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A Supplement to

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Part 2 of a 3-Part Series

EVALUATING EVIDENCE-BASED MEDICINE: CLINICIAN AND PAYER PERSPECTIVES AND APPLICATIONS FOR SCHIZOPHRENIA

This supplement to *The American Journal of Managed Care* is based on presentations and discussions from a roundtable meeting comprising expert consultants. This meeting was sponsored by Eli Lilly and Company, held in Detroit, Michigan, on July 18, 2008. Part 1, published in December 2008, covered the *Importance of Early and Effective Pharmacologic Treatment in Schizophrenia* (www.ajmc.com). The third installment in the series, *The Application of Evidence-Based Medicine in Evaluating Formulary Options: Payer Perspectives*, will be published in March.

INTRODUCTION TO EVIDENCE-BASED MEDICINE

What is evidence-based medicine?

Evidence-based medicine (EBM) is an integrated approach to the decision-making process, using individual clinical expertise in combination with the best research evidence and patient preferences.^{1,2} The goal is to achieve the most effective care, for improvement of quality and quantity of life for patients.¹ “Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.”¹

EBM guides clinical judgments based on individual experience, relevant scientific evidence, and patient values and preferences.¹ Scientific evidence may include both basic science and patient-centered research.¹ A common approach is the use of high-quality research, from which systematic reviews are written. These systematic reviews relieve the busy practicing clinician of reviewing an overwhelming amount of literature and direct practitioners, and payers alike, to high-quality research. Unlike strict research or cost-efficacy-driven guidelines, EBM practice incorporates individual clinician experience and patient preference as a key feature. “Evidence-based clinical practice is an approach to decision making in which the clinician uses the best evidence available, in consultation with the patient, to decide upon the option which suits that patient best.”^{2,3}

At the core of EBM—evaluating research and interventions

Three important questions must be asked when evaluating an intervention: Can it work? Will it work? Is it worth it?^{3,4}

- Based on efficacy in a clinical trial, can the intervention work?
- What is the effectiveness in the real world?
- Evaluate the risk–benefit to determine if it is worth the risk.

The first question is straightforward: “Is there efficacy data to support the use of an intervention?” For some conditions and diseases that are less common, only



Table 1

Levels of Evidence for Therapeutic Studies⁷

Level of Evidence	Type of Study
1a	Systematic reviews (with homogeneity) of randomized controlled trials
1a-	Systematic review of randomized trials displaying worrisome heterogeneity
1b	Individual randomized controlled trials (with narrow confidence interval)
1b-	Individual randomized controlled trials (with a wide confidence interval)
1c	All or no randomized controlled trials
2a	Systematic reviews (with homogeneity) of cohort studies
2a-	Systematic reviews of cohort studies displaying worrisome heterogeneity
2b	Individual cohort study or low-quality randomized controlled trials (<80% follow-up)
2b-	Individual cohort study or low-quality randomized controlled trials (<80% follow-up/wide confidence interval)
2c	“Outcomes” research; ecological studies
3a	Systematic review (with homogeneity) of case-control studies
3a-	Systematic review of case-control studies with worrisome heterogeneity
3b	Individual case-control study
4	Case series (and poor-quality cohort and case-control studies)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or “first principles”

Adapted from Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=1044>; Essential Evidence Plus: Levels of evidence—Centre for Evidence-Based Medicine, Oxford (1a-5). http://www.essentialevidenceplus.com/concept/ebm_loe.cfm?show=oxford.

lower-quality evidence, such as case reports, are available to evaluate an intervention. Evidence-based practice guidelines focus on the most common clinical decision points; however, the principles may also be used for evaluation of any clinical decision. The next question—“Is there effectiveness data to support the applicability of the intervention to this clinical circumstance”—involves evaluation of the research

evidence on implementation of treatment interventions in as close to “real world” practice settings as possible. Finally, the question of whether a treatment intervention is worth it is based on an evaluation of the risks and benefits of an intervention.^{3,4} All 3 of these concepts will be discussed in further detail below. Careful upfront consideration of the question and the validity of the intervention will simplify the search

for evidence, and guide the evaluation of evidence and implementation into patient care.⁵

