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Physician Staffing Patterns and Clinical Outcomes in Critically Ill Patients

A Systematic Review

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APPROXIMATELY 1% OF THE US gross domestic product is consumed in the care of intensive care unit (ICU) patients.¹ Despite this considerable investment of resources, there is wide variation in ICU organization,^{2,3} and studies have suggested that differences in ICU organization may affect patient outcome. For example, staffing ICUs with critical care physicians (intensivists) may improve clinical outcomes.⁴ A conceptual model that explains this finding is that physicians who have the skills to treat critically ill patients and who are immediately available to detect and treat problems may prevent or attenuate morbidity and mortality.² Staffing ICUs with intensivists may also decrease resource use because these physicians may be better at reducing inappropriate ICU admissions, preventing complications that prolong length of stay (LOS), and recognizing opportunities for prompt discharge.²

Intensive care unit staffing is typical of an organizational issue in health care in that, despite its potential importance in clinical and economic outcomes, it is not studied by using randomized trials. For example, the widely

Context Intensive care unit (ICU) physician staffing varies widely, and its association with patient outcomes remains unclear.

Objective To evaluate the association between ICU physician staffing and patient outcomes.

Data Sources We searched MEDLINE (January 1, 1965, through September 30, 2001) for the following medical subject heading (MeSH) terms: *intensive care units, ICU, health resources/utilization, hospitalization, medical staff, hospital organization and administration, personnel staffing and scheduling, length of stay, and LOS*. We also used the following text words: *staffing, intensivist, critical, care, and specialist*. To identify observational studies, we added the MeSH terms *case-control study* and *retrospective study*. Although we searched for non-English-language citations, we reviewed only English-language articles. We also searched EMBASE, HealthStar (Health Services, Technology, Administration, and Research), and HSRPROJ (Health Services Research Projects in Progress) via Internet Grateful Med and The Cochrane Library and hand searched abstract proceedings from intensive care national scientific meetings (January 1, 1994, through December 31, 2001).

Study Selection We selected randomized and observational controlled trials of critically ill adults or children. Studies examined ICU attending physician staffing strategies and the outcomes of hospital and ICU mortality and length of stay (LOS). Studies were selected and critiqued by 2 reviewers. We reviewed 2590 abstracts and identified 26 relevant observational studies (of which 1 included 2 comparisons), resulting in 27 comparisons of alternative staffing strategies. Twenty studies focused on a single ICU.

Data Synthesis We grouped ICU physician staffing into low-intensity (no intensivist or elective intensivist consultation) or high-intensity (mandatory intensivist consultation or closed ICU [all care directed by intensivist]) groups. High-intensity staffing was associated with lower hospital mortality in 16 of 17 studies (94%) and with a pooled estimate of the relative risk for hospital mortality of 0.71 (95% confidence interval [CI], 0.62-0.82). High-intensity staffing was associated with a lower ICU mortality in 14 of 15 studies (93%) and with a pooled estimate of the relative risk for ICU mortality of 0.61 (95% CI, 0.50-0.75). High-intensity staffing reduced hospital LOS in 10 of 13 studies and reduced ICU LOS in 14 of 18 studies without case-mix adjustment. High-intensity staffing was associated with reduced hospital LOS in 2 of 4 studies and ICU LOS in both studies that adjusted for case mix. No study found increased LOS with high-intensity staffing after case-mix adjustment.

Conclusions High-intensity vs low-intensity ICU physician staffing is associated with reduced hospital and ICU mortality and hospital and ICU LOS.

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held belief that outcomes are better after surgery performed by experienced surgeons or hospitals is based solely on observational data.⁵ Practical and ethical reasons exist to explain why such organizational characteristics are not subjected to randomized trials. Yet, as changes occur in the way health care is organized, financed, and delivered, it will be important to understand the impact of organizational characteristics, such as ICU physician and nurse staffing, on patient outcomes through systematic reviews.⁶ To inform health policy, we will need to synthesize evidence that is predominantly observational. Accordingly, the goal of this systematic review was to examine the effect of ICU physician staffing on hospital and ICU mortality and LOS.

METHODS

Study Selection Criteria

We sought to identify and review all studies that met the following criteria: randomized or observational controlled trials of critically ill adults or children, ICU physician staffing strategies, hospital and ICU mortality, and LOS.

Citation Search Strategy

To identify literature in electronic databases, we searched MEDLINE from January 1, 1965, through September 30, 2001, by using the following medical subject heading (MeSH) terms: *intensive care units, ICU, health resources/utilization, hospitalization, medical staff, hospital organization and administration, personnel staffing and scheduling, length of stay, and LOS*. We used the following text words: *staffing, intensivist, critical, care, and specialist*. We used the search strategy for retrieval of controlled clinical trials proposed by Robinson and Dickersin.⁷ To identify observational studies, we added the MeSH terms *case-control study* and *retrospective study*.

We also searched EMBASE, Health-Star (Health Services, Technology, Administration, and Research), and HSRPROJ (Health Services Research Projects in Progress) via Internet Grateful Med and The Cochrane Library (1998, issue 3), which contains the

CENTRAL Database of Controlled Trials, the Database of Abstracts of Review Effectiveness, and the Cochrane Database of Systematic Reviews.

In addition, we used the *related articles* feature of PubMed, which identifies related articles by using a hierarchical search engine that is not solely based on MeSH headings. This search was completed with articles selected by 2 of the authors (P.J.P. and D.C.A.).⁸⁻¹² Although we searched for non-English-language citations, subsequent article review involved only English-language publications. To identify studies published in abstract form only, we hand-searched the abstract proceedings from the annual scientific assemblies of the Society of Critical Care Medicine, the American College of Chest Physicians, and the American Thoracic Society from January 1, 1994, through December 31, 2001.

Study Selection

After all citations based on our search strategy were identified, 2 of the authors (P.J.P. and D.C.A.) independently reviewed each abstract to confirm eligibility. If an abstract was selected as eligible, the same authors independently reviewed the respective article, if available, to confirm that it met inclusion criteria. Abstracts from meeting proceedings were included if the data were not published as peer-reviewed articles. To resolve discrepancies, the 2 reviewers either had to reach consensus, or use a third reviewer (T.D.).

Data Extraction

Using a data collection form, we extracted data from the studies to describe patient characteristics, study methods, and study findings. We also abstracted quantitative data regarding the intervention, cointerventions, study design and duration, unit of analysis, risk adjustment, degree of follow-up, adjustment of historical trends, and type of ICU. All data were abstracted independently by each of the 2 primary reviewers and verified for accuracy by the third reviewer, again with discussion used to resolve differences among re-

viewers. All reviewers were intensivists with formal training in clinical epidemiology and biostatistics. We did not mask the reviewers to author, institution, or journal because such masking reportedly makes little difference to the results of a systematic review.¹³

Data Synthesis and Analysis

We measured the percentage of agreement before discussion among reviewers in study selection, study design, and data abstraction. For data synthesis, we constructed evidence tables to present data separately for the 4 main outcome variables: hospital mortality, ICU mortality, hospital LOS, and ICU LOS. Because of wide variation in the methods used to evaluate hospital costs, we did not include cost as an outcome.

We classified the study design as a randomized clinical trial, cohort study (prospective, retrospective, or historical control), case-control study, or outcomes study (cross-sectional). We classified the method of risk adjustment as follows: validated physiologic method (discrimination and calibration of the model previously reported), selected clinical data (discrimination and calibration of the model not reported), and no risk adjustment.

