]. The pharmacist's view of cost, which tends to stop at the price list, is therefore only one part of a larger picture that includes ward days, monitoring, complications and the downstream effects of resistance.

This review draws on published trials, observational cohorts, economic evaluations and guidelines to describe what antibiotic treatment of CAP costs, which factors move that cost, and where the evidence remains thin. It reports no new data and does not claim a systematic search. The sections that follow deal in turn with the components and methods of cost analysis, empirical regimens, duration and route of therapy, severity and site of care, stewardship and resistance, and the limits of the existing evidence. Where a figure is quoted it comes from the cited source, and where studies disagree the disagreement is stated rather than smoothed over. The intended readers are hospital and community pharmacists, formulary committee members and clinicians who have to defend a prescribing choice on cost as well as on efficacy.

A short note on terminology avoids confusion later. Cost, charge and price are not the same thing: a price is what a supplier asks, a charge is what a provider bills, and a cost is the value of resources actually consumed. Many older pneumonia papers use hospital charges as if they were costs, and charges can overstate resource use by a wide margin. Where this review compares studies, it therefore treats charge-based figures with more caution than micro-costed ones [11, 14]. Currency and price year matter as well, since a figure from the 1990s cannot be set beside one from the 2010s without adjustment. The cost of the drug itself, which pharmacy departments see, differs from the cost of the episode, which finance departments see, and the two rarely move together [14, 15].

2. COST COMPONENTS AND METHODS

Studies of pneumonia costs usually split spending into direct medical costs, direct non-medical costs and indirect costs. Direct medical costs cover admission, nursing time, diagnostics, antibiotics and other drugs, oxygen, and outpatient follow-up. Indirect costs capture lost working days and informal care. The perspective chosen decides what is counted: a hospital budget holder sees ward days, a payer adds readmissions, and a societal analysis adds lost productivity [11, 13]. Bottom-up costing follows individual resource use, whereas top-down approaches divide departmental budgets by activity, and the two can give quite different totals for the same ward [11]. Reporting standards such as the CHEERS statement ask authors to state perspective, time horizon, discount rate and price year, which is exactly the information that is often missing from older pneumonia papers [12].

Where the money goes is fairly consistent from one country to the next. A United Kingdom estimate from the 1990s found that hospital care accounted for the bulk of the total cost of managing adult CAP, with drugs a minor fraction [16]. A Spanish population-based study reached the same conclusion, showing that admission was the main cost driver [17], and a United States analysis from the same period reported that inpatient care made up most of the expenditure [15]. Later reviews for Europe and North America describe the cost of a hospitalised episode as many times that of an episode managed at home [4, 18]. Antibiotic acquisition is therefore rarely the line that matters most, though it is the line that pharmacists and formulary committees control most directly.

That finding changes how an antibiotic should be judged. A saving of a few currency

units on the drug is trivial next to a single avoided hospital day, so the useful question is what a regimen does to length of stay, to the probability of treatment failure, and to the chance of readmission. Treatment failure is expensive in its own right: a failed first-line course means a second prescription, further investigation, sometimes transfer to a higher level of care, and a longer stay [19, 20]. For this reason, analyses that compare drugs only by price per day are of limited use, and the better economic studies follow patients from the first dose to the end of the episode, or at least to a fixed follow-up point such as thirty days.

Modelling extends what a single trial can show. A decision-analytic model lays out the pathway a patient may follow, for example discharge, readmission, ICU transfer or death, attaches a probability and a cost to each branch, and then compares regimens over a defined horizon [14]. The approach is useful when trial follow-up is short or when no trial has measured cost directly, and it allows the effect of uncertain inputs to be explored through sensitivity analysis. Its weakness is that the answer is only as good as the inputs. Many pneumonia models borrow probabilities from trials in younger patients and costs from a different health system, and the result can look more precise than it is. Readers should look for the source of each input before trusting the headline figure [11, 13, 14].

