

# EVIDENCE- BASED MEDICINE:

Optimizing Decision-Making to Improve Patient Care

May 19-20, 2000  
Washington, DC



**AACC**

Advancing  
Clinical Laboratory  
Science Worldwide

*Proceedings from the Evidence-Based Medicine conference, sponsored by AACC and supported with a generous educational grant from Bayer Corporation.*

**Bayer**   
Diagnostics Division

Dear Colleague:

On May 19-20, the Association conducted a highly rated and successful conference on Evidence-Based Medicine, which brought together the key government and private sector leaders in this area. We heard presentations from AHRQ, HCFA, NCQA and other important players regarding the application of EBM to scientific research and public policy. I am pleased to provide a summary of the key remarks made at that meeting.

This monograph provides you the most up-to-date information on the field of EBM-its problems and limitations, as well as some specific recommendations for improvement. It also reviews how the government agencies are applying EBM to make research decisions, how accrediting organizations are using it to establish benchmarks for evaluating health care services and how practitioners are using it to improve patient care.

As laboratorians and health care providers, it is our responsibility to ensure that patient's receive the best care possible. To do that, we must become involved. As clinical laboratory scientists, our research, test ordering and interpretive skills provide us with a unique opportunity to participate in and guide the direction of this movement. Let's not miss the boat. As you read this monograph, I encourage you to think of ways that you can apply EBM within your institution. Hopefully, this conference and monograph will be just the first steps down the long road to an evidence-based health care system.

Putting together this conference and monograph was no easy task. It involved a lot of hard work and planning. I would like to take this opportunity to personally thank the members of the Evidence-Based Medicine Advisory Group, which put together this productive and exciting program: Robert Christenson, PhD, Chair; James Boyd, MD; D. Robert Dufour, MD; and Christopher Price, PhD. Thanks for a job well done. Also, I would like to extend a special thanks to Bayer Corporation for recognizing the significance of EBM to our profession by their generous support for this educational program.

Sincerely,  
Frank Sedor, PhD  
President

**AACC**



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*The conference moderator was George D. Lundberg, MD, Editor-In-Chief and Executive Vice President of Medicalogic/Medscape and founding Editor-in-Chief of both Medscape General Medicine site and CBS HealthWatch.com.*

**Friday, May 19, 2000**

## Opening Remarks

***Rolf Classon, President***

*Bayer Diagnostics*

*Tarrytown, NY*

The demands and the burden on the healthcare industry are growing. Today patients have greater expectations and want only the best care available, including state-of-the-art diagnostics and therapeutic modalities. They want care as quickly as possible. Patients are becoming more informed and educated about medicine. These forces make the decision-making process more demanding. As the population ages, there are more patients, more tests, more information, more interventions, and more and more knowledge.

As a diagnostics manufacturer, Bayer believes it can make an important contribution to evidence-based medicine (EBM). Each time we develop a new product, we have to go through a series of fact-finding questions, such as: What is the nature of the disease? What is the diagnostic problem, and how does the diagnostic problem relate to the natural history of the disease or condition? Will the test device answer the question being asked by the physician? Finally, would a new test answer the question better? Would this test make the decision faster or make the information more useful? Will it improve the patient's outcome?

Increasingly, when developing new tools, we must ask if there will be an operational benefit for the institution, and in the bigger picture, if there will be an economic benefit to the healthcare system as a whole. Bayer and other manufacturers must consult with medical professionals, especially clinical chemists. We must work more closely together in the future than we have in the past. "This is the major reason I am here at this conference: to learn more and to receive input from informed users."

Unfortunately, recent technology assessments of diagnostics are not encouraging. Few publications review the quality standards required to provide clear evidence of the benefit of diagnostic tests to patients, to patient outcomes, and to economics, but even fewer publications address the decision-making process that involves the device. Thus, some diagnostic tests are perceived as being of limited value. "The problem for all of us is that if that perception is true for some or many diagnostic tests, then that perception may extend to the laboratory and its value in the delivery of quality healthcare."

Diagnostics manufacturers need the support of the entire healthcare chain (healthcare agencies, payers, laboratorians, clinicians). Without this support, manufacturers will not be able to implement EBM and offer the clinical, economic, and time benefits of EBM on the scale needed.



# Keynote: The Importance of EBM in the Health Care System

**Henry J. Aaron, PhD**

*Bruce and Virginia MacLaury Senior Fellow*

*Economic Studies Program*

*Brookings Institution*

*Washington, DC*

The advent of rationing (budget limits) has upped the ante on the quality and character of evidence we need in order to make medical decisions. “The qualitative difference that made a point of inflection in the emphasis on evidence-based medicine is the advent of cost control. We now need to know how much something helps and how much it costs to have an understanding of the ratio of benefits to costs.... Operating efficiently now is operating ethically as well.”

Applying classical microeconomics to medicine, it becomes clear that when calculating marginal benefits (the benefit of doing one more thing to a certain patient versus the extra cost of that intervention), you must make sure that anything you don't do does not have a benefit: cost ratio higher than anything you do, because then you would be wasting resources. You would not be providing as much care to as many patients as possible.

Evidence-based medicine is the response to this pressure to measure and demonstrate the value of our decisions.

There are some bumps on the road to achieving EBM:

- Condition-treatment pairs are not standardized. Health care practitioners in various health care settings may treat the same condition differently. Also, an intervention that may be very beneficial to one patient may provide marginal to nil benefits to another.
- Physiologically, we all differ. Patients' histories differ and our willingness to follow treatment differs, so the likelihood of a beneficial outcome depends on the patient. All medical results are probabilistic.
- Patient tastes and preferences in treatments, and their tolerances for certain risks vary. For men with prostatic cancer and prostatic hypertrophy, one man might opt for chemical treatment, while another might prefer surgery. One might be willing to risk impotence but would not want to risk becoming incontinent as a result of treatment.
- Costs are not unique. The measurement of costs is not a simple task. For example, a laboratory may be well staffed and not too busy, so the incremental cost of doing another test may be small. But if the hospital and

laboratory are congested, then doing something more creates real costs of a much higher magnitude, because you may be squeezing out another patient or creating pressures for new construction.

- With regard to managed care, these different factors have caused managed care plans to find niches in which to operate to cater to particular groups of patients. Most want to attract low-cost enrollees and repel the high-cost enrollees. There is variation in outlays from year to year. If a plan does a bad job of screening its patients, it can cost the viability of the whole organization if these patients incur high enough costs.
- We need a research agenda that goes beyond the average efficacy of treatment and average cost. The agenda of EBM is only the start, because other factors are relevant in different patient populations. We must be realistic enough to consider the variability that exists in the real world.

The problems we have in practicing EBM, in drawing conclusions from such research, are not just analytical, but also political. Services important to the alleviation of pain, to mastering survival, to raising children, are often in the hands of third parties, who are often under the control of the bottom line.

Other nations have imposed budget limits on their health care. We are not doing that here, except with respect to some public benefits, mostly for the poor. We are trying out private-market regulation, creating a tension between the wants and desires of insured patients, who are aggressive, literate, and aware of advances in medicine, and external budget controls that mean they can't have it all. The experiment is whether we can make that system work. I don't think it can work as it is now. There are lots of people who disagree with me, who think we have developed a framework that other countries will emulate.

Whom will we trust with evidence-based decisions? As currently constituted, managed care should not be the decision-maker. There is a conflict of incentives between those who run these organizations and the patients they serve. Managed care will need tremendous outside supervision if it wants to play a role as a major decision-maker. Psychological, medical, and biological studies and the economic evaluations of health care are tools to be used in "the squabble."

"We don't know how this will turn out, but I am absolutely convinced that evidence-based medicine will be a central element in the story, because it will be the weaponry with which the various sides contend."

### **Audience Interaction:**

**Questioner:** Where will we get the resources to do the amounts of testing we need to do, to show that certain drugs or certain tests will shorten length of stay and improve patient health?

**Dr. Aaron:** My own view on the issue of budgets for medical research is that they should remain high and go higher, because we are in the midst of a flowering of opportunity, of a magnitude that rivals the physics revolution early in the 20th century. The answer for how to support research is to make trade-offs.

You in the laboratory know, sometimes long before a fact is published, that certain diagnostic tests or methods work. They may work in the laboratory with you top-rate physicians and scientists, but there are physicians in general who may not listen or apply procedures or tests exactly as they should. Just remember that you must do it, communicate it, and supervise physicians and medical professionals in order to hasten the introduction of demonstrably effective progress.



## EBM: What It Is, What It Isn't

**Robert Andrew Moore, MA, DPhil, DSc**

*Managing Director, Bandolier Ltd.*

*Oxford, UK<sup>1</sup>*

David Sackett, MD, said in the *British Medical Journal* (1996; 312:71-2) that “evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.” But what about his use of the words “current,” “best,” and “evidence”—what do these words mean?

“We in the laboratory world need to think of the general practitioners who use our evidence.” We all are limited by the time we have to learn and absorb news. Thirty minutes per week of reading about the profession is all that we manage. Physicians need to get their information in an immediately useable form.

Patient perspective is another key to practicing the best medicine. The patient needs to have a response to treatment, and we need to remember what aspects of treatment are most important to the patient, which outcomes the patient believes to be valuable.

Several systematic reviews of literature have led to the finding that many studies are woefully inadequate, without quality enough to warrant publication. “If only a few percent of the papers that appear in the medical literature are scientifically sound, then we have a problem.”

No one can read the millions of papers that apply toward the medicine they practice. Even in a narrow specialty, reading the right papers is difficult. We can narrow down topics through the web, and look for particular papers that have been published on particular subjects. We are trying to find the small nugget of information (from all of the articles) that is true.

Not all systematic reviews are equal. When you have a good one, it is a real jewel. How we use the information depends on the biology of the patient, the society in which we practice—on many factors.

Thus, we need to be concerned about the architecture of the clinical studies we are comparing to each other.

We must eliminate bias, which is the one-sided inclination of the mind. Some of the problems with studies: they are not random, not double-blinded, duplicate information exists (the same set of researchers may write up the same research results for different journals and these studies may all be counted in a meta-analysis, which could place undue importance on those findings. Another major problem is trials without enough patients. Poor reporting quality is another common problem with clinical trials.

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<sup>1</sup> *Editor and founder of Bandolier, an evidence-based healthcare journal provided free within the National Health Service, and director of a related web site, [www.ebandolier.com](http://www.ebandolier.com) The magazine comprises bullet points about medical effectiveness; hence the journal is named for the object that holds bullets, a bandolier.*

The importance of randomization is considerable. Using double-blind studies is very valuable. A look at the literature demonstrates our bias. Open (unblinded) trials have shown that acupuncture is effective. But acupuncture doesn't work for anything. Homeopathy doesn't work for anything. Randomization is important to avoid bias.