Because ICU physician staffing varied widely among studies in the control and intervention groups, we initially classified ICU physician staffing as follows: (1) closed ICU (the intensivist is the patient's primary attending physician), (2) mandatory critical care consultation (the intensivist is not the patient's primary attending physician, but every patient admitted to the ICU receives a critical care consultation), (3) elective critical care consultation (the intensivist is involved in the care of the patient only when the attending physician requests a consultation), and (4) no critical care physician (intensivists were unavailable). Because it is difficult to distinguish between a closed ICU and a mandatory critical care consultation, and because in several studies we were not able to do so, we further grouped ICU physician staffing into high intensity (mandatory intensivist consultation or closed ICU) or

Table 1. Characteristics of Reviewed Studies Concerning ICU Physician Staffing and Outcomes*

Source	Population	Study Design	ICUs Studied, No.	High Intensity†		Low Intensity†		Outcome Measures
				Patients, No.	Physician Staffing	Patients, No.	Physician Staffing	
Pronovost et al, ² 1999	Surgical (AAA repair)	Outcomes CS	39	2036	MC	472	EC	Hospital mortality, hospital and ICU LOS, rates of complications
Brown and Sullivan, ⁸ 1989	Medical or surgical	Cohort HC	1	216	CU	223	NI	Hospital and ICU mortality
Baldock et al, ⁹ 2001	Medical or surgical	Cohort HC	1	330	CU	295	EC	Hospital mortality
Kuo et al, ¹⁰ 2000	Surgical	Cohort HC	1	491	CU or MC	176	NI or EC	ICU mortality, ICU LOS
Multz et al, ¹¹ 1998 (retrospective)	Medical	Cohort HC	1	154	CU	152	EC	Hospital mortality, hospital and ICU LOS, non-ICU LOS, procedure use, duration of MV
Multz et al, ¹¹ 1998 (prospective)	Medical	Cohort CC	2	185	CU	95	EC	Hospital mortality, hospital and ICU LOS, non-ICU LOS, procedure use, duration of MV
Reynolds et al, ¹² 1988	Medical (sepsis)	Cohort HC	1	112	CU or MC	100	NI	Hospital mortality, hospital and ICU LOS, hospital costs, discharge status, LOS by survivorship, No. of interventions, No. of consultations
Al-Asadi et al, ²⁷ 1996‡	Medical	Cohort HC and CC	2	1005	CU	1404	EC	ICU mortality
Carson et al, ²⁸ 1996	Medical	Cohort HC	1	121	CU	124	MC	Hospital mortality, hospital and ICU LOS, hospital costs, duration of MV, subgroup analysis, patient and family perceptions
Ghorra et al, ²⁹ 1999	Surgical	Cohort HC	1	149	CU	125	EC	ICU mortality, ICU LOS, 30-day mortality, complications with procedure use
Li et al, ³⁰ 1984	Medical or surgical	Cohort HC	1	517	CU	480	NI	Hospital mortality, ICU LOS, 1-year mortality, tests, monitoring, post-ICU LOS
Jacobs et al, ³¹ 1998‡	Surgical	Cohort HC	1	1108	CU	1051	EC or NI	ICU bed use efficiency, ICU readmission
Manthous et al, ³² 1997	Medical	Cohort HC	1	930	EC	459	NI	Hospital and ICU mortality, hospital and ICU LOS
Marini et al, ³³ 1995‡	Surgical	Cohort HC	1	112	CU	65	EC	ICU mortality, ICU LOS, duration of MV, No. of consultations
Pollack et al, ³⁴ 1988	Pediatric	Cohort HC	1	113	MC	149	NI	ICU mortality, ICU LOS, admission criteria, difference of case mix, TISS
Reich et al, ³⁵ 1998‡	Medical or surgical	Cohort HC	1	830	CU	826	NI	ICU mortality, PA catheter use, No. of patients requiring MV, nursing hours per patient
Tai et al, ³⁶ 1998	Medical	Cohort HC	1	127	CU	112	NI	ICU mortality, hospital and ICU LOS, PA catheter use, arterial catheter use, readmissions
Pollack et al, ³⁷ 1994	Pediatric	Outcomes CS	16	2606	MC	2809	NI	Hospital and ICU mortality
DiCosmo, ³⁸ 1999‡	Medical	Cohort HC	1	1292	MC	1667	EC	ICU mortality, ICU LOS, LOS with MV, MV mortality
Dimick et al, ³⁹ 2001	Surgical (esophagectomy)	Outcomes CS	35	182	MC	169	EC	Hospital mortality, hospital LOS, hospital costs, postoperative complications

(continued)

Table 1. Characteristics of Reviewed Studies Concerning ICU Physician Staffing and Outcomes* (cont)

Source	Population	Study Design	ICUs Studied, No.	High Intensity†		Low Intensity†		Outcome Measures
				Patients, No.	Physician Staffing	Patients, No.	Physician Staffing	
Dimick et al, ⁴⁰ 2000‡	Surgical (hepatectomy)	Outcomes CS	NR	276	MC	275	EC	Hospital mortality, hospital LOS, hospital costs
Rosenfeld et al, ⁴¹ 2000	Surgical	Cohort HC	1	201	MC§	225	EC	Hospital and ICU mortality, hospital and ICU LOS, complications, ICU and hospital costs
Diringer and Edwards, ⁴² 2001	Neurological (intracerebral hemorrhage)	Outcomes CS	42	266	CU	772	EC	Hospital mortality, hospital and ICU LOS
Goh et al, ⁴³ 2001	Pediatric	Cohort HC	1	355	CU	264	EC	ICU mortality, ICU LOS
Blunt and Burchett, ⁴⁴ 2000	Medical	Cohort HC	1	393	CU	328	EC	Hospital mortality, hospital and ICU LOS
Topeli, ⁴⁵ 2000‡	Medical	Cohort HC	1	149	CU	200	NI	ICU mortality, MV mortality
Hanson et al, ⁴⁶ 1999	Surgical	Cohort CC	1	100	MC	100	NI	Hospital mortality, hospital and ICU LOS, hospital costs

*All studies were observational and control groups varied. ICU indicates intensive care unit; AAA, abdominal aortic surgery; CS, cross-sectional with concurrent control; MC, mandatory critical care consultation; EC, elective critical care consultation; LOS, length of stay; HC, historical control; CU, closed unit; NI, no intensivist; MV, mechanical ventilatory support; CC, concurrent control; TISS, Therapeutic Intervention Scoring System; PA catheter, pulmonary artery (Swan-Ganz) catheter; and NR, not reported.

†High-intensity physician staffing is either mandatory intensivist consultation or closed ICU. Low-intensity physician staffing is either no intensivist or elective intensivist consultation.

‡An abstract was reviewed; in all other instances, full journal articles were considered.

§Intervention was remote ICU management (telemedicine) using videoconferencing.

low intensity (no intensivist or elective intensivist consultation).

Evaluation of Study Quality

We elected to evaluate study quality as the risk of bias caused by temporal trends, confounding, and incomplete follow-up. We classified the risk of bias caused by temporal trends as low if the study duration was shorter than 2 years, medium if 2 through 4 years, and high if longer than 4 years. We classified the risk of bias from confounding as low if the authors used a validated physiologic method of risk adjustment, medium if the authors used selected clinical data, and high if the authors used no risk adjustment. We classified the risk of bias from incomplete follow-up as low if it was 90% to 100% complete; medium for 80% to 89% complete; and high for less than 80% complete.

