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# REPORT

# Laboratory Medicine Best Practices: Developing Systematic Evidence Review and Evaluation Methods for Quality Improvement Phase 3 Final Technical Report

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## EXECUTIVE SUMMARY

**BACKGROUND AND PURPOSE**: This report summarizes the third phase of an ongoing effort sponsored by the Division of Laboratory Science and Standards (formerly Division of Laboratory Systems), Centers for Disease Control and Prevention. (CDC. The purpose is to develop new systematic evidence review and evaluation methods for identifying pre- and post-analytic laboratory medicine practices that are effective at improving healthcare quality.[1] This effort began in 2006, when CDC convened the Laboratory Medicine Best Practices Workgroup (Workgroup), a multidisciplinary panel of experts in such fields as laboratory medicine, clinical medicine, health services research, and health care performance measurement. The Workgroup also includes two ex officio representatives from two federal agencies-Centers for Medicare and Medicaid Services (CMS) and the Food and Drug Administration (FDA).

An outcome of Phase 1 (2006 – 2007) was to act on a Workgroup recommendation and enlarge the search for evidence to unpublished studies, including assessments performed for the purposes of quality assurance, process improvement and/or accreditation documentation. Phase 2 (2007-2008) involved a pilot test of further refined methods to obtain, review, and evaluate published and unpublished evidence, along with collecting observations via key informant interviews about organizational and implementation issues successfully addressed by other recommending bodies about the development and dissemination of guidelines and best practice recommendations. These evidence review methods were adapted from those established by the GRADE group, The Guide to Community Preventive Services (Community Guide), the Agency for Healthcare Research and Quality (AHRQ) (US Preventive Services Task Force (USPSTF), Evidence-based Practice Centers (EPCs), and Effective Healthcare Program), and others, and modified to better accommodate the non-controlled study designs typically found in quality improvement research.

Phase 3 (2008-2010), the subject of this report, involved further development of methods for identifying evidence-based laboratory medicine quality improvement best practices, and validated these methods with reviews of practices associated with three topics: patient specimen identification, critical value reporting, and reducing blood culture contamination.

**SYSTEMATIC EVIDENCE REVIEW AND EVALUATION METHODS**: Methods developed in earlier phases were refined and applied to identify and frame review topics and questions, and then collect, screen, abstract, standardize, summarize, and evaluate evidence from published and unpublished sources for specific practices/interventions. The approach to implementing these evidence review steps adopted the vocabulary of a framework commonly used in evidence-based medicine (Ask-Acquire-Appraise-Analyze-Apply-Assess, or “A-6”, (Shaneyfelt et al 2006)). These methods include the guidance provided to expert panelists, who were asked to (1) review and finalize study quality ratings drafted by the review team; (2) evaluate and rate

[1] The LMBP Initiative relies on the Institute of Medicine’s six healthcare quality domains of safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity for measuring and evaluating laboratory medicine practice effectiveness (Committee on the National Quality Report on Health Care Delivery, 2001).

the magnitude of effect sizes obtained from these studies and their consistency; (3) use these ratings to assess the overall strength of a body of evidence for a given practice; (4) present their evaluation findings; and then (5) translate their findings for each practice into a draft evidence-based recommendation.

The expert panels' evidence reviews, evaluations, and draft recommendations became the basis for consideration of best practice recommendations by the Workgroup (serving in its capacity as the "Recommending Body"). As with earlier phases, methods for including, rating and evaluating study findings for a practice-specific evidence base were adapted from protocols from several organizations involved with public health and healthcare-related evidence reviews and recommendations.[2]

A key Phase 3 objective was to examine the utility and feasibility of including unpublished assessments/studies in systematic evidence reviews of laboratory medicine practices. Established steps for collecting evidence from unpublished sources included:

1. Obtaining the support and endorsement of key stakeholder organizations to encourage clinical laboratories and healthcare organizations to participate in the LMBP pilot test.

2. Identifying healthcare organizations/facilities likely to have completed relevant unpublished laboratory medicine practice assessments, based on:
   a. Conference papers or other public presentations.
   b. Relevant publications that implied the author(s) or others might have additional data beyond what was reported (e.g., more recent data, or data more encompassing in scope or care setting)
   c. Personal knowledge of Workgroup and Expert Panel members and the CDC/Battelle team.
   d. Calling attention to an online site where facilities could voluntarily register their interest in being contacted to gauge whether available data would be appropriate for inclusion.