Outcomes, the consequences of research, must be chosen carefully. Rarely does anyone ask the patient what he or she wants. It is important. Migraine patients want no recurrence, and complete pain relief. So we must measure not only that the pain has gone away, but also whether it returns. Another challenge is to apply these patient-preferred outcomes to the clinical trial data and express it in a way that nonmedical parties, such as politicians and patients, can understand, and even apply health economics to the results.

**Output:** Think about the value of what you are reporting. Don't merely tell that a treatment works—tell how well it works: for how long, in which set of patients, to what extent (complete versus partial relief).

I would criticize the evidence-based world for not asking this question: how effective are we at describing what we do and quality checking what we do?

In a surprising outcome, general practitioners (GPs) surveyed felt uncomfortable with many statistical concepts, such as heterogeneity and odds ratios—why include these in studies that physicians read? A more meaningful number is the number of patients needed to treat in order to get a response (Number Needed to Treat, NNT). For example, thiopental eventually puts everyone to sleep. For patients taking thiopental versus no treatment, the NNT is 1, which is perfect, because every patient has a response with the study drug, while no one falls to sleep after taking a placebo. A very good treatment has an NNT of from 2 to 5, to give some idea.

This statistic, NNT, is an expression of an outcome that is valuable to and comprehended easily by GPs. But in a study, only 35% could explain what NNT meant to others. GPs are at the heart of what we do in the evidence-based world. They need to get information they can process easily and understand.

Size or magnitude of the study is very important. Often, clinical studies have small numbers of patients. At low numbers our confidence in the result is poor. Only at high numbers of subjects are we confident at the results that show how well a treatment works. The heart of the matter is: can we trust meta-analysis? (Meta-analysis is the study of several studies at once, in an attempt to come to one answer about the effectiveness of a treatment).

Studies with smaller numbers of patients have a tremendous variation in results. The bottom line is that if you get garbage and gather it together, you have a big pile of garbage.

**Take home message:** utility.

Utility is the key to EBM. Physicians, patients, policymakers, and politicians share a limited ability to take in information and understand it. Few people understand odds or other statistics. We have got to keep it simple.

We cannot use relative measures. Relative risk is for researchers only. All policy decisions should be based on absolute measures of risk.

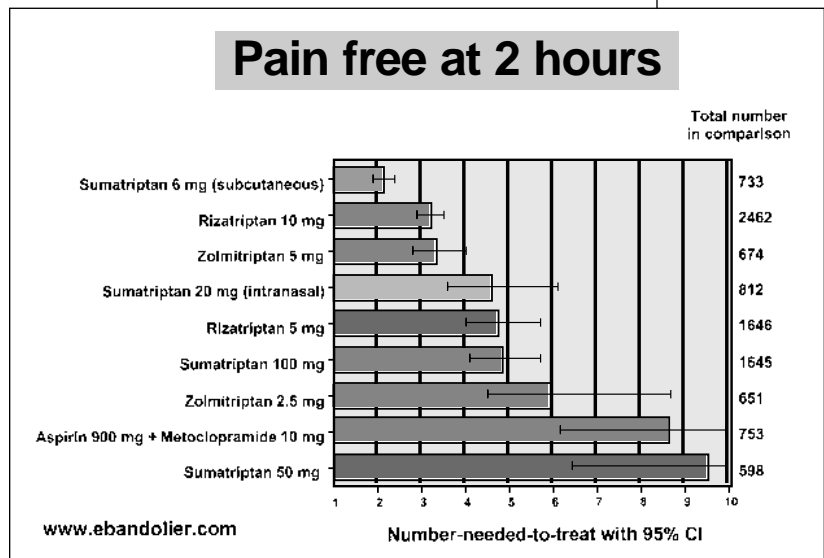
We need to think conscientiously about the best ways to present information. Here we see the numbers of patients in each study. With a 95% confidence interval, we see the percentage that reach pain relief and the percentage of pain relief. We can directly compare treatments. Some of the triptan drugs may have undesirable effects; some are more expensive than others. If we know how the various treatments work, we can suit the

treatment to the patient. A young woman who jets around the world sealing large deals may well be more prone to migraines than the average woman, and so the treatment with sumatriptan 6 mg subcutaneously, which affords the highest chance of total pain relief at 2 hours, is probably the best treatment for her, for whom cost is not an issue.

Doctors and patients need help making decisions. In a study published in the *Annals of Internal Medicine*, actors portraying patients with arthritis-related problems presented doctors with a challenge in treatment. While most physicians got the treatment decisions right, 30-40% still made suboptimal choices or downright unsafe choices about treatment, for a variety of reasons.

One reason is that the physician may be overburdened. One particularly frustrated GP in England stacked up all of the guidelines he had been issued. It was over a meter high, and most of it was not helpful.

“In the United Kingdom, 4 to 5 million decisions a day are made about patient care. The number of those truly influenced by evidence or policy or half-remembered guidelines is probably unknown. I hope it is by evidence, but I fear it is by guideline, and the major fear is that the guidelines themselves are often wrong.”





# The Role of EBM in Public Policy and Healthcare Decision-Making

## Panel Discussion

**Douglas Kamerow, MD, MPH,**

*Director, Center for Practice and Technology Assessment*

*Agency for Healthcare Research and Quality*

*Washington, DC*

The mission of AHRQ is to “support, conduct, and disseminate research that improves access to care, reduces its cost, and improves the outcomes, quality, and appropriate use of health care services.” In particular, the reassembled agency has a focus on looking at medical errors and patient safety.

Laboratorians should be aware of the 12 evidence-based practice centers (EPCs) at AHRQ, which produce evidence reports and technology assessments. They should consider nominating topics for EPC review for their own projects. AHRQ also asks for topics via the Federal Register publication.

The EPCs are responsible for the “front-end of guidelines” in the evidence reports. The EPCs produce systematic reviews, as defined in Cynthia Mulrow’s book, “Systematic Reviews.”

“Concise summaries of the best available evidence addressing sharply defined clinical questions, using explicit and rigorous methods to identify, critically appraise, and synthesize relevant studies.”

In an old-style review article, you never knew how the author approached the topic, where the material came from. Today that is not good enough. We must let people know what the study questions are, how we derived them, how we systematically searched the literature and how we evaluated it and reached conclusions.

Some evidence reports (now on the web at [www.ahrq.gov](http://www.ahrq.gov)) deal with: autopsy as a diagnostic aide; medical errors; cancer decision aides; and chronic fatigue syndrome.

The U.S. Preventive Services Task Force looks at preventive services, including screening tests, and tries to make recommendations based on carefully considered evidence. The screening tests, including lipids, PSA, and diabetes screening, are of particular use to laboratorians.

### 2000 EPC Topics (Tentative)

- Autopsy as Dx aide
- Acute bronchitis
- Amb. BP monitoring
- Congestive heart failure
- Repetitive motion disorders
- Parkinson’s Disease
- Medical errors
- Stroke diagnosis
- Cancer decision aides
- Chronic fatigue syndrome
- Speech/language disorders
- Bioterrorism



Laboratorians should know about the web-based repository of guidelines, the National Guideline Clearinghouse (NGC). These evidence-based guidelines are live on the web at [www.guideline.gov](http://www.guideline.gov). These can be searched by term, such as “heart failure.” The site is cross-linked with guidelines written by other medical associations.

Another part of AHRQ is Translating Research into Practice (TRIP), which is implementation research. This is the next step, which puts evidence-based recommendations into practice in various settings and populations. It is behavior change research, and the behavior we are trying to change is that of clinicians, their patients, and also systems, if you believe that systems can have behaviors. In 2001 and 2002, TRIP will be gearing up with more publications. Grant proposals can be submitted to AHRQ and information is on the agency web site.

For NGC, any AACC or other laboratory guidelines can be contributed (email: [info@guideline.gov](mailto:info@guideline.gov), Vivian Coates, NGC Project Director). For TRIP, lab scientists can submit grant proposals to AHRQ.

For more information, visit the AHRQ web site: <http://www.ahrq.gov> or email AHRQ staff: [Use first name initial] + [up to 7 letters of last name] @ahrq.gov.

***Hugh Hill III, MD, JD***  
*Acting Director*  
*Coverage and Analysis Group*  
*Office of Clinical Standards and Quality*  
*Health Care Financing Administration*  
*Baltimore, MD*

HCFA has tied quality to Medicare coverage. The link was presented in a 1996 report of the Administrator’s Quality Initiative Team. “We recommend that HCFA establish the impact on quality of care as a consideration in coverage decisions.”

For the Medicare program, two methods are used to make coverage decisions:

1. Medicare contractors can develop coverage policies, known as local medical review policies, and
2. HCFA can develop national coverage policies.

Coverage decisions must satisfy HCFA’s process for determining whether the service can be considered “reasonable and necessary.” Most new items that are covered come in through the local review process.

In 1999, the process for making coverage decisions changed, and Medicare will start using evidence-based decision-making.

Medicare introduced a new Medicare Coverage Advisory Committee (MCAC), which replaced the old Technical Advisory Committee. The MCAC has panels on the laboratory, medical devices, diagnostic imaging, DME, drugs/biological/therapeutics and medical/surgical. All of these panels are run through an executive committee.

HCFA has defined four new steps in applying its criteria:

1. Is there sufficient evidence that the item is medically beneficial for a defined population?

*If there is not sufficient evidence, it is not covered. If yes, go to 2.*

2. Is there a medically beneficial alternative item or service in the same clinical modality that is currently covered?

*If no, the item/service will be covered under Medicare. If yes, go to 3.*

3. Is it substantially more or less beneficial than the Medicare-covered alternative?

*If it is substantially more beneficial, it is covered. If it is equally beneficial, go to 4. If less beneficial, then it is not covered.*

4. Will it result in equivalent or lower total costs for the Medicare population than the Medicare-covered alternative?

*If yes, then covered. If no, then not covered.*

A Notice of Intent (NOI) for proposed rulemaking, to more clearly define Medicare's terms of what is "reasonable and necessary," has posed questions that still need to be answered. Laboratorians are urged to weigh in during the comment period to answer these questions:

- What is the proper evidentiary standard?
- How should we deal with bias and external validity when applying clinical trials to coverage decisions in the real world? A related problem is that the over-65 population often is not included in studies on these subjects.
- Should there be different standards for the different health care sectors? For example, should the standards be different for diagnostic tests than for surgical procedures?

The Notice of Intent (NOI) includes HCFA's interpretation of what is "reasonable and necessary." The text can be read at [www.hcfa.gov/quality/8b2-b.htm](http://www.hcfa.gov/quality/8b2-b.htm). Contact Hugh Hill at [hhill@hcfa.gov](mailto:hhill@hcfa.gov) or (410) 786-7176.

## *The Use of EBM*

“[W]e would measure both the medical benefit and the added value criteria by clinical scientific evidence.”