Data Analysis

Because the studies varied markedly in design, risk adjustment method, and ICU physician staffing in the control and intervention groups, we performed a qualitative and quantitative assessment of heterogeneity among trials.

Because we considered the qualitative heterogeneity among studies to be significant, we were reluctant to perform a quantitative synthesis of study results.¹⁴ Nevertheless, we used the test for quantitative heterogeneity.^{15,16} We present a random-effects, summary relative risk (RR) by using the methods of DerSimonian.¹⁷ When the data were available, we summarized mortality data from each study with RRs, odds ratios (ORs), and estimated 95% confidence intervals (CIs) for the ORs by using Woolf's method.¹⁸ We summarized LOS data as a relative reduction. We evaluated for publication bias with a funnel plot. All statistical calculations were performed with STATA 7.0 statistical software (STATA Corp, College Station, Tex). When possible, we reported unadjusted and adjusted outcomes for baseline severity of illness. When absolute rates of hospital mortality were unavailable, we reported the observed-expected mortality rate, and when the SD of LOS data were unavailable, we assumed it to be equal to the mean.² We used mean rather than median LOS because few studies reported medians. Results were considered significant at $P < .05$.

RESULTS

Study Selection and Characteristics

We identified 3544 citations from the electronic search, of which 660 were duplicates and 294 were unavailable in English and were excluded. We also identified 13 citations from hand searching meeting proceedings. Of the 2590 abstracts reviewed, we rejected 2556 (99%) because the intervention was not ICU physician staffing or because the published abstract was superseded by the subsequent article. We rejected an additional 8 abstracts after reviewing and discussing the corresponding article because the intervention was not ICU physician staffing or because the reviewers were not able to determine the type of ICU physician staffing.¹⁹⁻²⁶ Twenty-six studies^{2,8-12,27-46} met selection criteria (19 articles and 7 published abstracts). The reviewers had 99% crude agreement in the selection of eligible abstracts and 96% crude agreement in the selection of eligible articles (TABLE 1). FIGURE 1⁴⁷ presents the study search strategy (QUOROM: Quality of Reporting of Meta-analyses).

Twenty studies (77%) were from North America,^a 3 (12%) were from Eu-

^aReferences 2, 8, 11, 12, 27-29, 30-35, 37-42, 46.

rope,^{9,44,45} and 3 (12%) were from Asia.^{10,36,43} Eleven (42%) were from academic medical centers,^b 6 (23%) were from community teaching hospitals,^{11,27,32,33,36,41} 4 (15%) were from non-teaching community hospitals,^{30,35,38,44} and 5 (19%) included a variety of hospitals in Maryland^{2,39,40}. One article included a prospective and retrospective control arm.¹¹ Because our goal was to describe the available literature, we treated this article as 2 studies and thus had 27 studies for qualitative synthesis (Table 1).

Table 1 summarizes important aspects of these 27 studies, which included ICU patients treated between 1979 and 2000. Study populations included medical patients in 11 studies (41%),^c surgical patients in 9 (33%),^{2,10,29,31,33,39-41,46} mixed medical and surgical patients in 4 (15%),^{8,9,30,35} and pediatric patients in 3 (11%).^{34,37,43} Sample sizes varied from 177 to 5415 patients, with a mean sample size of 1001 patients (SD, 1190) and a median sample size of 551 patients (25%-75% interquartile range, 277-1213).

Study Design

All of the studies used an observational design (Table 1). Twenty-two were cohort studies, with 19 using historical controls (before-and-after design),^d 2 using concurrent controls,^{11,46} and 1 using both.²⁷ Five studies were cross-sectional with concurrent controls.^{2,37,39,40,42} In one study, the ICU physician staffing in the intervention group was via remote videoconferencing.⁴¹ Twenty of the studies evaluated a single ICU,^e 2 evaluated 2 ICUs,^{11,27} 1 evaluated 16 ICUs,³⁷ 1 evaluated 35 ICUs,³⁹ 1 evaluated 39 ICUs,² 1 evaluated 42 ICUs,⁴² and 1 did not report the number of ICUs evaluated.⁴⁰

ICU Physician Staffing

Twenty-five studies compared high- with low-intensity ICU physician staffing. Of

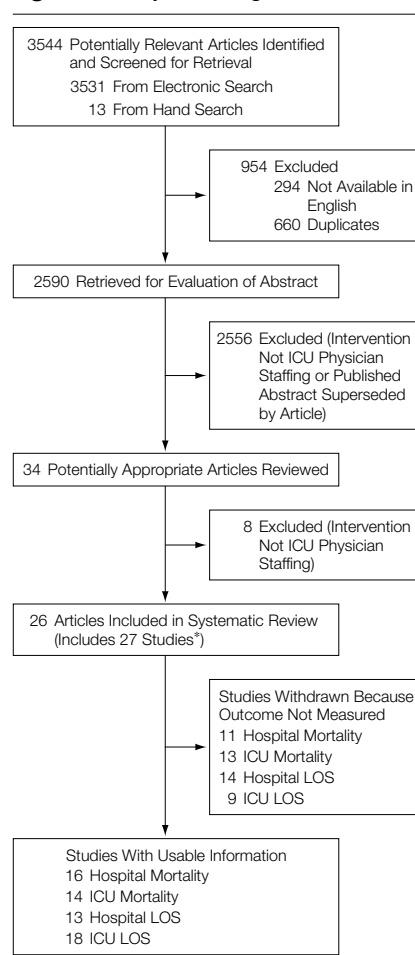
the remaining 2, one compared a closed ICU with a mandatory consultation²⁸ and the other compared elective consultation with no intensivist involved.³² Of the 25 studies comparing high- with low-intensity staffing, 9 compared a closed ICU (intervention group) with elective consultation (control group),^{9,11,27,29,33,42-44} 3 compared mandatory consultation (intervention) with no intensivist (control),^{34,37,46} 5 compared mandatory consultation (intervention) with elective consultation (control group),^{2,38-41} and 5 compared closed ICU (intervention) with no intensivist (control).^{8,30,35,36,45} In 2 studies, we could not differentiate between a closed ICU and a mandatory consultation,^{10,12} and in 2 studies^{10,31} we could not differentiate between an elective consultation and no intensivist.

Quality Characteristics

The quality characteristics of the studies are listed in TABLE 2. Fifteen of the 24 studies that reported the study period had low risk of bias from temporal trends, whereas 8 studies had medium risk and 1 had high risk. All 27 studies had complete follow-up and thus a low risk of bias from incomplete follow-up. No study followed up patients after hospital discharge.

Twenty-one of 27 studies had low risk of bias from confounding, whereas 6 studies had medium risk. All studies reported some form of risk adjustment. Twenty-one studies used a validated physiologic method (15 used the Acute Physiology and Chronic Health Evaluation Score [APACHE] only,^{48,49} 2 used the Mortality Prediction Model,⁵⁰ 2 used the Pediatric Risk of Mortality Score,^{51,52} 1 used the Physiologic Severity Index [PSI],⁵³ and 1 reported both APACHE II and the Glasgow Coma Scale⁵⁴). Six studies used selected clinical data (the first used nursing hours per patient,³⁵ a second used age, reason for admission, and mental status,³⁰ a third used a customized case-mix index and patient acuity measured by percentage of patients requiring mechanical ventilatory support,³⁸ and 3 others used discharge data in a regression model to adjust for patient demographics, severity of illness,

Figure 1. Study Flow Diagram



ICU indicates intensive care unit; LOS, length of stay. The asterisk indicates that the article by Multz et al¹¹ had 2 comparisons (retrospective and prospective).

comorbid disease, and hospital and surgeon volume^{2,39,40}) (Table 1).