Four broad types of economic evaluation turn up in this literature. Cost-minimisation analysis compares regimens assumed to be equally effective and simply picks the cheaper one. Cost-effectiveness analysis relates the extra cost of one option to the extra health gained, for example per death avoided or per life-year gained. Cost-utility analysis uses quality-adjusted life-years so that very different conditions can be compared. Cost-benefit analysis expresses both sides in money [11, 13]. Most pneumonia studies are cost-minimisation or simple cost-comparison exercises, built on trials designed to show noninferiority, and decision-analytic models are used only occasionally to extend the time horizon [14].

3. EMPIRICAL REGIMENS AND THEIR COST

Guideline regimens differ by setting and severity. For previously healthy outpatients the recommended options include amoxicillin, doxycycline or a macrolide where local pneumococcal resistance is low. For outpatients with comorbidities, and for patients admitted to a general ward, a β-lactam combined with a macrolide or a respiratory fluoroquinolone alone is advised [8, 9, 10]. In severe disease a β-lactam is paired with a macrolide or a fluoroquinolone. The acquisition costs of these regimens span a wide range. Generic amoxicillin and doxycycline are cheap, intravenous combination therapy with a second agent is dearer, and some newer agents are far dearer still. The question for budget holders is whether the dearer choices buy anything that offsets their price, and the trial evidence on this is more reassuring for the cheaper options than might be expected [21, 22, 23].

For adults admitted to hospital with moderately severe disease, two randomised trials bear directly on the cost of combination therapy. A Swiss noninferiority trial found that β-lactam monotherapy was not worse than β-lactam plus macrolide for clinical failure at the end of treatment in moderately severe CAP, although the monotherapy group needed a little more retreatment early on [22]. A Dutch cluster-randomised crossover trial compared β-lactam monotherapy, β-lactam plus macrolide and fluoroquinolone monotherapy, and found that the monotherapy strategy was noninferior for ninety-day mortality [21]. If a second drug can be omitted in a large part of the ward population, the saving across a hospital year is considerable. The main cost-relevant studies are summarised in table 1 and counted by theme in fig. 1.

The picture is less secure for outpatients. A Cochrane review of antibiotics for adult outpatients with CAP concluded that no class of antibiotic had been shown to be superior to another, although the underlying trials were mostly small and old, and many predated current resistance patterns [23]. That reading supports the use of cheap narrow-spectrum drugs where local resistance allows it, but it

cannot be stretched into a claim that all drugs perform alike in every population. Pooled data on the more expensive agents also come largely from trials designed for registration, which enrol selected patients and may not reflect the older, multimorbid patients who dominate admission statistics [20, 24].

Table 1: Published findings relevant to the cost of antibiotic treatment in CAP

Strategy or setting	Principal finding reported	Ref.
Three versus eight days of amoxicillin adults admitted, mild to moderately severe	Clinical success was similar after the short course, with fewer treatment days	[25]
High-dose levofloxacin for five days compared with ten days	Cure rates comparable with the standard longer regimen	[26]
Five days after clinical stability multicentre randomised trial	Shorter treatment noninferior to a longer course in stable patients	[9, 27]
Early intravenous-to-oral switch severe CAP, day three	Similar effectiveness to continued intravenous treatment with a shorter stay	[28]
Critical pathway controlled hospital trial	Fewer days of intravenous therapy and shorter hospital stay without harm	[29]
β-Lactam monotherapy versus combination moderately severe CAP	Monotherapy not worse for clinical failure; slightly more early retreatment	[22]
Three empirical strategies cluster-randomised crossover	β-Lactam monotherapy noninferior for ninety-day mortality	[21]
Guideline-concordant therapy older adults and ICU patients	Associated with lower mortality and shorter stay in observational cohorts	[19, 20]
Outpatient care for low-risk patients emergency department trial	Outcomes comparable with admission and higher patient satisfaction	[30, 31]
Share of total episode cost UK, Spanish and US analyses	Hospital stay accounted for most spending; drugs were a minor part	[15, 16, 17]

Adherence to guidelines is itself linked to outcome and cost. In an international cohort of older adults hospitalised with CAP, therapy that followed national guidelines was associated with lower mortality and a shorter stay than discordant therapy [20]. A study of patients admitted to intensive care (ICU) found that concordant antibiotic use was associated with better survival [19]. These are observational findings, and sicker patients may well have been the ones who received discordant regimens, so causation cannot be assumed. Still, the direction is consistent: prescribing outside guidance has not been shown to save money, and in the sickest patients it may cost lives, which is the largest cost of all.

