Improving outcomes from community-acquired pneumonia.

Grant Waterer MBBS PhD MBA FRACP FCCP

Professor of Medicine, University of Western Australia
Adjunct Professor of Medicine, Northwestern University, Chicago

Lesley Bennett MBBS FRCP

Consultant Respiratory Physician
Royal Perth Hospital

Corresponding author: Dr Grant Waterer

Level 4 MRF Building
Royal Perth Hospital
GPO Box X2213
Perth 6847
Australia

Ph +61892240245
Fax +61892240246
Email grant.waterer@uwa.edu.au

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Abstract

Purpose of the review: We are entering to a new era of healthcare where patient outcomes are increasingly being publically reported, not just by institution, but by individual clinicians. This review focuses on the issue of quality of care of patients with CAP, in particular the choice of outcome, quality of data needed and recommendations of the current bundle of care suggested by the available literature as delivering the best chance of favorable outcomes for patients.

Recent findings: There is increasing evidence that pneumonia outcomes have improved over the past decade, particularly mortality. However we have been over simplistic in setting quality targets and that a bundle of care is required to deliver best outcomes, such as has been shown with the surviving sepsis campaign. Equally the quality of data available to compare outcomes needs to be significantly improved on what is currently available.

Conclusion: To achieve best outcomes for their patients physicians must be actively comparing their outcomes against other institutions and not rely on historical data. A bundle of care that includes rapid administration of antibiotics, use of combination antibiotic therapy including a macrolide and early mobilization is a good starting point.

Introduction

We are entering a new era of healthcare that many physicians may find confronting and challenging. Both health payers and health consumers are driving increasing analysis and public reporting of differences in patient outcomes between institutions and even between individual practitioners. Such analysis has been enabled by the enormous amount of healthcare data now in accessible electronic form. In turn the internet has enabled healthcare consumers much greater access to analysis of healthcare data by a variety of sources including government agencies, health insurers and healthcare providers themselves.

Community-acquired pneumonia (CAP) remains a major cause of hospital admissions[1]. CAP, unlike for example an exacerbation of chronic airways disease, has a gold standard for diagnosis based on radiology and we have a large number of validated methods for predicting patient outcomes based on comorbidities and clinical presentation. It is therefore not surprising that CAP is the respiratory condition that has probably most been targeting for performance measures and comparative outcome analysis.

While it is understandable that physicians may be concerned about comparative analysis of patient's outcomes, especially when it is dissected down to individual specialist level, our view is that this is something that should be embraced. In CAP in particular there is good evidence that some patient outcomes like mortality and length of stay have improved over the past few over the past few decades, at least in some centers[2-6]. To deliver the highest quality of care to their patients, physicians need to know what the best outcomes

are that are currently being achieved and how their own outcomes compare. Equally since there is evidence that there are differences in patients outcomes not explained by current measures of severity of CAP[7], analyzing the differences in medical care between sites and how they influence outcome is a key avenue for research.

What are the important outcomes in CAP?

To improve an outcome it has to be measurable, able to be compared to some benchmark, and it has to be amenable to intervention. Which outcomes in CAP then can be objectively measured, have sufficient clarity around the contributing factors that we can compare between institutions and be sure that we are comparing “apples with apples”, and can be modified by available treatments.

Mortality has unquestionably been the primary outcome of interest in CAP, for understandable reasons. However while there is no doubt mortality is an objective outcome, it has many problems as a marker of quality of care. First there is the question of at what time point is mortality assessed. Inpatient mortality is complicated by the issue of the adequacy of medical care after discharge, with half of all deaths by 30-days in the over 65 age group dying after discharge from hospital[8]. It has been well document that CAP survivors have elevated 30-, 90- and one-year mortality rates compared to age, gender and comorbidity matched controls[9-14]. The impact of inpatient treatment on after discharge mortality has been poorly assessed and any possible connection is likely to vary markedly between different health systems with different primary care capabilities.

