Medication Use Evaluation: Pharmacist Rubric for Performance Improvement

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Despite rigorous expert review, medications often fall into routine use with unrecognized and unwanted complications. Use of some medications remains controversial because information to support efficacy is conflicting, scant, or nonexistent. Medication use evaluation (MUE) is a performance improvement tool that can be used when there is uncertainty regarding whether a medication will be beneficial. It is particularly useful when limited evidence is available on how best to choose between two or more medications. MUEs can analyze the process of medication prescribing, preparation, dispensing, administration, and monitoring. MUEs can be part of a structured or mandated multidisciplinary quality management program that focuses on evaluating medication effectiveness and improving patient safety. Successful MUE programs have a structure in place to support completion of rapid-cycle data collection, analysis, and intervention that supports practice change.

KEY WORDS medication use evaluation, drug utilization, target drug program, drug therapy management guidelines.
(**Pharmacotherapy 2014;34(12 Pt 2):5S–13S) doi: 10.1002/phar.1506**

The U.S. Food and Drug Administration (FDA) approves medications for clinician prescribing with the intent of ensuring that the agents marketed are safe, effective, and ultimately improve patient health. Despite rigorous review by expert physicians, statisticians, chemists, pharmacologists, and other scientists, the FDA can approve medications that have unrecognized and unwanted complications. Medications have been marketed with reported increased risk of adverse effects (e.g., rofecoxib and myocardial infarction),[1] no overall improved survival (e.g., bevacizumab and metastatic breast cancer),[2, 3] marginal symptomatic benefit (e.g., nesiritide and dyspnea improvement in decompensated heart failure),[4] or the need to target laboratory results (e.g., erythropoietin and hemoglobin level).[5, 6] Medications may also fall into routine use outside of their FDA-approved indications, only to be later shown to offer no value for those indications compared with current treatments (e.g., *N*-acetylcysteine or fenoldopam for prevention of contrast medium–induced nephropathy).[7] Some combinations of medications give rise to lethal adverse drug events (e.g., terfenadine and macrolide antibiotics).[8] Other agents (e.g., anticoagulants, antibiotics) have required support structures to ensure optimal outcomes.[9, 10] Finally, agents exist whose use remains controversial (e.g., albumin use in fluid resuscitation, intravenous immune globulin use for immunologic conditions) because information to support efficacy is conflicting, scant, or nonexistent.[11, 12]

Professional societies, government, regulatory, benevolent, and not-for-profit entities have developed clinical practice guidelines and position

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statements based on available evidence and expert opinion. Similarly, disease state management programs have been identified as a tool to improve the care of chronic health conditions while reducing costs. Results have been unremarkable, with only modest improvements in quality of care measures and little impact on utilization and cost savings.[13, 14] Yet despite standards intended to ensure trustworthy, quality, and reliable guidelines, problems have emerged.[15] These include poor compliance with development standards,[16] outdated guidelines, limited external review, conflict of interest concerns, and recommendations that are so narrowly focused, they may actually produce undesirable effects in patients with comorbidities.[17]

The current generation of pharmacists has been charged with taking responsibility for medication use outcomes by evaluating the effectiveness, safety, and affordability of each medication prescribed.[18, 19] In addition, pharmacists are accountable for performing quality reviews of medication use in hospitals and health care systems patient populations.[20]

Medication use evaluation (MUE) is a performance improvement tool that can be used when there is uncertainty over whether a medication will be beneficial, if a limited evidence base is available for a choice between two or more medications,[21] as well as for analyzing the process of medication prescribing, preparation, dispensing, administration, and monitoring. In this article, we review the development and application of MUE and provide case examples of success.

Medication Use Evaluation Definition

An MUE can be defined as a focused effort to evaluate medication use processes or medication treatment response, with a goal of optimizing patient outcomes.[21] MUE, synonymous with "target drug" or "drug use" programs, also fits into disease state management programs that look to improve outcomes in patients with chronic illnesses.[22, 23] Performance or quality improvement concepts and methodologies focus on measuring a process or outcome, and then making modifications to improve efficiencies or effectiveness.[24] Because it entails the collection of data, it becomes a formal evidence-based analysis that provides an opportunity to determine what is working well and where there is an opportunity for change.

