

Evidence Based Medicine and POCT

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POCT Definition

Point-of-Care Testing (POCT):

Diagnostic testing conducted close to the site where clinical care is delivered.

Point of Care Testing

- Advantages

- Immediate results - no lab transportation
- Small blood volume
- Wide menu of tests available
- Whole blood and other samples available
- Works within clinical patient flow

- Disadvantages

- More expensive than traditional laboratory tests
- Quality is questionable as anyone can run the analysis
- Difficulties with regulatory compliance and documentation
- Lack of staff appreciation preanalytic, analytic, postanalytic issues
- Compliance issues with billing and charge capture

What is Evidence-Based Medicine?

- Evidence-based medicine (EBM) is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.
- Sackett et al BMJ 1996;312:71-2.

Evidence-Based Medicine

- Goal of Evidence-Based Medicine (EBM) is to develop pathways of care, guidelines for achieving optimal patient outcomes based on existing evidence
- EBM blends research evidence with clinical experience
- EBM does not dictate patient management nor does it tell physicians how to practice medicine
- EBM indicates the most cost-effective manner for treating the average patient with a specific condition to obtain the best health outcome
- Individual patients vary considerably and may deviate from the average patient pathway which is where clinical judgment is required.

The Evidence Based Process

- Differs from the peer consensus conference
- Comprehensive examination of the available literature
- Grading criteria is determined in advance and applied equivalently to minimize individual bias or influence on committee
- Recommendations are developed to support or exclude the use of a procedure or test based on the strength of the supporting literature/evidence.

Three Levels for Evaluating Evidence

- Individual study (internal/external validity)
- Linkage in analytical framework (coherence, aggregate internal/external validity)
- Entire Service – degree to which the evidence connects the test, procedure or service directly to health outcomes

Current Methods of the U.S. Preventive Services Task Force: A review of the process. *Am J Prev Med* 2001;20(3S);21-35.

Grading Individual Studies

- I At least one randomized controlled trial
- II-1 Well-designed controlled trials without randomization
- II-2 Well-designed Cohort or case-control analytic studies, preferably from more than one center or research group;
- II-3 Multiple time series with or without intervention.
Dramatic results in uncontrolled experiments.
- III Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

Current Methods of the U.S. Preventive Services Task Force: A review of the process. Am J Prev Med 2001;20(3S);21-35.

Benefit/Harm

- Separate criteria from judging quality of evidence.
- Measures net benefit to be expected from implementing service, test or procedure.
- Four point scale:
 - Substantial
 - Moderate
 - Small
 - Zero/Negative

Principles for Making Recommendations

- Evidence-based – require evidence that persons receiving service/procedure experience better outcomes than those who do not and benefits outweigh harm
- The outcomes that matter most in weighing evidence are health benefits and harms
- Where possible total economic costs are considered but not a first priority
- Recommendations are not modified to accommodate concerns over insurance coverage, medicolegal liability or legislation (this is a consumer issue!)
- Recommendations apply to a specific population, as in the U.S. Preventive Service Task Force and asymptomatic patients for which preventive service is targeted.

Translating Evidence into Recommendations

- A – strong recommendation to support procedure
- B – recommendation to support procedure
- C – no recommendation for or against
- D – recommends against procedure
- I – insufficient evidence for or against