**Grant Bagley, MD, JD**  
*Partner, Arnold & Porter*  
*Washington DC<sup>2</sup>*

The problem of evidence, before we deem something a benefit and worthy of being in the armamentarium, is a chicken-or-egg problem.

Say we have a new technology, and we have some evidence that shows it is clinically valuable. Then a policymaker asks for the evidence. The manufacturer says, "If you pay for it, I can give you the evidence."

Remember that just because something has been FDA approved as safe and effective does not mean that HCFA will perceive it to be "reasonable and necessary" and will cover it under Medicare.

The difference is that it must progress up stairs. Health plans look first at safety and effectiveness. They ask questions. Is the benefit greater than the risk? Is there an improved outcome through this service or procedure? The newest mantra is: "Does it add value?"

In essence, the clinical studies become the responsibility of the healthcare provider, the physician and the patient. We have to consider direct outcome measures, such as survival and indirect outcome measures, such as metabolic and physiological changes.

Well-designed clinical trials of adequate size to measure an effect and that also deliver the goods to payers in terms of comparative effects, become very expensive and complex. We need a system that helps us accumulate complex and expensive information, not one that demands it.

Tests differ from treatments. Evidence of a test's value needs to be published, peer-reviewed, presented, available in abstracts, or can even be unpublished and anecdotal. Ideally, evidence should be analyzed in public, in an open forum, particularly on the issue of diagnostic testing.

Tests are often compared to gold standards. The problem with a diagnostic test is that it is not a replacement technology, and it is held to a higher standard. HCFA's coverage advisory committee combines both clinicians and lab scientists, so clinical value is important.

Regarding diagnostic tests, there are not a lot of randomized controlled trials from which to draw any conclusions about tests. Thus, HCFA uses alternative sources, such as textbooks and consensus within the provider community.

Diagnostic testing has a distinct burden. It must provide information that is otherwise not available or that constitutes an improvement in already available information. The information must lead to interventions that will have positive and predictable effects on a patient's health status. Merely showing improved sensitivity and specificity is not enough. While a therapy generally replaces another therapy, a diagnostic test can add to the information, not necessarily replace another test, for example.

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<sup>2</sup> *Dr. Bagley is the former director of the Coverage and Analysis Group at HCFA*

It is very difficult from a policy standpoint to implement new diagnostic testing procedures. We need to see what the difference will be clinically, and it requires different criteria and thus, differences in policy. This is why HCFA is issuing sector-specific guidance documents.

From a development point of view, there has to be an incentive to make the product available. Now HCFA will explicitly tell us what evidence is needed for a new technology and will tell what kind of coverage it might get. Today, HCFA is saying that if a manufacturer provides evidence that a test is an improvement in efficiency and value, then HCFA not only will pay for it but also will insist on this technology.

Both HCFA and FDA have to play a role in forwarding a new diagnostic test to the marketplace. The two agencies are now trying to work in tandem. At FDA, in the Center for Devices and Radiological Health, the director says that FDA sets up protocols and talks about evidence and tells what a manufacturer needs to get coverage for a new device or product. HCFA also is looking for evidence and outcomes. These two agencies will begin to approve protocols jointly. Things could move in a parallel fashion through the agencies.

In fact, in some cases, Medicare payment is provided during investigative trials. Both HCFA and FDA are trying to make joint definitions and coordinate their efforts. "Evidence-based medicine becomes refined, and it may be our friend if we use it right. All of us must learn to use it, as sponsors of technology, as consumers, as providers, and as those involved in setting policy."

***Phyllis Torda***

*Vice President, Product Development*

*National Committee for Quality Assurance*

*Washington, DC*

NCQA is a major dispenser of EBM nationally. NCQA's vision is to become the most widely trusted source of information that drives health care quality improvement.

HEDIS is NCQA's set of standardized measures that allows for comparisons between and among health plans. HEDIS is used by 90% of the managed care industry, and the Committee on Performance Measurement (CPM) oversees its content. CPM comprises 1/3 employers, 1/3 representatives of managed care organizations and 1/3 represent consumer organizations and other quality experts.

One subset of HEDIS measures, the Effectiveness of Care measures, must be evidence based.

All HEDIS measures are weighed for these desirable attributes: relevance, scientific soundness, and feasibility. (If possible and there is space available, insert slides on the components of each of these three attributes).

A 1999 survey on the state of managed care found:

- A huge gap between the top- and bottom-performing plans;
- Clinical quality correlates with member satisfaction;
- Accountability drives quality—plans that report results over time have better results; and
- NCQA-accredited health plans outperform non-accredited plans.

HEDIS measures were mostly geared toward preventive care until recently, but now include more measures involving chronic conditions.

## *Desirable Attributes*

### Scientific Soundness

- Clinical Evidence
- Reproducible
- Valid
- Accurate
- Case-mix/Risk Adjustment
- Comparability of Data

NCQA

## *Desirable Attributes*

### Feasibility

- Precisely Specified
- Reasonable Cost
- Confidential
- Logistically Feasible
- Auditable

NCQA

## *Desirable Attributes*

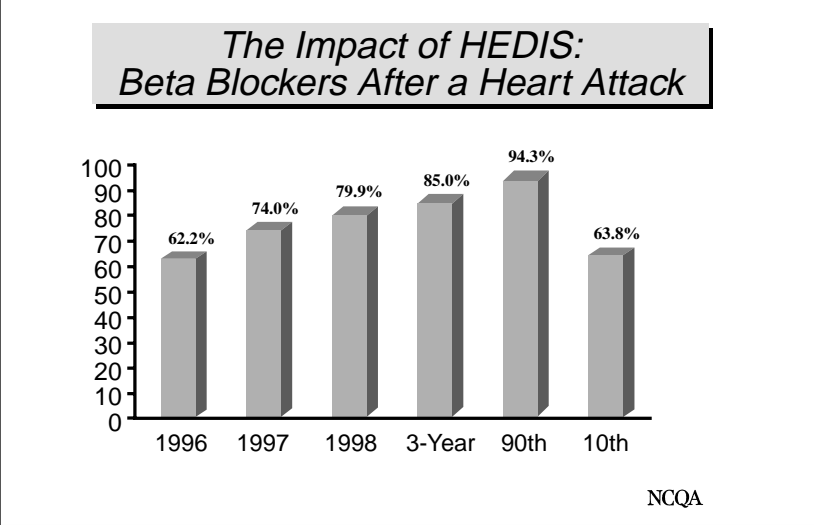
### Relevance

- Meaningful
- Health Importance
- Financial Importance
- Cost Effectiveness
- Strategically important
- Controllability
- Variance among systems
- Potential for Improvement

NCQA

HEDIS measures appear to encourage plans to implement the measures and improve each year. The impact of HEDIS is evident on the rate of giving beta-blockers after heart attack:

In 1996, 62.2% of patients in health plans received beta-blockers when the measure indicated they should have received it. The measure was new in 1996. In 1997, 74% of patients in the same category received beta-blockers, and in 1998, the percentage rose to 79.9. By 1999, the 90th percentile of plans showed that 94% of patients in these plans got beta blockers as needed, and at the 10th percentile, 63.8% got beta blockers, which reflects an improvement over all of the plans in 1996.



We do attribute the changes to HEDIS measures, which very dramatically shine a light on areas for clinical improvement. When we pick a measure, resources get poured into these areas. We do not deny that a lot of the improvement is related to documentation, and ability to measure what should be measured.



# The Role of EBM in Public Policy and Health Care Decision-Making: Case Studies

## Panel Discussion

### Diabetes

**William E. Winter, MD**

*Professor*

*Pathology and Immunology*

*Laboratory Medicine, Pediatrics and*

*Molecular Genetics and Microbiology*

*University of Florida*

*Gainesville, FL*

*Dr. Winter examined the question of how to use the medical literature to better manage and diagnose diabetes. Diabetes is the eighth leading cause of death in the U.S. A total of \$98.2 billion is spent annually (1997 dollars) in direct and indirect costs of care. He presented two cases studies.*

The first case study asked the question: does tight control improve microvascular and neuropathic outcomes in Type 1 diabetes?

An 11-year-old African-American female patient named Tabitha had been diagnosed with Type 1 diabetes for 18 months. She had mild diabetic symptoms and did not complain of hypoglycemic episodes. Her self-monitoring results often showed blood glucose levels above 200 to 300 mg/dL. Her hemoglobin A1c often was more than 10% (Upper Limit of Normal (ULN): 6.1%). Was it worth the extra effort and worry of tight controls for this patient?

A search of the literature led to the results of the Diabetes Control and Complications Trial (DCCT), which was NIH-funded between 1984 and 1993. Subjects were type 1 diabetics with 1441 subjects enrolled, aged 13 to 39 years.

Patients were subdivided into groups that received conventional therapy versus a group that received intensive therapy. Outcome measures were retinal photographs (retinopathy); urinary albumin excretion (UAE, a laboratory parameter for nephropathy); and for neuropathy, clinical assessment, autonomic nerve study or a nerve conduction velocity study. In each case, for retinopathy, nephropathy, and neuropathy, the intensive therapy group had fewer patients suffering from these complications, had better outcomes and sustained benefits longer.

The cost, however, for tight control is that as glycohemoglobin drops, the rate of severe hypoglycemic episodes rises. There is a trade-off.

Summarizing the DCCT results, they showed improved reduction of the three areas of complications. The benefits of reduced risk of retinopathy and nephropathy persisted even four years after the trial ended.

The lab can play a role in long-term glycemic control with hemoglobin A1c. This

was the primary measure of long-term glycemic control. Nephropathy was measured by an elevated urinary albumin excretion.

A review of the results of the United Kingdom Prospective Diabetes Study (UKPDS) found that tight control reduced any diabetes-related complication by 12% (with a statistical significance of  $P < 0.029$ ). This study showed specifically that retinopathy was reduced by 21% at 12 years and albuminuria was reduced by 33%.

Practice guidelines developed by the American Diabetes Association have a goal of hemoglobin A1c of less than 7%; the guidelines require action when it goes above 8%. Tabitha's often was more than 10%.

There is "compelling evidence in both type 1 and type 2 diabetes that improved glycemic control can alter outcomes for the better."

In a second case, a 51-year-old professor at the University of Florida was previously diagnosed with type 2 diabetes. Even though he was treated with glucophage and glucotrol, he had lost 25 lbs. (and was 6'2", 174 lbs.) Nonetheless, his hemoglobin A1c stood at 11.4%, with glucose values consistently near 300 mg/dL. Why did he fail the standard therapy for type 2 diabetes? Was he a type 1 diabetic?

The question from the second case was: How can the laboratory assist in diagnosing type 1 diabetes in this case?

The goal was to demonstrate the value of selected islet autoantibody testing in such a diagnosis. Using a novel approach, the lab determined whether islet autoantibodies were present, because the presence definitively indicated type 1 autoimmune diabetes. Additionally, many people with these autoimmunity conditions are at high risk for other endocrine and related autoimmunities, like thyroiditis, gastritis and adrenalitis. The laboratory's role is to screen for islet cell autoantibodies (ICA) in diabetes and to screen for organ dysfunction before treatment is developed.

