
Guideline Implementation Research: Exploring the Gap between Evidence and Practice in the CRUSADE Quality Improvement Initiative

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Abstract

Translating research results into routine clinical practice remains difficult. Guidelines, such as the 2002 American College of Cardiology/American Heart Association Guidelines for the Management of Patients with Unstable Angina and non-ST-segment elevation myocardial infarction, have been developed to provide a streamlined, evidence-based approach to patient care that is of high quality and is reproducible. The Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation (CRUSADE) Quality Improvement Initiative was developed as a registry for non-ST-segment elevation acute coronary syndromes to track the use of guideline-based acute and discharge treatments for hospitalized patients, as well as outcomes associated with the use of these treatments. Care for more than 200,000 patients at more than 400 high-volume acute care hospitals in the United States was tracked in CRUSADE, with feedback provided to participating physicians and hospitals regarding their performance over time and compared with similar institutions. Such access to data has proved important in stimulating improvements in non-ST-segment elevation acute coronary syndromes care at participating hospitals for delivery of acute and discharge guideline-based therapy, as well as improving outcomes for patients. Providing quality improvement methods such as protocol order sets, continuing education programs, and a CRUSADE Quality Improvement Initiative toolbox serve to actively stimulate physician providers and institutions to improve care. The CRUSADE Initiative has also proven to be a fertile source of research in translation of treatment guidelines into routine care, resulting in more than 52 published articles and 86 abstracts presented at major emergency medicine and cardiology meetings. The cycle for research of guideline implementation demonstrated by CRUSADE includes four major steps—observation, intervention, investigation, and publication—that serve as the basis for evaluating the impact of any evidence-based guideline on patient care. Due to the success of CRUSADE, the American College of Cardiology combined the CRUSADE Initiative with the National Registry for Myocardial Infarction ST-segment elevation myocardial infarction program to form the National Cardiovascular Data Registry–Acute Coronary Treatment & Intervention Outcomes Network Registry beginning in January 2007.

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The practice of translating the best available research evidence into clinical practice often meets significant obstacles. The publication of treatment guidelines does not guarantee their dissemination, acceptance, or routine use for patient care. Hence,

the translation of knowledge regarding the best approaches to providing patient care through evidence-based guideline implementation remains complex. Careful study of the process of successful guideline adherence and reporting of the results of these investigations is

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critical to decreasing the time required from establishing best practices to routine following of evidence-based guidelines in hospitals across the United States.

Many physician groups and institutions attempt to facilitate guideline adoption through quality improvement (QI) initiatives. Often, implementation strategies have to be multifaceted and include the use of physician champions; education of physicians, nurses, pharmacists, and administrators; audit and feedback to physicians and hospitals; the use of opinion leaders to visit an institution; and the introduction of QI tools such as nursing order sets, wall charts, and patient discharge instructions to facilitate change in practice. Furthermore, addressing individual institutions and clinicians and focusing on their specific concerns and culture increases the likelihood of guideline uptake.¹ It has also been shown that preexisting knowledge of, attitudes about, behaviors toward, and barriers to standardized approaches to care can have a significant impact on an institution's adherence to guidelines. Another investigator group performed and analyzed comprehensive interviews of physicians and nurses to identify themes and develop a framework by which to implement a protocol for ventilator management.² They found barriers to guideline use included a lack of awareness of the evidence basis for the protocol, unclear guideline format, and reluctance about changing usual practice. Unexpectedly, the consequence of limiting clinical autonomy through standardization of practice by a guideline was not found to be a deterrent to utilization. Clinicians tended to use the guidelines variably as educational resources, to access monitored beds, to avoid clinical conflicts, and to leverage professional credibility.²

THE CRUSADE QI INITIATIVE

The developers of the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines (CRUSADE) QI initiative intended to provide a method to observe, research, and improve the bench-to-bedside translation of the thorough but complex ACC/AHA guidelines on the treatment of unstable angina and non-ST-segment elevation myocardial infarction (NSTEMI),³ the two conditions that collectively make up non-ST-segment elevation acute coronary syndromes (NSTE ACS). These extensive guidelines were subsequently summarized for emergency physicians.⁴ Whereas the CRUSADE QI initiative is not the first registry of its type, the sheer magnitude and diversity of patient enrollment, the comprehensive QI efforts, and the prolific publication of results make the CRUSADE QI initiative a unique example of guideline implementation research.