A further problem with mortality as a quality of care indicator is that existing methods of correcting for comorbidities fail to adequately capture key clinical decisions around limitations of treatment imposed by the patient or the physician. For example, in one hospital with a proactive approach to end of life decisions a 95 year old with significant dementia but living at home with family may receive only palliative care for his CAP as a result of his or his families wishes and succumb. A similar patient in another health system may receive full care, and present another half a dozen times over the next three years and finally succumb to another illness. The second hospital will have much better mortality rate, but is it really providing better quality of care?

The final problem with mortality is that while different interventions have been associated with better outcomes, careful analysis of hospital deaths typically fails to reveal any significant deficiencies of care that would have both been appropriate (taking into account limitations of care as above) and would have had a reasonable likelihood of changing the outcome[15,16]. While this does not mean that the mortality rate can be ignored, it does underline the complexity of using death as a quality of care endpoint in CAP.

Readmission rates are another common quality endpoint derived from administrative databases, but it is often complex to sort out whether a readmission is related or unrelated to the primary pneumonia episode. There also appears to be no correlation between a hospitals mortality rate and 30-day readmission rate, at least in the United States[17], indicating that entirely different factors are involved (patient factors and treatment factors). Many healthcare payers, including the United States Centers for Medicare and Medicaid have also introduced financial penalties targeting readmissions. There

is however a dearth of literature showing specific interventions reduce readmission rates, although some trends and predictors of patients likely to require readmission are emerging[18-21], so this should be a focus of future research.

Length of hospital stay is a very popular endpoint with healthcare payers as it has a major influence on the cost of care. Whether health consumers consider length of stay to be a measure of quality is debatable with conflicting reports from a limited amount of studies not specific to pneumonia[22-26]. Due to the vagaries of individual decision making on when patients can be discharged, there is a strong push to use more objective endpoints like time to clinical stability (see below) rather than length of stay for assessing the effect of interventions. Given the importance to healthcare payers, clinicians do need to know how their patients average length of stay compare to benchmarks and understand what may be contributing to any differences, including interventions that have been shown to have a positive impact[27-29].

The final outcome of interest that is reasonably commonly reported is the time to clinical stability (or time to clinical response). This is one outcome where there has been significant interest in biomarkers to define the at risk population as early as possible[30,31]. Patients who develop complications such as non-resolving pneumonia (including empyema and lung abscess), a secondary nosocomial infection or have delayed respiratory failure or septic shock requiring admission to the intensive care unit after a period of care in a normal ward environment can have a major effect on this outcome[32]. While inappropriate initial antibiotic therapy clearly can be a reason for failure to respond to treatment, the proportion of patients who receive guideline

compliant empiric antibiotic but have a slower than hoped for clinical response is far larger and no interventions have been clearly shown to affect this. In addition, relatively little focus has been given in CAP to preventing and diagnosing additional complications that can affect clinical stability such as deep vein thrombosis and pulmonary embolism, myocardial infarction, stroke, sepsis related to nosocomial infection and fractures related to falls. All of these however have been studied in other conditions and been shown to be affected by changes in hospital management and therefore should be considered as part of the overall package of care to patients with CAP.

A slight variation on time to clinical response is early clinical response, typically defined as improvement in at least some key clinical features in the first 24 hours. Early clinical response has received endorsement from the United States Food and Drug Administration as an endpoint for clinical trials in CAP. This endpoint appears to have some validity[33] but further research is required to determine if it really is a robust measure of quality of care as defined above.

What data sources are available for comparing outcomes?

Having decided on which outcomes are important, the next step is to find comparative data to measure up against. While there is some value in comparing against historical data from your own institution, comparison against other institutions is obligatory. To achieve the best possible quality benchmarks the sample of institutions you can compare against should be as large as possible.

Individual clinicians are likely to find a marked difference in the availability of data against which they can compare their own outcomes depending on the sophistication of their health system and the amount of

investment in information technology support that has occurred to enable this type of activity. For example, in Australia we have The Health Roundtable, which provides comparative analysis of outcomes across 147 facilities in 87 health service organizations. The United Kingdom has a variety of databases and has been very proactive in making health outcomes data available to the general public. In the United States a variety of databases are available including those from Government sources (such as the Healthcare Cost and Utilization Project from the Agency for Healthcare Research and Quality), academic hospitals (such as the University Health System Consortium Database) and large private healthcare providers (such as the Kaiser Permanente Division of Research databases).