Eleven studies reported differences in severity of illness between the high- and low-intensity groups. In 4 studies,^{28,31,45,46} the high-intensity group compared with the low-intensity group had significantly higher APACHE scores, suggesting higher baseline severity of illness. Three studies reported higher severity in the low-intensity group by using different severity instruments.⁴²⁻⁴⁴ Two studies reported higher baseline severity in the high-intensity group by using the distribution of the PSI score³⁴ and APACHE II score.¹⁰ Another study reported higher ICU nursing hours per day and suggested that this represented

^bReferences 8-10, 12, 28, 29, 31, 34, 43, 45, 46.

^cReferences 11, 12, 27, 28, 32, 36, 38, 42, 44, 45.

^dReferences 8-12, 28, 29, 30-36, 38, 41, 43-45.

^eReferences 8-12, 28, 29, 30-36, 38, 41, 43-46.

higher severity in the high-intensity physician staffing group.³⁵ The author of the study,³⁸ which used patient acuity and case-mix index, also suggested greater severity in the arm with the high-intensity physician staffing. There was no evidence of publication bias on a funnel plot of hospital mortality (FIGURE 2).

Impact of High- vs Low-Intensity ICU Physician Staffing

Hospital Mortality. Seventeen studies (63%) reported hospital mortality according to ICU physician staffing as a pri-

mary outcome measure (TABLE 3). The hospital mortality rate ranged from 6% to 74% in the low-intensity staffing group and from 1% to 57% in the high-intensity staffing group (Table 3). Overall, 16 (94%) of the 17 studies showed a decrease in hospital mortality rate for ICU patients with high-intensity physician staffing; in the one study that showed increased mortality with high-intensity physician staffing, the increase was not statistically significant.²⁸ In 10 (67%) of 15 studies^{2,8,9,12,32,39-42,44} that reported unadjusted mortality and 9

(64%) of 14 studies^f that reported adjusted mortality, the decrease was statistically significant (Table 3). No study reported a statistically significant increase in hospital mortality with high-intensity ICU physician staffing. The random-effects pooled estimate of the unadjusted RR for high-intensity vs low-intensity staffing is 0.71 (95% CI, 0.62-0.82) (FIGURE 3A).

ICU Mortality. Fifteen studies (56%) evaluated the impact of ICU physician

^fReferences 2, 8, 12, 30, 32, 37, 40, 41, 44.

Table 2. Quality Characteristics of Reviewed Studies*

Source	Study Period	Risk for Bias Due to Temporal Trends	Adjustment for Confounding Variables	Risk for Bias Due to Confounding Variables
Pronovost et al, ² 1999	1994-1996	Low	†	Medium
Brown and Sullivan, ⁸ 1989	1984-1986	Low	APACHE II	Low
Baldock et al, ⁹ 2001	1995-1998	Medium	APACHE II	Low
Kuo et al, ¹⁰ 2000	1986-1996	High	APACHE II	Low
Multz et al, ¹¹ 1998 (retrospective)	1992-1993	Low	MPM	Low
Multz et al, ¹¹ 1998 (prospective)	1992-1993	Low	MPM	Low
Reynolds et al, ¹² 1988	1982-1984	Low	APACHE II	Low
Al-Asadi et al, ²⁷ 1996‡	1991-1995	Medium	APACHE II	Low
Carson et al, ²⁸ 1996	1993-1994	Low	APACHE II§	Low
Ghorra et al, ²⁹ 1999	1995-1996	Low	APACHE III	Low
Li et al, ³⁰ 1984	1979-1981	Low	Age, reason for admission, mental status	Medium
Jacobs et al, ³¹ 1998‡	1995-1997	Low	APACHE III§	Low
Manthous et al, ³² 1997	1992-1994	Low	APACHE II	Low
Marini et al, ³³ 1995‡	1993-1994	Low	APACHE II	Low
Pollack et al, ³⁴ 1988	1983-1984	Low	PSI§	Low
Reich et al, ³⁵ 1998‡	Not stated		Nursing hours per day§	Medium
Tai et al, ³⁶ 1998	1993-1994	Low	APACHE II	Low
Pollack et al, ³⁷ 1994	1989-1992	Medium	PRISM	Low
DiCosmo, ³⁸ 1999‡	1994-1997	Medium	†	Medium
Dimick et al, ³⁹ 2001	1994-1998	Medium	†	Medium
Dimick et al, ⁴⁰ 2001‡	1994-1998	Medium	†	Medium
Rosenfeld et al, ⁴¹ 2000	1996-1997	Low	APACHE III	Low
Diringier and Edwards, ⁴² 2001	1996-1999	Medium	APACHE II§ Glasgow Coma Scale§	Low
Goh et al, ⁴³ 2001	1996-1997, 1999-2000	Medium	PRISM II	Low
Blunt and Burchett, ⁴⁴ 2000	Not stated		APACHE II§	Low
Topeli, ⁴⁵ 2000‡	Not stated		APACHE II§	Low
Hanson et al, ⁴⁶ 1999	1994-1995	Low	APACHE II§	Low

*Risk of bias due to temporal trends is classified as low if study duration was 2 years or less, medium if 2 to 4 years, and high if more than 4 years. Risk of bias from confounding is classified as low if validated physiologic method of risk adjustment was used, medium if selected clinical data were used, and high if no risk adjustment was used. Risk of bias from incomplete follow-up is classified as low if follow-up is 90% to 100% complete, medium if follow-up is 80% to 89%, and high if less than 80%. Risk for bias due to incomplete follow-up was low in all studies. APACHE indicates Acute Physiology and Chronic Health Evaluation Score; MPM, Mortality Prediction Model; PSI, Physiologic Severity Index; and PRISM, Pediatric Risk of Mortality.

†Patient demographics (age, sex, race), comorbidity (diseases in Romano-Charlson index) for the study by Pronovost et al,² severity of illness (urgent or emergent admission, ruptured aorta for the study by Pronovost et al²; case-mix index for the study by DiCosmo³⁸ and the 2 studies by Dimick et al^{39,40}; percentage of patients requiring mechanical ventilation for the study by DiCosmo³⁹), hospital volume, and surgeon volume for the study by Pronovost et al² and the 2 studies by Dimick et al.^{39,40} These studies reported the distribution of severity scores by subgroups rather than the means for the low-intensity and high-intensity groups. Pollack et al³⁴ reported statistical difference between the low-intensity and high-intensity groups, whereas distributions were comparable in the study by Kuo et al.¹⁰

‡Abstract was reviewed; in all other instances, full journal articles were considered.