The CRUSADE QI initiative followed the progression and impact of this major guideline and its implementation on the care of patients with NSTE ACS. Now, after enrollment of more than 200,000 patients with high-risk NSTE ACS, CRUSADE is considered an outstanding example of a QI program that emphasizes the collaboration between emergency medicine, cardiology, nursing, pharmacists, hospital administrators, existing hospital QI programs, industry, and academic institutions. Diverse hospital types from across the country collected data regarding

patient management practices in the United States and used these data to target educational interventions intended to advance adherence to guideline recommendations.

The CRUSADE QI initiative was launched in late 2001 by a collaborative leadership of cardiologists and emergency physicians, with the Duke Clinical Research Institute serving as the data coordinating center.⁵ The goal of this effort was to provide a continuous cycle of data collection, audit, feedback, and educational interventions to each hospital compared with like hospitals and national standards. Data included patient risk factors and presenting symptoms, use of medications and invasive procedures, in-hospital clinical outcomes, and discharge interventions and recommendations collected retrospectively using a Web-based data collection form. Local hospital institutional review boards individually determined the need for institutional review board review for participation in CRUSADE, as well as the need for informed consent. Individual patient identifiers were not used, and data from sites were published only in aggregate.

The rich database generated from CRUSADE reflects the heterogeneous practice patterns of more than 400 hospitals from 46 states across the United States and includes more than 200,000 patients (Figure 1). In comparison with other major acute cardiovascular trials, such as Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PURSUIT),⁶ Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE),⁷ and Superior Yield of the New strategy of Enoxaparin, Revascularization, and Glycoprotein IIb/IIIa inhibitors (SYNERGY),⁸ the patients in CRUSADE were older, had more comorbidities, and were generally at higher risk (Table 1). The robust CRUSADE database, from a diverse unselected patient population, offers the remarkable opportunity to study guideline implementation, patient outcomes based on guideline adherence, the influence of QI measures on guideline uptake, and, uniquely, further implementation of guideline recommendations after publication and feedback of previous results.

The success of the CRUSADE QI initiative in improving patient care and publishing research attracted national attention from the Joint Commission, private payers, Medicare, and specialty groups such as the ACC. The ACC Foundation's National Cardiovascular Data Registry (NCDR) decided to combine several QI initiatives, including CRUSADE and the National Registry of Myocardial Infarction, to launch a new initiative to improve the safety and outcomes for patients with ACS through the development of the NCDR-Acute Coronary Treatment & Intervention Outcomes Network (ACTION) Registry. This initiative will combine the data collection and quality reporting features of these two leading national ACS registries to create a larger and more comprehensive cardiovascular patient database of both ST-segment elevation myocardial infarction (STEMI) and NSTEMI. It is anticipated that the NCDR-ACTION Registry will establish a national approach through the enrollment of most U.S. hospitals to improve understanding of STEMI and NSTEMI treatment patterns, clinical outcomes, drug safety, and the overall quality of care provided for patients with ACS through a registry that will provide direct feedback to physicians and institutions pioneered through the CRUSADE QI initiative. The National