3. Identifying and contacting a senior laboratory scientist, laboratory director, or other appropriate representatives (e.g., involved in patient safety, quality management, clinical research, regulatory/accreditation compliance) to describe the aims of the LMBP project and explore the circumstances under which the organization would consider participating in the pilot test.

4. Providing additional information about the project to the facility point-of-contact to share with colleagues and obtain a preliminary assessment from the organization's Institutional Review Board (IRB) chair for release of previously completed studies with de-identified data.

5. Extending a formal invitation to the organization and providing more general guidance about the type of information needed for unpublished studies.

[2] The Guide to Community Preventive Services (http://www.thecommunityguide.org/index.html), the US Preventive Services Task Force (http://www.ahrq.gov/clinic/uspstfix.htm), The GRADE Working Group (http://www.gradeworkinggroup.org/index.htm), AHRQ (EPCs http://www.ahrq.gov/Clinic/epcpartner/epcresmat.htm and Effective Healthcare Program http://www.effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productid=318) The Cochrane Collaboration (http://www.cochrane.org/).

6. Establishing any formal confidentiality safeguards or conditions under which the information would be provided for the purposes of the pilot test of LMBP systematic review methods.

7. Reviewing study information and other material received, and follow-up with additional information requests as needed.

To minimize the burden on pilot test participants and maintain consistency with published evidence, only previously completed studies were requested (i.e., no new data), and it was suggested that these studies might be derived from multiple types of sources, including internal assessments, case studies, Failure Mode and Effects Analyses (FMEA), and quality improvement project studies. Facilities were also requested to provide data that contained no personal patient health information. A commitment was made to de-identify all data and studies submitted, and each facility was offered the option to remain anonymous in the pilot test evidence summaries and findings.

All studies and/or assessments, published and unpublished acquired for the pilot LMBP evidence reviews were screened using the same criteria for relevance and completeness (i.e., had at least one effectiveness finding for a practice being reviewed with an outcome measure associated with the review question). Studies that met the inclusion criteria were then abstracted by at least two independent reviewers, summarized in a standardized format, and included in evidence summaries and meta-analyses for each practice reviewed. The evidence summaries and LMBP study quality rating criteria were used to categorically rate individual study quality, and the individual study and meta-analysis summary effect sizes were also categorically rated to produce an overall strength of evidence rating for each practice, using the following four-step approach:

1. Categorically rating individual study quality (good, fair, poor), based on a 10-point scale with specified criteria evaluating four quality dimensions
   a. Study
   b. Practice
   c. Outcome measure(s)
   d. Findings/result(s)

2. Categorically rating the observed effect size(s) (substantial, moderate, minimal/none) reported in each individual study with a “good” or “fair” study quality rating and relevance to the review question (direct, less direct, indirect). (Studies with “poor” quality ratings are excluded from the practice evidence base and the effect-size meta-analyses).

3. Assessing the consistency of all study effect sizes based on their direction and magnitude.

4. Rating the overall strength of a body of evidence using the ratings from the three previous steps is based on the number of good and fair quality studies that found a substantial or moderate effect size.

The following are the established rating categories for the overall strength of a body of evidence:

**High**: An adequate volume of evidence is available and includes consistent evidence of substantial healthcare quality impact from studies without major limitations.

**Moderate**: Some evidence is available and includes consistent evidence of substantial healthcare quality impact from studies without major limitations; OR an adequate volume of evidence is available and includes consistent evidence of moderate healthcare quality impact from studies without major limitations.

**Suggestive**: Limited evidence is available and includes consistent evidence of moderate healthcare quality impact from a small number of studies without major limitations; or the quality of some of the studies' design and/or conduct is limited.

**Insufficient**: Any estimate of an effect on healthcare quality impact is too uncertain. Available evidence of effectiveness is:

- Inconsistent or weak; OR
- Consistent but with a minimal effect; OR
- Contained in an inadequate volume to determine effectiveness

**EVIDENCE-BASED IDENTIFICATION OF BEST PRACTICES:** The rating categories for the overall strength of a body of evidence related to a potential best practice translates into recommendation rating categories. These rating categories reflect the extent to which there is confidence that the available evidence demonstrates that the practice(s) will do more good than harm:

**Recommend**: The practice should be identified as a "best practice" for implementation in appropriate care settings, taking into account variations and applicability in implementation and/or care settings. This recommendation results from a "High" or "Moderate" overall strength of evidence rating for improving healthcare quality, and accounts for available information related to additional harms and benefits.