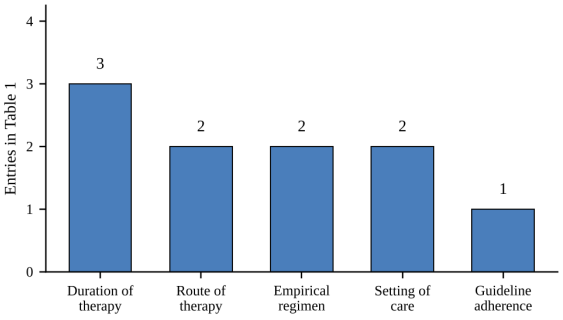


Fig. 1: Number of entries in table 1 by theme of the cost comparison

Matching the intensity of treatment to the severity score may offer some saving. A British cohort analysis reported on antibiotic therapy guided by the CURB-65 score, with low-risk patients receiving oral therapy and higher-risk patients receiving broader or parenteral cover, and described acceptable outcomes in the lowest-risk group [32]. The design was observational, so the finding is suggestive only. Even so, it fits the logic of the guidelines, which reserve intravenous combinations for the patients who stand to gain most from them [10, 32]. Whether the approach lowers total spending, as opposed to simply moving it between drug and bed budgets, has not been tested directly.

Severity-guided prescribing offers a further route to savings. The idea is to give the narrowest effective regimen that matches the CURB-65 category, using oral monotherapy for patients with a low score and reserving intravenous combinations for those at higher risk. A cohort analysis from the United Kingdom, in which therapy was matched to the score, reported acceptable outcomes in the low-risk group [32]. The BTS guideline makes the same link between score and regimen [10]. Evidence of this kind is observational, and should be read as

consistent with the guidelines rather than as proof that stepped treatment lowers cost. What it does show is that tiering of treatment by risk is feasible in routine practice and is not a purely theoretical proposal [10, 32].

4. DURATION AND ROUTE OF THERAPY

Treatment duration was long for many years, with seven to fourteen days a common instruction. Trials have since tested much shorter courses. A Dutch double-blind study in adults admitted with mild to moderately severe CAP found that three days of intravenous amoxicillin was as effective as eight days, as judged by clinical success at the end of the period [25]. A high-dose levofloxacin regimen of 750 mg for five days produced clinical cure rates comparable with the standard 500 mg dose for ten days [26]. A Spanish multicentre randomised trial found that stopping antibiotics after five days, provided clinical stability had been reached, was noninferior to a longer course [27]. The 2019 American guideline now recommends a minimum of five days, extended only when stability has not been reached [9].

The cost implications of shorter courses are easy to see. Fewer days of drug means lower acquisition cost, fewer doses to prepare and give, fewer opportunities for adverse effects such as diarrhoea, and less exposure of the gut flora to selective pressure. Where the course is given intravenously, each day saved also saves cannula care and nursing time. These benefits are individually small. Across the large numbers of patients treated each year, they add up. Because the three trials above showed no excess failure with shorter treatment, the shorter option looks dominant in economic terms, meaning cheaper and no worse, at least in the patients who were enrolled in them [25, 26, 27].

Route matters as much as duration. Many patients with CAP who are admitted are given intravenous therapy by default and remain on it longer than necessary. A Dutch multicentre randomised trial in severe CAP tested a switch from intravenous to oral therapy on day three, once criteria for improvement were met, and reported that the early switch was as effective as continuing intravenous treatment for the full course, with a shorter hospital stay [28]. A controlled trial of a critical pathway in Canadian hospitals also reduced the number of days of intravenous therapy and the length of stay without harming patients [29]. The saving here comes less from the drug than from the ward bed that is released when intravenous access is no longer needed.