Recommendation Grid

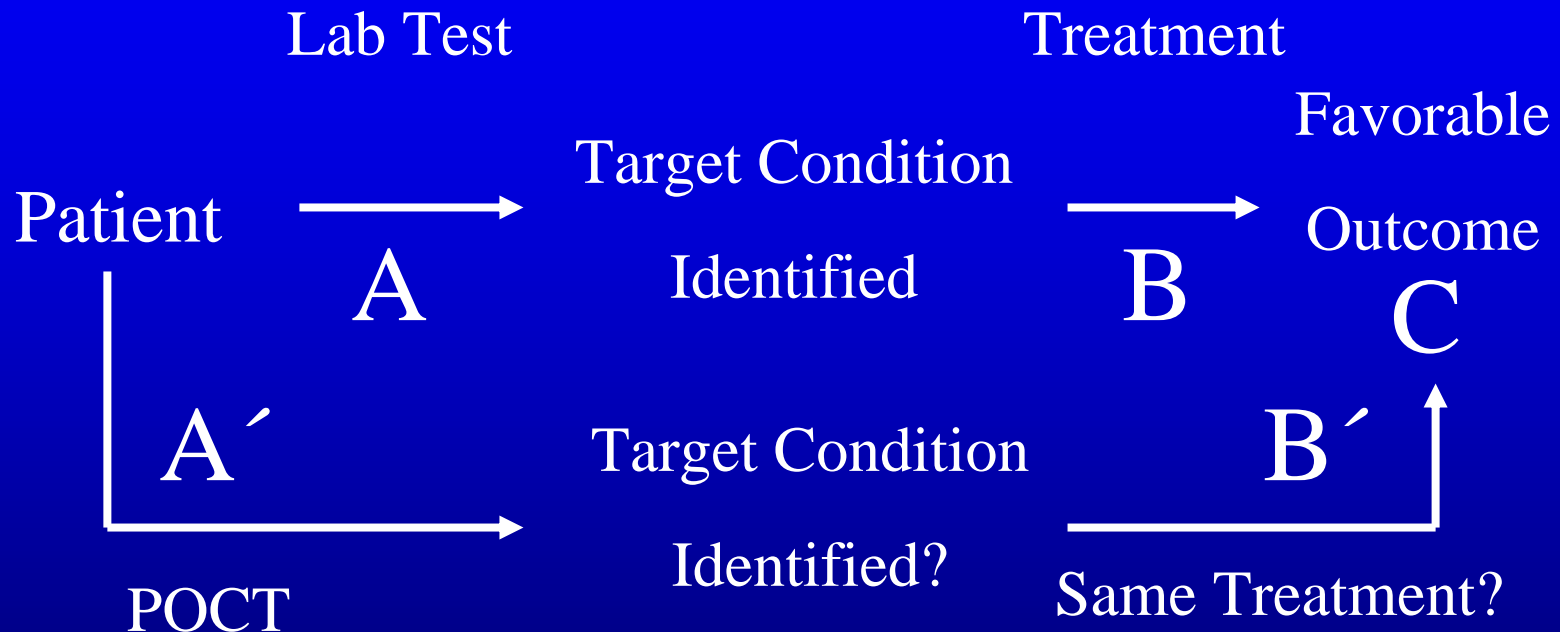
| Quality of Evidence | <u>Net Benefit</u> | | | |
|---------------------|--------------------|----------|-------|----------|
| | Substantial | Moderate | Small | Zero/Neg |
| Good | A | B | C | D |
| Fair | B | B | C | D |

Poor = I

POCT Literature Evidence

- Few randomized or case-controlled studies.
- Majority of literature is method comparison.
- POCT compared to a core lab method and assumed to obtain same clinical outcomes.
- This is not necessarily true in all patients and devices

Why doesn't $A + B = C$?



- Consider sensitivity vs. specificity of test method (core lab vs. POCT)
- Is treatment identical for both test results?
- Is a confirmation test or procedure performed with POCT?)

Generalizing Literature

- Biologic plausibility – do study results make sense?
- Study population comparability to real world – similarities in terms of risk factor profile, demographics, ethnicity, gender, clinical presentation and similar factors
- Similarities of the test or intervention studies to those that would be routinely available (methodology and compliance- will staff perform POCT correctly and with same emphasis as in study?)
- Clinical or social environmental circumstances in the studies that could modify results from those in routine practice

Evidence-Based POCT

- Assessment of patient outcome from obtaining a “quality” test result
- Integration of the laboratory into overall healthcare management
- Understand the process or processes that lead to the desired outcome
- The laboratory is quantitative and quality focused and therefore uniquely positioned to consult on critical pathways of care and development of practice guidelines.

Evidence-Based Medicine

Example: Blood Glucose Meters

- Recent NACB Guidelines and Recommendations for Laboratory Analysis in the Diagnosis and Management of Diabetes Mellitus:

- Recommendation: Use Diagnosis/Screening

There are no published data to support a role for portable meters in the diagnosis of diabetes or for population screening. The imprecision of the meters, coupled with the substantial differences among meters, precludes their use in the diagnosis of diabetes and limits their usefulness in screening for diabetes

Level of Evidence: Peer Consensus

Sacks D et al. Clin Chem 2002;48(3):436-472.