The patient had a positive ICA Screen and an ICA titer of 80 JDF units (a JDFU of more than 10 is significant).

The patient began insulin therapy and was able to improve his metabolic control.

Thus, islet autoimmunity testing can play an important role in selected patient cases.

## **Heart Disease**

*Ethan Balk, MD, MPH*

*Associate Professor of Medicine and Clinical Investigator*

*Division of Clinical Care Research*

*New England Medical Center*

*Boston, MA*

*Dr. Balk explained the steps that an Evidence-Based Practice Center (EPC) takes when it performs a systematic review of literature and meta-analysis. The EPC at Tufts-New England Medical Center (T-NEMC) examined treatment modalities for cardiovascular disease.*

This project stemmed from a congressional mandate to the National Heart, Lung and Blood Institute, which formed the National Heart Attack Alert Program. The program was charged with reducing morbidity and mortality from acute myocardial infarction (MI) and to focus on rapid response to acute cardiac ischemia in acute-care settings.

In 1997, AHRQ directed EPCs to prepare evidence reports, technology assessments, and focus on various aspects of diagnostics, treatment or management of a condition. The EPC would perform rigorous systematic reviews, and include meta-analysis and cost and decision analyses. EPCs have to document their methods, rationales, and assumptions.

Of interest to laboratorians is the EPC's assessment of biochemical markers, including CK, CK-MB, myoglobin, troponin I, and troponin T. The presentation focused specifically on laboratory tests that were done upon arrival to the emergency room and serial testing done in the emergency room to diagnose acute MI that setting.

The specific questions of interest were:

- What is the diagnostic accuracy of various technologies, specifically the biochemical markers, in the emergency department setting?
- What is the clinical impact of the use of these technologies in the ER setting?

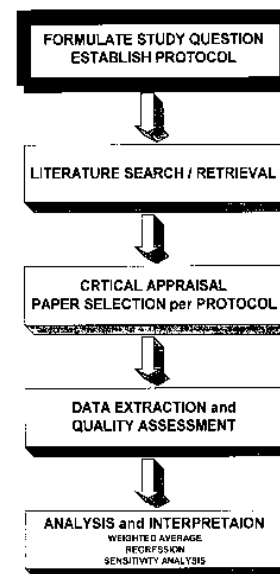
The EPC extracted data from the 407 full-length articles (1966 through January 1999, English-language literature, human subjects) that were worthy of retrieving. The EPC decided on 108 articles to include in their evidence report; 56 of these articles were on biomarkers. Each accepted article was read and reviewed so the EPC could extract data and assess the study quality.

Studies were included if the investigation was performed in the emergency department (ED) setting. Study sample was of patients seen in the ED who were suspected of having acute cardiac ischemia, which included both acute MI and unstable angina. Biomarkers were drawn as a single initial test or in multiple samples (serial tests).

Data were extracted on the setting, eligibility criteria of the study, test description, outcomes description and blinding of the study. Data were also extracted on the results and included information on demographics, subject dropout rate, and test performance data. Quality data included such factors as internal validity of the study, method, and the result reporting and accuracy of reporting.

Quality appraisal of all trials included in the systematic review is important. By assessing the quality of the studies included in the systematic review, investigators can estimate the degree to which the trials' design and methods prevented systematic errors. Variation in quality might explain differences in the results that are uncovered during a systematic review. Finally, quality appraisal is needed even if there is not much variability

#### STEPS OF PERFORMING A META-ANALYSIS



among the trials—we must make sure that what goes in is not trash. Consistent trash is still trash.

Three methods were used to assess the diagnostic utility of the tests:

1. Independently combined sensitivity and specificity values
2. Diagnostic odds ratios
3. Summary Receiver Operator Characteristic (ROC curves)

### Results: Presentation Biomarkers

Biomarker	# of Studies (Total N)	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic Odds Ratio (95% CI)	Overall Quality
Creatine Kinase	12 (3,195)	37 (31 - 44)	87 (80 - 91)	3.9 (2.7 - 5.7)	C
Creatine Kinase MB	19 (6,425)	42 (36 - 48)	97 (95 - 98)	25 (18 - 36)	C
Myoglobin	18 (4,172)	49 (43 - 55)	91 (87 - 94)	11 (8.0 - 15)	B
Troponin I	4 (1,149)	39 (10 - 78)	93 (88 - 97)	11 (3.4 - 34)	C
Troponin T	6 (1,348)	39 (26 - 53)	93 (90 - 96)	9.5 (5.7 - 16)	C

The overall quality of the first test drawn upon presentation in the ED, showed that only myoglobin was graded a B. The four other biomarkers were scored as C. The sensitivities were similar but low in the presentation studies. The specificities tended to be high, and were very similar. Thus, the diagnostic odds ratios were similar and helped to compare the diagnostic technologies to each other.

In terms of the overall quality of the serial biomarker tests, only troponin I and troponin T were rated a grade of A/B and A/B/C respectively. Myoglobin, CK, and CK-MB were all rated as a C.

Heterogeneity of the results could be due to varying test thresholds (e.g., in the CK-MB, range was from 4.7 to 9.0 ng/ml  $\pm$  4% - 5%). Patient populations also varied from patients with symptoms of acute cardiac ischemia to patients with chest pain. Another possible reason for different results was setting. Some studies used all eligible patients seen in the ED, and some included only patients eventually admitted to the coronary care unit. For all of these reasons, the prevalence of acute MI in the studies ranged from 1% to 78%. None of these truly explain the variability among the studies; this might indicate incomplete data information within the studies.

### Results: Serial Biomarkers

Biomarker	# of Studies (Total N)	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic Odds Ratio (95% CI)	Overall Quality
Creatine Kinase	2 (786)	[69 - 99]	[68 - 84]	[12 - 220]	C
Creatine Kinase MB	14 (11,625)	79 (71 - 86)	96 (95 - 97)	140 (65 - 310)	C
Myoglobin	10 (1,277)	89 (80 - 94)	87 (80 - 92)	84 (44 - 160)	C
Troponin I	2 (1,393)	[90 - 100]	[83 - 96]	[230 - 460]	A/B
Troponin T	3 (904)	93 (85 - 97)	85 (76 - 91)	83 (33 - 210)	A/B/C

The limitations of EBM applications include:

- Few studies examine multiple test thresholds;
- Very few studies exist of clinical impact of testing;
- Very few studies exist of combination tests (e.g., CK-MB and troponin T);
- A limited number of studies have been published, especially on troponin I and T; and
- The quality of methods and reporting was frequently poor.

There are a number of ways EBM can assist in the clinical management of patients with acute MI:

- If applied earlier, EBM might have saved lives and improved medical care through the earlier use of thrombolytic drugs and earlier abandonment of lidocaine use.
- EBM provides a better description of diagnostic utility of various biomarker tests, and better clarification of populations, settings, test thresholds, and test timing than single studies usually provide.
- EBM can clarify areas where further research is needed and how research can be improved.

## Bleeding Disorders

***Michael Laposata, MD, PhD***

*Professor of Pathology*

*Harvard Medical School and*

*Director, Clinical Laboratories*

*Massachusetts General Hospital*

*Boston, MA*

*Dr. Laposata looked at the consequences that can occur when a laboratory does not study evidence-based medicine, when the test selection process is complex and interpretation of test results is even more difficult. Too often, results leave the clinical lab and go directly back to the ordering physician without any further information based on the evidence that laboratory experts can leverage to fully inform a diagnosis.*

“There has to be a systematic practice change so that the evidence that is in the head of someone practicing laboratory medicine ends up contributing to the diagnosis.”

Dr. Laposata presented dramatic cases in the area of coagulopathy to demonstrate his point that laboratory experts must be integrated into the information loop with

clinicians. While vascular surgeons who cut out clots have heard of the various coagulation tests, for example, for a deep vein thrombosis, they still need to call the laboratory to learn more about the diagnostic issues and confounding variables. Laboratorians are the experts on laboratory testing issues and need to be consulted.

What options do physicians have to gather information they need for evidence-based diagnosis? None of the choices are attractive, and they vary in the degree of money, time, and accuracy.

The physician could:

- Make a formal consultation with a laboratory for evaluation of the abnormality. This option is highly accurate, but costly. Managed care discourages this loss of income by the primary care physician.
- Obtain friendly advice from a colleague as an informal referral. With this option, the data are evaluated by a specialist—the consultant laboratorian—who is not reimbursed for his or her services and does not see the patient or have access to all patient information.
- Obtain necessary information from textbooks or literature searches. This option provides a learning experience for the physician, but it is time consuming. There is a high risk for error, and there is no doctor-to-doctor consultation.
- Guess about the appropriate selection and interpretation of laboratory tests. With this option, turnaround time would be short but error rate would be high and the lab would have to perform many excess tests.

A solution is for the laboratory to offer valuable added services to enhance evidence-based medicine use in practice. These value-added laboratory services include:

- Directing test selection by algorithms within the lab to maximize efficiency of test selection for specific diagnoses. “Let us (in the laboratory) pick the most useful tests for the particular coagulopathy and if it is a more common test, we will put it at the top of the list, not at the bottom.”
- Providing a paragraph that interprets the results when a complex battery of tests has been performed.
- Rapidly consulting on laboratory test selection and interpretation.
- Informing patients about their diagnosis.

There is a tremendous financial savings from these services as well. The problem of not providing such services is considerable: every day at our hospital, we interpret about 35 complex batteries of coagulation tests. At least two to three cases per day are a serious

or irreversible problem, because the doctor could not get the evidence-based answer needed from a lab expert to make a conclusion.

Two tragic patient cases underscore the need for consulting laboratory experts who have a store of evidence about alternative diagnoses. Consulting the laboratory could have saved both patients' families much grief.

The first case was a 33-year-old woman who was pregnant. Early in her pregnancy, she mentioned shortness of breath during her first pregnancy, in which she was treated with a four-day course of IV heparin. No evidence for a pulmonary embolism was produced at that time, however.

The obstetrician for the second pregnancy ordered several tests for hypercoagulability, including a functional protein S assay.

The protein S result came back low, a condition that may indicate thrombosis. That combined with the previous history of treatment for thrombosis, and the obstetrician recommended that she terminate her pregnancy. Reluctantly, she did so.

The doctor, however, was unaware that protein S drops during every pregnancy. The abortion was unnecessary.

When the woman came to the laboratory for testing for a tubal ligation, her protein S was normal, and there was no documentation in her record of any evidence that her earlier bout of shortness of breath was associated with a pulmonary embolism. A laboratory consultation at the outset was needed.

