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Decreased mortality resulting from a multicomponent intervention in a tertiary care medical intensive care unit

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Abstract

Objective—To evaluate whether a multicomponent intervention, particularly increasing staff, can achieve reductions in patient mortality in an already high-intensity, Leapfrog-compliant medical intensive care unit.

Design—Retrospective, observational study.

Setting—Medical intensive care unit of a tertiary care, academic medical center.

Patients—A total of 1,263 patients admitted between April 19, 2004 and April 18, 2006 (before the organizational change) were compared with 2,424 patients admitted between September 5, 2006 and September 4, 2008.

Interventions—A multicomponent intervention including the physical move from a 10-bed to a 29-bed medical intensive care unit with larger patient rooms, the initiation of 24-hr critical care specialist coverage in the medical intensive care unit, an increase in the respiratory therapist:patient ratio, and the addition of a clinical pharmacist to the multidisciplinary team.

Measurements and Main Results—Measurements were made based on mortality in the intensive care unit and in-hospital. Patient comorbidity as measured by the Charlson score did not change after the intervention (2.7 ± 2.7 vs. 2.8 ± 2.6, $p = .62$), nor did the acuity of illness as measured by the case mix index (3.0 ± 3.7 vs. 3.1 ± 3.8, $p = .69$). The unadjusted medical intensive care unit mortality decreased from 18.4% to 14.9% ($p = .006$), as did in-hospital mortality (from 25.8% to 21.7%, $p = .005$). The reduction in medical intensive care unit mortality was consistent in the multivariable regression with adjustment for multiple possible confounders (odds ratio = 0.74, 95% confidence interval: 0.61– 0.91, $p = .003$), as was the reduction in hospital mortality (odds ratio = 0.74, 95% confidence interval: 0.62– 0.88, $p = .001$). In mechanically ventilated patients, there was an increase in median 28-day ventilator-free days (21, interquartile range 0 –25 vs. 22, interquartile range 0 –26, $p = .04$). An increase in median medical intensive care unit (2.4, interquartile range 1.1–5.2 vs. 2.7, interquartile range 1.3–5.9), $p = .009$) but not hospital (8.3, interquartile range 4.1–17.0 vs. 8.2, interquartile range 4.0 –16.8; $p = .851$) length of stay in days occurred with the intervention. The mean daily dosing of fentanyl and lorazepam decreased after the intervention.

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Conclusions—A multicomponent reorganization of medical intensive care unit services was associated with important reductions in mortality for medical intensive care unit patients, as well as an increased number of ventilator-free days. Substantial and sustained changes in clinically important outcomes may be obtained from organizational changes.

Keywords

critical care; health care quality assessment; quality indicators; health care; personnel staffing and scheduling; organizational innovation; outcomes and process assessment; health care

Wide variations in the quality of intensive care unit (ICU) care persist for critically ill patients. Better performing ICUs have 40% lower odds of death than poorly performing ICUs for mechanically ventilated patients (1). For acute myocardial infarction care, variations may be even wider (2–5). Since these variations exist in the face of medical knowledge that is uniformly available, there may be organizational factors that can be changed to improve patient outcomes. Appealingly, organizational changes can potentially be made now, without waiting for new fundamental biological discoveries into the basis of critical illness.

There have been significant improvements in critical care outcomes associated with closed-model ICUs and dedicated intensivist staffing (6 –13), and expert opinion has continued to search for the optimal ICU staffing model (14–19). Extending intensivist staffing to around-the-clock in the pediatric ICU was found to be associated with a reduction in mortality (20). In an adult medical intensive care unit (MICU), 24-hr coverage resulted in decreased length of stay (LOS) and increased adherence to patient care protocols but was not associated with an impact on mortality (21).

Most of these studies have sought incremental improvements in outcome by reorganization of physician staffing, either studying the improvements in low-performing ICUs gained with closed-model intensivist staffing or further improvements in closed-model ICUs utilizing 24-hr staffing. However, no previous study has evaluated just how much improvement can be gained by a multicomponent intervention to raise a high-intensity organizational model (defined by mandatory intensivist participation for all ICU patients [17]) to what expert opinion considers optimal organization. One model of such a multicomponent reorganization has been proposed by the American College of Critical Care Medicine of the Society of Critical Care Medicine in its recommendations for best “level I” ICU organization, which includes intensivist staffing, preferably around-the-clock, a complete multidisciplinary team, and complete consultative and hospital services support (Table 1) (16).

We hypothesized that a multicomponent intervention would improve clinical outcomes and are the first to evaluate the effect of bringing an ICU to a resource level equivalent to level I. The intervention consisted of a physical relocation of the MICU to new facilities, the institution of 24 hr/day, 7 day/week staffing by a critical care board-certified intensivist, the addition of a full-time clinical pharmacist to the multidisciplinary team, and a change in the respiratory therapist: patient ratio from 1:24 to 1:10. We assess the impact of this intervention on hospital and MICU mortality, 28-day ventilator-free days (VFDs) and sedative use.

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MATERIALS AND METHODS

Environment and Intervention

We conducted a single-center, quasiexperimental study (22, 23) of all patients admitted to the University of Maryland Medical Center MICU between April 19, 2004 and April 18, 2006 (24 months preintervention) and September 5, 2006 and September 4, 2008 (24 months postintervention). The University of Maryland Medical Center is a 705-bed teaching hospital. These dates reflect 2-year periods before and after the staggered implementation of a multistep intervention, which occurred between April 19, 2006 and September 4, 2006.