CRUSADE Site Distribution

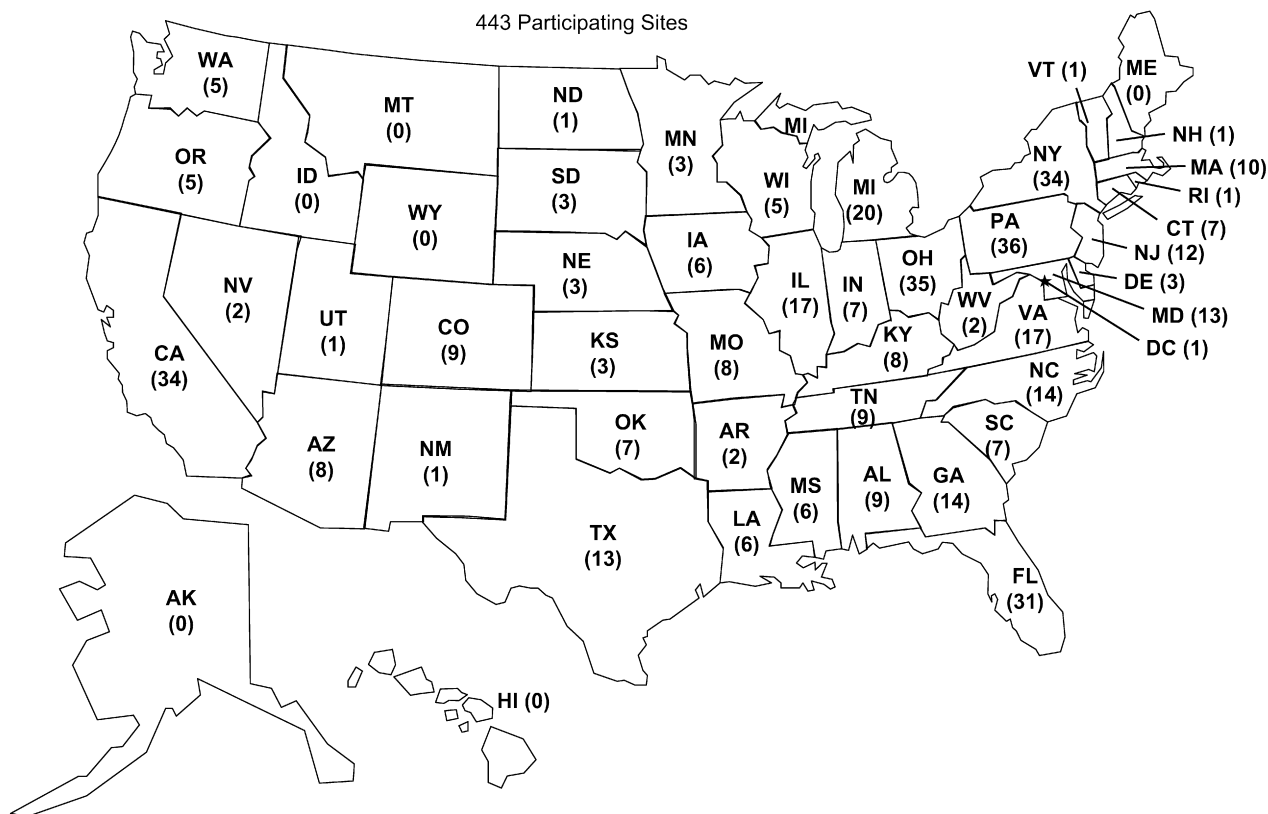


Figure 1. Geographic distribution of Can Rapid Risk Stratification of Unstable Angina Patients Suppress ADverse Outcomes with Early Implementation (CRUSADE) sites. Widespread data collection increases the validity of results.

Steering Committee and Publications Committee for the NCDR-ACTION Registry will again have both cardiology and emergency physician leadership.

