A CASE STUDY: HOW TO PUT CLINICAL STUDIES TO WORK FOR YOU

Developed by Pfizer Inc.

Monograph 3
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Getting started</td>
<td>3</td>
</tr>
<tr>
<td>Case study: Community-acquired pneumonia triage</td>
<td>5</td>
</tr>
<tr>
<td>Looking closer</td>
<td>11</td>
</tr>
<tr>
<td>Discussion</td>
<td>18</td>
</tr>
<tr>
<td>Conclusion</td>
<td>23</td>
</tr>
<tr>
<td>References</td>
<td>25</td>
</tr>
</tbody>
</table>
CHANGING TIMES

There has been an increasing interest in making sound clinical decisions based on current and valid evidence in published literature. This has formed the basis of evidence-based medicine—an efficient system for gathering and assessing information from various sources to apply to everyday clinical practice.

As times change, new approaches are needed to meet the challenges of today's healthcare environments. In this era of increased accessibility to information and increasing pressures of accountability, evidence-based decision making can help you effectively respond authoritatively to questions such as:

- Where did you learn about that treatment, prognosis, test, etc?
- How do you know that the information is believable and well founded?
- What would you do differently?
- What results do you expect? Why?

Obtaining current and relevant information is a critical part of caring for patients. It enables you to answer important clinical questions as they arise.
GETTING STARTED

APPROACH

An organized approach to finding and assessing clinical information can help you get the information you need in a timely way. These steps provide tips to help you conduct a successful search for and evaluation of the appropriate clinical studies.

Formulate questions

The first step in finding appropriate information is to convert your needs into answerable clinical questions. Asking the right questions can be a daunting task, requiring some understanding of the clinical challenges at hand. A question that is off-target, too broad, or too narrow in scope may lead to a time-consuming and fruitless search for information.

Identify appropriate clinical studies

Electronic databases easily accessed via the Internet can make this task less time consuming, and more efficient and productive.

Assess validity, accuracy, and relevance

Once you have located and acquired appropriate studies, you will need to assess their:

- Validity
- Accuracy of findings
- Relevance for clinical decision making

Such critical appraisal is an important step on the path to a well-founded conclusion. Reliable information, together with your own expertise and experience, helps guide your decisions regarding patient care.

This program illustrates the evidence-based–medicine process in action:

- Clinical questions are posed
- Information sources are discovered and assessed

The following case study provides a detailed example of the type of situations confronting clinicians.

NOTE: The case study is used for illustrative purposes only. There is no intention to either endorse or dispute the medical principles and/or practices advocated by the study authors.
SCENARIO

Community-acquired infections, especially community-acquired pneumonia (CAP), are a major concern in most medical practices. CAP is a major contributor to illness and mortality in the United States, causing 4 million episodes of illness and nearly 1 million hospital admissions each year. Pneumonia is the sixth-leading cause of death in the United States.¹

In all but the most ill patients, there may be questions regarding which patients may be safely treated via ambulatory care versus those requiring immediate hospitalization. “Safely“ implies reducing risks of mortality and morbidity. It suggests a form of triage in everyday medical practice, seeking to channel patients into the most efficient and effective modalities of care. Patient age might be an initial concern and departure point for decision making, with pediatric and geriatric patients possibly at greatest risk.

Health insurance and managed care organizations are concerned about unnecessary hospitalizations. Patients also would prefer to be cared for at home whenever possible.

However, making prognostic clinical decisions about which patients might not be appropriate for outpatient treatment and home care is an ongoing concern. This is largely due to the great potential for death from CAP. That is why being able to more confidently identify patients with CAP at low risk could result in:

• Lower mortality and morbidity
• Greater patient satisfaction and comfort
• Fewer unnecessary expensive hospitalizations

CASE STUDY: COMMUNITY-ACQUIRED PNEUMONIA TRIAGE
CLINICAL QUESTION

Based on the scenario described above, let's discuss how to formulate a clinical question that could guide a search for relevant information. For example, to begin, you may want to consider the following question:

*Which patients with CAP might be safely managed as outpatients rather than hospitalized?*

There are several points underlying the question:

- The desired goal is prognostic in nature: being able to predict outcomes based on patients' characteristics and/or physical conditions when pneumonia is diagnosed
- It has been noted that prognostic factors need not necessarily cause the outcomes, but must be associated with them strongly enough to predict their development²
- Specific application of risk factors are associated with initial development of the disease. At the time of diagnosis, prognostic factors are forward looking, whereas risk factors are retrospective
- The question is focused on the setting of care and not on therapy
- The term “manage as outpatients” implies the outcomes of interest are lower (or acceptable) levels of mortality and morbidity than those of inpatient management
- Although age is an issue, it is implied rather than stated
- The question as stated is also not limiting in terms of other patient demographic characteristics, such as gender, race, socioeconomic status, concurrent medical conditions, geographic region, etc

If, however, a specific practice population is of concern, the question could be narrowed to any extent desired by adding qualifying terms. *Example: Instead of “patients,” you might insert: “African American males, older than 50 years, living in southwestern United States.”*

It is important to note that the more narrowly defined the clinical question becomes, the less chance there will be of locating potentially relevant studies.
SEARCH STRATEGY

While there is always the chance of being overwhelmed with inappropriate studies, it is usually desirable to cast a wide net for information at first, then narrow the catch later in the search. Based on the problem description and clinical question described earlier, several broad query terms seem appropriate, including:

- Community-based infection
- Pneumonia
- Prognosis
- Age

Articles discussing a particular therapy for treating pneumonia, for example, can be excluded.

Where do you start looking for studies?

A good place to start is an electronic search of the MEDLINE® or EMBASE® databases. These can be accessed through various search engines, including PubMed and the National Library of Medicine (NLM) Gateway.