Evaluating the quality of the evidence

Many kinds of evidence are utilized in EBM, but not all are of equal quality. Randomized controlled trials are preferred,⁶ as controlled comparisons serve to eliminate or equalize other potential factors and bias influencing outcomes and focus on the difference in treatment effects between randomly assigned conditions (**Table 1**).⁷ Systematic reviews of randomized trials focus on a single question and then identify and evaluate all relevant research evidence. Systematic reviews use explicit criteria to identify and evaluate relevant research, thereby minimizing the possibility of bias. Meta-analyses are systematic reviews that merge data across multiple studies using quantitative statistics. Meta-analyses can give greater confidence to pooled data, such that the reader may use the aggregate information in clinical decision making; however, meta-analyses can be prone to analysis bias, and are therefore considered second-line evidence.⁶

EBM is not limited strictly to higher-level evidence; however, controlled research is preferred when available. Physiologic studies and unsystematic clinical observations, observational studies, and case reports may add additional information.⁶ Observational studies demonstrate effectiveness in less controlled conditions. Although uncontrolled, observational studies and case reports may address important patient outcomes and tap the resources of clinical experience. Finally, clinical guidelines are systematically developed recommendations, designed to assist in clinical decision making for specific clinical circumstances. Guidelines from reputable, authoritative organizations are usually based on the most current, relevant research and attempt to distill a large amount of information into an easily usable format. Guidelines



are developed using widely varying standards and may include value judgments about the relative importance of specific health outcomes, in addition to overall health outcomes and cost data. Because clinical guidelines make specific recommendations designed to influence practice, clinical guidelines are second-tier evidence for EBM reviews.^{6,8} For a quality EBM review, the best available evidence from various sources is carefully considered with the goal of providing provider–patient dyads the most accurate information to support informed decision making.

IMPLEMENTATION OF EBM PRINCIPLES IN PRACTICE

Defining a balance

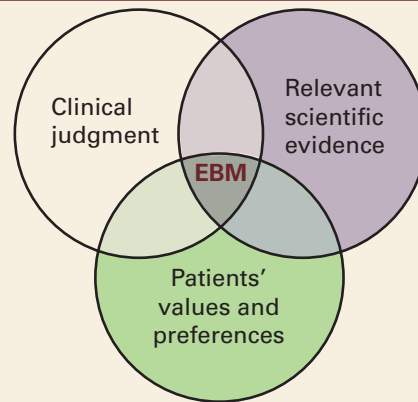
EBM is commonly described using a 3-sphere model, representing the key concepts of clinical judgment, relevant scientific evidence, and patients' values and preferences (Figure).^{1,3} There are no definitive rules for dividing the pieces of the pie. The sphere sizes may vary, larger and smaller, depending on the emphasis and the scenario. This fluidity of the process and adaptability may be the key to success. In one situation, the relevant scientific evidence may be lacking, but clinician experience and patient preferences are strong in the therapeutic decision-making process. In another scenario, a wealth of clinical data may outweigh some patient preferences and potentially even some clinical experiences.

Applicability to a practice setting

There are a number of challenges that all health systems face with implementation of any system change. Use of a professional, systematic approach is crucial for provider acceptance. Providers may view EBM as a suppression of clinical freedom¹ or complicated and only for those in academia.¹ Others view protocols and care pathways as “cookbook” medicine that doesn't apply to their patients.¹ In fact, surveys of non-academic practitioners revealed that

Figure

What Is Evidence-Based Medicine (EBM)?³



Adapted from Sackett DL, et al. *BMJ*. 1996;312(7023):71-72; Muir Gray JA. *Evidence-Based Healthcare*. 1997.

most already provide evidence-based care to the majority of their patients.¹ EBM systematic reviews relieve the busy practicing clinician of reviewing an overwhelming amount of literature, direct practitioners to high-quality research, and can help in the process of coordinating care throughout the spectrum of a health system.¹ The same is true for payers in the development of medical policies and usage guidelines.

The goal of EBM implementation is to attempt to avoid clinical decisions made without the benefit of relevant information (ie, likelihood of benefits of harm). Decision making

based solely on practitioner clinical experience commonly leads to biased observations and false-positive conclusions about efficacy. Obviously, not all clinical scenarios will have controlled trials to support treatment decisions, in which case, meta-analysis, case series, expert consensus, and practice guidelines would be used for clinical decision making.¹

Interpretation and application of data to patient care requires careful consideration, even in the best scenarios. Despite best efforts, no research is perfect. The data results produced by a study need to be understood in the context of the

“In EBM, there are 3 essential components: clinical evidence (eg, data, tools, and guidelines), individual clinical expertise (eg, education, judgment, experience), and patient values (eg, personal concerns, expectations, beliefs). Quite simply, optimizing treatment outcomes using EBM does not work unless these 3 components are considered simultaneously and with equal measure. Finding a balance is the key to success.”