The second case involved a father who alleged that he had dropped his 3-month-old while feeding her. To avoid letting the baby hit the ground, he grabbed her by the leg and lifted her sharply. She seemed fine but was crying and irritable the next day.

The baby was taken to the ER and seen by a neurologist. She had a subdural hematoma, and had bilateral retinal hemorrhages. She had no bruising. The neurologist concluded that, unless she had a bleeding disorder, this child was a victim of shaken baby syndrome.

They needed EBM to sort this out. The child had had bruises from seatbelts and was considered a very bruisable baby.

Tests were ordered. PT, PTT came back normal. Von Willebrand factor and ristocetin cofactor both came back in the low end of the adult normal range.

The physician concluded that the child had been abused. The father ended up in a state penitentiary. The mother, who had left the child in the care of the father, was deemed neglectful, and the child went into the foster care system.

After three months in foster care, the child had taken normal amounts of child's ibuprofen, which inhibits platelet function. If you have von Willebrand's disease, you already have platelet problems.

The baby ended up with meningitis and another bleeding episode. This time she was taken to a hospital that practices evidence-based medicine. A look at her history showed that her father and her father's brother had a low ristocetin cofactor and a history of nosebleeds. There was other evidence of bleeding disorders in the family.

“While we were working up the child, we were working up the family.” Two facts were unavailable to the neurologist who originally saw the baby:

- The normal range for von Willebrand is different for children—it is higher for children than for adults.
- With an injury, the von Willebrand factor level is above baseline as part of the acute phase response. The child would need to be tested again to determine the usual level in the blood. When she was tested at two weeks and then again at four weeks, the factor levels had dropped and dropped again. The diagnosis was von Willebrand’s disease.

If the physicians originally had taken the time to better establish the correct diagnosis, they would have learned from evidence in the literature that cases of spontaneous retinal hemorrhage are reported with von Willebrand factor levels even higher than those of this child. Furthermore, many reports of minor injury producing major bleeds in children with undiagnosed hemorrhagic coagulopathies result in false accusations of child abuse.

The father had received no justice, because of the political exigencies of the case—the prosecutor was running for state office, and it is politically valuable to prosecute child abusers, suspected or otherwise, as aggressively as possible.

As a result, we developed a new algorithm for evaluating children who may have been abused.

To reduce misdiagnosis in potential child abuse cases:

New algorithm:

- Extensive coagulation testing
- Quantitative approach to demographic analysis
- Take a thorough history and physical exam to better identify a hemorrhagic coagulopathy.

# Is EBM the Holy Grail?

## Panel Discussion

**Peter Lurie, MD, MPH**

*Deputy Director, Health Research Group*

*Public Citizen*

*Washington, DC*

The number of clinical trials has risen steadily. In 1962, it became federal policy that drugs demonstrate efficacy, in addition to safety. The FDA required all drugs to be subject to the Drug Efficacy Safety Implementation (DESI). Companies had to demonstrate efficacy through clinical trials if they had a drug on the market. (Not surprisingly, many drugs were pulled from the market because they were not effective.) Now the DESI review is complete, but that work is being undermined. The number of clinical trials mandated under DESI is an example of how EBM has made inroads.

EBM is also getting a boost from third-party payers who are refusing to pay for drugs without adequate evidence of their effectiveness or for experimental drugs. There is more dependence on pharmacoeconomic studies now, and there is controversy about sponsorship of studies and study results. There have been studies that have been manipulated to make drugs look cost-effective when they may not be or may not be as good as published.

Third-party payers, however, are not being consistent in their approach to coverage and the use of evidence-based medicine. Because consumers seem to be clamoring for alternative therapies, which are yet unproven, some payers are beginning to cover these treatments.

Many examples of unsafe drugs finally were publicized in the literature. Others prevail because of marginal efficacy. As long as you can show something works even marginally (like Relenza), it will get to market no matter the clinical context of the drug.

Another way in which the FDA ignores EBM is in the realm of dietary supplements. As long as medical claims appeal to functions and structures rather than medical diseases, they can be sold. Deregulation at the federal level has led to the growth of these supplements. Another more obscure example is pharmacy compounding—creating a drug from its elements. There is now a loophole for compounding pharmacists who can compound drugs that had been removed by DESI for reasons of inefficacy.

Evidence-based medicine also has been wrongfully deified. There is an overuse of placebo-based studies. For registration of a drug, much of the time the FDA will accept the mere proof that a drug is better than a placebo. This approach fails to provide relevant data to patients. Patients don't want to know that a new drug is better than nothing; they want to know how it compares to existing drugs. In hypertension, depression, or schizophrenia, the question is not whether to prescribe, but which drug to prescribe. Payers don't have the information they need, either.

EBM, as valuable as it is, is oversold. Viagra, for example, in the clinical trials excluded anyone with a hint of heart disease. But many of the people eligible for this drug in the real world will have some amount of cardiovascular disease. The labeling does not speak to this adequately, and there is potential danger to patients.

It strikes me that there are so many questions in clinical medicine that they can never all be answered. There are so many patient populations to study. In the end, important questions will always remain that will never be answered by evidence-based medicine.

***Gail J. Povar, MD, MPH***  
*Clinical Professor of Medicine*  
*The George Washington University*  
*Washington, DC*

Evidence-based medicine promotes the moral obligation of professionals to “do no harm.” Error is a major cause of death in the United States, exceeding motor vehicle accidents, AIDS, or breast cancer. Unnecessary or unindicated procedures or use of medications puts patients at risk for complications without reasonable likelihood of benefit. Attention to EBM should reduce misapplication of medical technology. Therefore, patients should embrace evidence-based medicine, because it promotes safe medical practice.

Evidence-based medicine helps to ensure fair use of the health care dollar:

- None of us would want to be treated any less well for a given condition, in terms of likelihood of a good outcome, than another person within the same framework (insurance, managed care entity, hospital, etc);
- EBM and the guidelines/algorithms that result help to reduce unwarranted variation in practice, for example, the underuse of beta blockers in the context of myocardial infarction;
- EBM helps to identify potential, if unintentional, discriminatory or unfair practices. We can uncover underuse of appropriate screening tests to certain populations, or under-diagnosis of myocardial infarction in specific groups of patients;
- EBM, through identification of the least costly, equally-or-nearly-equivalent effective and safe strategy for treatment of certain ailments (e.g. antibiotic choices), helps save money that can be applied to other health care needs.

Thus, EBM promotes fair application of health care resources and promotes like treatment for like people.

An important question: What counts as evidence for the sorts of decisions that are necessary for allocation of resources and for clinical decision-making? Consider screening tests: how many tests are required to make the diagnosis? At what cost?

Whether a test should be done, given the number needed to find a case, or the cost, is a social value decision. For instance, the NIH and the American Cancer Society have different recommendations with respect to mammography for women between the ages of 40 and 50. The reason for the difference was disagreement about the relevant outcome: case finding or case-fatality rates. Which outcome should be used is not an empirically solvable matter, and that is a problem.

Which evidence should count as determinative is a social matter that will affect the relative allocation of health care dollars, rather than a purely scientific matter. As such, the public and not merely the professionals will have to be party to and accountable for the choice. Therefore, public health recommendations or coverage decisions based on “evidence” must be transparent not only about the science, but also about the values that are implied in the decision. Ideally, the relevant public should play a role in identifying which values should be decisive.

Variation should reflect the goals and values of patients, not idiosyncratic clinician practice. Patients have a right to refuse any medical treatment, with the possible exception of treatments undertaken at least in part to protect the health of others (e.g., treatment of tuberculosis). Patients may request, and clinicians should give serious consideration to “n of 1” experiments, (an individual, rigorously observed, innovative care study). There are many aspects of medicine for which good or conclusive evidence is lacking.

Many patients suffer from conditions for which EBM has at various times had very little to offer. The strength of the patient’s claim on doing something depends on either the intervention being relatively low risk, or the patient being at high risk and having few or no other options.

Evidence-based medical practice can promote greater safety and less error in health care. EBM can also promote fair and just allocation of resources by providing relatively “objective” standards against which the care of individuals and populations can be measured. However, the nature and quality of the evidence used to set such standards should be a public discussion, not a professional decision. Individual variation in practice is justified to the extent that it respects individual patients’ goals and preferences, and is executed with rigor and responsibility that acknowledges that the patient is engaging in a de facto experiment.

The obligation to do good, to avoid harm, and to promote just use of resources commits professionals, institutions, payers and purchasers to an evidence based standard. Respect for individuals requires acceptance of appropriate variation, if not financial support, for every “n of 1” experiment.

**Brett Kay**  
*Health Policy Associate*  
*National Consumers League*  
*Washington, DC*

Evidence-based medicine makes sense. After all, if we require that medications be tested and approved for safety and effectiveness, shouldn't we hold our medical treatments to the same standard? There has been a great deal of attention paid to medical errors recently. The Institute of Medicine's report, "To Err is Human," has garnered a lot of publicity about a problem that has been left in the shadows for far too long. Evidence-based medicine can and should be a part of the solution.

Increased use of medical care outcomes measures has highlighted wide variations in outcomes among geographic regions and even among providers within a region. With doctors practicing very differently around the country, there is increased risk of error and a lot of waste and redundant care.

Evidence-based medicine is not the "Holy Grail" as it has been framed for this conference, and there are many issues yet to be resolved. As we all know, science and data can be used to support a wide range of positions and theories, many of which are based not on medical or scientific grounds, but on political, financial, or other factors. This is an important point for consumers and healthcare professionals to keep in mind as well. There can be repercussions if the public believes that they are being taken advantage of, whether this is a perceived or real situation.

Much of the managed care backlash we are seeing is the result of public cynicism and a belief that financial concerns, not scientific or medical concerns for a patient's well being. It is time for information to be shared openly with the public, but it is also necessary for the information to be put into context for the public. Otherwise, there will be more confusion and cynicism. Again, here is where the scientific and medical communities need to work with consumers and patients in a cooperative manner—the old "take two aspirin and call me in the morning" patriarchal, patronizing attitudes must change.

Evidence and data are important, but more important is what is done with the data, and who controls it. If large health care companies and other commercially-driven enterprises control the data, then there will always be a sense of mistrust. The perception exists now that there is bias when commercial and financial interests control the research agenda. I just read in the latest issue of the *New England Journal of Medicine* (May 19, 2000; Vol. 342, No. 20) an article addressing the uneasy alliance between clinical investigators and the pharmaceutical industry. The article points to several studies that show a direct relationship between favorable outcomes of studies funded by industry compared to research funded by the government or other non-profit institutions. This is something that must be addressed.

Consumers and health professionals need to keep a few things in mind as they move toward EBM. First, be a skeptic. Don't believe everything you hear or read. You need

to question the facts about the study, its design, patient populations, and wait for all the evidence to be in before making any final decisions.