The preintervention physician staffing was a high-intensity model (6) in a closed-model ICU (24) staffed by an intensivist ≥8 hrs daily, 7 days/week (25). Staffing was consistent with the recommendations of the Leapfrog Group, an organization founded by a consortium of Fortune 500 companies to provide advice on healthcare (26). Additionally, the MICU was staffed 24 hrs/day by house officers, consisting of one fellow, two residents, and four interns, and overnight call staffed by one resident and one intern. After January 1, 2006, there were also two nurse practitioners staffing the MICU preintervention. The preintervention nursing core consisted of trained critical care nurses, overseen by a qualified nurse manager. The preintervention patient:nurse ratio of 1:1.7 has been associated with improved outcomes (15, 27) and did not change over this period. As part of a large, tertiary academic medical center, the MICU preintervention resources included complete 24-hr laboratory and radiology services. Clinical pharmacists dispensed medication 24-hrs daily but did not routinely round in the MICU, and respiratory therapy (RT) provided around-the-clock care in the MICU. Full consultancy services were available 24 hrs daily. The medical center has been recognized for its quality of care by the Leapfrog Group, which placed it on its honor roll both pre- and postintervention. The decision to expand the ICU was made in response to increased demand for medical critical care, as a part of the move to a new hospital building, and was unrelated to prior clinical performance of the ICU.

This intervention consisted a physical relocation of the MICU to new facilities, the institution of 24 hr/day, 7 day/week staffing by critical care board-certified intensivists, the addition of a full-time clinical pharmacist to the multidisciplinary team, and a change in the respiratory therapist:patient ratio from 1:24 to 1:10. The change in RT staffing was part of a hospital-wide initiative to create a unit-based staffing initiative in all ICUs and to reduce RT staffing vacancies. All patients were staffed at least daily by an attending physician. The daytime staffing of the MICU consisted of two attending physicians, two fellows, four residents, four interns, and four nurse practitioners. There was no change in the scope of the nurse practitioners' duties. The overnight call team consisted of one attending physician, one resident, and one intern. In addition to the clinical pharmacists dispensing medication, a clinical pharmacist evaluated all patients daily during bedside rounds. The role of the respiratory therapists did not change. The medical director of the MICU did not change. The previous MICU was a 10-bed facility, consisting of all single rooms with a mean room size of 179.0 ± 6.1 square feet. The new MICU is a 29-bed facility, with all rooms being single and with mean room square footage of 380.7 ± 39.4. In addition to the stability of nursing staffing ratios over this period, the MICU nursing leadership remained unchanged. There was no change in laboratory, radiology, or consultant services after the intervention, which continued to be fully available 24 hrs daily.

The Institutional Review Board of the University of Maryland Baltimore approved this study with waiver of consent.

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Data Sources and Patient Selection

Data were abstracted from the hospital's electronic medical record and administrative record systems. We evaluated 4,107 consecutive patients in the 24 months preintervention and 24-months postintervention with first and single admissions on the data file to protect independence of observations and, to a lesser extent, comparability of the clinical courses studied. Patients missing All Patient Refined–Diagnosis-Related Groups codes and International Classification of Diseases, version 9 codes were excluded from analysis, as were patients with coded negative LOS.

Analytic Approach

Our primary outcome variable was mortality, both in-hospital and in-MICU mortality. We also provide comparisons on several other variables of interest. Baseline MICU admission characteristics pre- and postintervention are compared by using two-sample Student's *t* tests for continuous variables (28) and comparisons of proportions for categorical variables (29). The MICU, total hospital, pre-MICU hospital, post-MICU LOS, and median per admission total MICU and hospital variable costs before and after intervention were compared with two-sample Student's *t* tests and Mann-Whitney tests (30). Unadjusted hospital and MICU mortality and 28-day ICU-free days (31) before and after intervention were evaluated by comparison of proportions. We evaluated 28-day VFDs before and after intervention (32, 33). Rank-sum testing was performed (34, 35) to evaluate the composite end point of mortality and MICU LOS.

The effect of the intervention on hospital and MICU mortality was also evaluated by using logistic regression. To assess for confounding effects of patient characteristics on mortality, the analyses were also performed with variables chosen *a priori* on the basis of previous studies and biological plausibility: Age, gender, race, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category (36, 37), Charlson score (38, 39), for baseline characteristics, and to adjust for severity of illness, admission laboratory values (hemoglobin, white blood cell count, creatinine, sodium, potassium, glucose, and bicarbonate) (40–45), and the case mix index (CMI) weight, a Maryland state measure based on diagnoses and used to adjust hospital reimbursement for expected resource intensity of treatment. (CMI scores are weighted to a state average of 1.00 [46]). Each variable was evaluated individually for effect on the association of the intervention with mortality in logistic regression models. The variables that altered the odds ratio (OR) of the intervention by 15% were considered potentially significant confounders (47). The effect of the intervention on MICU, total hospital, pre-MICU hospital, and post-MICU LOS was evaluated with linear regression, with unadjusted and multivariable models.

Additional analyses were performed evaluating the period July 1, 2005 to April 18, 2006, preintervention, and September 5, 2006 to September 4, 2008, postintervention. These dates reflect the earliest availability of pharmacy data preintervention. Sedative and opiate use per MICU patient and per patient prescribed each agent was compared. To assess for any possible effect of seasonal variation, these baseline characteristic and outcomes were also evaluated comparing July 1, 2005 to April 18, 2006 and July 1, 2007 to April 18, 2008.

Analyses were performed using SAS version 9.1.3 (SAS Institute, Cary, NC). We applied the traditional definitions of statistical significance (48).

RESULTS

There were 1,263 patients preintervention and 2,424 patients postintervention for analysis. The proportion of patients with single hospital admissions did not change after the intervention (82.0% vs. 81.8%, $p = .92$). Within a hospital admission, the rate of MICU

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readmission was 6.0% preintervention and 9.6% postintervention ($p < .001$). Patients admitted after the intervention were similar to those preintervention (Fig. 1). There were no differences in gender, comorbidity (as measured by the Charlson score), or expected intensity of care (as measured by the CMI). After the intervention, patients were less likely to be non-White (53.8% vs. 58.0%, $p = .017$) and may have been slightly older (54.4 ± 16.4 vs. 53.4 ± 15.9 yrs, $p = .066$) (Table 2). There were clinically modest changes in the primary diagnosis of patients, with an increase in vascular-related and neoplasm admissions and corresponding modest declines in the relative incidence of other diagnoses. The relative proportion of admission sources did not change (Appendix Table 1).