Lawrence J. Cohen



“*Efficacy* is frequently used to describe results in clinical trials (eg, in a clinical trial the investigational antipsychotic demonstrated *efficacy* compared to placebo or an active comparator in controlling psychotic symptoms). In contrast, *effectiveness* implies not only efficacy, but also safety/tolerability and adherence. When considering EBM and our intent to optimize treatment outcome, *effectiveness* rather than *efficacy* becomes our principal consideration since it focuses our attention on the individual and their unique characteristics (eg, medical comorbidities, history of treatment response, and adherence/persistence).”

Lawrence J. Cohen

specific methodology utilized by the study. In psychiatric treatment research, relatively minor changes in methodology have often yielded different results. Selection bias in published research is a reality.⁶ Current research data do not answer every question; therefore, a series of interpretations must be made for application to a given patient. In the past, information was not always timely or consistently evaluated; however, clinical research is more rapidly available for integration into EBM reports than in the past. Standardized methods of grading quality of evidence for inclusion into EBM reviews have greatly improved consistency of evaluation and simplified grading of evidence and recommendations.⁶ EBM provides the evidence that must be integrated with, and is not intended to replace, clinician experience and patient preferences.¹

An obvious benefit of EBM implementation for payers is the potential for cost-containment. However, the goal is to look for the most effective therapies, which may result in cost increases or decreases.¹ EBM is a means of improving the quality and outcomes of clinical practice, and thus the accountability of practitioners to

payers and patients.⁶ Clearly, clinician judgment is an integral component of EBM and must be incorporated into payer policies.⁶

Bottom-line benefits

- EBM is an integrated and individualized approach to enhance the clinical decision-making process.
- EBM is intended to maximize the effectiveness of care, to improve health outcomes for patients, and to maximize cost-benefits for payers.¹
- EBM systematic reviews relieve the busy practicing clinician of reviewing an overwhelming amount of literature and direct practitioners to high-quality research.¹ These reviews also support payers in the development of appropriate usage guidelines and medical policy, enabling access to effective therapies.

DEFINING EFFECTIVENESS RESEARCH

While efficacy studies provide the greatest scientific integrity, “effectiveness” research provides a broader indicator of the effects of a treatment in actual clinical practice. Efficacy is

the impact of an intervention in a clinical trial, under controlled conditions where most potential contributors to outcome are eliminated or controlled. Effectiveness is the impact of an intervention in general without eliminating the many intervening factors that occur in general clinical practice, such as safety and side effects of a therapy along with patient acceptance and adherence. In addition, effectiveness takes into account balance of benefit to risk.⁹

Determination of effectiveness requires multiple levels of evidence, including assessment of time on treatment and adherence, in other words, the ability for people to accept and continue a treatment over time. A therapy with proven efficacy, but not well received by patients, is lacking in effectiveness. There is a process of balancing benefits and harms, which, of course, merges with patient preferences.⁵ Medication adherence is essential, particularly in the treatment of schizophrenia. Although many factors can influence patient compliance, recent evidence suggests that one of the most important reasons for antipsychotic discontinuation is lack of efficacy.¹⁰ Poor adherence with antipsychotic therapy is associated with increased relapses, hospitalizations, and costs.¹¹⁻¹⁴

For example, the *efficacy* of an antipsychotic drug reflects its ability to control psychotic symptoms. In contrast, the concept of *effectiveness* encompasses not only efficacy, but also safety/tolerability and persistence/adherence.⁷ In acute-phase schizophrenia—whether first episode or relapse—prompt antipsychotic treatment is recommended to reduce emotional distress, minimize disruption to the patient’s life, and reduce the risk of dangerous behaviors.¹⁵ In addition, prompt treatment may improve long-term outcomes. However, to realize these benefits, it is important to determine as quickly as possible whether the choice of antipsychotic drug is going to be effective for the individual patient.

CONCEPTS RELATED TO BENEFIT–RISK ANALYSIS

Risk–benefit analysis is a seemingly subjective concept that can be objectified by basic statistical evaluation. Statistical significance, in combination with clinical significance, adequate statistical power, and other analyses, can add to the strength of an *effectiveness* claim of a given intervention.