§Statistically significant difference ($P < .05$) in severity of illness (as defined by the risk adjustment methods used) between intervention and control groups.

staffing on ICU mortality, with 12 studies (80%) reporting ICU mortality adjusted for severity of illness (Table 3). Overall, 14 (93%) of these 15 studies⁸ showed a decrease in ICU mortality rate for ICU patients with high-intensity physician staffing. Nine (69%) of the 13 studies^{8-10,29,32,35,38,41,43} that reported unadjusted ICU mortality rates found a statistically significant reduction with high-intensity physician staffing in the ICU (Figure 3B and Table 3). In 9 (75%) of the 12 studies^{8-10,29,32,34,35,41,43} that adjusted for severity of illness, ICU mortality significantly decreased as well with high-intensity physician staffing. The random-effects, pooled estimate of the unadjusted RR for high-intensity vs low-intensity staffing is 0.61 (95% CI, 0.50-0.75).

Hospital LOS. Thirteen studies (48%) evaluated the impact of ICU physician staffing on hospital LOS (TABLE 4). The hospital LOS ranged from 8 to 33 days in the low-intensity group and 7 to 24 days in the high-intensity group. Ten (77%) of 13 studies reported a reduction in hospital LOS with high-intensity staffing (range of relative reduction, 5%-42%).^h In 6 of these studies, the reduction was statistically significant (FIGURE 4A).^{2,11,32,39,46} Only 1 study (8%) reported a statistically significant increase in hospital LOS with high-intensity physician staffing, but this study compared patients admitted to a neurosurgical ICU with patients admitted to a general ICU, and the results were not adjusted for baseline severity of illness.⁴² Only 4 studies adjusted hospital LOS for baseline severity of illness.^{2,39-41} Two of these studies^{2,39} showed a statistically significant decrease in hospital LOS with high-intensity physician staffing in the ICU, with the remaining 2 studies^{40,41} showing no significant difference in hospital LOS.³⁹

Intensive Care Unit LOS. Eighteen studies (67%) evaluated the impact of ICU physician staffing on ICU LOS (Table 4). The ICU LOS ranged from 2 to 13 days in the low-intensity group

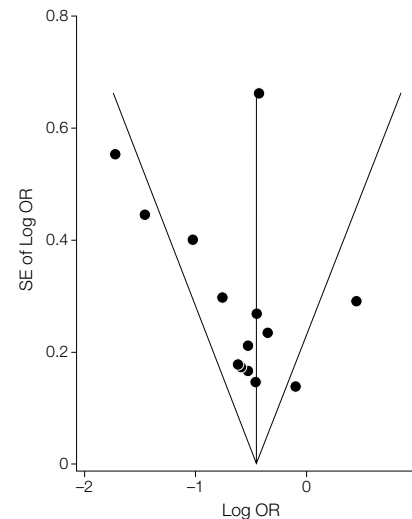
and 2 to 10 days in the high-intensity group. Fourteen (78%) of 18 studies reported that ICU LOS decreased with high-intensity physician staffing (Figure 4B).ⁱ In 11 of these studies, this decrease was statistically significant.^j The study that compared a closed neurosurgical ICU to a general ICU was the only one to report a statistically significant increase in ICU LOS with high-intensity ICU physician staffing in the neurosurgical ICU.⁴² Three of 18 studies reported higher severity in the high-intensity group,^{28,38,46} 2 reported higher severity in the low-intensity group,^{43,44} and the remaining 13 reported no difference between the 2 groups.^k Only 2 studies adjusted ICU LOS for baseline severity of illness^{2,42}; ICU LOS in both studies favored high-intensity physician staffing.

COMMENT

We found that greater use of intensivists in the ICU led to significant reductions in ICU and hospital mortality and LOS. These findings were consistent across a variety of populations and hospital settings and have potentially important implications for patient care. Given the variation in ICU physician staffing and the potential for reduced mortality implied by these studies, a more rigorous evaluation of the optimal ICU organization is essential.

Intensive care is one of the largest and most expensive aspects of US health care. There are approximately 6000 ICUs in the United States,⁵⁵ caring for approximately 55 000 patients daily,⁵⁵ with an annual budget of approximately \$180 billion.¹ The proportion of ICUs with high-intensity ICU physician staffing is unclear, but appears to be relatively small. In 1992, Groeger et al³ suggested that only 10% of ICUs in the United States require an intensivist to act as the patients' primary physician. In 1999, Schmitz et al⁵⁵ estimated that one third of all ICU patients in the United States were treated by intensivists acting as ei-

Figure 2. Funnel Plot of Hospital Mortality



The funnel plot provides an estimate of publication bias. In the absence of bias, the studies should be symmetrically distributed along the funnel. If small studies with negative results are unpublished, the plot will appear asymmetrical. Our plot suggests no evidence of publication bias. Log OR indicates log odds ratio.

ther primary physicians or consultants. Since most ICU patients are cared for with low-intensity physician staffing and high-intensity staffing appears to be associated with improved outcomes, mandatory ICU physician staffing may improve ICU process and outcomes.

The general lack of intensivist staffing in the United States contrasts with the usual closed ICU approach in Europe and Australia. A survey⁵⁶ by the Audit Commission for Local Authorities and the National Health Service in England and Wales found that closed systems are common and intensivists initiate care in 80% of all ICUs. The average 6-bed general ICU in the United Kingdom has 3 consultants with fixed commitments to the unit and 3 more taking part in the on-call rota.⁵⁶ According to Cole et al,⁵⁷ all ICUs in Victoria, the second most populous state in Australia, have been following the closed model for more than a decade. In 1997, a task force of the European Society of Intensive Care Medicine⁵⁸ issued recommendations on minimal requirements for intensive care departments (ICDs). Although the recommendations were not

^hReferences 2, 10, 11, 29, 30, 32, 33, 36, 38, 41, 43, 44, 46.

ⁱReferences 2, 10, 11, 32, 33, 36, 38, 41, 43, 46.

^jReferences 2, 10-12, 29, 30, 32-34, 36, 41, 42.

⁸References 8-10, 27, 29, 31-36, 38, 41, 43.

^hReferences 2, 11, 28, 32, 36, 39, 40, 44, 46.

evidence based, the task force emphasized that the director of an ICD should be an intensivist and that it is essential that a qualified intensivist provide 24-hour coverage in level II and III (moderate- and high-intensity care) ICDs.⁵⁸ The task force also recommended 24-hour coverage by an intensivist for level I ICDs.⁵⁸

Our review identified several issues that may be important for researchers studying health care organizational characteristics. Our initial search, based on MeSH terms and text words, yielded a large number of citations, yet failed to identify several relevant articles that we had previously identified.^{8,9,11,12,28,30,32,34} Although each shared

intensive care unit as a MeSH term, the assignment of other MeSH terms was inconsistent. By incorporating the related articles feature, we were able to identify additional relevant articles. The configuration of MeSH terms is not ideal for a comprehensive review of health care organizational characteristics, and investigators and library scien-

Table 3. Hospital and ICU Mortality With Low- and High-Intensity ICU Physician Staffing*