Mortality after the multicomponent intervention decreased. All-cause MICU mortality experienced a 19% relative reduction, from 18.4% to 14.9% ($p = .006$) (Table 2), whereas all-cause in-hospital mortality had a 16% relative reduction, from 25.8% to 21.7% ($p = .005$). In stratified analysis, MICU mortality among ever-ventilated patients was reduced from 31.6% to 28.7% ($p = .210$) and among never-ventilated patients was reduced from 5.6% to 4.2% ($p = .177$), although these reductions did not meet statistical significance.

The diminished likelihood of death after the intervention remained after adjustment for patient baseline and clinical variables (Table 3). Although none of these variables was found to change significantly the point estimate of OR of death, to assess for potential additive effect as well as to insure control for all clinical variables, we included them in the multivariable explanatory models. Our results for MICU mortality were consistent both in the unadjusted model (OR = 0.78, 95% confidence interval: 0.65–0.93, $p = .007$) and in the complete multivariable model with adjustments for patient age, gender, race, primary diagnosis category, Charlson score, MICU admission laboratory values, and CMI weight (OR = 0.74, 95% confidence interval: 0.62–0.88, $p = .003$). The OR for in-hospital mortality after the intervention was 0.80 (95% confidence interval: 0.68–0.93, $p = .005$) in the unadjusted model and 0.74 (95% confidence interval: 0.62–0.88, $p = .001$) in the complete explanatory model. A sensitivity analysis found these results robust (Appendix Table 2). The increase in MICU LOS remained significant after adjustment, and the lack of change in hospital LOS was consistent after adjustment. In subgroup analysis, these reductions were consistent in patients receiving renal replacement therapy, vasopressor therapy, mechanical ventilation, and with diagnoses of severe sepsis and septic shock (Appendix Table 3).

Whereas median MICU LOS increased from 2.4 (1.1–5.2) days to 2.7 (1.3–5.9) days ($p = .009$), there was no change in total hospital LOS 8.3 (4.1–17.0) days vs. 8.2 (4.0–16.8) days ($p = .851$), pre- or post-MICU LOS, or 28-day free ICU-free days (23.0 [0.0–26.0] vs. 23.0 [7.0–25.0[, $p = .224$). The proportion of patients receiving mechanical ventilation for one or more days was smaller postintervention, 49.2% vs. 43.6% ($p = .001$). There was a significant increase in median 28-day VFDs among the ever-ventilated, from 21 (interquartile range [IQR] 0–25) vs. 22 (IQR 0–26) ($p = .04$). Total per admission MICU variable costs increased from median $4071.10 (IQR from $1938.50 to $8988.40) to $6232.20 (IQR from $2999.00 to $13,969.20) ($p < .001$). The total per admission hospital variable costs increased from median $11,819.90 (IQR from $5631.20 to $25,027.60) to $13,178.90 (IQR from $6213.10 to $27,843.30) ($p = .005$). Rank sum testing showed no differences in the composite ranking of death and MICU LOS and reductions in composite ranking of death and hospital LOS (Appendix Table 4).

The intervention decreased sedation usage. Due to limitations in preintervention pharmacy data, these outcomes were evaluated by using a 10-month preintervention epoch compared with the 2-yr postintervention period. The characteristics of these patient groups are consistent with the 2-yr pre- and postperiod (Appendix Table 5). Identical 10-month intervals (from July 1, 2005 to April 18, 2006 and July 1, 2007 to April 18, 2008) were also

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compared to evaluate baseline characteristics and outcomes; these were similar to the 10-month pre- and 24-month postvalues (Appendix Table 6). There were substantial decreases in the mean daily doses of sedative medications for patients receiving these medications, as well as for total daily doses expressed as an average for all MICU patients (Table 4). These decreases were greatest for fentanyl and lorazepam, with no compensating increase in the use of propofol. The proportion of patients receiving midazolam increased but with reduced daily dosing after the intervention. The proportion of patients receiving haloperidol increased after the intervention.

We chose 365-day time periods pre-and postintervention to prevent results occurring from seasonal variation. Significant changes in MICU and hospital mortality and LOS were found comparing the periods of 4/19/05–4/18/06 and 9/5/06–9/4/07. We used 2-year epochs to increase statistical power and lessen the likelihood that any change detected was from year-to-year variation. The statistical comparison of 1-yr characteristics and outcomes are shown in Appendix Table 7.

DISCUSSION

In an already high functioning tertiary care ICU with a high-intensity staffing model and multiple other best practices, a reorganization of care was associated with substantial improvements in outcome, with 19% relative reduction in MICU mortality and a 16% relative reduction in hospital mortality, accompanied by a 1-day increase in 28-day VFDs in ever-ventilated patients. Additionally, there was a significant decrease in the use of sedative medications. This is the first study to find a survival benefit associated with improvements to an organizationally mature, Leapfrog-adherent MICU. Although these results may not be achievable by all ICUs at all points, they do suggest that the magnitude of feasible improvements in patient outcomes may be greater than is sometimes assumed.

Given the high volumes and high mortality associated with critical care services in the United States, our findings suggest that investing resources to bring select ICUs to the equivalent of full level I organization may have a profound impact. It has previously been estimated that approximately 53,000 lives would be saved yearly, if all urban hospitals implemented the ICU physician staffing recommendations of the Leapfrog Group (49, 50). Based on our findings, if these urban hospitals also adopted all the improvements seen in our MICU postintervention and had equivalent changes, an additional 10,400 lives would be saved each year. Among the 528,000 patients admitted yearly to urban ICUs already with intensivist staffing, there would be another 10,000 lives saved yearly. Thus, the adoption of level I organization in the United States could save a total of 20,000 additional lives each year in urban ICUs. While the Leapfrog guidelines provide a starting point for potential gains in survival, this suggests that further reductions in mortality may be possible with greater resources and further reorganization.