Statistical significance

Statistical significance is how efficacy is determined. A clinical intervention cannot be said to have efficacy unless its impact is statistically significant. A common statistical measure of significance is the “*P* value.” This number represents the probability that an observed difference is due to random error or chance. It is an indicator of how strong the likelihood that a finding is a true finding; the smaller the *P* value, the more convincing that a result is not simply due to random distribution of variation in outcomes. Although the sensitivity level may be adjusted to the requirements of a particular study, a *P* value of less than .05 is typically considered *statistically significant*, meaning there is a 95% probability that the finding is not due to chance.⁴ It is important to note that the *P* value does not indicate the size or the importance of the nonrandom effect, and the *P* value is not the same as effect size.⁴ Rather, the *P* value indicates how sure you can be that the difference measured is due to a difference between the conditions being compared. Effect size is better described by measures such as number needed to treat (NNT) or “risk reduction,” as discussed below.

Commonly, statistical significance in an adequately powered study is used to imply clinical significance.¹⁶ Although a significant *P* value indicates an effect that is likely to be “true,” the degree of meaningfulness and the clinical significance of that effect cannot also be automatically assumed.¹⁶ On the contrary, even if a study does not reach statistical significance, there can be clinically significant findings. However, without a significant *P* value, it is important to be sure that the study was sufficiently powered to determine if the findings are real or occurred by chance.¹⁶ When designing a study, researchers first need to determine the level of adequate power for a clinical trial to reach statistical significance. Power, which requires an adequate sample size, is needed to achieve statistical significance. To demonstrate adequate power for a study proposal, investigators need to declare a threshold of clinical significance, an effect size below which the treatment versus control difference would not be considered clinically significant.¹⁶ A trial may be powered to demonstrate statistical significance on a very small effect size; however, the reader may not agree that the effect size demonstrated in the trial is truly clinically meaningful.

Effectiveness and clinical significance

Effectiveness, also known as effect size, is the statistical measure of clinical significance. Clinical significance is determined based on disease outcomes, most frequently by using effect size, sometimes referred to as treatment effect. Effect size is a measure of the magnitude of treatment effect and

Table 2

Calculation of Absolute Risk Reduction (ARR), Relative Risk Reduction (RRR), and Number Needed to Treat (NNT)^{4,17}

$$\text{ARR} = \text{EER} - \text{CER}$$

$$\text{RRR} = (\text{EER} - \text{CER})/\text{CER}$$

$$\text{NNT} = 1/\text{ARR}$$

CER indicates control event rate; EER, experimental event rate.

independent of *P* value. It is important to note that effect size is used to determine clinical significance only for statistically significant findings.^{16,17} Effect size calculations include absolute risk reduction (ARR), relative risk reduction (RRR), and NNT, when an experimental treatment reduces the probability of a bad outcome. Absolute risk increase (ARI), relative risk increase (RRI), and number needed to harm (NNH) are used when an experimental treatment increases the probability of a bad outcome.¹⁷

Response rate and risk reduction.

Response rate, or percentage response, is a simple and commonly used type of outcome measure, used to describe efficacy.¹⁸ Response rate to a treatment is of limited value unless it takes into consideration a comparator. For example, if 50% of patients respond in the active treatment arm, yet 40% of patients respond in the placebo arm, the effect size of the active treatment is not as great as it appears at first glance.

Table 3

Sample Calculation of Absolute Risk Reduction (ARR) and Number Needed to Treat (NNT)³

$$\text{ARR} = \text{Frequency of outcome A} - \text{Frequency of outcome B}$$

$$\text{NNT} = 1/\text{ARR}$$

$$\text{ARR} = 52\% - 19\% = 33\%$$

$$\text{NNT} = 1/0.33 = 3$$



Table 4

Examples of Number Needed to Treat (NNT) for Medical Conditions^{3,5,21-23}

Condition	Intervention	Prevented Event	NNT
Diabetes ⁵	Insulin	Neuropathy	15
Acute myocardial infarction (MI) ²¹	Streptokinase and aspirin	Death in 5 weeks	20
Prematurely born baby ²²	Prenatal corticoid	Respiratory distress syndrome or prematurity	11
Diastolic blood pressure 115-129 mm Hg ²³	Antihypertensive drugs for 5 years	Death, stroke, or MI	3
Diastolic blood pressure 90-109 mm Hg ²³	Antihypertensive drugs for 5 years	Death, stroke, or MI	141