PubMed was used for the purposes of this case study. Our search was limited to a 5-year interval, and the following search terms and operators (eg, AND, NOT) were entered into PubMed:

```
Community-acquired infections AND pneumonia AND prognosis AND age factors NOT therapy
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This search retrieved 3 citations (arranged here alphabetically by author):


**NOTE:** *This search was conducted in 1999. A more current search would most likely result in different findings.*
The Fine et al study was the obvious choice for further review since it was in English, likely to focus on an American population, and found in an easily accessed journal. If this article turned out not to be of interest, we could have returned to PubMed and broadened the search by removing one of the less critical query terms (such as age factors or therapy), or tried a different database.

The complete text of the Fine et al article is available in PDF format as part of the Clinical Literature Evaluation and Assessment Resource CD-ROM of materials. Bracketed references in this booklet (eg, [xxx:x]) refer to the appropriate page number and column (L=left col, R=right col) in the article. For example, [243:L] is referring to page 243, left column, of the Fine et al article.
BEGINNING WITH THE ABSTRACT

Because a study abstract condenses all essential information, it can make it easier to quickly assess the appropriateness and relevance of the study to help you answer particular clinical questions. Services like PubMed allow you to retrieve and review the abstract—which is usually available online—before obtaining the full-text article.

The table on page 10 presents some analytical questions regarding the Fine et al study abstract: [243:L].

STUDY OVERVIEW

In general, the abstract of a study provides a succinct overview of the study background, study design methodology, clinical data, and author’s conclusions. In this particular study, for example, the abstract outlines the issue—considerable variation in hospitalization rates of patients with CAP—and describes the study design and the findings that lead to a concise conclusion. The full abstract appears below.

ABSTRACT

Background: There is considerable variability in rates of hospitalization of patients with community-acquired pneumonia, in part because of physicians’ uncertainty in assessing the severity of illness at presentation.

Methods: From our analysis of data on 14,199 adult inpatients with community-acquired pneumonia, we derived a prediction rule that stratifies patients into 5 classes with respect to the risk of death within 30 days. The rule was validated with 1991 data on 38,039 inpatients and with data on 2287 inpatients and outpatients in the Pneumonia Patient Outcomes Research Team (PORT) cohort study. The prediction rule assigns points based on age and the presence of co-existing disease, abnormal physical findings (such as a respiratory rate of ≥30 per minute or a temperature of ≥40°C), and abnormal laboratory findings (such as a pH <7.35, a blood urea nitrogen concentration ≥30 mg per deciliter [11 mmol per liter] or a sodium concentration <130 mmol per liter) at presentation.

Results: There were no significant differences in mortality in each of the 5 risk classes among the three cohorts. Mortality ranged from 0.1 to 0.4 percent for class I patients (P=0.22), from 0.6 to 0.7 percent for class II (P=0.67), and from 0.9 to 2.8 percent for class III (P=0.12). Among the 1575 patients in the three lowest classes in the Pneumonia PORT cohort, there were only seven deaths, of which only four were pneumonia-related. The risk class was significantly associated with the risk of subsequent hospitalization among those treated as outpatients and with the use of intensive care and the number of days in the hospital among inpatients.

Conclusions: The prediction rule we describe accurately identifies the patients with community-acquired pneumonia who are at low risk for death and other adverse outcomes. This prediction rule may help physicians make more rational decisions about hospitalization for patients with pneumonia. (N Engl J Med. 1997;336:243-50.)
## ANALYSIS OF THE ABSTRACT

<table>
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<th>Question</th>
<th>Response</th>
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<tr>
<td>Are the questions (hypotheses) addressed by the study relevant to your query?</td>
<td>Yes. The study concerns identifying patients with CAP who are at low risk for death and other adverse outcomes, allowing, as it states, “more rational decisions about hospitalization.”</td>
</tr>
<tr>
<td>Are the study subjects similar to your own patients?</td>
<td>The abstract merely indicates that the study included “adult inpatients,” without further demographic information. Thus, if your interest is pediatric patients, this study would not be appropriate.</td>
</tr>
<tr>
<td>Does the research design seem appropriate for the clinical question?</td>
<td>Yes. Clearly, the study concerns prognosis and develops a prediction rule that may be helpful in triaging patients with CAP to ambulatory versus hospital care.</td>
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<tr>
<td>Is the study based on strong evidence?</td>
<td>Large numbers of patients were included in the investigation, and the respective cohorts studied were significantly similar, adding to the validity of the design.</td>
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<tr>
<td>Are the results clear?</td>
<td>The results allow assigning patients to 1 of 5 prognostic risk classes, based on clinical and laboratory indicators. The practicality of using such a scheme in daily practice is less clear from the abstract.</td>
</tr>
<tr>
<td>Are the results significant?</td>
<td>The abstract focuses on mortality rates among the 3 lowest-risk classes, with 2.8% being greatest. It appears that the “prediction rule” successfully identifies low-risk patients; the full text must be consulted to see how this compares with higher risk classes IV and V.</td>
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In view of the clinical question posed and information provided by the abstract, it seems that this study is worth a closer look to assess its validity and applicability for everyday practice.