CRUSADE: GUIDELINE IMPLEMENTATION RESEARCH

At any given time, practice patterns for a particular disease process are dynamic. This flux can be based on many factors, including publications, reimbursement, media reporting, educational trends, and practice orga-

nization statements. Guideline writers are hampered by not really knowing real-world practice patterns at any given time. They must rely on the best available evidence collected from research trials, often in academic environments that reflect the best options for all patient care and outcomes in this setting. While findings from these trials and their reflected guidelines may represent the best known evidence, they do not address the feasibility and barriers to their execution in the “real world” environment outside of academic medical centers. Most patient care settings do not enjoy the benefits and peculiarities

Table 1
Comparison of CRUSADE QI Initiative with Large Trials of Patients with Non-ST-segment Elevation Acute Coronary Syndromes

Variable	PURSUIT (N = 9,461)	CURE (N = 12,562)	SYNERGY (N = 9,975)	CRUSADE (N = 189,065)
Mean age (±SD)	63 (±11)	63 (±12)	67 (±11)	67 (±14)
Female gender	36	39	34	40
Diabetes mellitus	23	23	29	33
Previous myocardial infarction	32	25	28	29
Previous congestive heart failure	11	8	9	18
Previous percutaneous coronary intervention	13	18	20	21
Previous coronary artery bypass graft	12	18	17	19
ST depression	50	42	55	34

All values are expressed as percentages unless otherwise indicated.
 CRUSADE = Can Rapid Risk Stratification of Unstable Angina Patients Suppress ADverse Outcomes with Early Implementation; QI = quality initiative;
 PURSUIT = Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy; CURE = Clopidogrel in Unstable Angina to Prevent Recurrent Events; SYNERGY = Superior Yield of the New strategy of Enoxaparin, Revascularization, and GLYcoprotein IIb/IIIa inhibitors.

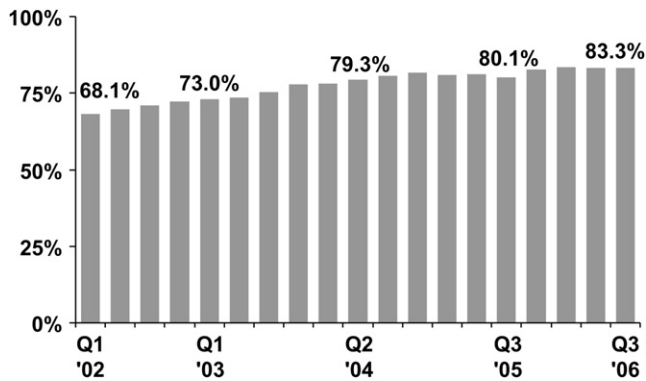


Figure 2. Overall adherence trends over time quarter 1, 2002, to quarter 3, 2006, in eligible patients without contraindications. The x-axis represents Can Rapid Risk Stratification of Unstable Angina Patients Suppress ADverse Outcomes with Early Implementation (CRUSADE) enrollment quarter, and the y-axis represents percent compliance with overall guidelines.

of an academic environment, yet it is in these institutions where guidelines are designed to have the greatest impact.

CRUSADE researchers initially reported the results of hospital adherence to guidelines, demonstrating improvement over time in overall adherence as well as the increased use of short-term and long-term therapies (Figures 2–4).⁹ When CRUSADE hospital study coordinators were questioned through a survey instrument to determine the factors most responsible for improvement in guideline adherence and improved quality, the following factors had significant association with QI: the use of CRUSADE QI tools, clinical commitment to quality by the cardiology coadvocate, barriers to QI-related resource availability, cultural and physician resistance to change, and financial commitment to quality. The following were found, in descending order, to have had the greatest