Critical care consumes substantial resources and its cost continues to increase (51, 52). With the realization of its expense, an impetus has emerged to improve care, which has resulted in guidelines and recommendations from a number of organizations (16, 25). There is often pessimism about the possibility of substantial improvements in outcomes in much of medical practice. However, our results provide evidence in the United States that accord with the results of the recent United Kingdom experience: That with increased resources expenditure–as evidenced by our greater postintervention MICU and total hospital variable costs–substantial improvements in patient outcomes are possible from the reorganization of critical care services. In the United Kingdom, the National Health Service increased spending on critical care by >40%, embarking on a multicomponent intervention consisting of a 35% increase in ICU beds, the creation of clinical networks, and adoption of clinical

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protocols. This resulted in an 11.3% decrease in adjusted ICU mortality and a 13.4% decrease in hospital mortality. These changes were deemed “highly cost-effective” by stringent U.K. standards (53).

Because the intervention in our MICU consisted of multiple components, it is difficult to elucidate the relative contribution of each discrete change. However, literature exists to suggest that each individual organizational change may have provided independent benefit. A high-intensity ICU staffing model consisting of 24 hr/day, 7 day/week intensivist staffing has been recommended (17) and has been associated with increased compliance with clinical protocols while reducing LOS (21), eliminating disparities arising from time of admission (54–59), and possibly reducing mortality (20, 60). The presence of a pharmacist in the ICU has been associated with reduced mortality, adverse events, infections, and drug charges (61–65). The effect of changing the respiratory therapist:patient ratio has not been previously evaluated; expert opinion suggests that the optimal ratio of patients to respiratory care practitioners is between 9:1 and 11:1 (66). This may facilitate increased use of patient-oriented, respiratory care-driven protocols (67–70). Overall, care by a multidisciplinary team has been found to be associated with reduced mortality (71). An around-the-clock physician likely maximizes the potential benefit of such a multidisciplinary team, especially one meeting the highest American College of Critical Care Medicine standards.

With the organizational changes, the MICU meets all guidelines set by the American College of Critical Care Medicine for the Society of Critical Care Medicine for the designation of a level I critical care setting (16). These include closed-model ICU staffed by intensivists, with the 24-hr coverage described as “ideal.” As per these guidelines, the multidisciplinary team of the MICU includes a nurse manager, trained critical care nursing, RT services, and critical care pharmacists. As a tertiary academic medical center, the availability of subspecialty consultants and diagnostic and laboratory resources also meet these guidelines. The reductions in mortality achieved through the full adoption of level I-equivalent critical care lends further weight to calls for regionalization of critical care in the United States (72–74). These recommendations are based on studies showing that outcomes are improved for critically ill patients in high-volume clinical centers (1, 3, 4, 75–77). Our findings suggest that increased resource allocation on designated level I centers will improve care and may facilitate a system that transfers critically ill patients, improving survival (73).

There are several limitations to consider. Because a randomized clinical trial was not feasible, a quasiexperimental design was utilized. Multiple control variables were used to adjust for potential changes in the patient population pre-and postintervention, with consistent results. However, the possibility of residual confounding or unobserved case mix changes, that our results may have occurred secondary to admitting patients who were not as ill, cannot be definitively excluded. Significant changes in patient diagnoses occurred after the intervention. Data were unavailable for the accurate calculation and use of common measures of acuity such as Acute Physiology and Chronic Health Evaluation (APACHE) scoring, although we used multiple, validated variables including Agency for Healthcare Research and Quality Clinical Classifications Software categories, CMI scores, and admission laboratory values. To assess the possible impact of residual confounding, a sensitivity analysis was performed, and it revealed that the reduction in MICU and hospital mortality was consistent in multiple models. We found an increase in MICU LOS after the intervention. While the etiology of this increase cannot be ascertained, the reduction in mortality may have resulted in patients who would have previously died with short LOS now surviving with commensurately longer LOS. Rank sum testing of the composite end point of MICU mortality and LOS pre- and postintervention were equivalent, suggesting that mortality was traded for LOS. In the rank sum testing of composite hospital mortality and

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LOS, all ranks were improved, consistent with the reductions in the component end points of mortality and hospital LOS (78).

In considering our outcomes, it should be noted that, as a single-center study, these results may not be generalizable to all ICUs. It is unlikely that un-targeted expenditures of additional resources in an ICU would result in patient improvements. Instead, reorganization and intensification may need to be customized to the particular ICU and hospital environment. Finally, it is essential to note that cost-effectiveness analyses (necessary from the distinct perspectives of the hospital, payers, and from society as a whole) are beyond the scope of the present manuscript but are essential to considering the policy implications of this finding.

CONCLUSIONS

Widespread variation in quality and outcomes is well documented in critical care. Our results demonstrate that even in a high functioning MICU already meeting national recommendations such as those of the Leapfrog group, targeted reorganization and investment has been associated with further, substantial improvements in patient outcomes. A multicomponent intervention including 24-hr intensivist staffing, the addition of a dedicated critical care pharmacist, increased RT staffing, and larger, more modern patient rooms was able to result in a 19% reduction in MICU mortality, a 16% reduction in hospital mortality, and a 5% increase in VFDs. Reductions in sedative use were also obtained. Hospital LOS did not change, although MICU LOS increased. By establishing an even higher standard of ICU staffing and care, it may be possible to effect even greater increases in survival than previously estimated, with potentially even greater overall cost effectiveness than previously estimated with traditional, high-intensity physician staffing (79).