Diabetes

- Criteria for diagnosis are based on outcome data (risk of micro-and macrovascular disease) correlated with plasma glucose concentrations (fasting and 2hr post glucose load) assayed in an accredited laboratory
- Whole blood is used in portable meters
- Although many devices have been programmed to report a plasma glucose, the imprecision of current meters precludes their use in diagnosis.
- Similarly, screening by portable meters, although attractive because of convenience, ease and accessibility, would generate many false positives and negatives.

Blood Glucose Meter Precision

- Statistically, 95% of results fall within $\pm 2SD$
- In our institution, Core Lab
 - 93.7 ± 0.9 mg/dL (1.0% CV)
 - 282.7 ± 1.9 mg/dL (0.7% CV)
- POCT is not equivalent to core lab
 - 49.0 ± 9.2 mg/dL (18.6% CV)
 - 283.0 ± 15.0 mg/dL (5.3% CV)
- Clinically the ADA has recommended glucose meters to have CV's of $<5\%$ at all levels and accuracy to within 5% of a lab result. (1987)

Blood Glucose Meter Accuracy

- Proficiency Survey (AAB 2nd Q 2001):

| | <u>Sample 1</u> | <u>Sample 2</u> | <u>Sample 3</u> |
|--------------------|-----------------|-----------------|-----------------|
| Bayer Glucometer | 153.7 | 76.1 | 34.1 |
| HemoCue | 284.8 | 155.4 | 68.3 |
| LifeScan OT II | 148.8 | 91.7 | 59.0 |
| LifeScan Sure Step | 190.6 | 116.7 | 74.7 |
| Medisense PCx | 164.6 | 96.3 | 55.2 |
| Roche Advantage | 154.7 | 88.6 | 45.6 |

- Glucose meters do not read the same on the same sample.
- While this may be due to matrix effects of the sample...

Blood Glucose Meter

- Most recent evaluation by FDA on patient samples:

| | <100 mg/dL | | >100 mg/dL | |
|---------|------------|----------|------------|------|
| | <20mg/dL | >20mg/dL | <20% | >20% |
| Meter A | 0% | 22% | 0% | 24% |
| Meter B | 0% | 14% | 0% | 0% |
| Meter C | 2% | 6% | 0% | 0% |
| Meter D | 4% | 10% | 4% | 0% |

- Currently marketed glucose meters fail to meet consensus criteria in the hypoglycemic range on actual patient samples.
- These same meters also fail FDA approval criteria:
 - 95% of results within $\pm 20\%$ if >100 mg/dL
 - 95% of results within ± 20 mg/dL if <100 mg/dL

Chen ET, et al. Clin Chem 2001;47(6S):A189.

How Precise does a Meter Need To Be?

- Monte Carlo simulation to generate random “true” and “measured” glucose based on mathematical model of meters having defined imprecision and bias. (N=10,000 - 20,000 pairs)

| <u>Analytical error</u> | <u>Insulin dose errors</u> |
|-------------------------|----------------------------|
| 5% | 8 - 23% |
| 10% | 16 - 45% |

- 2x or greater insulin dosage errors >5% of time when analytic error exceeded 10 - 15%
- Total error < 1 - 2 % required to provide intended insulin >95% of time.
- Boyd JC, Bruns DE. Quality specifications for glucose meters: Assessment by simulation modeling of errors in insulin dose. Clin Chem 2001;47:209-214

Practice Guidelines

- Recommendations are thus evidence-based and weighted by the strength of individual studies, the concordance of studies, the degree to which the procedure is linked to health outcomes, and the magnitude of the patient benefit.
- POCT up to now has been mentioned sporadically in practice guidelines related to specific disease states. The diabetes guidelines are one example.
- A project is currently being started to develop a more comprehensive collection of recommendations relating POCT to patient outcome.

Laboratory Medicine Practice Guidelines (LMPG)

Evidence Based Practice for Point of Care Testing

National Academy of Clinical Biochemistry (NACB) Mission

- The NACB is dedicated to advancing the science and practice of clinical laboratory medicine through research, education, and professional development.
- NACB publishes Laboratory Medicine Practice Guidelines (LMPGs) for the application of clinical biochemistry to medical diagnosis and therapy.

