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INSIDE

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Medical Emergency Teams: Does Rapid Response Make a Difference?

ABSTRACT & COMMENTARY

By Ruth Kleinpell, PhD, RN

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Dr. Kleinpell reports no financial relationship to this field of study.

Synopsis: *In this before-and-after study of more than 275,000 patients admitted to a Swedish hospital before-and-after implementation of a medical emergency team, in-hospital cardiac arrests decreased and overall in-hospital mortality fell by 10% in the 2 years following the team's implementation.*

Source: Konrad D, et al. Reducing in-hospital cardiac arrests and hospital mortality by introducing a medical emergency team. *Intensive Care Med* 2010;36:100-106.

THE USE OF A RAPID RESPONSE SYSTEM (RRS), OR MEDICAL EMERGENCY team (MET), has become established as a patient safety measure to ensure early detection of patient compromise. It has been demonstrated that 50%-80% of in-hospital cardiac arrests are preceded by some clinical signs of instability, such as abnormalities in pulse rate, respiratory rate, mental status, or oxygen saturation (SpO_2).[1-3] Early detection and response to promote timely recognition of patients with physiological deterioration with the use of a RRS has been identified as a way to decrease mortality rates by intervening and potentially preventing a cardiac arrest.

This prospective before-and-after trial of implementation of a MET at a hospital in Sweden examined the impact on hospital mortality rates over a 2-year intervention period that included 73,825 patients compared to a 5-year pre-implementation period with 203,892 patients. The MET team consisted of an ICU physician and ICU nurse who re-

sponded to calls based on one or more standard triggers, including vital sign changes, changes in mentation, or staff concern about the patient. The primary outcome was the number of cardiac arrests per 1000 admissions, and secondary outcomes included adjusted hospital mortality and 30- and 180-day mortality for patients receiving an MET intervention.

The number of MET calls was 9.3 per 1000 hospital admissions. In comparing pre-MET and MET intervals, the number of cardiac arrests decreased from 1.12 per 1000 patients to 0.83. MET implementation was associated with a reduction in total hospital mortality by 10% ($P = 0.003$). The results of the study indicated that the introduction of the MET improved outcomes for hospitalized patients.

■ COMMENTARY

The findings of the study provide further evidence on the benefit of the use of RRSs in decreasing mortality rates in hospitalized patients. Support for the use of RRSs by quality organizations such as the Institute for Healthcare Improvement, in conjunction with the 2008 Joint Commission's designation of the use of systems to promote health care clinician response to a patient's worsening condition as a National Patient Safety goal have led to widespread implementation of RRSs. However, while studies have shown that an RRS may improve outcome, questions remain about the specific components, best format, and ultimate benefits of the RRS.[4]

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Interpreting the Evidence Related to the use of Rapid Response Teams. The findings by Konrad and colleagues support the results of other studies that have demonstrated a reduction in in-hospital cardiac arrests with the use of a RRS.[4-7] Yet, ongoing debate continues regarding the advantages of implementing a RRS as other studies have found no difference in reducing hospital mortality. The MERIT (Medical Early Response Intervention and Therapy) study, a large 23-hospital Australian study evaluated the use of METs with 12 hospitals receiving training in the MET process and implementing a program, compared to 11 hospitals that did not receive training and were asked to delay introduction of a MET system during the study period.[8] During a 6-month follow-up period after implementation, no differences were found in cardiac arrests, unplanned ICU admissions, or unexpected death.[8] However, the authors cited inadequate utilization of the MET for patients who met clinical criteria and concluded that despite similar outcomes in both study groups, system-based interventions can have an impact on improving monitoring of patients and promoting appropriate clinician response. Additionally, the use of the randomized clinical trial design in demonstrating benefit of the RRS has since been debated.[9,10]

The findings by Konrad and colleagues also support prior research that has demonstrated a reduction in overall hospital mortality with the use of a RRS. An overall reduction in hospital mortality of 10% was found, lending support to other studies that have shown a reduction in hospital mortality of up to 26%.[6] A recent meta-analysis of 18 randomized clinical trials and prospective studies of the use of a RRS found a 33.8% reduction in rates of non-ICU cardiac arrests, but no significant differences in hospital mortality rates for adult patients.[11] However, for children, implementation of an RRS was associated with a 37.7% reduction in rates of non-ICU cardiac arrests and a 21.4% reduction in hospital mortality rates.[11]