Medication Use Evaluation Objectives and Methodology

For health care systems, MUEs can be part of a structured or mandated multidisciplinary quality management program. The Joint Commission emphasizes the need for hospitals to develop a safe and effective medication management system.[25] For the individual practitioner, an MUE may represent a simple criteria-based bedside review of a medication's performance in a specific patient care unit or population. The stimulus to complete an MUE usually rises from a clinical question or operational concern (Table 1). MUE objectives typically attempt to evaluate medication effectiveness; improve patient safety, or avoid medication misadventure including adverse drug events; standardize therapy to reduce variation; optimize therapy; meet federal, local, regulatory, professional, or accreditation standards; or minimize costs.

Although various management methods have been popularized over the last 40 years, they are all based on or analogous to the scientific method (Table 2).[26–28] The Plan-Do-Study-Act (PDSA) method is most commonly used and provides a framework for problem solving. Although PDSA supplies the structure, it does not specifically identify the ideal intervention, best data collection methods, or end points. Furthermore, PDSA is intended to be applied in repetitive, rapidly completed cycles, coupled with action steps that continuously introduce change. However, some MUEs may facilitate marginal change but also identify additional opportunities or problems, generating new project cycles. This contrasts with clinical trials that enroll large numbers of patients, have a long duration of surveillance, and take a long period of time to complete.

Medication Use Evaluation Logistics

Support

Organizations must have a support structure in place to ensure successful completion of MUEs and implementation of change. Organizational administration and leadership must acknowledge that MUE work is important, establish authority for the initiation, and remove obstacles as they arise. Numerous stakeholders are involved in medication use, and many will have an interest in the design and the results.

Table 1. Objectives for Completing a Medication Use Evaluation

Clinical or operational question	Description	Objective	Example
Effectiveness of a therapy or alternative therapy	Evaluate medication for therapeutic response or in comparison with another agent or intervention	Evaluate effectiveness	Therapeutic substitution of patient response to tbo-filgrastim vs filgrastim
Clinical equipoise	Evaluation of patient response compared with case reports, conflicting evidence, or absence of evidence		Use of albumin vs crystalloids in extrapleural pneumonectomy
Follow-up response	Durability of treatment, signs of treatment failure		Return of rheumatoid arthritis symptoms in patients treated with infliximab
Off-label medication use	Evaluate outcomes of treatment		Intravenous immune globulin use in multiple sclerosis
Toxicity	Identify incidence or magnitude of an adverse reaction	Improve patient safety	Incidence of major bleeding in patients with pulmonary embolism treated with thrombolytic therapy
Narrow therapeutic index	Incidence of event in relation to laboratory monitoring both within and outside of therapeutic range		Incidence of intracranial hemorrhage in patients with atrial fibrillation treated with warfarin
High-alert medications	Medications commonly implicated in medication errors or sentinel events		Surveillance of errors associated with insulin therapy
Patient population management	Identify characteristics of patients receiving or failing to receive a medication	Standardize therapy to reduce variation	Hospitalized patients > 65 years old receiving pneumococcal vaccination
Medication process analysis	Evaluate a medication process step: prescribing, preparation, dispensing, administration		Adherence to prescribed pharmacologic venous thromboembolism prophylaxis in high-risk patients
Monitoring or laboratory testing use	Determine the impact of a laboratory test on medication use		Appropriateness of clinical response to vancomycin trough concentration
Institutional benchmark	Comparison with practices at other facilities		Immunosuppressant use in solid organ transplantation
Patient satisfaction	Subjective patient evaluation of treatment		Pain control after surgery
Disease or treatment guideline	Comparison of local practice to national or local hospital guideline		Time to first antibiotic dose in the emergency department in patients with septic shock
Optimization	Identifying optimal dose	Optimize drug therapy	Determining optimal anesthetic gas flow rates for general anesthesia
Regulatory requirements	Adherence to federal and state legislation	Meet quality or regulatory standards	Documentation of narcotic administration and subsequent waste
Evaluate job/task performance	Completion of patient education		Percentage of patients receiving medication discharge education
Value analysis	Comparison of treatment costs, drug vs drug, or drug vs response	Minimize costs	Treatment costs of dexmedetomidine vs midazolam for sedation in mechanically ventilated patients

Table 2. Medication Use Evaluation Methodologies

Step	Method			
	Scientific	PDSA	DMAIC	SDCA
1	Construct a hypothesis	Plan: plan the test or observation	Define: define the problem or process	Standardize: identify process or treatment, and substitute or insert a new one
2	Test the hypothesis by completing an experiment	Do: try the test on a small scale or sample	Measure: collect information on performance	Do: collect data on outcomes
3	Analyze the data and draw a conclusion	Study: study and analyze the data and the results	Analyze: study and analyze the data and the results	Check: evaluate outcomes
4	Communicate the results	Act: make the process permanent or study the adjustments	Improve and control: intervene with change or maintain existing process	Act: continue, revert to existing treatment, or institute a new one

DMAIC = define, measure, analyze, improve, control; PDSA = plan, do, study, act; SDCA = standardize, do, check, act.