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APPENDIX

Sensitivity Tests, Particularly for Residual Confounding

Residual confounding is a major challenge to the potential validity of the study. We have conducted several analyses to assess the possibility that changes other than the intervention might account for the changes in mortality we documented. Of particular concern is the possibility of changes in severity of illness of patients. Our results appear to be robust.

In Appendix Table 1, we show that there was no significant change in the Admission Source for patients between the pre- and postintervention period.

To further assess the plausible extent of residual confounding, recall that our basic adjusted model included age, gender, race, primary diagnosis (categorical variable), Charlson Score (a measure of comorbidity), and the CMI (a measure of expected resource intensity). The model with adjustment for laboratory value included the values on MICU admission of glucose, sodium, potassium, bicarbonate, and creatinine, as well as the white blood cell count and hematocrit; all laboratory values were made into categorical variables as per the APACHE II Acute Physiology score cutoffs.

We performed a sensitivity analysis by examining the absolute difference in mortality in unadjusted models and in models with progressively greater adjustment. These mortality differences were based on the predicted probabilities from the logistic regression model, implemented by using the STATA (STATA, College Station, TX) "adjust" command. (Identical results were obtained from predicted probabilities in SAS [SAS, Cary, NC].) If there was substantial confounding of the MICU reorganizations with severity of illness, we would expect to see smaller and smaller differences in mortality between pre- and postintervention periods as we included better and better risk adjustment. The results of this analysis are in Appendix Table 2.

In fact, the mortality difference was unchanged by adjustment for confounding. If anything, the association with hospital mortality becomes greater with more extensive controls.

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There are two possible interpretations for this. The first is that our association is relatively independent of confounding by severity of illness. The alternative interpretation is that there exists some form of severity of illness that was much more common before the MICU reorganization than afterward *and* that this form of severity of illness is uncorrelated with *all* the covariates included in the fully adjusted model. This second potential explanation is highly implausible. Our fully adjusted model includes primary diagnosis, comorbid disease, age, and other demographics–all key components of major severity of illness scores such as APACHE. Further, our results were further unchanged by including presentation laboratory values for sodium, potassium, white blood cell count, bicarbonate, glucose, creatinine, and hemoglobin. Although not a full APACHE score, our results were remarkably robust to inclusion of most of the domains of the APACHE score and therefore likely to be quite robust to unmeasured domains of severity of illness to the extent that those unmeasured domains are correlated with our many measured domains.

To extend this analysis further, we replicated our model in several pertinent subgroups, as documented in Appendix Table 3. Here we see that all point estimates show a consistent pattern of lower mortality after we frankly acknowledge there is some variation in the particular odds ratio for the association between the intervention and mortality. In some cases the SEs have increased such that the point estimate in a subgroup is not, on its own, statistically significant. (Note, of course, that in no case is the point estimate statistically significantly different from the overall group point estimate, either.) However, there is a clear consistent direction of effect.

Appendix Tables 4–7 document other sensitivity tests referred to in the main text.

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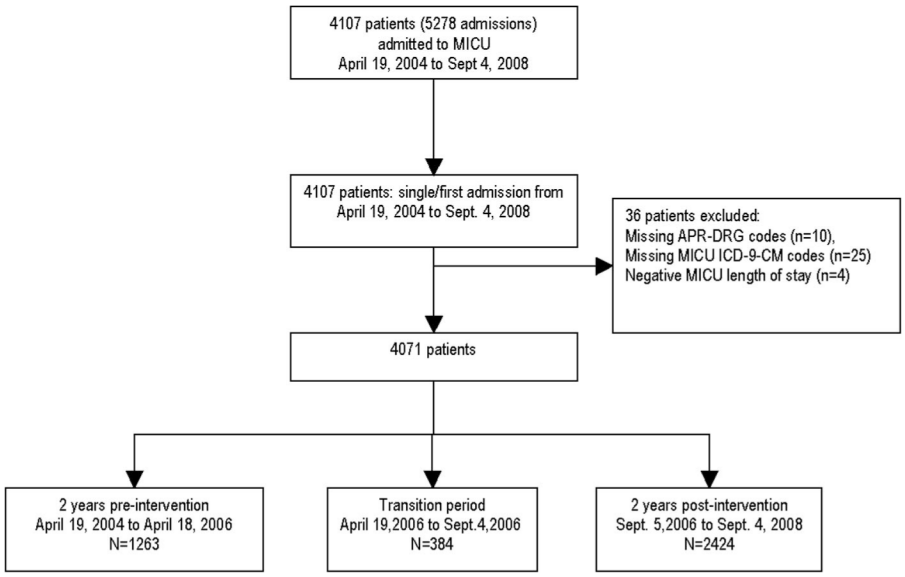

Figure 1.

Enrollment of study participants. *MICU*, medical intensive care unit; *APR-DRG*, All Patient Refined–Diagnosis-Related Groups; *ICD-9*, International Classification of Diseases, version 9.

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Table 1

American College of Critical Care Medicine guidelines for level I critical care centers

Staffing	Characteristics
Physician staffing	Board-certified intensivists
	24-hr in-house coverage (“ideally”)
	Intensivist intensive care unit director
Nursing staffing	Critical care nurses
	Qualified nurse manager
Respiratory care	24-hr availability
	Qualified respiratory therapists
Pharmacy services	Dedicated registered pharmacists
	Pharmacist should participate on rounds
Laboratory services	24-hr clinical laboratory
	Ability to perform rapid laboratory testing
Radiology services	24-hr radiologic services including radiography, interventional radiology, computerized tomography, ultrasound, magnetic resonance imaging
Consultant services	Full array physician subspecialists able to provide care within 30 mins