To establish consensus on issues related to use of the RRS, a consensus conference of international experts examined characteristics of an "ideal" monitoring system.[12] Four specific components of the RRS were considered, including the afferent or crisis detection and response triggering mechanism, an efferent or predetermined rapid response team, the governance/administrative structure, and a mechanism to evaluate crisis antecedents and promote hospital quality improvement processes.[12] The findings designated sufficient data to support that hospitals implement a RRS and that outcome benefits exist in terms of reduced deaths, cardiac arrest, hospital length of stay, ICU length of stay, and costs. However, additional research was advocated to determine the magnitude and benefit.[12]

It becomes evident that hospital-wide initiatives to educate and assist clinicians in early identification and

rapid treatment of life-threatening conditions that include a team response and protocols based on best practice guidelines can improve outcomes.[13,14] In addition, the use of track and trigger systems, combined with appropriate response algorithms, has been advocated to improve the recognition and management of critical illness.[1] As the severity of illness among hospitalized patients continues to increase, it becomes intuitive that RRS would be beneficial in promoting early detection of compromise. The results of research support that rapid response does make a difference, yet the quality of evidence that currently exists necessitates further work to validate the full utility of the RRS. ■

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Do Rapid Response Teams Reduce Hospital Mortality or Simply Increase Costs?

ABSTRACT & COMMENTARY

By Michael Young, MD

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Dr. Young reports no financial relationship to this field of study.

Synopsis: *This meta-analysis casts serious doubt on the ability of rapid response teams to significantly reduce hospital mortality.*

Source: Chan P, et al. Rapid response teams: A systematic review and meta-analysis. *Arch Intern Med* 2010;170:18-26.

Editor's Note

This issue deals with two key topics in the ongoing discussion about how critical care should be organized: rapid response systems (also called medical emergency teams or rapid response teams) for identifying patients not in ICUs who are at risk for life-threatening deterioration, and around-the-clock intensivist staffing in the ICU. The first of these topics is the subject of two abstract/commentaries highlighting both the importance and the unclear status of rapid response systems. Dr. Ruth Kleinpell summarizes an important new study from Sweden that found significant decreases in cardiac arrests and overall hospital mortality after a rapid response system was implemented. She points out that while improvements in the process of care associated with the introduction of such systems are clearly beneficial, the quality of the evidence supporting them needs improvement. This conclusion is emphasized by new contributing editor Michael Young, MD, who reviews a new meta-analysis of available studies on rapid response teams. Noting important gaps and design deficiencies in the studies comprising this literature, Dr. Young points out several important questions that are yet to be answered before the value of such teams can be considered established.

The second topic relating to ICU organization is whether all ICUs should have on-site intensivist coverage around the clock, seven days a week (24/7), the subject of a pro-con special feature. The presence of qualified intensivists in the ICU is associated with better patient outcomes. Given this, it stands to reason that having them present 24/7 would be the ideal medical staffing arrangement for the ICU. However, financial constraints, a substantial shortage of intensivists, and other considerations make this matter far from settled. Summarizing the pros and cons of 24/7 intensivist staffing, I describe some alternative staffing options that are currently being employed, and refer to several additional organizational measures that have recently received attention. ■

—David J Pierson, MD

In the past decade, rapid response teams (RRTs) were broadly implemented to identify and treat patients on medical and surgical wards at risk for catastrophic deterioration and thus prevent death. The impetus to form RRTs came after multiple observational studies in the 1990s suggested that ward patients who experience a marked clinical deterioration often suffer excess morbidity and mortality from delayed treatment and under-resuscitation. A number of single-center studies indicated that RRT implementation was associated with reductions in cardiopulmonary arrests outside the ICU and decreases in hospital mortality. However, two meta-analyses on RRTs published in 2007 were far more cautionary on their purported benefits. Despite equivocal evidence favoring RRTs, RRT implementation was an integral part of the "Save 100,000 Lives Campaign" lead by the Institute of Healthcare Improvement (IHI), and in 2008 the Joint Commission listed implementation of a RRT (or equivalent) as a National Patient Safety Goal.