MUE results should always provide a next actionable step, intervention, or change. Because clinical information flows in numerous locations, multidisciplinary collaboration, defined responsibilities, and accountability are important for access to data and critical for communication of results and effecting change (Figure 1).

Data and Data Collection

Treatment algorithms, critical pathways, care plans, and disease-based guidelines for drug use are often established and serve as a good starting point for MUEs. Once a clinical or operational question has been poised, the measurement variables and end points must be decided. It is important to distinguish between measured variables, which may constitute a combined end point, and the end point, which is a clinically relevant outcome. For example, the dose of an opioid is a measured variable, whereas the change in opioid dose or consumption is an end point. Similarly, a pain score is a measured variable, and the change in pain score is an end point. Measured variables can be quantitative or qualitative. Qualitative variables can be simpli-

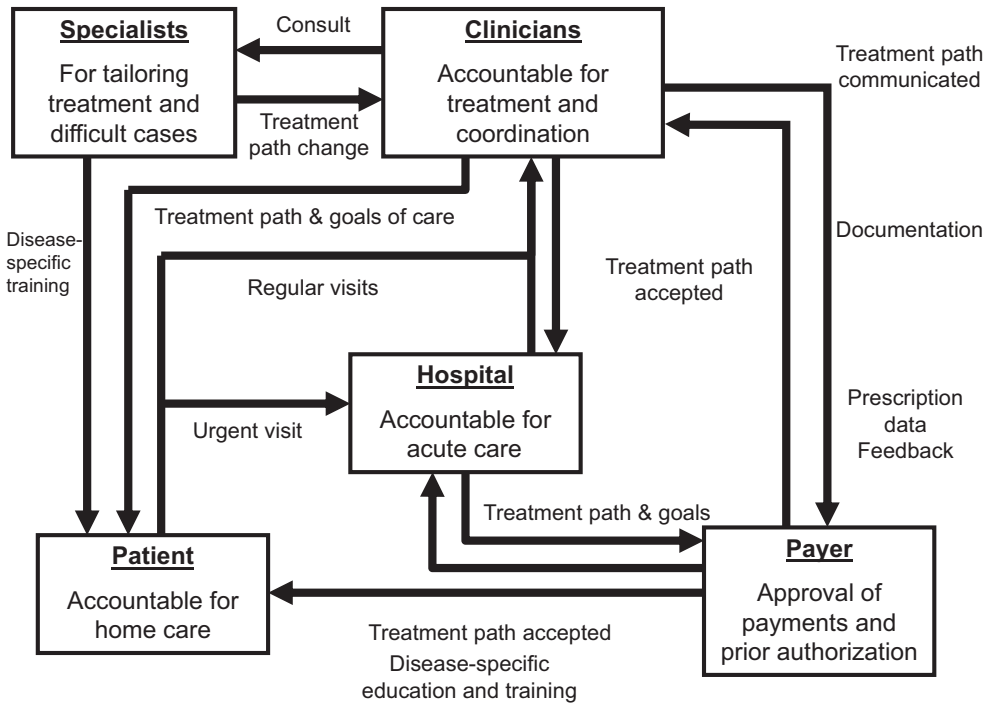

Figure 1. Stakeholders, roles, and responsibilities in medication use.

fied to a binary format (e.g., 0 = absent, 1 = present) to indicate the presence of a characteristic or comorbidity. Surrogate end points, events that substitute for or correlate to a clinical end point, are often used in MUEs to ensure an adequate number of events, shorten the data collection period, and still reflect clinical efficacy.[29] Continuous data—variables measured on a continuum or scale—can be recorded as numeric values or converted into a group, categorical data, to be made more meaningful.