LOOKING CLOSER

ASSESSING VALIDITY

Determining the validity of a study requires a thorough reading and close examination of the article. This should provide insights into methods and procedures used by the authors to draw conclusions.

Validity may be categorized as follows:

- **Internal validity** is the degree to which the study results and recommendations are likely to be true and free of bias (systematic errors). Internal validity also determines the extent to which the observed effects are true for the subjects in the particular study (as opposed to generalizability). The findings may be valid for the particular study but not applicable to your own clinical practice.

- **External validity**, also called *generalizability, relevance, or transferability*, is the degree to which the results of an investigation hold true in other settings and/or apply to populations, such as your own patients, beyond those included in a study. When assessing external validity, here are a few questions to consider:

  - Were subjects in this study and the setting similar to those in your own practice?
  - Can the recommendations be applied to your patients?
  - Will your patients be better off as a result of applying the recommendations? To what extent?

Assessing validity is the primary exercise that drives all other activities involved in a critical interpretation of the study.

CLASSIFYING THE STUDY

In accordance with the search criteria, this is a primary study focusing on prognosis:

- Among patients with CAP, the study seeks to project outcomes (eg, mortality risk) and the frequency with which the outcomes may occur as the result of specific predictive factors (eg, age, gender, coexisting illness, physical examination, and laboratory findings).

The Fine et al study design uses a case-control methodology—also called *case referent or retrospective*. It identifies nonrandomized groups or cohorts of patients with the outcomes of interest and looks back in time to see whether they had the same predictive factors of interest.

The typical protocol for this methodology involves gathering “cases” of individuals who have experienced the outcome event(s) of interest and comparing them with “controls” who have not been similarly affected. Usually the groups are drawn from the same population. The investigators then look for factors (exposures) in each cohort to determine which are most predictive of the outcome.2
In this study, however, each of the 3 cohorts represented a separate cross-sectional study—also called a prevalence or disease frequency study. Such studies examine the relationships between diseases or health conditions and other variables of interest (eg, mortality) as they exist in defined populations at particular points in time.

The Fine et al study surveyed different populations and used cohorts in distinct ways for developing a prediction rule, which was the objective of the investigation:

- A derivation cohort—coming from the 1989 MedisGroups Comparative Hospital Database—served as the cohort for comparison with the control groups
- 2 separate groups—the 1991 Pennsylvania MedisGroups study and the Pneumonia Patient Outcomes Research Team (Pneumonia PORT study)—were validation cohorts, essentially serving as 2 “control groups” that were compared with the cases (derivation) cohort

The authors used the 2 validation cohorts to independently assess whether the prediction rule, as developed from the derivation cohort, was accurate and reliable. Reliability implies that the results and trends observed in the derivation cohort would not differ significantly from those of the 2 validation cohorts—eg, it was verifiable in other populations.

Disadvantages of case-control studies

One potential problem with case-control methodology is a likelihood of having inconsistent or incomplete medical records for accurately determining exposure statuses of the patients. Records may not have been kept according to a study protocol, and/or staff and patients may not recall important details.

As a control for this situation, the authors relied on the Pneumonia PORT cohort for verification, since it followed patients prospectively for 30 days. Data collection involved both patient interviews and chart reviews using a standardized protocol. Underlying and immediate causes of death were assigned independently by 2 investigators, with a panel of 5 investigators resolving any disagreements. [244:R] Thus, if a comparison of the 1989 MedisGroups’ derivation cohort with this Pneumonia PORT validation group produced no significant differences in outcomes, it would help validate data-collection accuracy in the derivation cohort.
LOOKING CLOSER

PATIENT SELECTION BIAS

In virtually any investigation, there will likely be conditions that influence or limit the selection of patients for study, which may affect external validity. Recognizing such biases allows for more prudent application of study results for clinical decision making.

For internal validity, the 3 cohorts needed to be equally matched for a fair comparison. The 3 cohorts were drawn nonrandomly from different populations at different points in time, but Table 1 [245] shows the groups were generally equivalent.

From an external validity perspective, it is important to define the characteristics of the study subjects to determine whether they match those of your own patients. By careful examination of the patient selection criteria and demographics described in the Fine et al study, several observations regarding the 3 cohorts can be made:

- Males and females were equally represented. Further demographics by race, ethnicity, and socioeconomic status were not reported
- All of the subjects were older than 18 years, so the study would apply to an adult population
- From Table 1 [245] it appears that roughly half of all patients were older than 50 years. A more precise determination of age ranges cannot be determined since additional data (eg, mean, standard deviation) are not given
- The authors acknowledged a bias in the Pneumonia PORT cohort—with enrolled patients younger than eligible nonenrolled patients and more often classified as at low risk for mortality [244:R]