The present meta-analysis by Chan and colleagues examines the effect of RRT implementation on cardiopulmonary arrest rates and hospital mortality. The authors' search strategy yielded 143 potentially relevant articles on the basis of title and abstract. Additional articles were excluded because they were simply review articles, lacked a control group, failed to evaluate mortality or CPR rates, were duplicates of other articles, or provided insufficient data. Eighteen articles, including 13 adult and 5 pediatric studies, published between 2000 and 2009, were included in the meta-analysis. Of the 6 studies classified as "high-quality," 2 were randomized clinical trials and 4 were observational in design.

Some of the adult RRT studies included in the meta-analysis showed a reduction in cardiopulmonary arrest rates while others did not. Cumulatively, the adult high-quality studies identified a 21% decrease in non-ICU cardiopulmonary arrest rate compared to a 48% decrease in the other studies. In contrast, the pooled mortality rate for adult patients was unaffected by implementation of RRTs in both high- and low-quality studies, and in studies with high- vs low-RRT activation rates. In the pediatric population, there was a lower mortality rate (relative risk [RR], 0.79; 95% confidence interval [CI], 0.63-0.98) with RRT implementation, but the improvement was not robust. Furthermore, when the adult and pediatric results were pooled, mortality rate with RRT implementation did not change (RR, 0.92; 95% CI, 0.82-1.04).

Among the 5 studies that reported a lower mortality rate with RRT implementation, Chan et al measured whether the reduction in cardiopulmonary arrest rate could explain the improvement. Their analysis found that the observed reduction in cardiopulmonary arrest rates could explain < 1% to as much as 61% of the mortality reduction.

■ COMMENTARY

This study is now part of growing series of meta-analyses indicating that the benefit of RRTs may be more modest than widely believed. If RRTs' benefits are measured largely by their impact on hospital mortality, the enthusiasm for RRT formation by the Joint Commission and IHI is not easily supportable. On the other hand, the data do indicate that RRTs reduce the number of cardiopulmonary arrests outside the ICU among both adult and pediatric patients. Given the discouraging mortality and morbidity associated with in-hospital cardiopulmonary arrest, this is an important benefit. There may be other benefits that RRT implementation provides that have not been well quantified. Nurse and patient/family satisfaction are reported to be improved with RRT implementation. Clinician education may be improved and delays in transfer to the ICU from the ward may be decreased. More research in these areas is needed.

Perhaps equally important, this study reminds us how difficult it can be to interpret the results of single-center studies, especially those that use a "before-and-after" design. RRTs may be another example of where we, as clinicians, adopt therapies or interventions that simply make "sense" to us without waiting for well-done outcomes studies. Once rigorously studied, we may find the story more complex than we suspected and the therapy less helpful than we anticipated and sometimes even more harmful than helpful — for example, lidocaine post-myocardial infarction, aggressive use of total parenteral nutrition in the ICU, and routine use of pulmonary artery catheters among patients with acute lung injury and the ARDS.

Why the remarkable variation in outcomes seen in the before-and-after RRT implementation studies? There are probably a number of factors at play. RRT composition is widely variable. The clinical thresholds used to prompt RRT activation vary. What are the sensitivities and specificities of those clinical thresholds' ability to predict catastrophic deterioration? In about 50% of cases, RRT are activated because of a "worried clinician." When should clinicians become worried? What interventions should the RRT provide when the RRT arrives at the bedside of a patient suffering measurable physiologic or subjective deterioration? What is the right rate of RRT activation? Once activated, how long should the RRT stay at the patient's bedside? When and which patients should be transferred from the ward to the ICU? How often should the vital signs of patients on medical and surgical wards be measured and reported? How accurate are those measurements?

Should RRTs be disbanded? In my view, no. However, until we conduct serious research to find answers to these questions, the real potential of RRTs to prevent morbidity and mortality among patients on hospital wards will remain unknown. ■

Special Feature

Should All ICUs Have 24/7 In-house Intensivist Coverage?

By David J Pierson, MD, Editor

One of the hottest topics in critical care these days is whether all ICUs should be staffed around the clock, seven days a week (24/7), by physicians with special training and qualifications in critical care (intensivists). Four recent editorials[1-4] offer different perspectives on this topic and highlight its relevance to the readers of this newsletter. In this essay I will try to identify the key issues involved and summarize the pros and cons of 24/7 in-house intensivist coverage. The issues are not as straightforward, nor is the evidence as clear, as one might wish, and key aspects of the matter are beyond the control of individual clinicians working in the ICU.