Source	No./Total (%) of Deaths		OR (95% CI)†	P Value	
	Low-Intensity ICU Staff	High-Intensity ICU Staff		Unadjusted	Adjusted‡
Hospital Mortality					
Pronovost et al, ² 1999	52/472 (21)	131/2036 (6)	0.56 (0.40-0.78)	<.05	<.05
Brown and Sullivan, ⁸ 1989	79/223 (36)	53/216 (25)	0.59 (0.39-0.90)	<.01	<.05
Baldock et al, ⁹ 2001§	107/294 (36)	78/330 (24)	0.54 (0.38-0.77)	<.001	NR
Multz et al, ¹¹ 1998 (retrospective)	68/152 (45)	56/154 (36)	0.71 (0.47-1.12)	NS	NS
Multz et al, ¹¹ 1998 (prospective)	36/95 (38)	52/185 (28)	0.64 (0.38-1.08)	NS	NS
Reynolds et al, ¹² 1988	74/100 (74)	64/112 (57)	0.47 (0.26-0.83)	<.01	<.05
Carson et al, ²⁸ 1996	28/124 (23); O/E, 0.9¶	38/121 (31); O/E, 0.8¶	1.57 (0.89-2.78); O/E, 0.89¶	.12	NR
Li et al, ³⁰ 1984	153/480 (32)	154/517 (30)	0.91 (0.69-1.19)	NS	.01
Jacobs et al, ³¹ 1998§	O/E, 0.98¶	O/E, 0.81¶	O/E, 0.83¶	NR	NS
Manthous et al, ³² 1997	156/459 (34)	116/471 (25)	0.63 (0.48-0.84)	.002	<.05
Pollack et al, ³⁷ 1994	NR	.03
Dimick et al, ³⁹ 2001	24/169 (14)	7/182 (4)	0.24 (0.10-0.58)	.003	NS
Dimick et al, ⁴⁰ 2001	21/275 (8)	4/276 (1)	0.18 (0.05-0.50)	<.001	<.05
Rosenfeld et al, ⁴¹ 2000	26/225 (12); O/E, 1.1¶	9/201 (5); O/E, 0.7¶	0.36 (0.16-0.79)	.008	<.05
Diringier and Edwards, ⁴² 2001	0.39 (0.22-0.67)	.001	NR
Blunt and Burchett, ⁴⁴ 2000	113/328 (34); O/E, 1.1¶	93/393 (24); O/E, 0.8¶	0.59 (0.43-0.82)	.001	<.05
Hanson et al, ⁴⁶ 1999	6/100 (6)	4/100 (4)	0.65 (0.18-2.39)	NS	NS
ICU Mortality					
Brown and Sullivan, ⁸ 1989	62/223 (28)	29/216 (13)	0.40 (0.25-0.66)	<.01	<.05
Baldock et al, ⁹ 2001§	83/294 (28)	64/330 (19)	0.61 (0.42-0.89)	.01	.005
Kuo et al, ¹⁰ 2000	90/176 (51)	151/491 (31)	0.42 (0.30-0.60)	<.001	<.01
Al-Asadi et al, ²⁷ 1996	112/1404 (8)	66/1005 (7)	0.81 (0.59-1.11)	.19	NS
Ghorra et al, ²⁹ 1999	18/125 (14)	9/149 (6)	0.38 (0.17-0.88)	.01	<.05
Jacobs et al, ³¹ 1998§	O/E, 1.17¶	O/E, 0.99¶	O/E, 0.85¶	NR	NS
Manthous et al, ³² 1997	96/459 (21)	70/471 (15)	0.66 (0.47-0.93)	.02	<.05
Marini et al, ³³ 1995§	13/65 (20)	12/112 (11)	0.48 (0.21-1.13)	.09	NR
Pollack et al, ³⁴ 1988	10/149 (7)	4/113 (4)	0.51 (0.16-1.67)	.26	<.05
Reich et al, ³⁵ 1998	57/826 (7)	35/830 (4)	0.59 (0.39-0.92)	<.05	<.05
Tai et al, ³⁶ 1998#	O/E, 1.23¶	O/E, 1.0¶	...	NR	.29
DiCosmo, ³⁸ 1999	137/1667 (8.2)	63/1292 (4.9)	0.57 (0.42-0.78)	<.001	NR
Rosenfeld et al, ⁴¹ 2000	22/225 (10); O/E, 1.8¶	3/201 (2); O/E, 0.6¶	0.14 (0.04-0.48)	<.01	<.05
Goh et al, ⁴³ 2001	82/264 (31); O/E, 0.9¶	42/355 (12); O/E, 1.6¶	0.30 (0.20-0.45)	<.001	<.05
Topeli, ⁴⁵ 2000	42/200 (21)	45/149 (30)	1.63 (0.99-2.66)	.05	...

*ICU indicates intensive care unit; OR, odds ratio; CI, confidence interval; NR, not reported; and NS, not significant. Low ICU physician staffing is either no intensivist available or elective consultation; high ICU physician staffing is either mandatory consultation or closed ICU. Ellipses indicate studies in which outcome was not evaluated.

†The ORs are quoted from the studies or calculated from unadjusted high-intensity mortality rate vs low-intensity mortality rate where rates were available.

‡Results were adjusted for baseline severity of illness. Adjusted P values and ORs (where available) shown as reported by the authors.

§Studies have more than 1 observation period after intervention. Information from observation period closest to intervention is included.

||Multz et al¹¹ also pooled the data and found a significant reduction in hospital mortality (P<.04) with high-intensity ICU physician staffing.

¶O/E is the observed-to-expected mortality ratio based on risk adjustment using the Acute Physiology and Chronic Health Evaluation Score (APACHE) II (studies by Carson et al,²⁸

Tai et al,³⁶ and Blunt and Burchett⁴⁴), APACHE III (studies by Jacobs et al³¹ and Rosenfeld et al⁴¹), or Pediatric Risk of Mortality II (study by Goh et al⁴³).

#Data reported for survivors only.

tists should improve this indexing situation.

There are a number of potential limitations to consider regarding this literature. First, there is a risk of selection bias. Mark³⁹ describes 3 areas of possible selection bias in critical appraisal: selection of representative subjects (generalizability), selection of subjects to exposure (confounding variables), and selection of subjects at outcome (distorted samples). We believe the findings are generalizable because there was a consistent benefit associated with high-intensity staffing in studies of medical and surgical patients, studies from academic and community hospitals, and studies from inside and outside the United States. Because the studies are not randomized, the risk of confounding variables is considerable. However, an important strength of this literature was the consistent use of risk-adjustment methods. Critical care medicine has developed sophisticated, well-validated, risk-adjustment methods that use

multiple clinical and physiologic variables to predict the risk of in-hospital death.⁴⁸⁻⁵² In our analysis, 22 (81%) of 27 studies used such methods to minimize bias from confounding variables. Finally, all 27 studies had complete follow-up, and there was therefore no risk of bias from distorted samples.