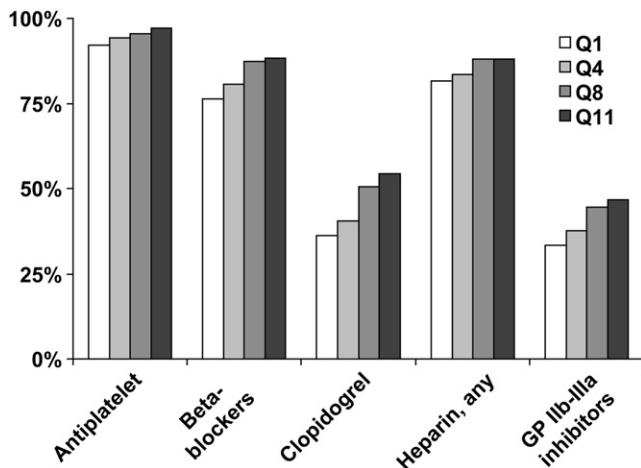


Figure 3. Trends in guidelines-recommended acute (<24 hours) therapy use over time (quarter 1 to quarter 11) in Can Rapid Risk Stratification of Unstable Angina Patients Suppress ADverse Outcomes with Early Implementation (CRUSADE) (in patients without contraindications). The x-axis represents acute therapy, and the y-axis represents percent compliance.

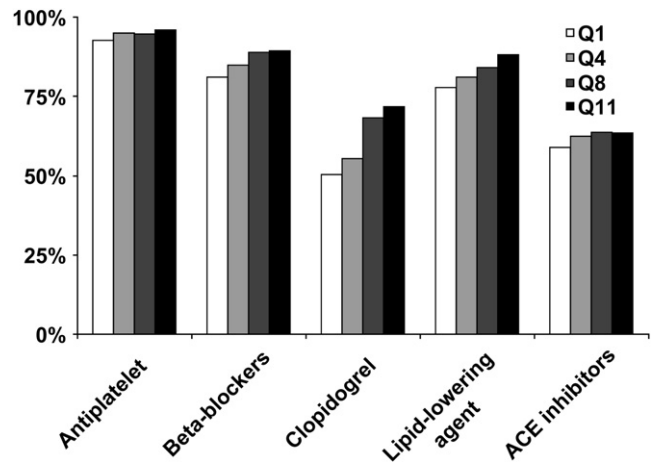


Figure 4. Trends in guidelines-recommended discharge therapy use over time (quarter 1 to quarter 11) in Can Rapid Risk Stratification of Unstable Angina Patients Suppress ADverse Outcomes with Early Implementation (CRUSADE) (in patients without contraindications). The x-axis represents discharge therapy, and the y-axis represents percent compliance. ACE = angiotensin converting enzyme.

impact on QI at CRUSADE hospitals: barriers related to resource availability, clinical commitment by the cardiology coadvocate, barriers related to culture, and financial commitment to quality.¹⁰

Previously, there have been little data to show the association between hospital process performance and outcomes. The substantial use of CRUSADE QI tools led to the largest absolute percent improvement in quality score. When later evaluation of patient outcomes demonstrating improved mortality was associated with higher levels of guideline adherence by a hospital, significant interest and enthusiasm for the CRUSADE QI initiative was achieved at all levels, from the physicians at individual hospitals to the national health care payers (Figure 5).¹¹ This robust database has since provided a remarkably successful mechanism by which to study and publish many aspects of the acute care of patients

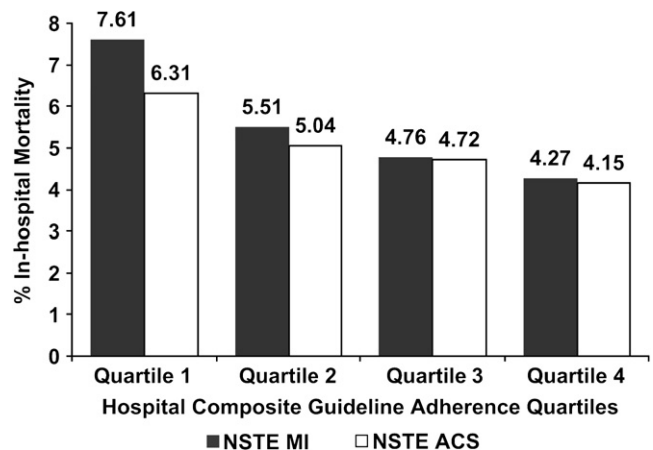


Figure 5. Association between hospital guideline adherence rates and in-hospital mortality. NSTEMI = non-ST-segment elevation myocardial infarction; ACS = acute coronary syndromes.