Origins of the Controversy

The current push for 24/7 intensivist staffing in ICUs has multiple origins, but its most prominent driver in the United States has been the Leapfrog Group. This is a consortium of health care purchasing organizations formed in response to ever-increasing health care costs in order "to trigger giant leaps forward in the safety, quality and affordability of health care by supporting informed health-care decisions by those who use and pay for health care and promoting high-value health care through incentives and rewards."[5] One of Leapfrog's core intended "leaps" is for all ICUs to be staffed by intensivists, although it does not specifically call for the physical presence of an intensivist in the ICU 24/7. However, a 2000 survey found that only 4% of U.S. ICUs met the Leapfrog physician staffing standard,[6] and available evidence suggests that while the proportion may be higher today, it is still far short of the goal. In fact, only a minority of critically ill patients receive any care by an intensivist, let alone 24/7 care.[2,6] In the United States there are numerous reasons for this, but a big one is that there are not enough qualified intensivists to go around.

ICU Physician Staffing Models

How ICUs are staffed by physicians and how this staffing affects the outcomes of critical care have been the subject of considerable study. Rubenfeld and Angus describe several models for such staffing,[7] depending on the degree of involvement of intensivists in the care of patients in a given ICU. These include the following distinctions:

- Admission and discharge decisions and all patient management in the unit are by intensivists (closed ICU) vs admission and discharge decisions by the patient's primary physician, with or without involvement of intensivists in management (open ICU);
- Closed ICU as above, or mandatory intensivist consultation for all patients (high-intensity ICU) vs open ICU as above, with or without intensivist consultation or availability (low-intensity ICU);
- At least 80% of patients managed by intensivist (high-intensity ICU) vs some but < 80% of patients managed by intensivist (intermediate-intensity ICU) vs no intensivist;
- Closed ICU, or open ICU with mandatory intensivist consultation ("no choice" ICU), vs open ICU with consultation of intensivist at discretion of primary physician ("choice" ICU) vs no intensivist available ("no choice" ICU).

Perhaps three-fourths of all critically ill patients in U.S. ICUs are managed under the low-intensity physician staffing model defined above.[8] However, most studies evaluating the association between ICU physician staffing and patient outcomes have shown lower hospital mortality and shorter ICU and hospital stays with high-intensity physician staffing.[8] A prominent exception, published 2 years ago, examined data from more than 100,000 patients in 123 American ICUs participating in Project Impact, a voluntary critical care database.[9] That study found that high-intensity ICU staffing (defined as having at least 95% of all patients cared for exclusively by an intensivist) was associated with higher, rather than lower, severity-adjusted mortality as compared to low-intensity ICUs (defined as 5% or less of critically ill patients receiving exclusively intensivist care). As discussed in a previous special feature in this newsletter *(see* Critical Care Alert*, September 2008, pp. 46-48)*, there are a number of potential explanations for these findings, including unaccounted-for differences in patient populations, severity and complexity of illness, and processes of care among the Project Impact ICUs.

The majority of studies dealing with ICU staffing have looked at patient outcomes before and after full-time intensivist coverage was introduced to the ICU. Usually when this happens, numerous other things change besides just the addition of intensivists to the unit — such as admission and discharge criteria, the use of protocols, and emphasis on evidence-based practice, to name just a few. Typically, multiple aspects of patient care improve when such changes are introduced, and it should be no surprise that better care results in better outcomes. These and other study design issues notwithstanding, though, the weight of available evidence strongly favors the closed-ICU and high-intensity intensivist staffing models.

If care by intensivists is associated with better outcomes, it stands to reason that having those intensivists in the unit 24/7 would be the best possible staffing arrangement. However, here the picture is less clear, and the supporting evidence more equivocal, than with the simple presence or absence of intensivist care.