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Table 2

Characteristics and outcomes, 2-yr preintervention vs. 2-yr postintervention

Characteristic	Preintervention (n = 1263)	Postintervention (n = 2424)	p^a
Age, years	53.4 ± 15.9	54.4 ± 16.4	.066
Gender, male	563 (44.6%)	1100 (45.4%)	.642
Race, non-Caucasian	732 (58%)	1305 (53.8%)	.017
MICU Charlson score [median (IQR)]	2 (1–4)	2 (1–4)	.360
CMI score [median (IQR)]	2.0 (1.1–3.3)	2.0 (1.1–3.2)	.351
MICU primary diagnosis[b]			
Disease of the respiratory system	249 (19.7%)	417 (17.2%)	.017[c]
Disease of the circulatory system	184 (14.6%)	470 (19.4%)	
Disease of the digestive system	148 (11.7%)	281 (11.6%)	
Infectious and parasitic disease	183 (14.5%)	320 (13.2%)	
Injury and poisoning	127 (10.1%)	235 (9.7%)	
Neoplasm	105 (8.3%)	212 (8.8%)	
Other	267 (21.1%)	489 (20.2%)	
Outcomes			
MICU LOS [median days (IQR)]	2.4 (1.1–5.2)	2.7 (1.3–5.9)	.009
Hospital LOS (days) [median days (IQR)[	8.3 (4.1–17.0)	8.2 (4.0–16.8)	.851
Pre-MICU hospital LOS [median days (IQR)]	0.2 (0.0–1.2)	0.1 (0.0–0.9)	<.001
Post-MICU hospital LOS [median days (IQR)]	3.0 (0.0–8.1)	2.2 (0.0–7.0)	.003
MICU mortality	232 (18.4%)	361 (14.9%)	.006
Hospital mortality	326 (25.8%)	525 (21.7%)	.005
28-day ICU-free days [median (IQR)]	23.0 (0.0–26.0)	23.0 (7.0–25.0)	.224

IQR, interquartile range; MICU, medical intensive care unit; CMI, case mix index; LOS, length of stay. Preintervention period: 4/19/04–4/18/06; postintervention period: 9/5/06–9/4/08.

[a] *p* values were obtained from tests of comparison of proportions, two-sample Student's *t* test and nonparametric Mann-Whitney test;

[b] first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category;

[c] the probability of observing an association as strong or stronger than observed, assuming no difference in the distribution of MICU primary diagnoses pre- and postintervention.

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Table 3

Mortality odds ratios, 2-yr postintervention vs. 2-yr preintervention

Mortality	Mortality Odds Ratio (95% Confidence Interval)	p^a
Unadjusted MICU mortality	0.78 (0.65–0.93)	.007
MICU mortality adjusted for age, gender, race, diagnosis, Charlson score, CMI[b]	0.75 (0.62–0.90)	.002
MICU mortality adjusted for age, gender, race, diagnosis, Charlson score, admission labs[c]	0.74 (0.61–0.91)	.003
MICU mortality adjusted for age, gender, race, diagnosis, Charlson score, CMI, admission labs[d]	0.74 (0.61–0.91)	.003
Unadjusted hospital mortality	0.80 (0.68–0.93)	.005
Hospital mortality adjusted for age, gender, race, diagnosis, Charlson score, CMI[b]	0.76 (0.64–0.89)	.001
Hospital mortality adjusted for age, gender, race, diagnosis, Charlson score, admission labs[c]	0.75 (0.63–0.89)	.001
Hospital mortality adjusted for age, gender, race, diagnosis, Charlson score, CMI, admission labs[d]	0.74 (0.62–0.88)	.001

MICU, medical intensive care unit; CMI, case mix index; labs, laboratory values.

[a] *p* values were obtained from logistic regression models;

[b] adjusted for age (continuous), gender (dichotomous), race (categorical), MICU primary diagnosis (categorical, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category), Charlson scores (continuous), CMI weight (continuous);

[c] adjusted for age (continuous), gender (dichotomous); race (categorical); MICU primary diagnosis (categorical, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category); Charlson scores (continuous); sodium, potassium, white blood cell, bicarbonate (ordinal per Acute Physiology and Chronic Health Evaluation II scoring categories); glucose, creatinine (ordinal); hemoglobin (continuous);

[d] adjusted for age (continuous), gender (dichotomous), race (categorical), MICU primary diagnosis (categorical, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category), Charlson scores (continuous), CMI weight (continuous), labs as above.

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Table 4

Intravenous sedative usage, preintervention vs. postintervention

Daily Sedative Medicine Usage[a]	Preintervention	Postintervention	p[b]
Fentanyl, μg/day			
Per MICU patient	835.0 ± 1897.0	380.4 ± 1399.0	<.001
Per patient receiving fentanyl	1915.0 ± 2490.0	888.7 ± 2030.0	<.001
MICU patients receiving fentanyl, n (%)	208 (43.6%)	979 (42.8%)	.749
Propofol, mg/day			
Per MICU patient	61.2 ± 129.9	50.6 ± 163.2	.124
Per patient receiving propofol	226.2 ± 158.4	192.7 ± 272.2	.061
MICU patients receiving propofol, n (%)	129 (27.0%)	601 (26.3%)	.730
Midazolam, mg/day			
Per MICU patient	1.0 ± 7.6	0.9 ± 7.4	.870
Per patient receiving midazolam	3.7 ± 14.3	2.8 ± 12.5	.480
MICU patients receiving midazolam, n (%)	129 (27.0%)	779 (34.1%)	.003
Lorazepam, mg/day			
Per MICU patient	8.3 ± 25.7	2.2 ± 11.9	<.001
Per patient receiving lorazapam	17.9 ± 35.6	6.4 ± 19.5	<.001
MICU patients receiving lorazepam, n (%)	220 (46.1%)	802 (35.1%)	<.001
Haloperidol, mg/day			
Per MICU patient	0.5 ± 1.9	0.6 ± 2.4	.195
Per patient receiving haloperidol	4.1 ± 4.1	4.4 ± 5	.664
MICU patients receiving haloperidol, n (%)	57 (12.0%)	326 (14.3%)	.185

MICU, medical intensive care unit.