Data collection requires time, effort, and labor expense, and it may be inconvenient for patients. It should never obstruct patient care. With the introduction of electronic health records, clinicians can perform more sophisticated longitudinal MUEs. However, information is now located in various software programs and numerous locations, and may create additional problems (Table 3). Choosing measured variables and end points that are available in adequate supply, relevant, accessible, reproducible, and agreed upon by clinical definitions among the MUE participants is important. For these reasons, objective measures (e.g., viral load, swollen joint count, walking distance) are preferable to subjective measures (e.g., fatigue, pain, breathlessness). A data collection plan that outlines who will collect measurements, where information will be collected from, and when it will be collected adds precision and consistency to the MUE design. Poor documentation is a common pitfall of MUEs (Table 4). In clinical trials, paper-based case report forms are used for recording information. Electronic data collection programs (e.g., REDCap, OpenClinica, StudyMaker) are being introduced to enhance data quality with standards being developed.[30] Data are typically recorded in binary format. MUEs can mirror these approaches with a paper-based data collection tool or by creating an electronic format with database management software

Table 3. Data Variables, Sources, and Potential Problems

Measurement	Example	Source	Problems
Patient characteristics	Age, sex, height, weight, ethnic origin	Direct measure, medical record, office visit, emergency department notes	Recorded often and in multiple locations, conflicting values
Comorbidities	Diabetes, metabolic syndrome, atherosclerosis, heart failure, depression	Objective laboratory test, invasive procedure, standardized criteria	Transfers from another facility
Physiologic measurement	Blood pressure, blood glucose level, temperature, tidal volume	Direct measure, medical record, office visit note, laboratory report, point-of-care testing device	Recorded often and in multiple locations, conflicting values
Health states	Alive, deceased, cause of death, illness present or absent	Medical record, Social Security Death Index, CDC National Death Index	Absence of information, database updates, lost to follow-up
Anatomic	Size, location, volume	Imaging studies, procedure results, biopsy results	Poor image quality, requires expert interpretation
Clinical events	Myocardial infarction, bleeding, stroke, vomiting episodes	Objective test, imaging study, scoring system	Multiple clinical definitions, severity scoring systems vary, canceled tests, ambiguous test results
Care delivery	Medication administration, medication commencement, invasive procedure	Nursing records, pharmacy records, procedure report	Inaccuracy, missing information, omitted values, poor documentation
Symptoms	Pain, nausea, diarrhea	Patient assessment, medical record	Patient access, poor documentation, unrecognized events
Physical function, daily activities	Walking distance, stair climb, orientation	Patient reporting, diaries, calendars	Patient access, accuracy
Resource use	Hospital admissions, length of stay, intensive care unit days, ventilation days, expense	Medical record, respiratory records, finance/billing systems	Encounters outside of hospital or system, access to records
Timing	Event onset, event conclusion	Patient reporting, medical records, pharmacy records	Inaccuracy, missing details, omitted values
Patient surveys	Satisfaction, opinions	Patient or family reporting	Patient access, poor historian

CDC = Centers for Disease Control and Prevention.

Table 4. Characteristics of Successful Medication Use Evaluations

Characteristic	Definition
Organization	Project leader, definition of roles and responsibilities for data collection, analysis, presentation, communication
Communication	Clear message of benefits and improvements, emphasis on importance, timely and effective communication by organization leaders
Documentation	Well-designed data collection tool, relevant, accurate, verifiable measures, processes, and process participants
Participation	Active clinician participation including meeting attendance, data review, early adopter of change, communicator of benefits
Follow-through	Commitment to project and process, methodical attention to detail, adjustments in the face of obstacles or problems
Access	Access to data through end user applications and software packages, retrievable data
Seamless	MUE tasks are integrated into routine patient care
Resourced	Appropriate, motivated clinician participants with protected MUE time

MUE = Medication use evaluation.

(e.g., Access, FoxPro, dBase). Data collection tools should be tested to ensure that variables and end points are feasible and collectively provide an answer to the clinical question or operational concern.