Pros and Cons of 24/7 In-house Coverage

Table 1 *(below)* summarizes the reasons that have been advanced for and against implementation of 24/7 in-house intensivist coverage.[1-4,8,10] Extrapolating from the evidence in support of intensivist care in general, advocates point out that critical illness does not respect "business hours," and that at least as many patients are admitted to ICUs at night and on weekends as during usual daytime hours. Evidence supporting early, aggressive intervention in sepsis, acute myocardial infarction, and trauma is typically offered in support of having an intensivist at the bedside whenever these or other critical illnesses are diagnosed. A number of studies document increased ICU mortality during nights and weekends, and also among patients initially admitted during these times. In contrast, several reports from units with 24/7 intensivist staffing find no increase in mortality during off-hours. Mortality among patients cared for in academic, teaching-hospital ICUs has been reported to be higher than in non-teaching settings, and adjustments for patient demographics and other factors have led to the conclusion that being managed by housestaff accounts for the difference. All these findings have been cited in support of 24/7 intensivist coverage. The devil, however, is in the details, and none of these arguments is as clear-cut as it first appears. For example, patients admitted at night and on weekends tend to be sicker than those admitted during the day, and teaching hospitals care for more complex, more severely ill patients than nonteaching hospitals.

One single-center, before-and-after study found that processes of care in the ICU were improved after 24/7 intensivist coverage was implemented.[11] There was better adherence to evidence-based practice guidelines, ICU-related complications decreased, and hospital length of stay was shortened. Staff satisfaction also improved under the new physician staffing paradigm. It may be argued, however, that the improved outcomes associated with

Table 1. Pros and Cons of Implementing 24/7 Intensivist Staffing in the ICU.

***Pro:* Potential Reasons for Implementing 24/7 Intensivist Staffing**

- Critical illness happens 24/7, not just during regular business hours; majority of ICU admissions occurs during off-hours
- Early intervention improves outcomes in sepsis, MI, trauma, etc.; immediate availability of intensivist at bedside will facilitate this
- Quicker/better responses to new admissions and changes in patient condition
- Mitigation of worse mortality and other outcome measures among patients admitted to or cared for during off-hours
- Mitigation of increased mortality observed in teaching hospital ICUs, presumed due to care by residents
- Improved house-staff education: more time for teaching; better supervision for procedures
- Shorter ICU length of stay: no waiting for decisions to transfer or discharge patients
- Improved cost-benefit for ICU care (one study concluded this)
- Improved processes of care: better adherence to evidence-based guidelines and fewer ICU-related complications (one single-center, before-and-after study)
- Greater intensivist satisfaction (one single-center, before-and-after study)
- Increased revenue generation: more time for documentation; ability to bill for supervised house-staff procedures

***Con:* Potential Reasons for Not Implementing 24/7 Intensivist Staffing**

- Evidence for improved outcomes with 24/7 intensivist staffing is weak: few studies; weak design; likelihood of other explanations for observed effects
- Increased mortality associated with off-hours admission and care likely due to severity of illness, comorbidity, and other patient factors rather than physician staffing
- Observation of worse outcomes in teaching hospitals likely reflects patient mix and other factors rather than care by housestaff per se
- Increased intensivist presence would not solve other staffing problems: nurses; respiratory therapists; consultants; availability of tests and procedures
- Lack of continuity of care: problems related to patient handoffs; adverse effects on communication with patients and families
- Disadvantages associated with shift work: circadian rhythm disruption; decreased staff satisfaction; lost productivity following overnight shifts
- Shortage of trained intensivists
- Adverse effects on the intensivists themselves: work-life conflicts; burnout; disproportionate burden on junior faculty and youngest practice members; critical care medicine as a less attractive specialty for future practitioners
- Increased costs to institution of hiring additional intensivists
- Improved processes of care do not necessarily require off-hours intensivist presence (implementation of evidence-based guidelines, protocols, checklists, etc.)

better implementation of evidence-based guidelines and systems approaches to reducing ICU infections have also been reported in other studies unrelated to physician staffing, so that it may be possible to achieve these improvements without the 24/7 presence of an intensivist. That is, systems approaches to implementing, for example, early goal-directed therapy for sepsis and lung-protective ventilation for acute lung injury may or may not require physical presence of the intensivist at the bedside.

Critical care is a multidisciplinary activity necessarily involving multiple individuals in the management of an individual patient. Still, several aspects of the shift approach to physician coverage pose challenges to both optimal patient care and efficient staff functioning. Handoffs between shifts have been identified as important sources of medical error, and the potential effects on patient and family satisfaction of multiple switches between managing physicians are important considerations in implementing 24/7 intensivist coverage. Also important are the effects on the intensivists themselves. In academic settings off-hours coverage may fall disproportionately on junior faculty members, interfering not only with work-life balance for these individuals,[12] but also with other activities upon which their long-term career prospects depend.[4] It is likely that analogous pressures affect more junior members of practice groups in non-academic settings as well. In addition, the prevalence of burnout and other consequences of work stress may have an adverse effect on the attractiveness of critical care medicine as a career choice for residents.