NACB Laboratory Medicine Practice Guidelines

- **Nutritional Status** 1994
- **Thyroid Disease (1st edition)** 1996
- **Newborn Infant** 1998
- **Therapeutic Drug Monitoring** 1999
- **Cardiac Markers** 1999
- **Hepatic Injury** 2000
- **Diabetes** 2002
- **Thyroid Disease (2nd edition)** 2002
- **Emergency Toxicology** in progress
- **Maternal / Fetal Health** in progress
- **Cardiac Risk Factors** in progress
- **Point of Care Testing** in progress

Evidence Based Practice for POCT

- POCT is an increasingly popular means of delivering laboratory testing.
- When used appropriately, POCT can improve patient outcome by providing a faster result and therapeutic intervention.
- However, when overutilized or incorrectly performed, POCT presents a patient risk and potential for increased cost of healthcare.

Evidence Based Practice for POCT

- Clinicians, staff and laboratorians need guidance to apply POCT in the most effective manner for patient benefit.
- This guidance should be based on a concurrence of the scientific evidence to date.
- This LMPG will systematically review the existing evidence relating POCT to patient outcome, grade the literature, and make recommendations regarding the optimal utilization of POCT devices in patient care.
- Develop liaisons with appropriate professional, clinical organizations: ADA, ACOG, American College of Cardiology, etc.

Evidence Based Practice for POCT

Organizing Committee

- James H. Nichols, Ph.D. (Chair)
- Naomi Aronson, Ph.D.
- Robert H. Christenson, Ph.D.
- Ellis Jacobs, Ph.D.
- Kent B. Lewandrowski, M.D.
- Rodney S. Markin, M.D., Ph.D.
- Christopher Price, Ph.D.
- David B. Sacks, M.D.
- Salvador F. Sena, Ph.D.
- William E. Winter, M.D.

Evidence Based Practice for POCT Schedule

- Fall 2002 - Form focus groups on specific topics composed of clinicians, laboratorians, industry and representatives of professional societies.
- Spring 2003 - Conduct a systematic review of literature and make specific recommendations.
- Summer 2003 – Internet availability of recommendations for public comment.
- Fall 2003/Spring 2004 – Groups resolve comments.
- Winter 2003/Spring 2004 – Internet publication of revised recommendations
- Summer 2004 – Present final recommendations.

Evidence Based Practice for POCT

Focus Group Chairs

- Cardiac – Robert H. Christenson, Ph.D., Univ of MD
- Diabetes – Glen L. Hortin, M.D., Ph.D., NIH
- Reproduction – Ann M. Gronowski, Ph.D., Washington Univ
- Infectious Disease
- Coagulation
- Parathyroid – Lori J. Sokoll, Ph.D., Johns Hopkins
- Toxicology/Addiction
- Bilirubin Screening
- Critical Care- Greg Shipp, M.D., i-Stat
- Renal – William A. Clarke, Ph.D., Johns Hopkins
- Occult Blood – Kent Lewandrowski, M.D., Mass General
- pH
- Provider Performed Microscopies covered in Renal and Reproduction focus groups.

Evidence Based Practice for POCT

- This LMPG promises to be the most comprehensive collection of our POCT knowledge base.
- Recommendations from this LMPG will be useful:
 - To define applications where POCT is more effective in patient care from those with little benefit.
 - To sort the facts from conjecture when implementing and utilizing POCT devices.
 - To establish proven applications from off-label and alternative uses of POCT
 - To outline the mechanisms and strategies for optimizing patient outcome.

Evidence Based Practice for POCT

THE NACB



WANTS
YOUR INPUT

Evidence Based Practice for POCT Levels of Participation

- Send POCT Concerns and Comments to Organizing Committee
- Focus Group Member
 - Participant in Systematic Review
 - Develop Practice Guidelines
- Review Draft Recommendations as a consumer and provide comment or suggestions.

1976-2001



For more information
visit the NACB at

www.nacb.org

Evidence Based POCT Summary

- POCT is an expanding delivery option due to increased pressure for faster results.
- POCT should not be utilized as a core lab replacement in all patient populations haphazardly without consideration of the test limitations and evaluation of a faster result on patient care.
- More quality POCT outcomes studies need to be conducted.
- Efforts are currently underway to develop recommendations for evidence-based “best” practice of POCT.