Implementation

MUE requires effective project management and implementation planning (Figure 2). It is not a task or responsibility of a single individual or department and is best accomplished with small multidisciplinary groups. Lack of organization is another common pitfall of MUEs. Successful programs incorporate the available infrastructure, information systems, and professional staff, and they rely heavily on education, communication, and monitoring information. Those contributing to the MUE should be supported with literature review and background knowledge. Once the objectives, variables, end points, and data plan are communicated and agreed upon, a timeline with milestones should be established with predefined meetings for progress reports. Because MUEs involve protected health information, institutional review board

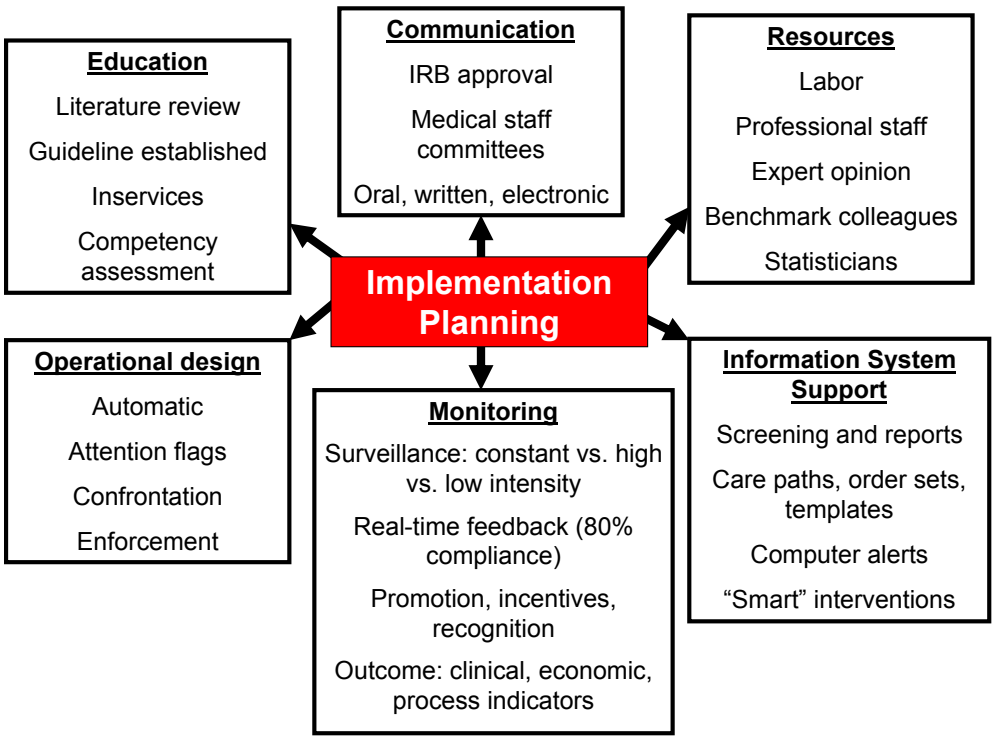

Figure 2. Medication use evaluation implementation planning. IRB = institutional review board.

approval or waiver is warranted. Labor resources must be identified for data collection. Although pharmacy, nursing, or medical students may be readily available, their depth of knowledge may not be sufficient to interpret data elements, or they may not understand the processes, medications, or conditions being evaluated. If they are enlisted, they should be supervised and data collection verified. Information systems and computer support can be used for patient screening and reporting. The monitoring requirements will vary based on the labor resources, measurement, and end point frequencies.

Once MUE results are analyzed and established, this cycle repeats with a focus on change. Results are translated into local guidelines and practice and care changes. The benefits and improvements are communicated to medical staff committees for approval and then broadcasted through existing channels. Regular meetings, newsletters, and electronic mail are effective ways to reach those who are impacted. It is important for professional staff and local and external experts to be engaged in promoting the practice change. Information systems can be recruited to change critical or care pathways, generate prescribing alerts, or intercept and change prescribing practices. Labor resources now shift from data collection to performance monitoring, with real-time feedback and recognition for those with ideal performance. Finally, to freeze the new practices, as it were, any final changes should be automated. Those drifting from the new practices should be notified with discussion and education steps initiated or exclusions granted.

Medication Use Evaluation Models

There are good examples of MUE work. In 2008, the Joint Commission initiated performance measures to prevent deep vein thrombosis by ensuring the use of appropriate venous thromboembolism (VTE) prophylaxis (Table 5)[31]. In this first-cycle MUE, the participants measured whether VTE prophylaxis, once prescribed, was actually administered.[32] They found that although 90% of prescribed pharmacologic prophylaxis was administered, patients frequently refused parenteral doses. Cycle 2 followed with a pharmacist-driven intervention to educate patients on VTE and the reasons for the injections.[33] Although prophylaxis rates improved, new concerns were raised about extending pharmacologic VTE prophylaxis after