Finally, prominent in any discussion of the possibility of implementing 24/7 intensivist coverage are the problems of money and manpower. Staffing an ICU around the clock with qualified intensivists requires a substantial commitment of resources on the part of the institution, with as many as 5 physicians required to fill one full-time equivalent position 365 days per year.[10] This is a big practical problem for the individual institution, albeit a potentially solvable one, but at the regional and national levels the shortage of qualified intensivists renders implementation of 24/7 intensivist staffing for all ICUs an impossibility — at least in the short term.

Options for Optimizing ICU Physician Staffing

Table 2 *(right)* lists 6 different options for staffing a "closed" ICU. All of these are currently used in the greater metropolitan area in which I practice. Of the medical ICUs in the main teaching hospitals of our university system, one relies on the first option and the other uses the fourth listed in the table, with "nocturnalists" (hospitalists, typically recent medicine residency graduates) covering the unit and supervising the residents at night. Other ICUs in these same institutions use other models on the list, as do the community hospitals around us. Some of our senior critical care fellows moonlight in option #3. One of the largest hospitals in the region recently went to 24/7 intensivist coverage, and another relies on ICU telemedicine.

Given the unfeasibility of providing an intensivist 24/7 for every ICU, the practical thing to do would seem to be to deploy intensivists where they can do the most good for the largest number of critically ill patients. To this end, several changes have been proposed for the way critical care is organized in the United States.[13] Because outcomes for patients with a given condition tend to be better at hospitals that manage more patients with that condition, the first proposal is tiered regionalization. This would involve categorizing hospitals according to the level of critical care they can provide, and systematically transferring high-risk patients to higher levels of care. For example, one study based on simulation of regionalized care for the majority of nonsurgical patients requiring mechanical ventilation found that managing them at a few high-volume centers would confer a substantial survival advantage.[14] For regionalization to be effective, however, would require major financial and organizational investment and the will to deploy it.[13]

A second systems-level organizational change would be more extensive utilization of ICU telemedicine, which is in use in some areas but not currently widespread. Although the evidence that telemedicine improves outcomes is inconsistent, this approach to intensivist staffing is particularly appealing for smaller hospitals and those geographically distant from large population centers.[13] Again, though, major changes in health care organization and clinician acceptance would be necessary if ICU telemedicine were to be broadly implemented.

A third approach to improving the quality of critical care and more efficiently utilizing the available intensivist workforce is quality improvement through regional outreach.[13] Instead of physically moving patients to higher-

Table 2. Potential Options for ICU Staffing

1. Current "business model" staffing: intensivists present 12h, on-call 12h
   - academic version with housestaff present in unit 24/7
   - community model with no physician present in unit at night
2. Intensivists present in unit 24/7
3. Senior-level critical care trainees staff unit during off-hours (moonlighting)
4. Hospitalists (nocturnalists) staff unit during off-hours
5. Mid-level practitioners (physician assistant, nurse practitioner) staff unit during off-hours
6. Telemedicine (with one or more ICUs covered electronically by off-site intensivist, the "E-ICU")

expertise hospitals or importing physician expertise via telemedicine, regional outreach involves cooperation among all hospitals in a given region to improve outcomes through benchmarking and quality improvement. Several studies have shown the effectiveness of this strategy in such areas as improving staff performance, increasing adherence to evidence-based guidelines, and reducing ICU-related complications.[13] For regional outreach to work, however, requires not only the willingness of different institutions to cooperate, but also the presence of an adequately supported central coordinating authority to facilitate education and data collection.