Conversely, risk reduction evaluates change from baseline or difference in response between 2 treatments. Whereas ARR is the absolute change in frequency,¹⁸ RRR is the comparative likelihood that some difference in outcome will occur between 2 treatment groups.⁴ RRR and ARR are simple calculations. ARR is calculated by subtracting the experimental event rate (EER) from the control event rate (CER). RRR is the ARR divided by the control event rate (Table 2).^{4,17} Using

the ARR allows the reader to take into account the frequency of the event, which relative risk does not allow. As an example, the Women’s Health Initiative study evaluated the risk of developing breast cancer for postmenopausal women who took daily aspirin versus placebo. The breast cancer risk for women who do not take daily aspirin is 955 per 194,884 person-years, or 0.49% (CER). Taking daily aspirin reduces breast cancer risk to 99 per 24,398 person-years,

or 0.41% (EER). The RRR is 20% ($[(0.49\% - 0.41\%)/0.41\%]$); however, the ARR is only 0.08% ($0.49\% - 0.41\%$).¹⁹ Despite a large RRR, the small baseline absolute risk (CER) results in a relatively low ARR.

NNT and NNH. NNT describes how many more patients you would need to treat with the experimental treatment instead of another treatment, such as placebo, or other control, to see 1 more patient benefit from

Table 5

Number Needed to Treat (NNT) in Psychiatry^{3,18}

Disorder	Treatment Comparison	Outcome Measure	NNT
Major depression	Antidepressant vs placebo	50% reduction in HAM-D	3
Acute mania	Valproate or lithium vs placebo	50% reduction in SADS-D	5
Bipolar disorder	Lithium vs placebo	Relapse	3
Schizophrenia	Antipsychotic vs placebo	40% reduction in BPRS or “much improved” CGI scale	2-5
Panic disorder	SSRI vs placebo	Panic free	3-6
Social phobia	Paroxetine vs placebo	“Much improved” CGI scale	3
Obsessive-compulsive disorder	SSRI vs placebo	35% reduction in Y-BOCS	4-5
Bulimia nervosa	Antidepressants vs placebo	Remission	9

BPRS indicates Brief Psychiatric Rating Scale; CGI, Clinical Global Impression; HAM-D, Hamilton Rating Scale for Depression; SADS, Schedule for Affective Disorders and Schizophrenia; SSRI, selective serotonin reuptake inhibitor; Y-BOCS, Yale-Brown Obsessive Compulsive Scale.



the experimental treatment.⁴ NNT is calculated from the ARR (1/ARR; **Table 3**).³ NNT is believed to be the most clinically useful measure of treatment effectiveness.¹⁸ The smaller the NNT, the greater the benefit of the experimental treatment, as a smaller number of patients requires treatment for 1 additional patient to benefit. In other words, the smaller the NNT, the more frequently the additional benefit of the experimental treatment will occur in clinical practice. There is no specific cutoff for what is a clinically significant NNT, as clinical significance is dependent on the gravity of the outcome measured. In general, NNT <10 is a big effect and >100 is a small effect. However, for prevention of death, >100 may still be clinically important. Cost per event avoided can be another helpful calculation, using NNT (Cost per event avoided = NNT x Cost of intervention). Payers and providers alike can use cost per event avoided for evaluation of clinical significance.¹⁷ It is important to keep in mind that NNT is only calculable for binary or dichotomous events that are either present or absent and not for continuous data, such as laboratory values. Continuous data can be converted to binary data, by using a clinically significant threshold, such as a greater than 10% decrease in blood pressure, after which calculation of NNT is possible.⁴

A negative NNT, or rate of adverse event occurrence, indicates that the study results favor the control group, also referred to as NNH. These adverse events can include side effects due to the medication or untoward events such as rehospitalization or even death. The calculation for NNH is the same calculation as NNT, but results in a negative number, indicating a negative outcome, sometimes referred to as 1/ARI.⁴

Application of significance to patient care

As discussed above, a statistically significant difference is not necessarily clinically significant. However,

“EBM requires us to use our clinical judgment in order to weigh benefits and risks for the individual patient in a number of ways.”

