

Evidence-Based Medicine: Defining Evidence

By Kit-Bacon Gressitt and Amy Fuller

A woman in California, diagnosed with multiple sclerosis (MS), was shocked to learn her insurance company would no longer cover her intravenous immune globulin (IVIG) therapy because of a lack of medical evidence supporting the treatment of MS with IVIG. After approving the IVIG infusions for three and a half years, at the recommendation of her physician and MS specialists, the insurance company suddenly denied coverage on the basis that IVIG is an experimental treatment for MS.

This was devastating news to the patient, who believes IVIG is her lifesaver, enabling her to once again do things, such as walking, that most people take for granted. The patient also reported that IVIG therapy had relieved her debilitating headaches, severe muscle weakness and cognitive dysfunction. She was convinced her quality of life would be dramatically diminished without the IVIG infusions prescribed by her physician and supported by her MS experts. So, the patient paid more than \$4,000 per treatment out of pocket for her monthly infusions, while she appealed her insurance company's coverage denial. But, when she could no longer afford the expense, she had to follow her insurance company's treatment recommendation to try those therapies considered standard treatment for MS: steroids and interferon.

At first glance, the insurer's recommendation seemed sound, claiming a basis in medical evidence-based decision-making. However, in this particular case, the insurance company's recommendation failed to include consideration of three other factors that had been considered by the patient's physician and experts:

1. The patient's experience with IVIG, that it was demonstrably effective in reducing her MS symptoms during the previous three and a half years, improving her physical and mental functioning and, thereby, enhancing her quality of life;

2. The patient's additional diagnosis of osteoporosis, a condition that is exacerbated by the use of steroids; and
3. The patient's history of treatment for depression, which is a side effect of interferon.

In fact, the insurance company's treatment recommendation increased the risks of serious side effects for the patient. Still, the company insisted that she first fail the standard MS treatments before they would reconsider IVIG.

Stories such as the California patient's are not rare. Over the past year, Michelle Vogel, director of the Alliance for Plasma Therapies, knows of more than 250 patients who have lost access to IVIG based on insurance company determinations that their IVIG treatment is not supported by evidence-based medicine.

What Is Evidence-Based Medicine?

"Evidence-based medicine is not what payers are claiming it is," said Dominick Spatafora, president of the Neuropathy Action Foundation (NAF) and CEO of the Los Angeles County Medical Association. He is concerned about "the growing misuse of so-called evidence-based medicine" (EBM) in payer decisions about IVIG reimbursement. "Evidence-based medicine is a great tool when it is used as it was intended—for medically based diagnosis and treatment decisions—but it can put patient care at risk when it is misused to achieve cost containment or cost reduction by government and commercial health insurance companies."



EBM was developed in the mid-1990s to help physicians avoid wide variations between clinical practices, unproven medical interventions and inconsistent application of practice guidelines, with the ultimate goal of improving the physician-patient relationship, patient care and outcomes. The early proponents of EBM claimed it would help ensure healthcare funds would be spent more efficiently,¹ while improving outcomes. They believed doctors who consistently used evidence in planning a course of treatment for their patients would be more likely to use new, more effective treatments and abandon treatments that failed to show results.

Spatafora explained that EBM was defined in the mid-1990s by David Sackett, MD, and others as the “conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.” Sackett and his colleagues stressed that doctors would be encouraged to keep up with the latest medical innovation and still have the ability to draw on their accumulated practical knowledge.²

As defined by Sackett and his colleagues, EBM essentially has three key elements:

1. **A physician’s clinical expertise**—the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice;
2. **The best available external clinical evidence**—the clinically relevant research, often from the basic sciences of medicine, but especially from patient-centered clinical research into the accuracy and precision of diagnostic tests (including the clinical examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative and preventive regimens; and
3. **The patient’s situation and preferences**—the thoughtful identification and compassionate use of the individual patient’s predicaments, rights and preferences in making clinical decisions about his or her care.

The EBM model dictates that the first element, a doctor’s clinical expertise, is integrated with the second, the best available external clinical evidence, to result in treatment decisions that match the patient’s clinical state, predicament and preferences.

“When all three of these components are combined, the best evidence-based medical decisions can be made,” Spatafora said to attendees at a September 2007 Alliance for Plasma Therapies meeting with the U.S. Department of Health and Human Services and the Centers for Medicare and Medicaid Services (CMS). “But,” Spatafora clarified recently, “the cost of clinical research prevents the body of scientific evidence EBM suggests and payers are now demanding for less common and rare diseases.”

At the same meeting, Lisa Christopher-Stine, MD, of Johns Hopkins University Department of Rheumatology, said that many patients who benefit from IVIG, such as some myositis patients, are unlikely to become the subjects of clinical trials because the number of these patients is too small to motivate drug companies to invest in the research necessary to meet U.S. Food and Drug Administration (FDA) guidelines. She said, however, that in informal clinical settings, when a person who had been dependent on a wheelchair for mobility stands up and walks, it’s obvious that IVIG has improved the quality of the patient’s life tremendously.

“Were EBM applied as intended in this instance, the treating physician’s clinical expertise and the patient’s situation and preferences could serve as proof that IVIG treatment is appropriate,” said Spatafora, “despite the off-label indication and lack of external clinical evidence. And this would be reasonable within the EBM model.”