Nguyen and colleagues have recently described an organizational framework for implementing all three of the above systems approaches.[13] Such implementation would require a unified national strategy for improving ICU care. In the meantime, even if one is convinced that it is the best thing to do, deciding to move to 24/7 intensivist coverage involves juggling the benefits and costs at the level of the individual hospital. Adopting 24/7 intensivist coverage for a particular ICU may be possible given enough financial support from the institution and enough trained critical care physicians in the community. However, although some regions of the country may be better stocked with intensivists than others, nationwide there are definitely not enough to go around. The staffing options listed in Table 2 provide possible alternatives, at least until this issue is addressed in a more global way and/or more definitive evidence becomes available. ■

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CME / CNE Questions

14. Which of the following components of the rapid response system refers to the crisis detection and response triggering mechanism?

a. Efferent response
b. Active response
c. Afferent response
d. Effector response

15. Which of the following is *true* regarding the criteria used to mobilize RRTs?

a. The sensitivity and specificity of the physiologic threshold (heart rate, blood pressure, respiratory rate, etc.) use to mobilize RRTs are well known.
b. RRT mobilization rarely occurs simply because of a "worried clinician."
c. The clinical criteria used to mobilize the RRTs may vary between institutions.
d. The clinical response by RRTs to altered physiology is highly protocolized
e. None of the above

16. Which of the following statements is *true*?

a. Mortality is higher among patients admitted to an ICU at night or on weekends.
b. Mortality is higher among patients admitted to an ICU in a teaching hospital.
c. The majority of ICU patients in the United States are cared for by intensivists.
d. All of the above
e. Answers a and b are true, but c is false

Answers: 14. c, 15. c, 16. e.

PHARMACOLOGY WATCH

Supplement to *Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.*

Aggressive Modification of Cardiovascular Risk Factors

In this issue: Aggressive approach to CVD reduces MI, folic acid and vitamin B12 for CAD, corticosteroids for acute exacerbations of COPD, prescription drug abuse among young adults, and ARBs and cancer risk.

CVD decreases with aggressive treatment

Aggressive modification of cardiovascular risk factors seems to be paying dividends, at least for a large population of insured patients in Northern California. In an analysis of nearly 18.7 million patient-years between 1999 and 2008, the rate of myocardial infarction (MI) increased in 1999 and 2000 and then decreased significantly every year thereafter (287 cases/100,000 person-years in 2000, decreasing to 208 cases/100,000 person-years in 2008; 24% relative decrease over the study period). The rate of ST-segment elevation MI decreased over the study period (133 cases/100,000 person-years in 1999 to 50 cases/100,000 person-years in 2008; $P < 0.001$) and the 30-day mortality rate decreased from 1999 to 2008 as well (adjusted odds ratio, 0.76; 95% confidence interval, 0.65-0.89). This occurred despite more aggressive diagnosis of MI.

The authors conclude, "The lower incidence of myocardial infarction — particularly ST-segment elevation myocardial infarction — is probably explained, at least in part, by substantial improvements in primary-prevention efforts, ..." including statins and aggressive blood pressure reduction, as well as use of cardioprotective medications such as aspirin (*N Engl J Med* 2010;362:2155-2165).

An accompanying editorial points out that while these trends are generally the case in the United States, there are significant geographic differences. "The risk among residents of Oklahoma, the lower Mississippi corridor, and Appalachia, for example, is double that among other Americans, ... " suggesting socioeconomic factors play a role. Hypertension and diabetes rates have increased slightly over the last decade, while smoking rates have decreased. Perhaps even more importantly, statin use has increased significantly (among those between age 45 and 64 years, statin use in men increased from 2.5% to 16.8% and from 1.9% to 13.5% in women; among those 65 years of age or older, statin use increased from 1.9% to 38.9% in men and from 3.5% to 32.8% in women). Aspirin, beta-blockers, and ACEIs/ARBs have also contributed to the decline in cardiovascular mortality in the United States (*N Engl J Med* 2010;362:2150-2153). ■

Folic acid and vitamin B12 for CAD

Unfortunately, lowering homocysteine with folic acid and vitamin B12 does not seem to be a benefit to patients with coronary artery disease. In a study from the United Kingdom, more than 12,000 survivors of myocardial infarction were randomized to 2 mg folic acid plus 1 mg vitamin B12 daily vs matching placebo, with the main outcomes being first major vascular event such as coronary event, stroke, or noncoronary revascularization. Folate and vitamin B12 were effective at reducing homocysteine levels by 28%; however, there was no difference in the rate of major vascular events over the 6.7 years of follow-up (25.5% active treatment vs 24.8% placebo; $P = 0.28$). Individually, there was no effect on major coronary events, stroke, or noncoronary

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revascularizations, nor was there a survival benefit from active treatment. Interestingly, the authors also looked at incidence of cancer and found no difference in that outcome either. The authors conclude that long-term reductions in blood homocysteine levels with folic acid and vitamin B12 do not have a beneficial effect on vascular or cancer outcomes (*JAMA* 2010;303:2486-2494). ■