A comparison of results between institutions in one of these databases should be considered the starting point, as all lack the granularity of data to tease out some of the complex clinical factors potentially affecting patient outcomes. Apparent poor performance against competitors does not necessarily mean patient outcomes are worse, but should trigger a much more detailed evaluation of patient outcomes to establish that current best practice is being delivered and no additional preventable factors can be identified. In our experience key researchers and research groups who regularly publish papers in CAP are excellent sources of comparative data with the granularity needed to establish benchmarks for patient outcomes.

Indicators of quality of care in patients hospitalized with CAP

A number of processes of care have been targeted as quality indicators because of their association with mortality. These indicators include rapid

administration of antibiotics, performing blood cultures (preferably prior to antibiotic delivery), measuring oxygen saturation on admission, using a validated severity scoring system (such as the pneumonia severity index or CURB-65) and prescribing an antibiotic therapy compliant with standard guidelines.

A common problem to all of these apparent indicators of quality of care is that mortality, as already discussed, is not a simple endpoint. In addition each individual intervention itself, perhaps with the exception of compliance with antibiotic guidelines as discussed below, is more likely to be a part of an associated package of care rather than a critical driver of outcome by itself. In this respect the sepsis community has done much better in defining the bundle of care that achieves best outcomes.

Administration of antibiotics within a fixed period, typically four to eight hours, was first suggested as a predictor of better outcomes by two large retrospective database studies[34,35]. Further studies have found similar associations[2,36], but clinical studies focused on more rapid administration of antibiotics have failed to show improved patient outcomes[37-39]. Equally there is evidence that the push to give antibiotics faster has resulted in adverse patient outcomes such as over use of antibiotic and antibiotic induced complications in patients who ultimately did not have pneumonia[40-43]. It therefore seems likely that while antibiotics should be given as promptly as possible[2], time to first dose of antibiotics is more a marker of an important package of care rather than a determinant of outcomes itself[44]. To be effective, rapid administration of appropriate antibiotics must also be accompanied by prompt attention to other medical issues such as fluid resuscitation, correcting electrolyte

imbalances, controlling arrhythmias, treating respiratory failure (including recognizing CO₂ retention), deep vein thrombosis and pulmonary embolism prophylaxis, recognition and treatment of myocardial ischemia, treatment of hyperglycemia etc.

Numerous studies have identified performing blood cultures as being associated with better patient outcomes including mortality. Given published data suggests that blood cultures rarely impact on clinical management[45-50], even when they should[45], it is very difficult to see how this is a directly causative relationship. Even more so than timely antibiotics, performing blood cultures is likely to be associated with a group of other interventions that do improve patient outcomes.

Empiric antibiotic regimes that are not compliant with guidelines are associated with worse patient outcomes[51-55], including mortality. When key pathogens such as *Legionella* have not been covered, this may clearly be causative. However physicians who are unaware or disregard published guidelines are probably less likely to comply with other standards of care, potentially impacting outcome as well.

The use of validated severity scores to determine the site of care (inpatient vs outpatient, ward vs intensive care) has attracted a lot of research attention, in part because it offers the elusive goal of being able to treat patients by a simple protocol without all the complexities of physician assessment of complicated patient comorbidities and physical signs. There is reasonable evidence to support using a validated pneumonia severity score as an adjunct to clinical judgment in determining the site of care[56,57], but data supporting the use of pneumonia severity scores to guide the selection of empiric antibiotic

therapy is more mixed[58]. Late admission to the intensive care unit has been associated with worse patient outcomes[59], but it is unclear if this is due to a delay in critical interventions or if patients who deteriorate on the ward represent a different subgroup of disease driving worse outcomes. Either way, use of one of the validated scoring systems[56] is helpful to flag patients who may need more attention, particularly to inexperienced medical staff, as long as they are not used to replace or over-ride experienced clinical judgment.