- Table 1 described coexisting medical conditions, physical examinations, and laboratory findings in the 3 cohorts. The authors noted that the prevalence of these was lower in the Pneumonia PORT group. This reflected the patients’ lower ages as well as lower prevalence of coexisting illness among the outpatient subjects in this cohort [245:L]
- Patients with a history of HIV infection or AIDS were excluded from the study
- There was no mention of pregnancy as a prognostic factor, although this might be relevant in some clinical populations
- The 2 MedisGroups’ studies did not collect data on injection drug use and alcohol abuse among the patients. Thus, the prediction rule would not account for these conditions
- The 1989 MedisGroups’ derivation cohort represented broad-based data from 78 hospitals in 23 states, so a regional bias was largely avoided
A final consideration regarding patient selection is expressed by what is called Berkson’s fallacy. Essentially, this proposes that disorders appearing to be related in hospitalized patients (eg, all subjects in the 2 MedisGroups’ studies) may merely co-occur because the samples are biased toward severity.

• In many cases, hospitalized patients are not representative of the population as a whole; their primary diagnosis may have progressed further than usual, or there may be special circumstances leading to hospitalization.

The Pneumonia PORT study, which included a large number of outpatients for comparative purposes, controlled for such bias. The mix of inpatients and outpatients in this cohort would help detect a trend toward greater severity among hospitalized patients when compared with the 2 MedisGroups’ cohorts.
METHODOLOGY/RESULTS
Quantitative clinical research methodology relies heavily on statistical measures and tests. Like many authors, Fine et al provide references to other resources that explain some of their test statistics in more detail.

DERIVING THE PREDICTION RULE
Fine et al explained that they determined significant predictors of mortality through logistic regression analysis. This statistical procedure is used to analyze the relationship between a dichotomous dependent variable (death vs survival in this case) and various independent variables. Results are often expressed by odds ratios or relative risks and 95% confidence intervals.

Using the logistic model, patients were ranked according to mortality risk, assigning those with the lowest risk to class I. Derivations of the point scoring system for the other 4 classes were explained in the text, following a procedure that appears to have “face validity”; that is, it seems to be reasonable and convincing.

A total-point score for each patient is achieved by adding age in years and specified point scores for other predictor variables that the patient evidences. Ten points are deducted from the age for women. This adjusts for the logistic regression analysis finding that male gender is a higher risk factor.

Figure 1 provided a schematic presentation of the rationale for assigning patients to the lowest risk class I. Table 2 showed point assignments for all 19 factors used in determining risk classes II, III, and IV.

STATISTICAL VALIDATION
For all statistical analyses, the authors indicated the two-tailed probability values of less than 0.05 were considered significant. Such two-tailed tests are preferred, since they account for scores that move in any direction: for example, mortality rates either increasing or decreasing. One-tailed tests are, essentially, unidirectional.

A probability value of less than 0.05, or $P<0.05$, indicates that for the reported “significant difference” there was a greater than 95% likelihood that the factors being compared were genuinely different, rather than being merely due to chance or some unknown reason. The $P<0.05$ level is commonly accepted by most researchers.
Fine et al reported 3 statistical methods for validating their prediction rule:

**Chi-square test**

- To show that the 3 cohorts were equally comparable, the authors needed to demonstrate that there were no significant differences in mortality rates among the 3 cohorts in terms of the 5 risk classes. Using the chi-square test, no significant differences were found, as reported in the notes to Table 3. [248]
- The chi-square test is generally used for categorical data (in this case, death versus survival) to determine if rates or frequencies differ significantly between groups. For the data labeled “% who died” in Table 3, a contingency table having 3 columns (cohorts) by 5 rows (risk classes) was most likely developed for the calculations.

**Receiver operating characteristic curves**

- This type of analysis depicts the extent to which a screening test can discriminate between persons with and without a condition or conditions of interest. The area under a graphically plotted curve (AUC) provides a measure of how well the test performs. An AUC of 1.0 is perfectly accurate, whereas a test with an AUC of 0.5 is performing no better than chance.
- Areas beneath receiver operating characteristic (ROC) curves for predicting mortality in each of the 5 risk classes were compared in each cohort [244:R].
- Fine et al reported generally equivalent AUCs of 0.84 for MedisGroups’ derivation cohort, 0.83 for MedisGroups’ validation cohort, and 0.89 for Pneumonia PORT’s validation cohort.
- The prediction rule was performing well in forecasting mortality rates in each risk class, much greater than by chance alone.

**Cochrane-Armitage test**

- The Cochrane-Armitage test is a computer-driven statistical model for detecting increasing or decreasing responses when categorical exposures are ordered, such as in dose-response measures or, possibly in this case, predictive factors within the 5 risk classes affecting hospital stay.
- The authors mentioned using a Cochrane-Armitage test for trend to assess associations between risk class and other medical outcomes, eg, subsequent hospitalization and admission to an intensive care unit. A trend test was also performed for length of hospital stay [245:L].
- The results of this test were not reported in the paper.
As a measure of internal validity, the authors commented: “The clinical profiles of patients within risk classes were nearly identical in the three study cohorts.” And, in answer to our search query regarding age factors, several trends were reported:

- Class I patients were all young (median age 35-37)
- Class II patients were typically middle-aged (median age 58-59)
- Class III patients were older (median age 72)
- Class IV and V patients were somewhat older (median age ≥75)
DISCUSSION

In their discussion, the authors noted: “The prediction rule identifies three distinct classes (I, II, and III) of patients who are at sufficiently low risk for death.” [249:L] These patients might be candidates for treatment as outpatients. The cumulative death rate for these 3 classes of inpatients in the MedisGroups’ derivation cohort was 3.9% [from Table 3]. The authors suggested that, for added safety, classes I, II, and III patients presenting with hypoxemia might continue to be treated as inpatients.3

BENEFITS

The authors used data from the Pneumonia PORT study to illustrate the potential benefits of their prediction rule. Assigning all class I and class II patients to outpatient care, would have reduced hospitalization by 31%. [249:L]

Calculation from Table 4: (class I + class II inpatients) / total patients = (185 + 233) / 1343 = 0.31 or 31%.

Another way of looking at this is that there was a 31% absolute reduction in hospitalizations, or for approximately every 3 patients evaluated using the prediction rule, an additional patient would be spared hospitalization. This is an interpretation of the number needed to treat (NNT), using the formula 1 divided by absolute risk reduction: in this case, 1/0.31.

The authors further note that those in class III treated as inpatients might have only a brief observational hospital stay, thus reducing full inpatient care by an additional 19%.3

Calculation from Table 4: 254 class III patients / 1343 total = 0.19 The NNT would be about 5 (1/0.19); eg, for every 5 class III patients, an additional patient might avoid an inpatient hospital stay.
CAVEATS

The study only included hospitalized patients, not outpatients: “It is important to note that the premise that a large proportion of low-risk inpatients could be treated safely in an outpatient setting or with very short hospital stays assumes the processes of care in the hospital setting are not critical determinants of medical outcomes among low-risk patients.” [250:L]

In addition, the authors suggested a number of important limitations of their prediction rule “before recommending its use in clinical practice.” In particular, the following patients might receive traditional inpatient care, even if they were classified in low-risk classes I, II, or III:

- All patients presenting with hypoxia. The authors noted that even if such patients with hypoxia in classes I, II, or III had been admitted as inpatients, there still would have been reductions in hospitalizations of 26%, and an added 13% of patients would have only been treated with a brief observational hospital stay (compared to the 31% and 19% reductions stated above) [249:R]

- Those with medical and/or psychosocial contraindications—eg, impaired cognitive function, treatment compliance problems, and other situations hindering home care. (Alcoholics and injection drug abusers, not accounted for in the prediction rule, might be considered noncompliant patients)³

- Patients with rare conditions—eg, neuromuscular disease or immunosuppression—that were not considered as predictor variables in the logistic regression model for developing the prediction rule³

- Pregnancy was not mentioned in the patient demographic information or included in the prediction rule model. This could have been a factor necessitating hospitalization in some women with CAP³

Residing in a nursing home is considered a risk factor (assigned a score of 10) and such patients might score in high-risk classes according to the prediction rule. However, the observational care and therapies available in those environments might have reduced the need for inpatient hospitalization in some cases.

In addition, the authors advised that the prediction rule should not override physicians’ judgments in clinical decisions. They acknowledged that the rule was constructed using dichotomous predictor variables—a condition or finding was deemed either normal or abnormal. “As a result,” they noted, “it may oversimplify the way physicians interpret the predictor variables.” [249:R]
DISCUSSION

CLINICAL APPLICATION

The external validity of this study seems to hinge on combining the prediction rule as a starting point with sound clinical judgment. In this sense, the “rule” appears more like a “guide.” The authors seem to acknowledge this by stating that adhering to the rule “assumes that the processes of care in the hospital are not critical determinants of medical outcomes among low-risk patients.” [250:L] In brief, some patients will benefit from hospitalization, regardless of which class they fall into.

Fine et al also suggested: “Firm recommendations for [the prediction rule's] clinical use will depend on future prospective trials to confirm its effectiveness and safety.” [250:L]

One approach, which might even be tested in small group clinical practice, would be to have physicians randomly assigned to either use the prediction rule (experimental group) or “standard practice procedures” (control group) when evaluating patients with pneumonia and assigning them to either outpatient or inpatient treatment. Ideally, patients would also be randomly assigned to physicians.

Patient records would then be assessed, perhaps by independent and blinded investigators, at follow-up intervals—30 days, 60 days, etc—to determine outcomes. The results should indicate whether the experimental group experienced fewer hospitalizations, along with decreased mortality and morbidity. Thus, the feasibility and benefits of the prediction rule in everyday use would be established, albeit for that particular medical practice environment.
SUMMARY

Although the study has limitations—eg, it only included hospitalized patients—it does help inform you of some of the risk factors and scenarios for assessing the initial clinical question: Which patients with CAP might be safely managed as outpatients rather than hospitalized? This, in turn, can help you use your clinical judgement to make an informed decision about how to evaluate a clinical study.