[a] Daily sedative usage shown in mean ± SD;

[b] *p* values calculated by comparing preintervention period (n = 477, 7/1/05–4/18/06) with postintervention period (n = 2287, 9/5/06–9/4/08) by using nonparametric Mann-Whitney test or chi-square test.

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Appendix Table 1

Admission source

Medical Intensive Care Unit Admission Source	Preintervention (n = 1263)	Postintervention (n = 2424)	p^a
Emergency department/emergency room	380 (30.1%)	789 (32.6%)	.484
Outside hospital transfer	285 (22.6%)	523 (21.6%)	
University of Maryland Medical Center floor transfer	369 (29.2%)	695 (28.7%)	
Unknown	229 (18.1%)	417 (17.2%)	

[a] *P* value obtained from test of comparison of proportions.

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Appendix Table 2

Sensitivity analysis of logistic regression model

	Between-Period Difference in:	
Variable	**Medical Intensive Care Unit Mortality**	**Hospital Mortality**
Unadjusted	3.5%	4.2%
Adjusted basic	3.7%	4.9%
Adjusted with labs	3.3%	4.8%

Performed by using the STATA (College Station, TX) “adjust” command.

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Appendix Table 3

Adjusted mortality odds ratios in subgroups

Variable	Mortality Odds Ratio (95% Confidence Interval)	p^a
Unadjusted MICU mortality	0.78 (0.65–0.93)	.007
MICU mortality adjusted for age, gender, race, diagnosis, Charlson score, case mix index[b]	0.75 (0.62–0.90)	.002
MICU mortality adjusted for age, gender, race, diagnosis, Charlson score, admission labs[c]	0.74 (0.61–0.91)	.003
MICU mortality adjusted for age, gender, race, diagnosis, Charlson score, case mix index, admission labs[d]	0.74 (0.61–0.91)	.003
Full model: Patients receiving renal replacement therapy	0.57 (0.36–0.91)	.019
Full model: Patients receiving vasopressors	0.81 (0.54–1.21)	.310
Full model: Patients undergoing mechanical ventilation	0.78 (0.61–0.99)	.040
Full model: Patients with severe sepsis or septic shock	0.89 (0.61–1.30)	.557

MICU, medical intensive care unit; labs, laboratory values.

[a] *p* values were obtained from logistic regression models;

[b] adjusted for age (continuous), gender (dichotomous), race (categorical), MICU primary diagnosis (categorical, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category), Charlson scores (continuous), CMI weight (continuous);

[c] adjusted for age (continuous), gender (dichotomous); race (categorical); MICU primary diagnosis (categorical, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category); Charlson scores (continuous); sodium, potassium, white blood cell, bicarbonate (ordinal per Acute Physiology and Chronic Health Evaluation II scoring categories); glucose, creatinine (ordinal); hemoglobin (continuous);

[d] adjusted for age (continuous), gender (dichotomous), race (categorical), MICU primary diagnosis (categorical, first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diagnostic category), Charlson scores (continuous), CMI weight (continuous), labs as above.

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Appendix Table 4

Rank testing using composite length of stay

Rank Test	4/19/04–4/18/06, n = 1263	9/5/06–9/4/08, n = 2424	p^a
Composite MICU LOS			
% deceased (LOS coded as 999)	232 (18.4)	361 (14.9)	
Minimal value	<0.1	<0.1	.965
25th percentile	1.4	1.5	
50th percentile	3.0	3.2	
75th percentile	10.2	9.6	
Maximal value	999.0	999.0	
Composite hospital LOS			
% deceased (LOS coded as 999)	326 (25.8)	525 (21.7)	
Minimal value	0.1	<0.1	.014
25th percentile	5.2	5.0	
50th percentile	13.1	11.7	
75th percentile	999.0	999.0	
Maximal value	999.0	999.0	

MICU, medical intensive care unit; LOS, length of stay.

[a] *p* values obtained from two samples Van der Waerden test comparing a 2-yr epoch preintervention with a 2-yr epoch postintervention. In surviving patients, composite length of stay = length of stay; in deceased patients, composite LOS = 999.0 (highest rank).

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Appendix Table 5

Ten-month preintervention vs. 2-yr postintervention

Characteristic	7/1/05–4/18/06 (n = 477)	9/5/06–9/4/08 (n = 2287)	p^a
Age, years	53 ± 15.6	54.7 ± 16.4	.043
Gender, male	212 (44.4)	1032 (45.1)	.786
Race, non-Caucasian	277 (58.1)	1235 (54)	.104
MICU Charlson score, 0–20	2.8 ± 2.7	2.8 ± 2.6	.890
Case mix index score	3.3 ± 4	3.1 ± 3.8	.426
MICU primary diagnosis[b]			
Disease of the respiratory system	100 (21)	393 (17.2)	.019[c]
Disease of the circulatory system	59 (12.4)	426 (18.6)	
Disease of the digestive system	52 (10.9)	269 (11.8)	
Infectious and parasitic disease	66 (13.8)	313 (13.7)	
Injury and poisoning	44 (9.2)	224 (9.8)	
Neoplasm	42 (8.8)	204 (8.9)	
Other	114 (23.9)	458 (20)	
Percentage of patients billed for ventilation	257 (53.9)	1586 (69.4)	<.001
Outcomes			
MICU stay, days	4.7 ± 6.1	5.5 ± 8	.012
Hospital stay, days	13.2 ± 15.2	13.8 ± 16.4	.395
Pre-MICU hospital stay, days	2.2 ± 6.2	2.4 ± 6.9	.660
Post-MICU hospital stay, days	6.3 ± 11.1	6 ± 11	.622
MICU mortality, deceased	100 (21)	360 (15.7)	.005
Hospital mortality, deceased	127 (26.6)	513 (22.4)	.048
28-day intensive care unit-free days	16.7 ± 10.7	17 ± 10.4	.610

MICU, medical intensive care unit; CMI, case mix index.