Thus, consumers need to know about study bias and other threats to internal validity. They need to understand the hierarchy of clinical study design, and why a double-blind, randomized control trial is considered the gold standard. They need to know that five or even 25 people in a study does not represent the universe, and why that is important. Scientists can help us learn more. When we are better educated consumers, then we can demand better quality health care. Doctors have to use terms consumers can understand and find ways to make the information meaningful to the patient. Just as clinicians need to find ways to make raw data meaningful so practitioners can actually adopt the new findings into their daily practice.

***Stephen E. Kahn, PhD***

*Section Chief and Director*

*Clinical Chemistry, Toxicology and Near-Patient Testing*

*Loyola University Medical Center*

*Chicago, IL*

I do believe that evidence-based medicine is the right way to go. However, we need to broaden the application of such care. Information technology is aligned to help us, both in acquiring data and in disseminating and using EBM.

From my vantage point in the laboratory, I know I have way too much data, and too much information, as do many of us. We have to get better at handling it, connecting it to other information systems, and apply this to the patient's health.

Students at Loyola are taught EBM in the core curriculum, for three years. But we also must enlighten our physicians and residents, and I don't see the carry-through about EBM for those doctors.

To effectively change physician behavior requires good planning and usually several kinds of actions. Obstacles to change should be identified first. EBM should be complemented by evidence-based implementation. Remember we all have different approaches to using healthcare that are based more on beliefs than scientific evidence.

The most important point in my message is that we need to go beyond EBM and have "Evidence-Based Healthcare." This concept comes from a book by the same title (Gray, JAM. Evidence-based Healthcare: How to Make Health Policy and Management Decisions, Churchill Livingstone, New York, NY, 1997). Individuals who practice evidence-based decision-making help to shape organizations, which can become evidence-based organizations that foster more evidence-based decision-making. This is the evolution of a culture, and it is a goal that those of us in hospitals should strive for.

The factors that demand a broader application of EBM include an aging population, higher professional expectations, higher patient expectations and patient desire to participate more in their own care, and new knowledge and technology, fueled by industry and research.

Regarding EBM: What we've got here is a failure to communicate. The idea of EBM has been around for over 100 years. There are so many publications and books, the electronic databases, the information explosion, the interest of the National Health System in the United Kingdom talk about EBM, but we just don't see the application of EBM or evidence-based healthcare that we would expect.

I conclude that EBM is the right thing to do, teach and practice. "I define and think of EBM "as physicians using best evidence and their individual clinical expertise, taking into consideration the patient's values, for effective healthcare."

Because we do work in a market-driven system, tying the best research to reimbursement and development of good practice guidelines is the way to extend the application of EBM. This presents opportunities for all of us in laboratory medicine and manufacturing. We must find ways to correct the failure to communicate.

***Saturday, May 20, 2000***

## The Role of the Clinical Laboratory in EBM

***Matthew J. McQueen, MD, PhD***

*Professor*

*Department of Pathology and Molecular Medicine*

*McMaster University and*

*Director*

*Hamilton Regional Laboratory Medicine Program*

*Hamilton, Canada*

A number of themes have emerged since the program began yesterday. We are not certain how the laboratory community fits into the scheme of EBM. We need better leadership, leading us into the practice of EBM. Simply teaching people to do something does not mean that they will practice it.

We need to have more research funding. The ongoing changes in the practice of better medicine require more resources than many of us have.

There is a lack of comfort with the whole area of EBM. Using an analogy, there is a similar lack of comfort within our profession about molecular diagnostics. It may have been embraced in the research site, but many of our colleagues feel uncomfortable about its importance and role in laboratory medicine.

The key is whether we want a healthcare industrial model or a clinical model. We are changing emphasis. We have begun asking clinical questions that incorporate not only a laboratory perspective, but thinking in terms of the hospital community perspective, we must also consider the clinic, individual physician, the hospital and a health economy viewpoint.

Another challenge that has arisen in the course of this conference is the role of the laboratory professional as a consultant. Moving into that clinical consultant role, however, is where the system begins to fall apart. We need to commit to demonstrating our value. We need to show that laboratory testing contributes to correct and timely decisions that improve the quality of healthcare by making better use of limited resources.

Three quality tools have been identified as helping to provide the best possible care with the best use of resources: clinical practice guidelines, care maps, and outcomes measures.

Clinical practice guidelines are intended for an institution or group of practitioners. Guidelines are a strategic method for assessing the appropriateness of an intervention, and they guide practice in an explicit manner. They generally extend beyond local conditions to the general. Guidelines can be bulky, slow to use, and expensive to produce, but they also serve to provide a guide to care based on evidence. It is true that sometimes they are not based on the very best evidence, however.

Care maps are an attempt to reduce unnecessary variances in care delivery. By reducing variation, we can streamline the services, including lab services. These can be

constantly updated based on evidence from key indicators. The lab has to help create and improve the care maps. Time delays, for instance, could involve the lab in achieving a workable solution. Most of these quality efforts, however, fall apart because of a lack of continuing commitment. Commitment is a key to successful change. Another way to place the laboratory in the circle of continuous quality improvement is to include laboratory services in impact analyses on physicians or changes in practice patterns, to learn how laboratory services impact on patient-focused care.

Outcome measures are difficult to assess, in terms of the laboratory contribution. There has been progress in assessing the process and the outcomes of medical care. The laboratory must demonstrate that its tests contribute to better overall resource utilization (reduced length of stay, less time in critical care unit, etc.).

Major morbidity and mortality are not the only outcomes. Other types of outcomes include cholesterol screening, Pap smears, and PSA tests. If cholesterol screening is deemed clinically useful by your institution, measurement of the proportion of patients undergoing this screening should rise and your institution needs to work to see that patients get this type of screening.

We do not have all of these quality indicators in place yet. But in long-term studies, we can look at laboratory tests as they relate to patient satisfaction, functional status, quality of life, and return to work rates. We need to address over-use and under-use of tests. We must explore further, ask some questions. For example, do we really understand how family practitioners use blood tests? Is it for direct diagnosis or for ruling out other things?

There is a much larger role for laboratories to play in randomized clinical trials. The laboratory information system, tied to other databases, is extremely valuable. Overall, laboratory data must be better integrated with clinical, diagnostic, pharmaceutical, statistical, and financial information in a repository of data, kept online longer.

As laboratorians, we should be ashamed of the types of reports we give out. They are singularly unhelpful. We need to produce reports that help to improve outcomes and clearly define and validate rules. We need to reduce practice pattern variations among physicians, so that one doctor does not use three times as many tests as another. We need to do some “what if” modeling, see what might happen if certain tests are reduced, for instance, which can yield tremendous directions for the laboratory services.

We need to know what appropriate use of laboratory medicine is. In one study of 4,100 citations of studies that purported to measure inappropriate use, only 44 were used in the systematic review—only 1%. In yesterday’s presentation on the systematic review of cardiac markers, less than 1% of articles were eligible to be included. That speaks to the standards of quality and relevance of all studies.

More bizarre is the conclusion from this systematic review on appropriateness. The rates of inappropriateness ranged from 4.5% to 95% for testing. Even in the area of therapeutic drug monitoring, where the lab naturally would figure as a consulting body, the study showed an inappropriate rate of lab tests of from 4.7% to more than 80%. These

kinds of results are embarrassing for the laboratory. It is bad for administrators to read these summary results.

We don't correct inappropriate test use very well. We have got to deal with this, or others will deal with it for us. We have also got to deal with under-use of tests, particularly in the instance of diabetic patients.

Systematic analysis can be expensive, costing \$150,000 and more. We do need to understand the guidelines for critical appraisal of the literature. If nothing else, we at McMaster teach students how to appraise the quality of a study. It is vitally important when a study is of high quality.

We need to learn to use the databases like Medline, M-Base, HealthStar, and recognize and understand the use of structured abstracts, various keywords, indicative titles, and critical commentaries. Access to information via the Internet is also important, yet many of us don't use all of the alternatives to find the evidence we seek.

We might think about changing the way we report results, to reflect the uncertainty of results. Instead of giving a single value for cholesterol, why not give the range of possible answers? Then we could adjust and review these every few months to see where we are in terms of laboratory test uncertainty.

A paper by Leslie Shaw and his colleagues was published in *Clinical Chemistry* (1998; 44:381-387). It reviews the potential value of prospective, concentration-controlled clinical trials for frequently measured drugs. It provides clearer definitions of risk: benefit for immunosuppressive drugs. This paper is a good example of a systematic review, and we need to emulate it.

We still need information that would enhance clinical usefulness. I maintain that cardiac troponin is still not clinically useful. We need to publish likelihood ratios associated with serum troponin for complications of ischemia and for myocardial infarction in the 72 hours after the patient's presentation. What is the role of troponin in managing ER patients, in discharging them versus admitting them? We need the likelihood ratios in the literature.

We need to enforce information that we have that shows that testing does not help or that testing is only valuable for patients with a certain history or certain health conditions, not all patients undergoing a procedure. For example, the complication rates of cataract surgery showed no differences whether the patients were tested preoperatively or not, in an article published in the *New England Journal of Medicine*.

We do need to perform prospective studies, but we don't need to be hamstrung by lack of funding. Grants are available. Giant clinical trials can include subgrants that study certain laboratory parameters. We need to be creative about finding funding sources and getting the laboratory involved.



## Techniques to Improve Physicians' Use of Diagnostic Tests

**Michael Laposata, MD, PhD**

*Professor of Pathology*

*Harvard Medical School and*

*Director, Clinical Laboratories*

*Massachusetts General Hospital*

*Boston, MA*

The clinical laboratory can and should claim a dynamic role in helping physicians to manage many of their patients. As test numbers have expanded greatly in recent years, at the same time that therapeutic options also have expanded, physicians are extremely challenged. Even within a specific medical specialty, it is difficult for them to know all of the information related to both the management and diagnosis of a disorder. Most focus on disease management, which opens a door for the laboratory.

We know the Institute of Medicine report of medical errors shows that up to 98,000 Americans die from hospital medical errors. But there are huge numbers of errors stemming from laboratory information that could have been provided but that wasn't. The real problem is preanalytical, helping physicians selecting the right test in the first place. The primary care physicians are just now beginning to admit they don't know that much about antibody and other forms of testing.

"No more, I get the blood and doctors get back the numbers," Laposata says. "Now we are going to have to give back the most current and applicable information that physicians can use."

A solution is for the laboratory to offer valuable added services to enhance evidence-based medicine use in practice. These value-added laboratory services include:

- Directing test selection by algorithms within the lab to maximize efficiency of test selection for specific diagnoses. These reflex testing algorithms also obviate the need for multiple visits by the patient for repeat blood collections, which often is necessary to obtain the correct diagnosis with the fewest possible laboratory tests.
- Automatically providing narrative interpretation in paragraphs when complex batteries of tests have been performed. These interpretations specifically describe the patient and include consideration of other laboratory test results and findings from the clinical history and physical exam when appropriate.