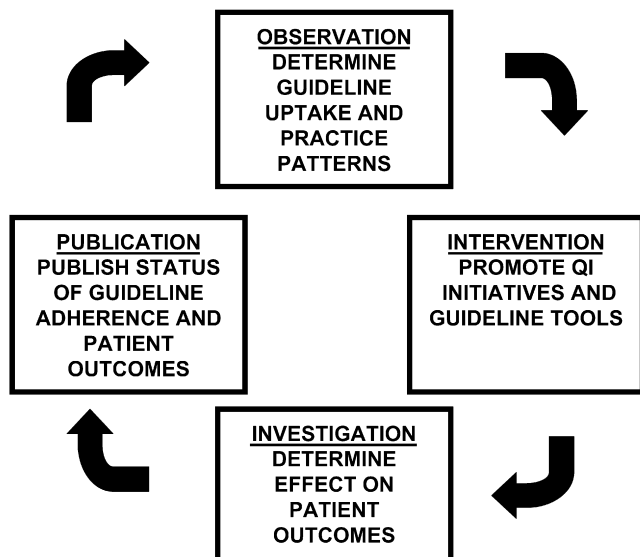


Figure 6. Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation (CRUSADE) QI initiative research using the continuous cycle of observation, intervention, investigation, and publication.

with NSTEMI ACS along the path of improved guideline implementation.

The information that has been collected by CRUSADE has been published in journal articles, presented in abstracts at major medical conferences, and shared in QI newsletters and reports. To date, 51 articles have been published and 86 abstracts have been presented at multiple national meetings in cardiology, emergency medicine, nursing, and other specialties. A listing of peer-reviewed papers published in 2006 is provided (see Appendix A, available as an online Data Supplement at <http://www.aemj.org/cgi/content/full/j.aem.2007.06.017/DC1>). The cyclical method of observation, intervention, investigation, and publication has proven successful in performing research that can be demonstrated to affect patient care. The cycle for research to guidelines to implementation is depicted in Figure 6.

It is intuitive that such a prolific research program would require the support and resources from a data coordinating center, which in the case of CRUSADE is the Duke Clinical Research Institute. Generally, large registries and QI programs suffer from lack of funding. Lack of funding translates into loss of interest and poor data collection unless specific benefits of participation can be demonstrated. Funding for this specific initiative has come from multiple pharmaceutical partners through unrestricted research grants representing a collaborative approach between industry and academia, resulting in improved patient care. Hospitals participate voluntarily and are compensated a small amount for each completed data collection form. These data are submitted through a Web-based enrollment program performed at each institution. The Duke Clinical Research Institute is responsible for details such as contracts and agreement documents, staff and physician training, feedback report generation, and data analyses.

Guideline implementation research for CRUSADE was based on the assumption that clinicians understand, agree with, and want to adhere to the recommendations provided in the ACC/AHA guidelines for treating patients with NSTEMI ACS. Demonstration of improved patient outcomes associated with better guideline adherence provided compelling evidence for continuing to increase guideline adherence. Benefits of participation in CRUSADE included automatic hospital reports on the use of these guidelines driving evidence-based management strategies and therapies, as well as performance ranking among “like,” national, and “best-practice” hospitals. In return for data collection and contribution, hospitals were able to meet existing hospital QI monitoring requirements and concurrently receive insights into their own care and how this compares with other institutions. Not only were hospitals provided with data as to how they were doing, but they were also given tools to help improve, such as continuing education programs, publications, postings, and protocol order sets as listed in the CRUSADE QI Toolbox (Figure 7, available as an online Data Supplement at <http://www.aemj.org/cgi/content/full/j.aem.2007.06.017/DC2>). The CRUSADE QI initiative provided substantial evidence that regular and repeated quarterly reports to hospitals, or the “audit and feedback” method, improved guideline adherence.