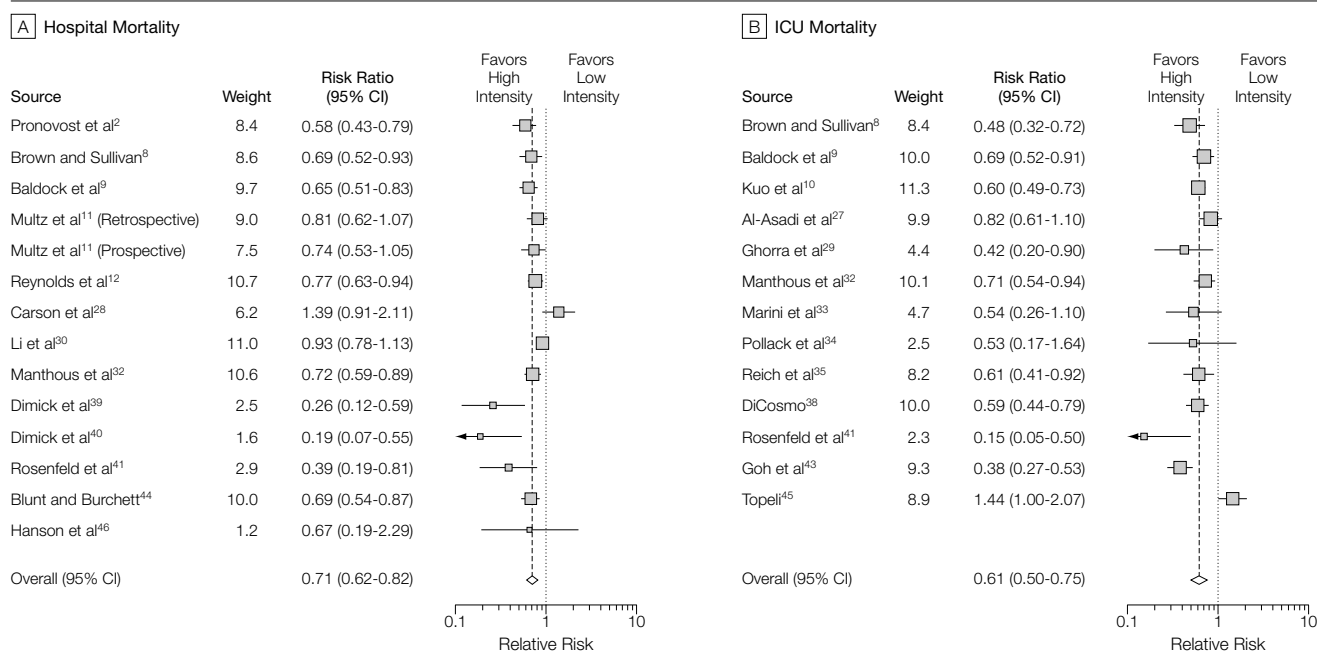
A second potential limitation is publication bias. However, the funnel plot suggested that risk for publication bias was not significant (Figure 2). There was no quantitative heterogeneity among studies, and the results were consistent across studies, increasing our confidence in the validity of our conclusions. Moreover, from our discussions with staff of critical care societies (American Thoracic Society, American College of Chest Physicians, and Society of Critical Care Medicine at their annual meetings during 1999-2001), we found no evidence of any relevant negative unpublished studies.

A third potential limitation is risk for temporal trends in mortality to bias study results. Temporal trends in any

before-and-after study design could affect the results of this review and reduce the strength of our inferences. We believe this source of bias is small for several reasons. First, evidence for the effectiveness of therapies in reducing mortality in critically ill patients occurred only at the end of the study periods.⁶⁰⁻⁶² Second, there were no trends for reduced mortality in critically ill patients during the study periods. Third, most of the studies were conducted during a short period, and thus the effect of any temporal trends is likely small.

A fourth potential limitation is the use of ICU mortality and LOS as outcome measures. Because no study described explicit criteria for discharge from the ICU, differences in discharge practices between the treatment and control groups may have influenced the results. For example, early ICU discharge may have artificially reduced ICU mortality without decreasing hospital mortality. However, the improvement in mortality and LOS observed with high-intensity ICU physician staff-

Figure 3. Unadjusted Hospital and ICU Mortality With Low- and High-Intensity ICU Physician Staffing



Data from studies demonstrate the relative risk (RR) with 95% confidence intervals (CI) of hospital and intensive care unit (ICU) mortality with high intensity vs low intensity ICU physician staffing. The RRs less than 1 suggest reduced mortality with high intensity staffing while RRs greater than 1 suggest increased mortality with high intensity staffing. The size of the data markers corresponds to the weight of the studies. Larger markers imply less uncertainty from the results of the individual study, and carry more weight in calculating the random effects pooled estimate from the systematic review.

ing was observed at ICU and hospital discharge.

There are also limitations in the way we conducted our review. First, 3 of the authors (P.J.P., D.C.A., and T.D.) are intensivists and potentially biased. The high degree of agreement among reviewers may be due to similar clinical and research interests and may have encoded systematic error. Second, we included only articles published in English, although we are not aware of relevant

non-English-language publications. The exclusion of non-English-language articles should not significantly affect the study results.⁶³ Third, we did not perform a formal evaluation of study quality, because the particular scale chosen may influence the results.⁶⁴ Rather, we identified relevant methodologic aspects of the study (a priori) and assessed these individually.

Our systematic review was rigorously conducted and transparently re-

ported, following recommendations outlined by the Meta-analysis of Observational Studies in Epidemiology Group.¹⁴ Because it is unclear how to proceed when there is qualitative but not quantitative heterogeneity among studies, we present pooled estimates by using the random-effects model and recommend cautious interpretation of these results.

We should attempt to identify the characteristics of high-intensity ICU

Table 4. Hospital and ICU Length of Stay with Low- and High-Intensity ICU Physician Staffing*

Source	Length of Stay (LOS)		P Value		Relative Reduction in LOS, %
	Low-Intensity ICU Staff	High-Intensity ICU Staff	Unadjusted	Adjusted†	
Hospital LOS					
Pronovost et al, ² 1999	12.5 (11.5)	10.8 (10.5)	<.05	<.05	14
Multz et al, ¹¹ 1998 (retrospective)	31.2 (31.2)‡	22.2 (22.2)‡	<.02	NR	29
Multz et al, ¹¹ 1998 (prospective)	33.2 (33.2)§	19.2 (19.2)‡	<.01	NR	42
Reynolds et al, ¹² 1988	21 (22)	24 (23)	NS	NR	-14§
Carson et al, ²⁸ 1996	16.7 (19.4)	15.9 (4.2)	.75	NR	5
Manthous et al, ³² 1997	22.6 (22.6)‡	17.7 (17.7)‡	<.05	NR	22
Tai et al, ³⁶ 1998	11 (11)‡	10 (10)‡	NS	NR	9
Dimick et al, ³⁹ 2001	15 (11-25)	9 (8-11)	<.05	<.05	40
Dimick et al, ⁴⁰ 2001	8 (6-11)	7 (6-10)	NS	NS	13
Rosenfeld et al, ⁴¹ 2000	9.2 (9.2)‡ O/E 0.63	9.3 (9.3)‡ O/E 0.6	NS	NS	-1§
Diringer and Edwards, ⁴² 2001	11.4 (5.8)	15.5 (24.0)	<.05	NR	-36§
Blunt and Burchett, ⁴⁴ 2000	14 (8-24)	13 (8-24)	NS	NR	7
Hanson et al, ⁴⁶ 1999	23.6 (23.6)‡	20.3 (20.3)‡	<.05	NR	14
ICU LOS					
Pronovost et al, ² 1999	6 (7)	3.8 (4)	<.05	<.05	37
Kuo et al, ¹⁰ 2000	11.8 (13.1)	10.1 (11.0)	<.001	NR	14
Multz et al, ¹¹ 1998 (retrospective)	9.3 (9.3)‡	6.1 (6.1)‡	<.05	NR	34
Multz et al, ¹¹ 1998 (prospective)	12.6 (12.6)‡	6.2 (6.2)‡	<.01	NR	51
Reynolds et al, ¹² 1988	8 (10)	10 (11)	NS	NR	-25§
Carson et al, ²⁸ 1996	4.4 (7.1)	4.9 (6.3)	.57	NR	-11§
Ghorra et al, ²⁹ 1999	5.8 (5.8)	5.5 (5.1)	.73	NR	5
Li et al, ³⁰ 1984	4 (3.9)	3.9 (4.9)	.05	NR	3
Manthous et al, ³² 1997	5 (5)‡	3.9 (3.9)‡	<.05	NR	22
Marini et al, ³³ 1995¶	9 (9)	4 (4)	<.05	NR	56
Pollack et al, ³⁴ 1988	2 (2)	2 (2)	NS	NR	0
Tai et al, ³⁶ 1998	3 (3)‡	2 (2)‡	.01	NR	33
DiCosmo, ³⁸ 1999	4.1 (4.1)‡	3.6 (3.6)‡	NR	NR	12
Rosenfeld et al, ⁴¹ 2000	2.7 (2.7)‡ O/E 0.96	2 (2)‡ O/E 0.86	<.01	<.01	26
Diringer and Edwards, ⁴² 2001	4.5 (6.2)	7.8 (12.5)	<.05	NR	-73§
Goh et al, ⁴³ 2001	6.8 (10.3)	4.0 (5.6)	<.001	NR	41
Blunt and Burchett, ⁴⁴ 2000	2.0 (95% CI, 0.8-4.2)	1.9 (95% CI, 0.8-3.5)	NS	NR	5
Hanson et al, ⁴⁶ 1999	2.8 (2.8)‡	2 (2)‡	<.05	NR	29

