one week, another resident the next week, and so on. Although there is sometimes very little continuity in our system, continuity is extremely important to the patient. One of the principles of palliative care is to provide continuity.

TOWARD BETTER PALLIATIVE CARE FOR ALL

The World Health Organization would like to see the philosophy and practice of palliative care integrated into routine cancer care, if necessary, from the time of diagnosis. Moreover, in Great Britain, we believe that the principles of palliative care should not be confined to cancer patients but should be applicable to all patients with chronic, difficult, terminal phases. Approximately 10% of the patients referred to the palliative care team our hospital have cardiac or respiratory disease, and others have renal or chronic neurological disease.

The priorities for the future are to take palliative care to where the patients are, to include palliative care in the core curriculum of every health care professional, and to establish the evidence base for palliative care with high-quality clinical and health services research.

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Evidence-based medicine in everyday practice

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ABSTRACT

The evidence-based medicine method of answering clinical questions involves searching the literature for relevant studies, assessing study quality, interpreting the findings, and applying them in light of patients' preferences and societal values. In this article, evidence-based methods are used to solve questions posed by two patients.

EVIDENCE-BASED MEDICINE should never be an impersonal "cookbook" approach to treating patients. Scientific evidence in and of itself never tells us how to treat a particular patient. Rather, our decisions are informed by the values and preferences of the patient, the physician, and society.

In the two cases below and the discussion that follows, I outline how evidence can guide a busy physician.[1]

CASE #1: MR. SMITH'S OPTIMAL TREATMENT

One day, Mr. Smith, a 70-year-old man, visits your office. He suffered an anterior myocardial infarction 2 years ago, complicated by heart failure. He is concerned because his shortness of breath seems to be getting worse, hampering his ability to take walks or do other activities he once took for granted. He takes an angiotensin-converting enzyme (ACE) inhibitor, digoxin, and a diuretic.

Despite the limitations imposed by his health, Mr. Smith enjoys life. He is worried about premature death and would like to live

as long as possible. He adheres to his medication regimens, and he is very willing to take additional medications if he is convinced that they will help him live longer.

CASE #2: MR. LEE'S QUALITY OF LIFE

Coincidentally, later the same day, another 70-year-old man with similar health problems comes in for an appointment. Mr. Lee also suffered an anterior myocardial infarction about 2 years ago and has worsening symptoms of heart failure, which are limiting his daily activities. He takes an ACE inhibitor as well as a diuretic. He was once offered digoxin but decided against taking it because he felt it did not offer enough benefit to be worth the hassle of taking another medication.

Mr. Lee is frustrated with his limitations and his medications, saying they make his life unpleasant. His highest priority is finding something to make him feel better. The only drug he would be willing to add to his regimen is one that will improve his quality of life, not one that would prolong his life with its current limitations.

What should be done for Mr. Smith and Mr. Lee, and how can evidence-based medicine help us come up with the right answers?

Evidence based medicine is not "cookbook" medicine

WHAT IS EVIDENCE-BASED MEDICINE?

Traditionally, physicians rely heavily on their own and their colleagues' clinical experience and on their training in pathophysiology to solve clinical problems like these. Yet most of us are willing to admit that our clinical experience may be limited by small sample size and unsystematic case selection. Experience has also taught us that therapies supported by persuasive physiologic rationales may turn out to be ineffective or even harmful when tested in patients.

Four levels of evidence

The evidence-based medicine movement, started in 1990 at McMaster University, proposes that clinical evidence is best for solving clinical problems. Those who advocate this approach argue that certain types of evidence are stronger than others.

- The most valuable clinical evidence comes from well-conducted **integrative studies**, such as systematic reviews and meta-analyses, which combine and review the evidence from strong randomized trials.
- Second in value are well-conducted individual **randomized trials**.
- Third are **observational studies**.
- Other types of evidence, such as **clinical experience** and **physiologic rationale**, are valuable but are more open to bias and therefore are ranked at the bottom of the hierarchy of evidence.

We apply these types of evidence to specific cases in light of the preferences and values of our patients and our society.

HOW TO APPLY THE EVIDENCE-BASED APPROACH

Identify the best evidence

Faced with the question of how to treat Mr. Smith and Mr. Lee, the first question the evidence-based practitioner would ask is, "What is the available evidence?" We would first search for the strongest type of evidence, integrative studies that focus on our question. A search of MEDLINE for recent meta-analyses of beta-blockade for heart failure turns up a promising article by Heidenreich et al.[2]

Assess study quality

To determine the quality of the meta-analysis, several questions could be considered.

First, were the inclusion and exclusion criteria explicit and reasonable? In this meta-analysis, the authors considered randomized trials evaluating the effects of beta-blockers on mortality in patients with heart failure, and included only those with intention-to-treat analysis and follow-up longer than 3 months. These seem very reasonable and appropriate inclusion and exclusion criteria that should yield high-quality evidence.

Second, we might consider whether the literature search was comprehensive. In this case, Heidenreich began with a MEDLINE search, then went through the reference lists from the articles they read, and sought abstracts from meetings. Again, such a procedure seems reasonably comprehensive.

Third, we might note that Heidenreich et al failed to critique the adequacy of the primary studies in terms of concealment of randomization or loss to follow-up. However, we may not consider this limitation so serious as to warrant disregarding the article.

Understand the results

We have determined that this meta-analysis is unlikely to suffer from major bias. Now, we should look at the results of the study and seek to understand how they would apply to our patients.