- Rapidly consulting on a 24-hour basis in a physician-to-physician consultation service on laboratory test selection and interpretation.
- Informing patients about their diagnosis and diagnostic findings.

Regarding testing algorithms, MGH offers six tests on its coagulation request form, as opposed to three single-spaced pages of every test a hospital offers. It is up to the laboratory director to think about the logical order of testing, which tests are needed for which condition, which drugs have an effect on results.

We have implemented the value-added services with goals in mind. The goals are a shorter time to diagnosis, shorter length of stay, and fewer laboratory tests. Our algorithm for thyroid testing has been successful. MGH has demonstrated success in thyroid-stimulating hormone as a screening test to limit subsequent thyroid testing. The endocrine laboratory saw its numbers decrease (for total T3 and total T4 assays) from \$16 per test to \$6.25.

*The same three goals also apply to the concept of narrative interpretations, similar to daily rounds to interpret complex test results. When physicians order nonroutine tests in certain areas of the lab (such as coagulation or toxicology), test results come back as numbers plus a narrative interpretation by a pathologist. The interpretation includes the differential diagnosis and recommendations for future testing.*

The interpretation services include a standing order for an interpretation by the attending physician, and this standing order can meet the definition of a physician request. Several interpretation codes have the technical components that are already paid under the national laboratory fee schedule. HCFA pays for 18 codes, mostly anatomic pathology in the clinical lab setting. The exception is that HCFA also pays for coagulation interpretations.

To maintain the respect of our physicians, however, we must do more than say “band seen” on a hemoglobin electrophoresis, for example. We must tell the physician about hemoglobin E and its relationship to anemia, whether it is a stable hemoglobin, and how it is inherited, in a concise paragraph.

*The interpretations have proven popular. Without advertising, MGH acquired the business of 17 hospitals to obtain the narrative interpretations, and then attracted the business of another 50 hospitals within the Mayo Medical New England Laboratory network.*

This type of interpretive service cannot be haphazard. It must be well staffed and well run, and there must be a commitment to it. The interpreters must be on call 24 hours for the service to be useful. The trick is organizing the work so that two interpreters are available in each area of testing. If one is traveling, the other remains available. To keep costs down, MGH residents are trained and can generally answer two thirds of the questions they field.

Other drawbacks that limit an interpretation service:

- interpreters without expert knowledge;

- illegible handwritten comments;
- comments without important clinical information about the patient; and
- comments that are too brief or too general.

We have begun to share health information with patients and in some cases, this has saved lives, when patients present in the ER or in some other health crisis situation. MGH takes the interpretation and puts it directly on a wallet-sized card. The cards have been well received by both patients and physicians.

Our many value-added services are well received at MGH. A survey showed that 97.8% of physicians reported that interpretations were useful or informative. Seventy-one percent said the interpretation helped them to avoid a misdiagnosis.

Looking at the savings from avoiding a misdiagnosis, we see that the services are financially sound. Annual savings generated amounted to an average of \$277 per case that might have been misdiagnosed—or a total of \$582,120 per year. In the case of preventing a misdiagnosis of a bleeding or thrombotic disorder, the savings amount to \$929,544 per year.

MGH is also looking at a web-based service that helps physicians to make laboratory-related decisions similar to the value-added laboratory services that exist at MGH.

“We need the information technology piece, which is missing. We need to get the billing people, the legal people,” Laposata says. “I need your help in putting together this national service. We have already done the hard part, figuring out how the evidence-based medicine should be offered.” Interested colleagues can contact Dr. Laposata directly at [MLAPOSATA@PARTNERS.org](mailto:MLAPOSATA@PARTNERS.org).



# Overview on How to Practice Evidence-Based Laboratory Medicine

**Robert Andrew Moore, MA, DPhil, DSc,**  
*Managing Director*  
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We should not succumb to using different levels of evidence among the studies we consult for evidence. The best studies are independent, use masked comparisons, have a clear reference standard and enter consecutive patients into the study. If we are performing a meta-analysis and choose these good studies but also use studies in which the reference standard is not universally applied or that do not use consecutively entered patients, then we are not insisting on proper evidence. We are contaminating our meta-analysis and its results. The poorer designed studies are so biased, as to be unusable, in many cases.

In the *Journal of the American Medical Association* (1995;274:645-651), an article looked at the percentage of studies that met a high reporting standard for diagnostic tests. For example, only about a quarter of papers about diagnostic tests explain the population characteristics of the group on which the tests were done. *Clinical Chemistry* (<http://www.aacc.org/ccj/infoauth.stm>) insists on these standards, too:

- spectrum composition (age distribution, sex distribution, et al.)
- accuracy in sub-groups in the study
- avoidance of workup bias
- avoidance of review bias
- test accuracy precision
- indeterminate test results
- test reproducibility

I have said that the size of the studies is very important, and that holds true for studies of diagnostic tests. A look at sperm counts since the 1940s has shown that sperm counts are falling. Is that true? No. All of the evidence for falling sperm counts is due to small numbers of samples in decades past. The variability of sperm counts in studies with small numbers of patients is enormous, varying from 40 million sperm/mL to 150 million/mL. Large studies more accurately measure it.

After 80 attempts to systematically review literature on diagnostic tests, I have failed at each. I have tried, like Ethan Balk, to conduct systematic reviews on cardiac markers and failed. The reason is simple: if you look at all of the studies, and try to find unbiased studies, the number of studies you have left for analysis is near zero. This is true in other areas of laboratory medicine. The data in these various studies, often with small populations, are not good enough to be combined. This is my thesis. These studies taken alone are likely to be giving you the wrong answer.

We need to know more about the way that physicians use tests. Reid and colleagues (*American Journal of Medicine*; 1998; 104: 374-380) asked various physicians how they used tests: did they use Bayesian methods, ROC curves or likelihood ratios. The answer was no, the physicians scarcely ever used these tests. The physicians don't use these methods to assess test accuracy.

What they want is what Michael Laposata and colleagues are giving them: simple computer-driven algorithms, or some other format that allows them to combine different sorts of data about their patients, demographics, signs and symptoms, other laboratory tests. They need an indication of where to go next; they need an interpretation.

Clinical diagnosis, based on signs and symptoms, is a mixed blessing. Take the case of dementia. Dementia rates in a population vary enormously—they are highest in California and lowest in China. A study published in the *New England Journal of Medicine* (1997; 337:1667-1774) showed that using difference systems for diagnosis yielded very different rates of dementia prevalence, from only 3% of the patients to nearly 30% of the patients examined.

Here are some points to keep in mind. Trials have been conducted on anti-dementia drugs. But if you can't diagnose dementia accurately:

- How can you perform a clinical trial?
- Explain the results of the trial?
- Decide which patient benefits?
- Advise clinicians on which patients to treat?
- Explain all this to the patients and their families?

There is a place for signs and symptoms in clinical testing. In some disease areas, we could score the prevalence of signs and symptoms at the same time a test is being ordered.

In 1978, when we set up a thyroid testing service in Oxford, we wanted to set up a service that went beyond checking boxes for tests, so that physicians could indicate what was wrong with their patient and why. The laboratory would do the appropriate tests and together with the endocrinologists would give them a report to explain it all. This system worked very well.

Note here: If you have a valuable idea, one of the best things to do is to put it in a letter to the editor of a medical journal. These can be more powerful than the longest, most sophisticated papers.

Scoring signs and symptoms can help. In a letter to the *Lancet* from Australia (White & Walmsley; *Lancet* 1978; ii:933-935), a set of 18 thyroid symptoms was considered: six cardiac symptoms, and a set of three additional symptoms (unspecified in the publication). If a patient had three or fewer symptoms, the testing was not useful. Five or more symptoms, and testing became useful. That is a huge number (96%) of laboratory tests that could have been saved. An interesting idea—an area we as a profession could examine more closely.

David Sackett and colleagues in Canada are gathering evidence about the usefulness of the clinical examination. The CARE study (Clinical Assessment of the Reliability of the Examination) is open to participation to everyone worldwide. Their web site is [www.carestudy.com](http://www.carestudy.com), and a paper explains the study: McAlister et al., *Lancet* 1999; 354:1721-11724.

These researchers are using the Internet to gather information via standardized forms. They started with chronic obstructive airways disease, and found in this study that the signs and symptoms in textbooks are wrong. The most important sign is not in textbooks. This is an interesting example of a mechanism that laboratory experts could use to start generating large amounts of information.

I don't think that meta-analysis in the area of diagnostic testing is worth a damn. We have to look forward. Here are the things that we in the laboratory need to do:

- Perform studies that minimize bias, using consecutively entered patients in real situations;
- Make studies large enough to avoid randomly introduced error; and
- Use the Internet to recruit many centers, emulating the example of the CARE study, and to make results meaningful.

In the new paradigm for tests:

- Perform a prospective comprehensive audit.
- Collect information on a large number of patients with a defined clinical problem.
- Assess clinical and laboratory findings, with eventual outcome and diagnosis.
- Determine which clinical and laboratory findings are strongly associated with outcome and diagnosis.
- Create decision rules.

- Assess these decision rules in randomized trials, where the unit of randomization is a hospital.

Examples of the new paradigm can be found. In both of the following studies, reductions in X-ray use, cost, and time were evident:

*BMJ* 1995; 311:594-7 (Ottawa ankle decision rules)

*JAMA* 1997; 278:2075-9 (Ottawa knee decision rules).

We need to think about the ways in which we can best describe results. In conclusion, we have found new and better ways of describing test results for treatments, for example, the information offered by Dr. Laposata and colleagues. We need to use these ways of describing results so that doctors can and will understand them and be able to apply them.

For diagnosis, we have to find better ways of describing results. The ways we use now are not acceptable or helpful.

Results will have to be available and useable in 15 seconds. This is the way we are moving.

We don't have time to debate these thorny problems. We have to get together and do something to change things. Summing it up, in my opinion:

Systematic reviews don't help. It is not possible to translate them, as they are now, into something that helps the typical doctor.

We must get together with our colleagues to connect clinical practice with academia and industry.

We must promote better research. We need funding.

We need to promote more useful research.

We need to do more research. "The only way to practice evidence-based laboratory medicine is to do research."

## Q&A Discussion:

### *Comment and Question/*

**Dr. Kahn:** We on the AACC Troponin I subcommittee have made excellent progress this year and have completed a round-robin study with manufacturers, which will be announced at the AACC Annual Meeting in July, and there will be a related poster session.

What examples at your institution highlight the biggest successes in working with other physicians, in terms of turning evidence-based information into guidelines, care paths, and algorithms?

**Dr. McQueen:** The laboratory got involved in the various care pathways set out for hip and joint replacements, and we were involved in the revision stage, because I reviewed them and realized there was no laboratory testing involvement. The ongoing monitoring and revisions of the care paths in a multidisciplinary situation is where we have tended to fail. Part of the problem is that we all like to work on new projects and not keep revisiting the same ones. I am not sure I know of good ways to keep up with the monitoring.