A rough sum shows why length of stay dominates. If one hospital day costs many times what a day of oral amoxicillin costs, then removing even a single day of admission outweighs a large premium on the drug. That arithmetic explains why pathway studies report savings far greater than the antibiotic budget itself [15, 28, 29]. It also shows the limit of what pharmacy-led savings alone can deliver. A hospital that substitutes a cheaper generic but leaves discharge practice untouched will save little, whereas one that introduces clear switch criteria, clinical stability criteria and a stop date may change expenditure substantially, even if the drug chosen is more expensive per dose.

Adverse effects and patient factors are part of the cost as well. Gastrointestinal upset, rash, tendon problems with fluoroquinolones, QT prolongation with some macrolides and fluoroquinolones, and antibiotic-associated diarrhoea can all prompt extra visits, tests or drug changes. Longer courses give more time for these to occur. Adherence also falls as courses lengthen, and a missed dose in the community may translate into relapse. The trials of shorter therapy do not usually count these events in monetary terms, but they point the same way as the drug-cost argument [25, 26, 27]. A pharmacist counselling an outpatient on a five-day course has an easier task than one explaining ten days of tablets.

Both routes have hidden costs. Intravenous therapy requires cannulae, diluents, infusion sets, pharmacy time and nursing time, and each cannula carries a risk of phlebitis and bloodstream infection. Oral therapy depends on adequate gut absorption and on the patient being able to swallow and keep medicine down, and in a small number of severely ill patients that cannot be assumed. Switch criteria in the trials typically combined temperature, heart rate, respiratory rate, oxygen saturation and the ability to take

tablets, so that the decision was based on stability rather than on a calendar date [28, 29]. A drug with good oral bioavailability makes such a switch straightforward, and that is one reason why agents such as amoxicillin and levofloxacin feature so often in the pathway trials.

5. SEVERITY AND SITE OF CARE

Because admission is the single biggest cost, the decision on where to treat a patient is the most expensive prescribing decision of all. Two scoring systems dominate practice. The Pneumonia Severity Index (PSI) assigns patients to five risk classes using age, comorbidity, examination findings and laboratory results, and was derived to identify low-risk patients who could be treated at home [31]. The CURB-65 score is simpler, counting confusion, urea, respiratory rate, blood pressure and age of 65 or more, and was validated across several countries as a tool for severity assessment at presentation [33]. Both are meant to support clinical judgement rather than replace it. They are, however, the main way that guidelines translate risk into a decision about admission.

The economic importance of these tools is shown by a randomised trial from Barcelona. In low-risk patients attending the emergency department, those who were discharged to receive oral therapy at home did as well as those admitted, and the home group reported greater satisfaction [30]. The saving came almost entirely from avoided bed days. Not every low-risk patient is suitable for home care, since social circumstances, ability to take oral medicine and access to follow-up all matter, and the trial excluded those with obvious problems of this kind. Even so, it shows that a proportion of admissions are discretionary, and that a well-run outpatient pathway moves cost from the ward to the community.

At the other end of the spectrum, sicker patients account for a disproportionate share of spending. Large registry data from Germany, covering several hundred thousand patients, showed that hospital mortality rose steeply with age, with certain comorbidities and with the need for ventilation, and that mortality differed markedly between groups of patients with the same diagnosis [24]. Patients who reach intensive care consume many times the resources of ward patients, and getting the first antibiotic right matters most in this group [19, 20]. For these patients, a cheaper drug that fails is not cheaper at all. Cost analysis in severe CAP should therefore be judged mainly on whether it preserves effective, guideline-concordant cover.