The Heidenreich study reports that for all-cause mortality, the pooled odds ratio (OR) for beta-blockers was 0.69. An odds ratio of 0.69 suggests that these medications are associated with a 31% reduction in relative odds, an approximation of relative risk (100% – 69% = 31%).

In seeking to understand the estimate of the effect of this drug, it is also important to look at the precision of the estimate. We see that the study reports a 95% confidence interval for the odds ratio of 0.54 to 0.88. Thus, we are fairly confident that the true value for this odds ratio lies between 0.54 and 0.88. Even the most pessimistic estimate, according to the study, would be a 12% reduction in relative risk (100% – 88% = 12%).

The Heidenreich study also shows that the beneficial effect was virtually identical for patients with ischemic cardiomyopathy (OR 0.69, 95% CI 0.49 to 0.98) and nonischemic cardiomyopathy (OR 0.69, 95% CI 0.47 to 0.99). Interestingly, carvedilol seemed to perform better (OR 0.54, 95% CI 0.36 to 0.81) than all non-carvedilol drugs (OR 0.82, 95% CI 0.60 to 1.12). However, this finding probably cannot be taken too seriously, because the confidence intervals around the two odds ratios are quite wide and overlapping, and a reported *P* value of 0.10 suggests that chance could explain the difference.

APPLYING THE EVIDENCE TO MR. SMITH AND MR. LEE

Can the treatment prolong Mr. Smith's life?

How can we apply these numbers to Mr. Smith's very concrete question about prolonging his life?

This meta-analysis, as well as other studies, suggests that Mr. Smith, with his moderate to severe heart failure, has a risk of dying in the next year of about 20%. The meta-analysis suggests that beta-blockers will reduce his risk by almost 30%. That is, his one-year risk of dying will drop from 20% to 14%.

Another way to look at the potential benefit is to calculate the absolute risk reduction (ARR), in this case, 20% – 14% = 6%.

Yet another way of interpreting the evidence is to calculate the number of patients who would have to be treated to save one life. This number, the number needed to treat or NNT, is the inverse of the absolute risk reduction (1/ARR). Dividing 1 by 6% or 0.06, we calculate an NNT of 16.66. Thus, about 17 patients would have to be treated with beta-blockers to save a single life.

The evidence shows that beta-blockers will likely prolong Mr. Smith's life. We can be fairly sure about the effectiveness of beta-blockers, but we have a variety of options about what to do with that evidence.

Making the treatment decision with Mr. Smith

In a **parental model of health care**, the physician might make the decision to prescribe beta-blockers on behalf of Mr. Smith, feeling certain that they may prolong his life in accordance with his wishes. In the **collaborative model**, we might tell Mr. Smith that beta-blockers are likely to reduce his risk of dying in the next year from 20% to 14% and discuss the decision with him, taking into account such factors as side-effects and cost. In the **technical model**, we might inform Mr. Smith about advantages and disadvantages and leave the decision to him.

Certain types of evidence are stronger than others

How will the treatment affect Mr. Lee's quality of life?

Unfortunately, the Heidenreich meta-analysis provides no evidence about quality of life that might apply to Mr. Lee's situation, and our literature search comes up with no other relevant meta-analyses. A MEDLINE search of the next level of evidence, the individual randomized trial, turns up 25 trials on the effect of beta-blockers on quality of life.

To narrow the field and select the strongest studies, we can set our own inclusion and exclusion criteria. We can choose to restrict our search to studies that indicated quality of life using a numerical measure such as New York Heart Association functional class. When we choose studies of more than 100 patients which reported a numerical quality-of-life value at the end of the study and which followed up at least 80% of patients, we find two interesting articles.

The first compared bisoprolol with placebo in 641 heart failure patients, losing only one patient to follow-up. New York Heart Association functional class improved in 21% of bisoprolol patients and 13% of placebo patients.[3]

However, a second study comparing carvedilol with placebo had a very different finding. The rate of improvement was higher in the placebo group and the rate of deterioration was lower.[4]

In light of this contradictory evidence, we cannot be sure what effect beta-blockers will have on quality of life. We can tell Mr. Lee that beta-blockers have a good chance of prolonging his life, but we will have to admit that it is not clear whether the medication will make him feel any better. Mr. Lee's values and preferences are likely to be the deciding factor in whether or not he accepts a prescription.

In the end, a decision depends on the patient's values and preferences

USING EVIDENCE-BASED MEDICINE IN A BUSY PRACTICE

Obviously, it would be impractical to conduct a full literature review every time a patient asks for advice. But it is important to realize that in every practice, certain clinical problems appear over and over again. Every physician could probably identify 100 clinical questions that would cover the vast majority of situations encountered in daily practice and for which good evidence is available.

Electronic resources

In addition, methodologically strong, up-to-date reviews of important clinical questions are published quarterly on CD-ROM and the Internet (www.cochrane.co.uk) by the Cochrane Collaboration. The website of the American College of Physicians (www.acponline) provides free access to articles and abstracts from *Evidence-Based Medicine* and *ACP Journal Club*, two evidence-based medicine journals. These resources will help clinicians ensure that they are providing their patients with evidence from the latest, strongest medical research.

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FURTHER READING

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CME ANSWERS

Answers to the CREDIT TEST on page 511 of this issue

1 **D** 2 **D** 3 **E** 4 **C** 5 **B** 6 **D** 7 **B** 8 **E** 9 **C** 10 **B** 11 **D** 12 **B**