Consistent with the clinical scenario and clinical question that initiated an exploration of this topic, the authors noted: “Given the prevalence of [community-acquired pneumonia], strategies that reduce the use of traditional hospital care could result in large aggregate cost savings.” [249:R]

In fact, in their introduction, the authors observed that 600,000 hospitalizations each year for CAP have an aggregated cost approaching $4 billion [243:R]—or $6700 per case. Therefore, the reductions in hospitalization presented in this study could have considerable economic impact.

The authors further observed that reducing hospitalizations would be consistent with patients’ preferences for home care rather than hospital care. [249:L] At the same time, this study demonstrated that mortality risks would not significantly (in a statistical sense) increase due to application of the prediction rule and that adult patient age does appear to be a factor in assigning risk.

In most regards, this study seems to respond well to our query. However, several questions might remain regarding:

- Selection biases in the study cohorts
- Limitations of applying the prediction rule (as expressed by the various caveats above, such as applying data about inpatients to an outpatient setting)
- The need for prospective investigations to confirm validity of the rule

Your next step might be to consult other studies for clarification and confirmation of the prediction rule. Or different strategies might be explored in answer to the clinical question.

In looking for additional studies on this topic, you might want to consider the references listed in the Fine et al study. Also, PubMed has a feature allowing a quick search for “Related Articles” linked to the Fine et al study. This could be used to extend your inquiry or to explore more targeted clinical questions.
DISCUSSION

FURTHER ACTION

When this search was done, PubMed produced 129 citations related to the Fine et al study, including:


The list above demonstrates that numerous other articles, including additional ones by Fine as lead author, might answer the clinical question. Deciding just when sufficient evidence-based research has been gathered for clinical decision-making purposes is always difficult.

Ideally, you will assemble several studies responding to your particular clinical question, so they can be compared and contrasted to help resolve any doubt about the best diagnosis and treatment. It is helpful to remember that healthy skepticism is a virtue when you are critically assessing the results and conclusions of any published study with the objective of making evidence-based clinical decisions.
CONCLUSION

BALANCING RESULTS AND REALITY

Successfully bridging the gap between your initial patient-care questions and search results that facilitate clinical decision making can require time and effort. That is why an efficient and productive approach is essential.

The evidence-gathering process, as demonstrated in this case study, follows a protocol:

- Formulate concise, answerable clinical questions based on the identified challenge
- Identify accessible resources for studies, such as local medical libraries, colleagues, and Internet databases (eg, MEDLINE, EMBASE, professional search services)
- Assemble abstracts or studies for preliminary review, selecting only those that seem to most appropriately respond to your clinical question(s) for further analysis
- Assess the validity, accuracy (reliability), and relevance of those studies for your particular patients

When evaluating studies, consider the following:

- Does the study’s purpose and hypothesis address your clinical question or query? (This can often be immediately gleaned from the title or abstract)
- Is the study population large enough and well defined? Are the subjects similar to your own patients?
- Is the study free of bias in the selection, assignment, and treatment of subjects? If there are biases, might they detract from or add to the applicability of the results to your patients?
- Do the study methods and measurements provide statistically significant results?
- Are the results clear, understandable, and presented in ways that aid your clinical decision making?

A study may have internal validity, yet the external validity may be questionable. That is, the observed effects may seem true for the subjects in the particular study, but you may still be uncertain about whether or not the conclusions can or should be applied to your specific patients.

Study results are based on average effects in a subject population statistically representative of a much larger population as described in the study. Individual patients, however, may differ from the average in ways that influence the ultimate effectiveness of any medical treatment or intervention. Plus, there are usually potential risks (eg, adverse reactions, morbidity, mortality) and economic costs to consider.

The role of the practitioner is to balance medical research findings and everyday clinical realities to determine appropriate treatment (intervention, test, etc) thresholds. In some cases, there is a need to gather further confirming evidence of therapeutic benefit or harm reduction before those treatment boundaries can be clearly defined.

Even the most rigorously designed and statistically significant studies will have limitations. For example, studies may provide results that are most valuable only
CONCLUSION

when applied in the right place and time, with the right patients, and in the right way. So, there is always the need to consider the opportunities or restrictions inherent in particular clinical settings and among specific patients.

Finally, implementing valid study results depends on the extent to which the conclusions agree or conflict with professional experience and beliefs. Evidence-based medicine approaches, above all, can assist in forming new beliefs that better meet today’s challenges of patient care.

For a review of key questions to ask when evaluating clinical literature, refer to the Clinical Literature Evaluation and Assessment Resource “Article Review Checklist” on the CD-ROM.
REFERENCES