Corticosteroids for exacerbations of COPD

Giving corticosteroids orally in lower doses is as effective as giving the drugs intravenously at higher doses for the treatment of acute exacerbation of COPD (ae-COPD), according to a recent study in the *Journal of the American Medical Association*. The records of nearly 80,000 patients in more than 400 hospital admissions for ae-COPD who received steroids were reviewed. The primary outcomes were treatment failure, defined as the initiation of mechanical ventilation, inpatient mortality, or readmission within 30 days. The vast majority of patients (92%) received IV steroids. After multivariate adjustment, the death rate was similar in the two groups (1.4% IV therapy vs 1.0% oral) and the composite outcome was also similar (10.9% IV vs 10.3% oral). In a propensity-matched analysis, the risk of treatment failure was actually significantly lower among orally treated patients (odds ratio, 0.84; 95% confidence interval, 0.74-0.95), as was the length of stay and cost. Of the orally treated patients, 22% were switched to IV therapy later in the hospitalization.

The authors conclude that for patients admitted for ae-COPD, low-dose steroids administered orally are as effective, and may be safer, than higher-dose IV steroids (*JAMA* 2010;303:2359-2367). An accompanying editorial suggests that rather than doing large non-inferiority studies to confirm these findings, sufficient evidence exists to change practice now with continued comparative effectiveness research via linked registries (*JAMA* 2010;303:2409-2410). ■

Prescription drug abuse in young adults

Prescription drugs are the new drugs of abuse among young adults. While drug use in general seems to be dropping in high schools, prescription drug abuse is skyrocketing. The recently published National Youth Risk Behavior Survey from the Centers for Disease Control and Prevention (CDC) showed that 1 of 5 high school students in the United States reported abusing a prescription drug at some time in their lives. The most commonly mentioned drugs were OxyContin®, Percocet®, Vicodin®, Adderall®, Ritalin®, and Xanax®. Prescription drug abuse was most common among white students (23%), followed by Hispanic students (17%), and then black students (12%). Not surprisingly, high school students were most likely to abuse drugs in their senior year (*MMWR* 2010;59:1-142). While many teens get their prescription drugs from medicine cabinets of family and friends, others order them online, and recently many drug dealers have begun specializing in prescription drugs.

Many young adults, however, seek opioids and benzodiazepines from physicians, especially in emergency departments (ED). A new report from *MMWR* reports that ED visits for nonmedical use of opioid analgesics increased 111% from 2004 to 2008 and increased 29% from 2007 to 2008 alone. The highest number of ED visits was recorded for oxycodone, hydrocodone, and methadone. ED visits for benzodiazepines also increased 89% over the same period. In 2008, the rates of visits for both opioids and benzodiazepines increased sharply after age 17 and peaked in the 21-24 year age group. During the 2004-2008 study period, the largest increase in ED visits to obtain drugs occurred among persons age 21-29 years. Findings were from the CDC and the Substance Abuse and Mental Health Services Administration, reviewing data from the Drug Abuse Warning Network (*MMWR* 2010;59:705-709). ■

ARBs and cancer risk

Do angiotensin receptor blockers (ARBs) increase the risk of cancer? In a widely reported study, researchers from Case Western Reserve performed a meta-analysis of 5 trials for which cancer data were available from more than 61,000 patients. Telmisartan was the ARB used in nearly 86% of the studies. Patients randomly assigned to receive ARBs had a rate of new cancer occurrence of 7.2% vs 6.0% for placebo (relative risk [RR], 1.08; 95% confidence interval [CI], 1.01-1.15; $P = 0.016$). The risk ratio was higher when the analysis was limited to trials where cancer was the prespecified endpoint (RR, 1.11; 95% CI, 1.04-1.18; $P = 0.001$). There was no difference in the rate of cancer deaths between the two groups. The authors conclude that this trial suggests that ARBs are associated with a modestly increased risk of new cancer diagnosis, but it is not possible to draw conclusions about the exact risk of cancer associated with each particular drug and further research is warranted (*Lancet Oncology* 14 June 2010; early online publication). ARBs are involved in the regulation of cell proliferation, angiogenesis, and tumor progression, which are possible mechanisms for these findings. ■