**No recommendation for or against**: A potentially favorable impact on healthcare quality is not of sufficient size, or not sufficiently supported by evidence to indicate that it should be identified as a "best practice" for implementation in appropriate care settings. This recommendation results from a "Suggestive" or "Insufficient" overall strength of evidence rating, and accounts for available information related to additional harms and benefits.

**Recommend against**: The practice should not be identified as a "best practice" for implementation because it is not likely to result in more good than harm. This recommendation results from a "High" or "Moderate" overall strength of evidence rating for adversely affecting healthcare quality, and accounts for available information related to additional harms and benefits.

There is an important distinction between evidence of effectiveness for healthcare quality improvement and evidence related to other aspects of implementation, such as feasibility, cost, applicability (e.g., to specific care settings and populations), and other harms and benefits. Only the evidence of effectiveness was systematically reviewed. Further methods refinements for these implementation aspects will be considered in future reviews.

***PHASE 3 EVIDENCE REVIEW RESULTS:*** Seven practices met the pilot test minimum criteria for available evidence to be considered for systematic reviews: two for the Patient Specimen Identification topic, two for the Communicating Critical Values topic, and three for the Blood Culture Contamination topic.

***Patient Specimen Identification***: Practices associated with this topic area are designed to reduce patient specimen and/or test result identification errors and assure accurate identification of specimens and/or test results. Practices for which enough evidence was available from unpublished and published sources to be included in the evidence review were:

- **Barcoding Systems** - Electronic bar-coding of both patient identification and specimen used to establish positive identification of specimen as belonging to patient. This involves the use of bar code scanners and capability to barcode specimens.
- **Point-of-Care-Testing Barcoding Systems** - Automated patient and sample/test result identification system using bar-coded patient identification and bar code scanners when using a testing device at or close to the patient.

***Critical Values Communication***: Practices associated with this topic area are designed to assure timely and accurate communication of critical value laboratory test results to a licensed responsible caregiver who can act on these results. Practices for which enough evidence was available from unpublished and published sources to be included in the evidence review were:

- **Automated Notification** – Automated alerting system or computerized reminders using mobile phones, pagers, email or other personal electronic devices to alert clinicians of critical value laboratory test results.
- **Call Center** – Critical value notification process centralized in a unit responsible for communication of critical value laboratory test results to the licensed caregiver.

***Blood Culture Contamination***: Practices associated with this topic area are designed to reduce blood culture contamination rates (i.e., false positive blood culture test results associated with contaminants in blood culture specimens), which routinely result in unnecessary repeat tests and antimicrobial drug therapy associated with adverse clinical and economic outcomes (e.g., increased hospital length of stay, side effects, and cost of therapy). Practices for which enough evidence was available from unpublished and published sources to be included in the evidence review were:

- **Dedicated Phlebotomy** – Use of certified phlebotomists (rather than nursing or other staff) to draw blood specimens for analysis, acknowledging that 100% of phlebotomist blood draws use venipuncture collection.
- **Venipuncture (vs. Intravenous catheter) collection** – Puncture of a vein through the skin *vs.* use of a thin flexible tube inserted into the body to withdraw blood for analysis
- **Pre-packaged Prep Kits** - Pre-packaged aseptic supplies for drawing blood specimens by venipuncture that are prepared in-house or commercially purchased

***Preliminary results (December 2009)***: Based on the strength of evidence, the following were identified as "best practice" recommendations.

Patient Specimen Identification:

- The use of barcoding systems (vs. no barcoding) is identified as a best practice for reducing patient specimen identification errors (8 studies, log odds ratio = 2.45; 95% CI 1.6-3.3).

- The use of point-of-care-testing barcoding systems is identified as a best practice for reducing patient test result identification errors (5 studies, odds ratio 6.55; 95% CI 3.1 – 14.0).

Critical Value Reporting:

- No recommendation is made for or against identifying the use of call centers (3 studies, Standard difference of means = 0.81, 95% CI -0.52 – 2.15) [3] or automated notification systems (3 studies, Standard difference of means = 0.51, 95% CI -0.4 – 1.4) as a best practice.