However, some public and private insurers appear to be making use of EBM primarily as a cost containment or cost reduction tool. “This is evidenced in the increasing reference to EBM in coverage denials for expensive therapies,” said Vogel, “even if the patient has used the therapy with good results for years. And now CMS has proposed making EBM the bedrock for deciding which treatments, devices and services Medicare will cover. Government and private payers must assure physicians and patients that they will use EBM, not a cost-cutting spin that emphasizes only one of the three elements over the other two.”

The director of CMS’ Coverage and Analysis Group, Dr. Steve Phurrough, offered an interpretation of EBM that appears to represent a policy shift from the EBM founders’ concept to an emphasis on clinical research: “Evidence-based medicine de-emphasizes intuition, unsystematic ➤

¹ “Some fear that evidence based medicine will be hijacked by purchasers and managers to cut the costs of health care. This would not only be a misuse of evidence based medicine but suggests a fundamental misunderstanding of its financial consequences. Doctors practising evidence based medicine will identify and apply the most efficacious interventions to maximise the quality and quantity of life for individual patients; this may raise rather than lower the cost of their care.” Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence-based medicine: what it is and what it isn’t. *BMJ*. 1996;312:71-77.

² Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence-based medicine: what it is and what it isn’t. *BMJ*. 1996;312:71-77.

clinical experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and *stresses the examination of evidence from clinical research.*"^{3,4}

This interpretation of EBM would likely deny IVIG access to many patients with rare diseases and complicating diagnoses, despite previously observed beneficial outcomes, as was the case with the MS patient. Because the numbers of these patients are, again, small and clinical research is expensive, manufacturers would likely need some financial incentive to invest in the clinical trials necessary to scientifically prove IVIG's efficacy to FDA standards. But the incentives do not exist, the research is not being done, and such indications for IVIG treatment are inevitably failing the external clinical evidence litmus test payers are mistakenly representing as EBM.

According to several critics of the CMS proposal to adopt EBM, the potential human cost of misuse of EBM would be great. The Alliance's Vogel said, "In short, misuse of EBM by payers to make coverage determinations threatens to weaken the doctor-patient relationship, to dismiss the importance of clinical experience and to de-emphasize the observable efficacy of a treatment for a single patient by focusing solely on the statistical outcomes for a group. If this is the intent, it is a dangerous course that could leave damaged patients in its wake," she concluded.

Pfizer's Health Reform Policies posted on the company's website clearly states the pharmaceutical manufacturer's position that EBM is a tool for practitioners: "Evidence-based medicine should be used by the medical provider—not the payer—as a factor in determining the most appropriate treatment for individual patients."

Indeed, as Spatafora indicated, the originally conceived EBM is a tool for experienced healthcare practitioners to plan a rational course of treatment with their patients: Physicians review external clinical evidence, draw on their experience, and make a judgment to match the treatment to the individual patient's situation and preferences.

Spatafora believes that if EBM is implemented with these principles in mind, quality of care can improve and healthcare dollars can be spent efficiently. However, said Spatafora, "when EBM is applied with an emphasis only on clinical research evidence, it results in predominantly a cost-cutting tool, diminishing or even rejecting the relevance of physicians' clinical expertise and judgment

and the patient's individual needs. Without consideration of all three elements, it is not EBM."

In the MS patient's case, Vogel said, "her doctor's opinion was not given adequate consideration compared to the medical evidence. Neither was the medical expertise of the MS specialists who concurred with her doctor's recommendation. Additionally, the patient's other diagnoses and positive clinical experience with IVIG were not considered relevant, and, instead, her insurer rejected her appeal for IVIG. She has been forced off a therapy that was proven to be effective for her and shifted onto interferon, a therapy that puts her health and well-being at risk."

Since starting interferon, the patient reports that her muscle weakness and cognitive dysfunction have increased, and her quality of life has decreased. She said she will continue to appeal to restore her access to the one therapy that has proved effective for her, IVIG. But, as she struggles through the complexities and frustrations of her current appeal process, she is afraid she will not regain access to IVIG before her MS has progressed to the point that the IVIG treatment will no longer be effective.

This situation leaves the patient and those who care for her seriously questioning the insurer's decision-making. "This does not appear to be true evidence-based medicine," Spatafora said. "The insurer's disregard of the treating physician's expertise, along with the patient's situation and preferences, is a perversion of EBM—apparently with the sole purpose of cutting costs. And it appears to be a trend in this country, one with potentially devastating human cost."⁵

One day, a patient, a physician, a manufacturer, a politician or perhaps a payer will manage to elevate the bottom-line question to the public ear: What human cost will we tolerate to achieve cost containment? ■

For More Information

Read the British Medical Journal editorial, "Evidence based medicine: what it is and what it isn't" BMJ 1996;312:71-72 www.bmj.com/cgi/content/full/312/7023/71.

Pfizer's Health Reform Policies www.pfizer.com/about/public_policy/pfizer_health_reform_principles.jsp
Copyright © 2002-2008 Pfizer Inc., Last Updated September 2007.

³ Evidence-Based Medicine Working Group, JAMA 1992.

⁴ Emphasis is the editor's.

⁵ Pfizer's Pharmaceutical's Health Reform Policies. Copyright © 2002-2008 Pfizer Inc. Last Updated September 2007. www.pfizer.com/about/public_policy/pfizer_health_reform_principles.jsp.