LESSONS LEARNED FROM THE CRUSADE QI INITIATIVE

In summary, some of the most important advances realized from the CRUSADE QI initiative include the following.

1. The most effective translation and implementation of treatment guidelines occur through the collaborative integration of health care providers and administrators.
2. Publishing and wide dissemination of guidelines alone do not guarantee adherence to guidelines or a change in patient outcomes.
3. Measurement and timely feedback to hospitals of practice patterns can decrease the gaps between usual and evidence-based care.
4. Demonstration of improved outcomes in actual patient care environments offers the most compelling data to clinicians and administrators to change practice and adhere to guidelines.
5. Data collection, reporting, and analyses appeal to the national focus on improving QI efforts.
6. Clear institutional benefits for participation encourage patient enrollment, guideline adherence, and QI efforts.
7. Rapid assessment and publication of practice patterns and outcomes is an effective feedback loop to boost enrollment in a registry and improve guideline adherence.
8. Retrospective observation of practice patterns can improve future patient outcomes.

The lessons and advances enjoyed through implementation of the CRUSADE QI initiative will provide a firm foundation for the NCDR-ACTION Registry and hopefully will encourage the enrollment of the majority of

U.S. hospitals in this new initiative to improve health care for all patients with ACS.

References

1. Doherty S. Evidence-based implementation of evidence-based guidelines. *Int J Health Care Qual Assur Inc Leadersh Health Serv.* 2006; 19:32–41.
2. Sinuff T, Kahn moui K, Cook DJ, Giacomini M. Practice guidelines as multipurpose tools: a qualitative study of noninvasive ventilation. *Crit Care Med.* 2007; 35:776–82.
3. Braunwald E, Antman EM, Beasley JW, et al. American College of Cardiology; American Heart Association. Committee on the Management of Patients with Unstable Angina. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction—summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients with Unstable Angina). *J Am Coll Cardiol.* 2002; 40:1366–74.
4. Gibler WB, Cannon CP, Blomkalns AL, et al. American Heart Association Council on Clinical Cardiology; American Heart Association Council on Cardiovascular Nursing; Quality of Care and Outcomes Research Interdisciplinary Working Group; Society of Chest Pain Centers. Practical implementation of the guidelines for unstable angina/non–ST-segment elevation myocardial infarction in the emergency department. *Ann Emerg Med.* 2005; 46:185–97.
5. Hoekstra JW, Pollack CV Jr, Roe MT, et al. Improving the care of patients with non–ST-elevation acute coronary syndromes in the emergency department: the CRUSADE initiative. *Acad Emerg Med.* 2002; 9: 1146–55.
6. The PURSUIT Trial Investigators. Platelet Glycoprotein IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatid e in patients with acute coronary syndromes. *N Engl J Med.* 1998; 339:436–43.
7. Clopidogrel in Unstable Angina to Prevent Recurrent Events Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *N Engl J Med.* 2001; 345:494–502.
8. SYNERGY Trial Investigators. Enoxaparin vs. unfractionated heparin in high-risk patients with non–ST-segment elevation acute coronary syndromes managed with an intended early invasive strategy: primary results of the SYNERGY randomized trial. *JAMA.* 2004; 292:45–54.
9. Mehta RH, Roe MT, Chen AY, et al. Recent trends in the care of patients with non–ST-segment elevation acute coronary syndromes: insights from the CRUSADE initiative. *Arch Intern Med.* 2006; 166: 2027–34.
10. Mehta RH, Newby LK, Patel Y, et al. The impact of emergency department structure and care processes in delivering care for non–ST-segment elevation acute coronary syndromes. *Am Heart J.* 2006; 152: 648–60.
11. Peterson ED, Roe MT, Mulgund J, et al. Association between hospital process performance and outcomes among patients with acute coronary syndromes. *JAMA.* 2006; 295:1912–20.