Doug Noordsy

clinical significance should not normally be considered if the finding is not statistically significant, as the finding may be due to chance.¹⁶ On the contrary, failure to find a statistically significant difference does not necessarily mean that 2 treatments are equivalent. It is possible that the sample size was too small to detect a difference, and higher-powered, larger studies may demonstrate a significant difference between the treatments being compared.¹⁶

Despite use of NNT and NNH calculations, there is no specific cutoff for determination of clinical significance. NNT is a more intuitive way of interpreting clinical benefit and presenting it to patients.⁴ Some authors suggest a threshold for clinical significance is an ARR of 10% or greater or an NNT of 10 or less, whereas others recommend an ARR of 25% or greater or an NNT of 4 or less.²⁰ Clearly the threshold for significance must be put in context with importance or severity of the outcome, frequently in combination with cost and other factors. Using NNT and NNH as measures of treatment benefit and risk quantifies probability of successful outcome and simplifies calculation of cost per event avoided, such as relapse or rehospitalization

(Cost per event avoided = NNT x Cost of intervention). Presenting the likelihood of help or harm allows the relative valuation of benefit versus harm. These numbers can be presented to a patient, to involve them in evaluation of a proposed therapy, along with the associated risks. On a global payer level, NNT and NNH assist in the calculation of cost to society and cost avoidance with intervention and can be quite helpful in the development of both clinical practice and public treatment policy. The standard in health policies is evaluation of cost per death avoided or cost per year of life gained. The nature of psychiatric medications do not readily lend themselves to direct calculation of deaths avoided or years of life gained, as is standard with other treatments, such as cardiac intervention post-myocardial infarction (**Table 4**).^{5,21-23}

Application to the treatment of schizophrenia

Kinon et al evaluated early responders to antipsychotic therapy versus nonresponders and found a statistically significant difference in responsiveness to treatment over time. Early response was defined as ≥20% improvement on the Positive and

“Evidence-based medicine goes beyond anecdotal evidence and beyond mere calculation of statistical significance and allows the integration of clinical research into clinical practice.”

Doug Noordsy



Negative Symptom Scale (PANSS) total score at 2 weeks. Fifty-two percent of early responders versus 19% of early nonresponders achieved a $\geq 40\%$ improvement on the PANSS total score (moderate improvement) at end point (6 months, or at early discontinuation, whichever occurred first).^{3,24} The finding is statistically significant ($P < .001$), with the response rate more than doubling in the responder group. A significant P value indicates the finding is likely to be valid and not due to chance; however, it does not necessarily indicate clinical significance, relative to the disease. To determine clinical significance, calculation of NNT is needed.

In other words, for every 3 patients who improved by at least 20% at 2 weeks versus those who did not, there was an additional patient who had a robust response at 6 months. This difference is clinically significant; the advantage would be seen commonly in clinical practice.^{3,24} Overall for patients with schizophrenia, between 2 and 5 additional patients must be treated with antipsychotics to achieve 1 additional 40% reduction on the Brief Psychiatric Rating Scale or to achieve a “much improved” rating

on the Clinical Global Impression scale (Table 5).¹⁸

EBM resources

There are a growing number of EBM resources, both in print and on the Web. Below is a list of selected references. Many health-system libraries have specific collections of EBM educational materials along with other training and implementation resources.

- Straus SE, et al. *Evidence-Based Medicine: How to Practice and Teach EBM*²⁵
- OpenClinical²⁶
- Centre for Evidence Based Medicine (Oxford)²⁷
- Centre for Evidence-Based Medicine (University of Toronto)¹⁷
- Duke University Medical Center Library/Health Sciences Library, University of North Carolina-Chapel Hill²⁸
- Ruth Lilly Medical Library, Indiana University School of Medicine²⁹
- Lamar Soutter Library, University of Massachusetts Medical School³⁰
- “What is...?” series³¹

SUMMARY

EBM is not a single-step process. It involves a number of points of assessment: formulation of a specific question regarding a specific point in treatment of a particular patient, evaluation of relative literature, determination of effectiveness in clinical practice, assessment of risk–benefit, as well as statistical and clinical significance, culminating in a decision that takes into account the overall clinical picture of that particular patient and includes patient values and preferences. Implementation of EBM treatment is a valuable process, yet requires time and dedication. Clinicians need to learn and understand the information to implement EBM in clinical practice, then communicate with and educate patients and peers. Payers and providers alike can use cost and effectiveness data for evaluation of clinical significance and provision of coordinated care. Payers and providers must adopt flexible and prompt mechanisms that allow the evidence-based guidelines to be applied to individual patients. By use of an EBM process with practice standards, providers and payers may coordinate efforts to provide seamless, high-quality patient care.

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