Table 5. Medication Use Evaluation Model: Anticoagulant Safety

Cycle	Clinical question	Variable measure	End point	Lesson learned	Action step, intervention
Cycle 1	What is our compliance with VTE prophylaxis orders?	Doses administered	Percentage of doses administered	85% of prescribed doses administered, but patients rarely informed about VTE and often refused injections	Design pharmacist-driven patient education module
Cycle 2	Does patient education improve VTE prophylaxis compliance?	Doses administered	Percentage of doses administered	90% of prescribed doses administered, but extended prophylaxis beyond discharge is cumbersome	Evaluate efficacy and safety of VTE prophylaxis after discharge
Cycle 3	Is extended VTE prophylaxis safe and effective?	Agents prescribed, dose, and frequency	Bleeding episodes, adverse effects, VTE events	Extended prophylaxis was not effective in medically ill patients; adverse effects are problematic	Review discharge medications, intervene and stop extended prophylaxis, evaluate HIT management
Cycle 4	Evaluate clinical and economic outcomes of HIT	Identify cause and outcomes	HIT Incidence, mortality, cost	HIT more common with unfractionated heparin than low-molecular-weight heparin	Develop internal HIT management guideline; identify methods to improve diagnostic accuracy
Cycle 5	Evaluate heparin–antiplatelet factor 4 antibody levels in suspected HIT	Heparin–antiplatelet factor 4 antibody levels	Rates of thrombosis	Higher levels of antibody associated with increased thrombosis risk; better assays may exist	Change laboratory report of antibody levels from qualitative to quantitative
Cycle 6	Evaluate different heparin–antiplatelet factor 4 assays	HIT incidence	Patient diagnosed as HIT positive	IgG-specific assay associated with a lower rate of positive test results; direct thrombin inhibitor prescribing significantly altered	Evaluate efficacy and safety of direct thrombin inhibitor use

HIT = heparin-induced thrombocytopenia; IgG = immunoglobulin G; VTE = venous thromboembolism.

discharge in medical patients, where limited evidence exists.[34] Cycle 3 found that extended VTE prophylaxis was not effective, and heparin-induced thrombocytopenia (HIT) emerged as a concerning adverse effect.[35] In cycle 4, HIT diagnosis and management was explored,[36] leading to an assessment and change in the diagnostic assay that was then evaluated in cycle 5.[37, 38] A diverse group (pharmacists, physicians, nurses, laboratory staff) participated in this MUE, and each cycle led to a follow-up cycle, all with continuous measurements and practice changes.

Future Opportunities

FDA labeling and package inserts may take decades to reflect changes in indications and dosing recommendations for use in routine practice. Furthermore, clinical trials are often not large enough and exclude patients for whom the medication information is most needed. Pharmacists are the practitioners who are most commonly searching for, and making decisions with or without, this information. MUEs can fill gaps in clinical knowledge and process improvement. Although most MUEs are performed in single centers, have small patient numbers, and have an impact on local practice patterns, there is an opportunity for far greater impact.

The United States has almost 6000 hospitals. Now, with electronic health records, the ability to collect MUE measures in larger patient numbers, across health care networks, and with much finer detail is upon pharmacists. Similar retrospective projects have emerged from large group purchasing organizations by surveying practice patterns and outcomes with procedural and medication charge codes.[39, 40] Pharmacists and pharmacy organizations should begin to align themselves around disease states and begin collaborating on multicenter MUEs, mirroring what is accomplished in multicenter clinical trials. Retrospective studies are often plagued by data inconsistencies and collection bias. Single-center studies often represent narrow patient populations and hence may fail to support widespread practice changes. Some of these hurdles can be overcome by using existing technologies in the MUE process. Personal digital assistants (e.g., laptop computers, tablets, smartphones) are becoming ubiquitous. Software applications that allow bedside prospective data collection and link small community hospitals to large academic medical centers may overcome these deficiencies. Although sufficient labor resources may never be allocated to a single site, small patient enrollment at a large number of sites will lead to a number of events or end points that can be statistically meaningful. Rapid PDSA cycle quality improvement efforts have become embedded or are emerging in most health care organizations and serve as the model rubric of support.

Conclusion

MUEs provide much needed information to answer clinical questions, improve operational processes, and optimize medication use. Successful MUEs are built on multidisciplinary participation and organization, with continuous cycles of intervention and change. More opportunities remain to improve MUE vigor, which should be a focus of clinicians moving forward.

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