Blood Culture Contamination:

- The use of venipuncture for sample collection when this option exists in the clinical setting is identified as a best practice for reducing blood culture contamination rates (7 studies, OR = 2.63, 95% CI 1.85-3.72).

- The use of dedicated phlebotomy (teams) to collect blood culture specimens is identified as a best practice for reducing blood culture contamination rates (6 studies, OR = 2.76, 95% CI 2.2 - 3.5).

- No recommendation is made for or against identifying the use of pre-packaged preparation kits (4 studies, OR =1.1, 95% CI 0.99-1.41)[3] as a best practice.

## CONCLUSIONS

Methods

- Findings from pilot LMBP systematic reviews (2006-2009), demonstrate that LMBP systematic review and evaluation methods may be applied to evaluate quality improvement practices.

- Systematic evidence review and evaluation methods developed and tested during Phase 2 were refined and adapted to better address the evidence available from laboratory medicine quality improvement studies resulting in greater consistency and transparency of evidence rating and evidence.

- Unpublished and published data from laboratory quality improvement efforts provide evidence of effectiveness for inclusion in systematic evidence reviews.

[3] When the Confidence Interval (CI) for the Odds Ratio extends below 1.0 (or below 0.0 for the Standard Difference of Means), we cannot determine whether there is an effect that favors the intervention over the comparator.

- The Phase 3 pilot test findings demonstrate that LMBP systematic review methods for quality improvement practice evidence reviews support evidence-based recommendations. The LMBP methods for summarizing and evaluating practice evidence of effectiveness, and rating the overall strength of a body of evidence are comprehensive, appropriate and can be efficiently implemented on an ongoing basis given sufficient organizational resources and appropriately qualified staff, but still require further specific refinements in Phase 4 (ending in 2011) discussed below.

Network for unpublished evidence

Phase 3 efforts to recruit healthcare organizations to participate in a network to provide unpublished evidence provided considerable insight into the factors that constrain and encourage participation, and the likelihood of obtaining usable evidence, including:

- Contacts with knowledgeable representatives invested with appropriate decision-making authority,
- Identification and participation of organizations that use the practices being reviewed,
- Clear communication of specific requirements for what constitutes includable effectiveness evidence (i.e., relevant practice and at least one outcome measure/finding, preferably with a baseline comparison),
- Appropriate formal letters of invitation and endorsement of professional, accreditation and industry organizations, and
- Information that meets the needs of relevant IRB chairs and other administrative review offices; assurances of confidentiality when requested.

Organizational Development and Sustainability

- Characterization of the roles and responsibilities of the LMBP Workgroup, Expert Review Panels, and the staff support team evolved over the course of this phase, helping to further specify organizational requirements to support systematic evidence reviews and the production of best practice recommendations on an ongoing basis.
- Several key factors are necessary to support and sustain the development and implementation of the LMBP process:
    - **Transparency**. The process must be open to all relevant stakeholders and the public; no part of it should be conducted behind closed doors. All evidence should be clearly presented and the review process should be clearly defined so that it can be replicated and produce the same results.
    - **Timeliness of recommendations**. Sufficient resources must be allocated to the LMBP process to ensure that reviews are completed in a timely fashion so that recommendations are disseminated while they are still relevant and likely to improve healthcare quality outcomes.
    - **Collaboration**. CDC should not operate independently, but instead should collaborate with existing stakeholder, professional and guideline-setting organizations, as well as those recognized independently as subject matter and methods experts.

- **Involvement of Partners**. It is critical to ensure that the process be inclusive of not only representation of all laboratory medicine stakeholders but sufficiently responsive to the needs and input of all relevant perspectives and disciplines involved in all phases of the testing process. The partners should be diverse and multi-disciplinary, and must have real opportunities for providing input to impact the LMBP process and outcomes.

- **Independent Recommending Body**. The evidence review results and identification of evidence-based best practices should be issued by a recommending body that is perceived to be independent, not subject to the influence of any particular faction within the field, the sponsoring agency, nor political considerations.

- **Organizational Commitment to Sustainability**. The model must be sustainable, with resources available to support the process for the long-term. If the process is perceived as an initiative that will fade away, it will not garner the support necessary to make it effective.

- **Integration with Existing Efforts (Without Duplication).** A number of organizations are already in the process of identifying and disseminating best practices recommendations. The CDC-led LMBP effort should integrate with these efforts to the extent possible through its evidence-based methods, and should not duplicate them.