Measuring oxygenation was once more complicated than it is now with the widespread availability of cheap oximeters and it is now so routine that it has been dropped off many quality frameworks. However, recognition of type II respiratory failure has become more critical given the evidence that, at least in some patients, early institution of non-invasive ventilation reduces the need for mechanical ventilation and its attendant morbidity, mortality and cost[60-62].

What is the “gold standard” of care for patients with CAP?

In the absence of studies clearly defining a gold standard of care for each outcome, any recommendation of the “package” of care that is optimal management must be a subjective analysis of the available literature and clinical experience. The following recommendations are a starting point for achieving the best patient outcomes, and there is some evidence that applying some of them as a bundle of care does lead to better mortality outcomes[6,63], although this is still an active area of debate[64]. Ultimately clinicians will only truly be able to be comfortable they are achieving the best for their patients when they can compare their patient outcomes with others with the level of granularity of data needed to account for all known variables.

1. A validated severity score should be calculated as an aid to clinical judgment in determining the site of care. There is little to choose between pneumonia scores that have been studied[56].
2. Empiric therapy should be consistent with local guidelines as this is associated with improved patient outcomes[51,52,65-67]. It is very important that clinicians do have guidelines that take into account local differences in etiology (e.g. such as *Acinetobacter* being a common pathogen in many tropical countries).
3. A macrolide should be part of the empiric regime in hospitalized patients. This is a controversial area, but the wealth of retrospective data[65], particularly in sicker patients[2,68,69] and in patients with pneumococcal pneumonia[70,71], that macrolides are associated with better outcomes and especially mortality. This recommendation is also supported by a recent randomized controlled study of 580 patients where patients with pneumonia severity index grade IV disease had a better clinical response if they received a macrolide compared to a beta-lactam alone[72].
4. Antibiotics should be given as fast as possible, ideally within four hours of presentation[2,34,35].
5. Within the same time for antibiotics administration attention should be given to ensuring the patient has adequate fluid resuscitation, electrolyte disturbances are being addressed, hyperglycemia is being corrected, thrombosis prophylaxis is considered and myocardial ischemia is considered and prophylaxis considered if appropriate.

6. Hypoxic patients with any risk factor for CO₂ retention should have this assessed and managed if present.
7. A process needs to be put in place to ensure that patients who begin to deteriorate are identified early and appropriate interventions started.
8. Patients should be encouraged to ambulate as early as possible[27,29].
9. Failure to clinically improve within 48 hours should prompt early review of potential complications such as empyema.
10. A protocol should be in place to encourage physicians to switch from intravenous to oral therapy at the earliest appropriate time point[73].
11. Given the long-term poorer outcomes in CAP survivors[9-14], cardiovascular risk factors should be assessed during admission and after discharge. A recent study suggested aspirin reduces the rate of cardiovascular events in patients with pneumonia[74] indicating prophylaxis may be an effective and relatively low risk strategy.

Conclusion

All clinicians want to believe they are delivering quality care. The only way to be sure you are delivering quality care is to measure patient outcomes and compare them against the widest selection of other physicians possible. To date this is something that has been done poorly, but new tools and pressure from both healthcare funders and patients are driving a new era and good clinicians will embrace it.

Current assumptions around the ability to compare patient outcomes are overly simplistic and ignore some very complex issues. In particular mortality is not a simple outcome and the granularity of clinical detail needed to be sure that comparisons are fair and accurate far exceeds that currently available in administrative databases. This limitation accepted, there is more than sufficient comparative data available to being the process of identifying potential deficiencies that should drive further research.

Finally we do have a suite of measures that have reasonable validity as the starting point for a “bundle of care” in patients with CAP. Further research will determine the relative contributions of these, refine recommendations and hopefully develop new strategies to further improve both the short and long-term outcomes from CAP.

- Outcomes from CAP have improved over the past decade
- Physicians must compare their patient outcomes to achieve best practice
- Optimal care is a bundle of clinical behaviors, not a single activity

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