*Results are presented as means (SDs) except where noted. ICU indicates intensive care unit; NR, not reported; NS, not significant; and O/E, observed-to-expected mortality ratio based on risk adjustment using the Acute Physiology and Chronic Health Evaluation Score II. Low ICU physician staffing is either no intensivist available or elective consultation; high ICU physician staffing is either mandatory consultation or closed ICU.

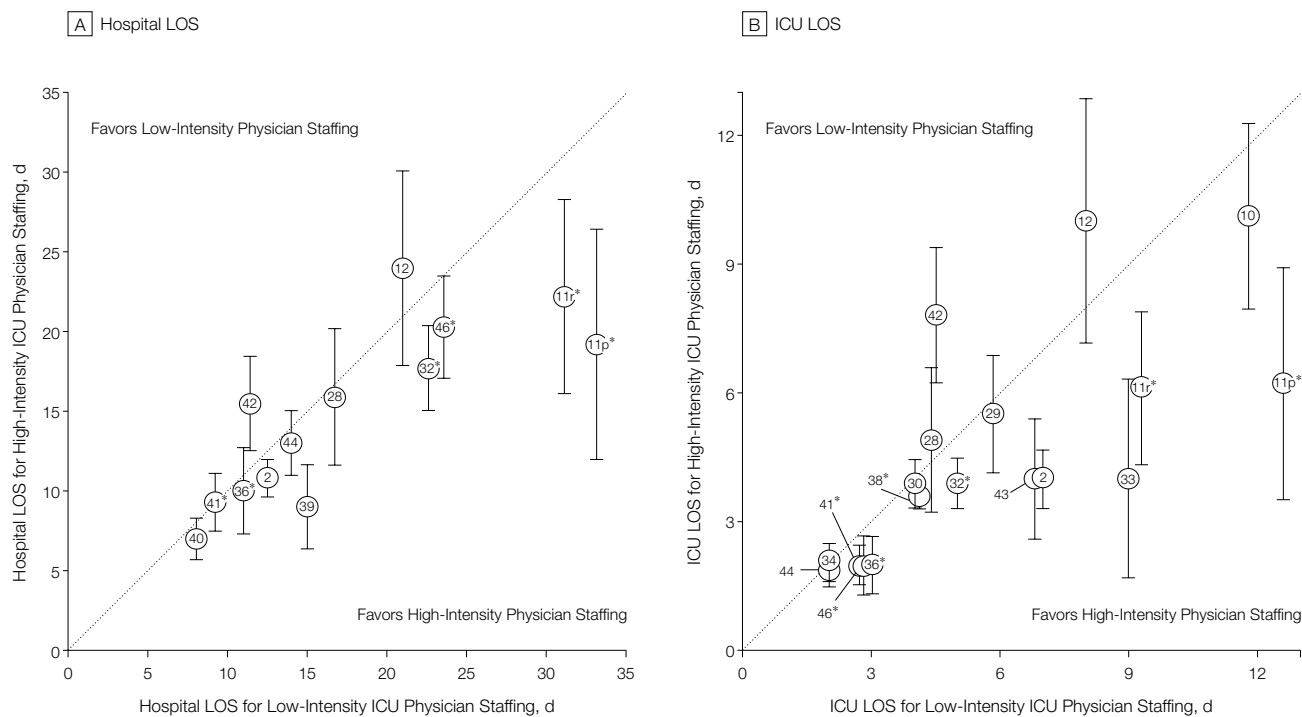
†Results were adjusted for baseline severity of illness. Unadjusted and adjusted P values shown as reported by the authors.

‡The SD was not provided in the original study and was assumed to be equal to the mean LOS.

§Relative risk increase.

¶Medians reported instead of means. Range is shown in parentheses.

||Studies have more than one observation period after intervention. Information from the observation period closest to the intervention is included. Data shown are for survivors only.

Figure 4. Unadjusted Hospital and Intensive Care Unit (ICU) Length of Stay (LOS) With Low- and High-Intensity ICU Physician Staffing

Data from studies are plotted with the high-intensity mean LOS as a y-coordinate and the low-intensity mean LOS as an x-coordinate with the 95% confidence intervals (error bars) calculated by the authors of the systemic review. A discrepancy exists between the plotting of the error bars for study 10 in panel B (error bar crosses the line of equivalency) and $P < .001$ (as reported by Carson et al). The diagonal line represents the line of equivalency. Data points below the line of equivalency suggest shorter LOS in the high-intensity group, and those above the line suggest shorter LOS in the low-intensity group. Numbers refer to references (r indicates retrospective; p, prospective). Asterisks indicate SD, assumed to be equal to the mean LOS.

staffing that improved outcome. We found previously that daily rounds by an ICU physician were associated with improved outcomes in patients who underwent abdominal aortic surgery. Yet how daily rounds translate into improved outcomes remains unclear.² For example, were the improved outcomes due to specific critical care training and expertise or to increased availability, perhaps with reduced response time, of a team of physicians whose sole responsibility was to provide care in the ICU? Some of the improvements may be possible through alternative staffing models, such as telemedicine.⁴¹ Finally, other ICU characteristics, such as nurse-to-patient ratios, also affect patient outcomes.⁶⁵ Determining how to best organize ICU staffing from a multidisciplinary standpoint to optimize patient outcomes is a high research priority. Meanwhile, our findings provide evi-

dence to support the recommendations by the Leapfrog Group^{66,67} and Society of Critical Medicine for ICU physician staffing.⁶⁸ We believe this systematic review summarizes and clarifies the available literature, helps guide public policy, and provides a basis for future research.

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Author Contributions: Study concept and design: Pronovost, Angus.

Acquisition of data: Pronovost, Angus, Dremsizov, Young.

Analysis and interpretation of data: Angus, Dorman, Robinson, Dremsizov.

Drafting of the manuscript: Pronovost, Angus, Young.

Critical revision of the manuscript for important intellectual content: Pronovost, Angus, Dorman, Robinson, Dremsizov.

Statistical expertise: Pronovost, Angus, Robinson.

Administrative, technical, or material support: Angus, Dremsizov, Young.

Study supervision: Pronovost, Angus, Dorman.

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