**Dr. Kahn:** The ongoing monitoring issue in our lab, we have incorporated NCCLS GP-26-A is the guideline we're following, in a quality systems approach. This has enhanced our ability to provide the ongoing and periodic monitors in key areas throughout all of our laboratory services. I understand in the final CLIA quality control rules will advocate a quality systems approach. That might be part of the answer.

I have a comment about giving out expert opinions in the lab. We introduce our own form of tyranny when we make an expert judgment about a case. How do we ensure when we give out these interpretations that we are reflecting the expertise of all of our colleagues?

**Dr. Laposata:** Although we take the evidence from literature, we have had some very heated discussions of how we will deal with the PTT mixing study or the diagnosis of HIT. We don't use this as a reason to not have a decision. We realize the decision may change.

You may think that once an algorithm is made, it is fixed. Or that once coded comments are made they are written in stone. In fact, our coded comments. Of our 100 or so coagulation comments, we are probably going to modify 20 of them in the next few months. The testing algorithms change, too. This is a dynamic process.

**Dr. Moore:** One thing that has worked at Oxford is staff in training in the lab and on the clinical side working together to produce updates to their bosses at suitable times. This helps them learn to appraise literature and find evidence for themselves. A lovely thing happens, too: early in their careers, laboratorians and clinicians work together.

**Dr. Laposata:** Our clinical residents have been educated. They used to bail out at level three difficulty (out of 10) on my cases. Now most of them can go through all levels and demonstrate understanding. I asked how they came to improve so

dramatically. They said that they had been reading the lab interpretations through their entire residency and had learned a lot from these interpretations. A fair amount of learning can happen when you give physicians more than numbers.

**Question/**

**David Bruns, MD, PhD, University of Virginia, Editor of Clinical Chemistry journal:** On the Internet we can correct errors online and keep the older versions. This is called versioning. But when you change guidelines or algorithm, don't you have to hold onto the old version so that when the lawyer looks at the way you tested a patient in the older algorithm, you can show what you were doing then was the state of the art.

**Dr. Laposata:** That is a very good idea. As the commercial viability of our coded comments became clearer, our hospital has taken control of the coded comments and all of our electronic programs that provide suggested interpretations and have called inventors so we receive some royalties. But we should probably document these different versions by date.

**Question: Unidentified speaker:** Dr. McQueen recommended publishing confidence intervals for test results. Are there any publishing institution-specific likelihood ratios for cardiac markers? Does anyone do that and if not, why not?

**Dr. Moore:** I have seen one or two papers that have attempted to do this, but they have not included any outcomes from it. I think the difficulty with likelihood ratios

is the busy doctor, who is too busy to sit down and sort out likelihood ratios. A small algorithm—put it all in and get a result out—that is what's needed.

**Question/**

**Richard Flaherty, Executive Vice-President, AACC:** Many laboratory experts are perceived as just running numbers factories. They don't get the reimbursement they deserve. What public policy changes would you like to see? How would you like others outside the laboratory to facilitate the diffusion of EBM in the field?

**Dr. Laposata:** A comment: nurses and laboratory technologists both go to college for four years, but technologists always make less than nurses. It's true on all levels. Why are laboratory scientists viewed as less contributory than others in the field? The patients don't really understand our contributions or the idea that we could be involved in clinical care.

That perception of our contribution will change if we take the necessary steps and work together as a team. We have to show how we contribute significantly to clinical care, all of us, the technologists, scientists, and pathologists in the laboratory. I think it will be a battle, but maybe we can win with the younger internists, who will begin to see the value of the narrative interpretations we provide.

**Dr. McQueen:** In Canada, I have always worked with a fixed budget in my laboratories. The emphasis has been on our clinical value. We have probably suffered less downsizing than any other department in

our hospital because we made sure that all of our clinical pathologists are also clinicians. I visit patients. When our two senior microbiology experts retired, the administration tried to eliminate those positions. I noted that they would lose infection control coverage for two hospitals. The positions stayed. That is the added value. The impact analyses have borne out our utility, because of our clinical value.

**Dr. Lundberg:** In the early 1970s, I had a fixed budget lab and they were going to lay off many of my people. We stopped answering the phone. It took about 30 minutes, and we had our new positions. That hardball may get some results, but it won't work for culture change. We are going to have to change physician behavior delicately. It is not easy. It is a matter of incentivizing—persuading them that they can do a better job if they go along with certain other things that we can provide.

**Comment/**

**Tadd Scott Lazarus, MD, Medical Affairs Director, PCR Diagnostics, Roche:** My comments are from by background as an internist in HIV primary care. There are dirty little secrets we need to talk about. One of the reasons why physicians are reluctant to utilize algorithms is their training. That training was abhorrent to anything that could be considered “cook-book” medicine, instead of a thinking person's resource. I think we have to re-formulate the world of primary care.

I didn't realize that you have felt devalued. We in primary care have always looked toward our laboratory colleagues to assist us. The archetype pathologist

who went into the laboratory so as not to deal directly with patients—those stereotypes must be broken down so that we know that you are accessible. Similarly, you have to understand that we are thinking professionals. We have to do so much in so little time.

The other dirty secret about algorithms is that physicians want to know that these expert algorithms are not going to be disseminated in patient portals until we get a chance to live by them and discuss them with you. Similarly, we don't want direct-to-consumer advertising for Claritin to get to our patients before we've seen the product and learned more. We need that kind of chance. We don't want to be replaced in the patient's mind by algorithms.

When you have 12 minutes to see a patient, how do you get the information quickly? I don't mean to be pejorative, but CD-ROMs are passe, unless they are web based, too. Now internists need to have a live DSL line (rapid Internet connection) while they're seeing the patient. The secret to practicing primary care is knowing what you need most of the time and being able to access it instantaneously. Moving these algorithms to web based models in professional portals—that is the start.

**Dr. Lundberg:** American medicine is in a horrendous mess every way you look. Specifically, we know there are pathologists who don't like to deal with patients. At UCLA and UC—Davis, we had an interview method with knock-out questions for those applying for pathology residencies that were trying to run away from people contact.

As for your comment of keeping information away from patients until you have had your opportunity for review, you are living in the wrong decade. For right or wrong, patients and physicians are getting information from the Internet as soon as possible, whether the data or information is scientifically sound or not.

**Dr. Laposata:** There was opposition in the Department of Medicine to having our algorithms advance. I put everything on the line, and I went ahead with the algorithm for coagulation testing, because that is my area of expertise. My job was in jeopardy. But the 2,000 other doctors benefited from this so much, the department chairs were over-ruled. If we had passed it around for comments, it would never have happened.

About the web-based system, we have been working with American Medical Laboratories and Park City Systems on this. Our experts said that answers must appear within seconds or they wouldn't be useful to the internist who sees so many patients in an hour. This project is web based, and the whole purpose is to pick the right test and assist in diagnosis.

**Question/**

**Eleanor Travers, MD, US Department of Veterans Affairs:** If decisions on policy are politically motivated and if medical research data cannot be trusted to scientists, and compliance with federal regulations inhibits the logical patient-care thinking process, then should cost be used as one of the relevant factors used in evidence-based medicine?

**Dr. McQueen:** We are using costs all the time. We must remember that lowest cost, however, is not always best. It may be a good idea to spend \$500 on a diagnostic test that would keep a patient out of the hospital for 4-5 days. We'll never be able to move away from cost. But we can't embrace the idea that the lowest cost of testing is always for the best.

**Dr. Moore:** The combination of good evidence and an understanding of how to use health economics is a terribly powerful combination. If you have enemies and you have evidence and you can present costs, you can smite them. My advice to anyone working with evidence is to find out how to do costing work, find the sensitive points, and go for them.

**Dr. Laposata:** If I am addressing administrators, the focus of my talk becomes cost. It is important to be able to use different aspects for different audiences. With administrators, your arguments should be cost based.

**Dr. Lundberg:** As we move into gene-based diagnostic technologies, costs will be fantastically high. The idea will be to save money while remaining within ethical guidelines, which still to be developed. This is a new challenge for us.

**Question:/**

**Dr. Joe Boone, PhD, CDC:** In our current research environment, how do we prioritize our research questions? How do we even know who is doing what, particularly laboratory medicine, in single institutions? How can we design low-cost prospective

studies? How do we collect and analyze all this data? How do we educate everyone about this new information? I think the new focus on medical errors is an opportunity for laboratory medicine to pull this together.

**Dr. Lundberg:** To change the government, we must use the public media, using anecdotes during Congressional hearings. This proves the power of anecdotes as surpassing hard data. If we can include laboratory medicine representatives in these hearings on Capitol Hill, we can make cultural changes more rapidly. If Dr. Laposata could show the senators his photographic proof of how difficult it is to tell the difference between a bleeding disorder and an abused child, and how failing to do testing could result in a wrongful incarceration, this could help to change a culture. But you have to be willing to become a public figure and deal with scrutiny from the media and others. That is how culture changes in this country.

**Dr. Moore:** To communicate and educate, you need people who can work well together. There are unsung heroes in every institution, who make an impact. What is it about that person that makes

that service sing, when someone right next door can't? Those are management issues, team issues—we must start talking about these.

**Dr. McQueen:** Using specific examples is the best solution. There is no across-the-board solution. One example: We had a situation in which we saw that we could use the medical microbiologist and infection control practitioners beyond the walls of the hospital to help the community. We are looking at how we can take this service seamlessly out to cover a whole city, into other hospitals and long-term care institutions. We want to ask, in a major area where resistant organisms are a problem: Can we integrate with others, including public health agencies and epidemiologists that might look suspiciously upon the laboratory, and get a team working on this and collect evidence and see if we can make a difference? This is a project that will demonstrate value to many parties in our community.

**Comment: /**

**Dr. Bruns:** I would like to have case reports of medical errors sent to *Clinical Chemistry*. Please send them to the journal. I think that would be useful.



## Closing Remarks

***Frank Sedor, PhD***

*President, AACC and*

*Director, Clinical Chemistry Services*

*and Administrative Director,*

*Core Laboratory*

*Duke University Medical Center*

*Durham, NC*

I want to take this opportunity to thank our moderator, Dr. Lundberg, our speakers and you the participants for attending this forum on EBM. I think this program highlights what we in the laboratory community have known for years—that clinical laboratory testing is a key element of the medical-decision making process. However, with that recognition comes an enhanced responsibility to make sure that the tests we offer, and the data we provide, is accurate and useful.

This conference should serve as a wakeup call, to all of us in the laboratory community, that we all need to work together—manufacturers, laboratories, physicians and government agencies—to ensure that patients receive the best medical care that we can provide. Thank you for joining us today and making this scientific and policy forum possible. And I would like to extend a special thanks to Bayer Diagnostics for their generous support for this program.

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