## RECOMMENDED NEXT STEPS

In moving towards sustained implementation, it is recommended that the Laboratory Medicine Best Practices systematic evidence review and evaluation methods for assessing the effectiveness of quality improvement practices be further refined and enhanced to include some or all of the following activities.

Methods: *Topic Area Selection*

Refine and standardize the process by which systematic review topic areas are selected and associated candidate practices are nominated. Topic selection criteria established early in the Initiative's development still apply (burden of problem/quality gap; preventability, availability of existing knowledge, potential effectiveness, operational management, and potential economic benefit), but further refinements are needed in soliciting and responding to suggestions from the field.

Methods: *Analytic Framework*

Refine and standardize methods for schematic representation of a topic area analytic framework for each review question including:

- Formalize a process for establishing functional requirements for practices associated with a selected topic area. A "process mapping" approach may help to outline work flows and common points of intervention at which practices can achieve improvements in healthcare quality outcomes.

- Identify processes from domains of application outside of laboratory medicine that meet the same functional requirements, increasing the likelihood that evidence of effectiveness from these other domains will be regarded as relevant to laboratory medicine practices.

Methods: *Search, Screening and Data Abstraction Methods*

Make further improvements to the review methods and electronic data abstraction tool including:

- Refine, standardize, and document literature search strategy to generate relevant published materials in a broader array of journals and published conference proceedings.
- Develop standardized search and reporting functions for reference and study databases.
- Improve guidance and standardization for screening and abstraction methods for reviewers.
- Refine reviewer/user interface enhancements for data abstraction.
- Structure and formatting of data abstraction template more directly linked with evidence summary templates and individual study evaluation criteria.
- Further standardization of outcome measures, definitions, and their categorization to minimize topic area-specific programming and maximize comparability.
- Develop and implement standardized methods for screening and capturing non-effectiveness evidence related to feasibility of implementation, applicability, economic evaluation and harms and benefits and/or other newly developed criteria.

Methods: *Evidence Summary and Evaluation*

- Finalize evidence summary presentation formats along with development of standardized content and terms to facilitate and ensure consistent evaluations, and when applicable statistical meta-analyses, and recommendation statements (for the LMBP topic area Expert Panels and Workgroup), and for publishing and disseminating evidence reviews and evidence-based recommendations.

- Specify methods for including, evaluating and synthesizing additional non-effectiveness evidence related to implementation feasibility, economic evaluation, applicability (settings, populations, contextual variables) and harms and benefits, incorporating concepts of external validity and internal validity.

- Further refine protocols for nominating, selecting, and guiding the work of expert panelists so that panelists have a clear idea of their roles and responsibilities relative to the Recommending Body and support staff, and panel composition is adequately diversified to represent key stakeholders' perspectives to produce unbiased and scientific evidence reviews.

- Further refine protocols for guiding the work of the LMBP Workgroup (or if not overlapping a Recommending Body) so that members of this body have a clear idea of their roles and responsibilities relative to the expert panelists and support staff.

Network Development for unpublished evidence

- Further develop the network as the principal source for unpublished evidence. Expanding and maintaining this network is essential to the future sustainability of an evidence-based laboratory medicine practice recommendations process, as the main challenge to its success remains insufficient published evidence.

- Further refine guidance to network participants on informational requirements for submitting evidence.

- Develop and implement an education / curriculum strategy that familiarizes laboratory managers with methods for improving the quality of unpublished process improvement / quality assurance studies so that data from these studies are consistently available to inform “best practice” recommendations.

- Expand strategies to extend the breadth and depth of the network to provide greater opportunities for identifying participating organizations and individuals within those organizations responsible for relevant practice evaluations and quality improvement initiatives.

- Maintain a network tracking database with strategic information to facilitate contacts, targeted follow-up as well as routine communication with network affiliates.

Organizational Development and Sustainability

- Create a specific business plan for implementation and funding potential based on collaboration with key stakeholders.

- Develop and implement communication, publication and other dissemination strategies based on collaboration with key stakeholders to optimize impact of evidence reviews and further the implementation of evidence-based methods and standards for quality improvement in laboratory medicine.

Development of a process for assuring a pipeline of future topic areas and priorities for evidence reviews based on broad stakeholder engagement, including identification of appropriate evidence.

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