[a] *p* values were obtained from tests of comparison of proportions/two-sample Student's *t* test;

[b] first-level Agency for Healthcare Research and Quality Clinical Classifications Software 2010 diag nostic category;

[c] the probability of observing an association as strong or stronger than observed, assuming no difference in the distribution of MICU primary diagnoses pre- and postintervention.

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Appendix Table 6

Matched months, 10-month preintervention vs. 10-month postintervention

Characteristic	7/1/05–4/18/06 (n = 477)	7/1/07–4/18/08 (n = 880)	Before vs. After p^a
Age, years	53 ± 15.6	54.8 ± 16.7	.058
Gender, male	212 (44.4)	401 (45.6)	.691
Race, non-Caucasian	277 (58.1)	486 (55.2)	.313
MICU Charlson score, 0–20	2.8 ± 2.7	2.8 ± 2.7	.730
Case mix index score	3.3 ± 4	3 ± 3.6	.191
Primary diagnosis (International Classification of Diseases-9-Clinical Modifications Clinical Classifications Software level I)			
Disease of the respiratory system	100 (21)	156 (17.7)	.196
Disease of the circulatory system	59 (12.4)	158 (18)	
Disease of the digestive system	52 (10.9)	94 (10.7)	
Infectious and parasitic disease	66 (13.8)	119 (13.5)	
Injury and poisoning	44 (9.2)	81 (9.2)	
Neoplasms	42 (8.8)	82 (9.3)	
Other	114 (23.9)	190 (21.6)	
Percentage of patients billed for ventilation	257 (53.9)	859 (97.6)	<.001
Outcomes			
MICU stay, days	4.7 ± 6.1	5.5 ± 7.2	.044
Hospital stay, days	13.2 ± 15.2	13.8 ± 16.5	.460
Pre-MICU hospital stay, days	2.2 ± 6.2	2.6 ± 8.2	.349
Post-MICU hospital stay, days	6.3 ± 11.1	5.8 ± 10.5	.440
MICU mortality, deceased	100 (21)	153 (17.4)	.106
Hospital mortality, deceased	127 (26.6)	208 (23.6)	.223
Intensive care unit-free days	16.7 ± 10.7	16.9 ± 10.3	.857

MICU, medical intensive care unit.

[a] p values were calculated comparing a 10-month epoch before move (7/1/05–4/18/06, n = 477) vs. a 10-month epoch after move (7/1/07–4/18/08, n = 880) by chi-square for categorical variables, two-sample Student's t test for continuous variables (means).

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Appendix Table 7

One-yr epochs pre- and postintervention, transition period

Characteristics	4/19/04–4/18/05 (n = 635)	4/19/05–4/18/06 (n = 628)	4/19/06–9/4/06 (n = 384)	9/5/06–9/4/07 (n = 1317)	9/5/07–9/4/08 (n = 1107)	p^a
Age, years	53.8 ± 16	53 ± 15.7	54.2 ± 15.8	54.7 ± 16.3	54.1 ± 16.5	.030
Gender, male	286 (45)	277 (44.1)	188 (49)	619 (47)	481 (43.4)	.231
Race, non-Caucasian	376 (59.2)	356 (56.7)	213 (55.5)	703 (53.4)	602 (54.4)	.171
MICU Charlson score, 0–20	2.7 ± 2.7	2.8 ± 2.6	2.8 ± 2.6	2.8 ± 2.6	2.8 ± 2.6	.906
Case mix index weight, fiscal year 2009	2.9 ± 3.4	3.2 ± 4	2.8 ± 3.4	3 ± 3.6	3.3 ± 4.1	.187
Primary diagnosis (International Classification of Diseases-9-Clinical Modification)						
Respiratory disease	124 (19.5)	125 (19.9)	58 (15.1)	220 (16.7)	197 (17.8)	.013
Infectious and parasitic disease	94 (14.8)	89 (14.2)	36 (9.4)	171 (12.9)	149 (13.5)	
Circulatory disease	101 (15.9)	83 (13.2)	58 (15.1)	266 (20.2)	204 (18.4)	
Injury and poisoning	64 (10)	63 (10)	40 (10.4)	135 (10.3)	100 (9)	
Neoplasm	54 (8.5)	51 (8.1)	32 (8.3)	104 (7.9)	108 (9.8)	
Digestive disease	76 (12)	72 (11.5)	37 (9.6)	154 (11.7)	127 (11.5)	
Other	122 (19.2)	145 (23.1)	123 (32)	267 (20.3)	222 (20.1)	
MICU stay, days	2.5 (1.1–5.5)	2.3 (1.1–5.1)	2.3 (1–5)	2.7 (1.3–5.6)	2.8 (1.2–6.1)	.051
Hospital stay, days	8.4 (4.1–16.8)	8.2 (4–17.1)	7.5 (3.7–15.5)	7.9 (3.8–16.3)	8.7 (4.1–17.7)	.356
Pre-MICU hospital stay, days	0.2 (0–1.1)	0.2 (0–1.3)	0.1 (0–0.8)	0.1 (0–0.6)	0.1 (0–1.4)	<.001
Post-MICU hospital stay, days	3 (0–8)	2.9 (0–8.6)	2.1 (0–6.4)	2.2 (0–6.9)	2.1 (0–7.5)	.016
MICU mortality, deceased	114 (18)	118 (18.8)	55 (14.3)	185 (14.1)	176 (15.9)	.007
Hospital mortality, deceased	170 (26.8)	156 (24.8)	76 (19.8)	273 (20.7)	252 (22.8)	.041
28-day intensive care unit-free days [median (interquartile range)]	23 (0–26)	23 (3–26)	24 (15.5–26)	23 (11–25)	23 (5–25)	.758

MICU, medical intensive care unit.

[a] *p* values for comparison of 4/19/05–4/18/06 and 9/5/06–9/4/07.