Host factors modify both risk and cost. Age, chronic lung disease, heart failure, diabetes, alcohol excess, smoking and immunosuppression have all been linked to a higher incidence of CAP in European data [5]. They also lengthen admission and increase the chance of readmission, which in turn raises the cost per episode. Pharmacists reviewing a formulary should be aware that average cost figures from trials tend to understate the cost in older, frailer patients. A regimen that looks economical in a trial population with a median age in the fifties may behave differently in a ward where most patients are over seventy and several take five or more regular medicines [18, 20].

Prevention deserves a mention in any cost discussion. In a large Dutch randomised trial of older adults, a 13-valent pneumococcal conjugate vaccine reduced first episodes of vaccine-type pneumococcal CAP, though not CAP from all causes [34]. A prevented admission is the cheapest admission, and the vaccine effect therefore shifts the economics of antibiotic treatment indirectly, by reducing the number of patients who need it. How far this shifts the balance depends on vaccine price, uptake and the serotypes circulating locally, none of which can be generalised from one country to another. Older adults, who carry the highest admission rates, are also the group in whom vaccine effectiveness is hardest to establish.

Prevention sits outside the antibiotic budget but changes the denominator. The conjugate vaccine trial in older adults found fewer first episodes of vaccine-type pneumococcal CAP after vaccination, which means fewer admissions and fewer courses of antibiotics [34]. The same logic applies to influenza and smoking cessation, which act on risk factors identified in European surveys [5]. A formulary committee may feel that

vaccination is not its concern, but a hospital that treats several hundred pneumonia admissions a year has an interest in how many of those might be avoided. Cost per case prevented can then be set against the cost per case treated, giving a fuller account of the choices available [5, 34].

6. STEWARDSHIP AND RESISTANCE

Antimicrobial stewardship programmes try to make sure that each patient receives the right drug, dose, route and duration. Guidelines from the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America describe the core strategies: prospective audit with feedback, formulary restriction and preauthorisation, and education, supported by de-escalation, intravenous-to-oral conversion and dose optimisation [35]. In CAP, the strategies with the clearest evidence are those already discussed, namely early oral switch, shorter courses and avoidance of unnecessary combination therapy [21, 25, 28, 29]. These strategies align economic and microbiological aims, since a shorter and narrower course costs less and exerts less selective pressure.

Resistance is the cost that economic evaluations are least able to capture. Macrolide resistance in pneumococci, fluoroquinolone resistance in Gram-negative organisms, and the spread of *Clostridioides difficile* infection have all been linked to heavy use of particular classes, and the consequences fall on later patients, not on the one being treated [35, 36]. Such externalities are rarely monetised in a trial-based analysis, which is limited to the follow-up window of the study. A review of the health and economic outcomes of antimicrobial resistance showed that resistant infections raise morbidity and cost, so individual prescribing decisions have consequences beyond the patient in front of the clinician [36]. Any cost comparison that ignores this will tend to favour broad-spectrum agents.

Diagnostics and microbiology also enter the calculation. Pathogen-directed therapy is cheaper when a narrow drug can be chosen with confidence, but testing itself has costs and often returns results after the first treatment decision has been made. Most patients with CAP never have a pathogen identified, and the guidelines accept empirical treatment as the norm [8, 9, 10]. A Swiss trial of monotherapy is a useful reminder that when an atypical pathogen is not the dominant concern, it may not be necessary to cover for it routinely [22]. Reviews of CAP management describe how the balance between empirical cover and targeted therapy shifts with local epidemiology, which is another reason why economic findings do not travel easily between settings [2, 3, 37, 38].

Implementation is where many cost savings are lost. A guideline recommending five days of treatment achieves nothing if the electronic prescribing system defaults to seven, and a switch policy fails if nobody reviews the chart on day three. Stewardship teams have therefore moved towards structured prompts, automatic stop dates and review by a pharmacist at forty-eight to seventy-two hours [35]. The evidence on pneumonia pathways shows that these local arrangements, and not the choice of antibiotic, account for much of the observed saving [28, 29]. Auditing concordance with local guidance, and feeding results back to prescribers, is relatively cheap and has repeatedly been associated with better prescribing [19, 20, 35].

Local data matter. Pneumococcal resistance to penicillin and macrolides varies widely between regions, as does the prevalence of organisms such as *Legionella pneumophila* and *Mycoplasma pneumoniae*. A hospital antibiogram, updated regularly and shared with prescribers, is the cheapest stewardship tool there is. It permits an informed choice between narrow and broad empirical regimens and gives a reasoned basis for departing from a national guideline where local resistance demands it [35, 37]. Pharmacists are well placed to produce and maintain it, because they already hold the dispensing data and sit on the committees that decide formulary policy. Without it, empirical choices tend to drift towards whatever is familiar.

7. LIMITATIONS AND FUTURE DIRECTIONS

Several features of the literature limit what can be concluded. The cost studies come from different decades, health systems and perspectives, and their results are expressed in different currencies and price years, which makes direct comparison unreliable. Many of the most informative trials were designed to test clinical noninferiority, with cost as a secondary or post hoc outcome, so they were rarely powered to detect differences in expenditure [22, 25, 26, 27]. Observational studies of guideline adherence are open to confounding by severity [19, 20]. Hospital cost data are often based on charges, and data on outpatient costs are much scarcer than data on inpatients, even though most episodes of CAP in the community are managed outside hospital [4, 7, 18].

Future work could usefully do several things. Prospective trials of short courses and early switch could collect resource use alongside clinical endpoints, using standard reporting frameworks [12]. Studies from low- and middle-income countries are needed, since the global burden of lower respiratory infection falls heavily there and the relative price of drugs and bed days is very different [1]. Models should attempt to include the downstream cost of resistance, even if only as scenario analyses [36]. Finally, economic evaluations should consider the older, frailer patient, who is the typical person admitted with CAP and who is underrepresented in most trials [20, 24]. Until then, cost advice remains a matter of informed judgement.

One more limitation concerns the way outcomes are measured. Most studies use short-term clinical cure or mortality, and do not capture recovery of function, return to work, or the lingering fatigue many patients report for weeks after pneumonia. Cardiovascular events after pneumonia are also increasingly recognised, and those add cost that lies outside the usual thirty-day window [2, 3, 7]. Where quality of life has been measured, the instruments differ and are seldom linked to cost. The result is that cost-effectiveness ratios, which need a common measure of benefit, can seldom be calculated from the CAP literature, and most conclusions have to rest on cost-minimisation reasoning [11, 13].

8. CONCLUSION

Across the published work, the cost of treating community-acquired pneumonia is governed far more by where and for how long a patient is treated than by which antibiotic is chosen. Hospital admission accounts for most of the spending, so pathways that safely treat low-risk patients at home, switch to oral therapy early and stop at a defined point offer the largest savings [15, 16, 17, 28, 29, 30]. Trials of short courses and monotherapy suggest that these savings need not cost anything in clinical outcome for the patients studied [21, 22, 25, 26, 27], and guideline-concordant prescribing has been associated with better results in older and critically ill patients [19, 20].

For pharmacists and formulary committees, the practical message is to judge regimens on episode cost and not on price per dose, and to build switch criteria and stop dates into prescribing. The weaknesses of the evidence are plain: mixed methods and currencies, few trials with cost as the primary endpoint, thin data on outpatients and on lower-income settings, and almost no valuation of resistance [1, 4, 12, 36]. Better-designed economic analyses, run alongside clinical trials and reported to a common standard, would let local decisions rest on firmer ground.

9. ABBREVIATIONS

CAP-Community-acquired pneumonia, PSI-Pneumonia Severity Index, CURB-65-Confusion, urea, respiratory rate, blood pressure, age 65 score, ICU-Intensive care unit, CHEERS-Consolidated Health Economic Evaluation Reporting Standards, IDSA-Infectious Diseases Society of America, ATS-American Thoracic Society, BTS-British Thoracic Society

10. FUNDING

Nil

11. AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

12. CONFLICT OF INTERESTS

Declared none

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