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Pharmacist Contributions as Members of the Multidisciplinary ICU Team

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Critical care pharmacy services in the ICU have expanded from traditional dispensing responsibilities to being recognized as an essential component of multidisciplinary care for critically ill patients. Augmented by technology and resource utilization, this shift in roles has allowed pharmacists to provide valuable services in the form of assisting physicians and clinicians with pharmacotherapy decision-making, reducing medication errors, and improving medication safety systems to optimize patient outcomes. Documented improvements in the management of infections, anticoagulation therapy, sedation, and analgesia for patients receiving mechanical ventilation and in emergency response help to justify the need for clinical pharmacy services for critically ill patients. Contributions to quality improvement initiatives, scholarly and research activities, and the education and training of interdisciplinary personnel are also valued services offered by clinical pharmacists. Partnering with physician and nursing champions can garner support from hospital administrators for the addition of clinical pharmacy critical care services. The addition of a pharmacist to an interprofessional critical care team should be encouraged as health-care systems focus on improving the quality and efficiency of care delivered to improve patient outcomes.

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Abbreviations: ACLS = advanced cardiac life support; ADE = adverse drug event; ADR = adverse drug reaction; aPTT = activated partial thromboplastin time; QTc = corrected QT interval; SCCM = Society of Critical Care Medicine

Critical care pharmacy has evolved over the past 30 years and is now recognized by the pharmacy profession and critical care practitioners as an advanced discipline within pharmacy practice. This is not surprising given the growing number of ICU beds, increasing complexity of critical care medicine, and a focus on multidisciplinary care to optimize patient outcomes. Moreover, technological advances (eg, computerized provider order entry, integrated health-care records, automated distribution systems, robotic fill devices, bar coding), scope of practice changes (eg, technician check technician), safety and cost-containment mandates, and competitive pressures are enabling pharmacists to be physically present in the ICU, often providing direct patient care and acting as the expert pharmacotherapy manager of a multidisciplinary ICU team.[1] This article delineates pharmacy services commonly provided in the ICU, reviews the existing literature on the contribution of clinical pharmacists in the management of critically ill patients, and provides recommendations for future study.

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Defining Direct Critical Care Pharmacy Services

The American College of Clinical Pharmacy defines clinical pharmacy practice as a "health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health and

disease prevention."[2] Clinical pharmacists contribute to the generation of new knowledge that advances health and quality of life. Direct patient care is described in the Scope of Pharmacy Practice as the pharmacist's observation of the patient and his or her contributions to the selection, modification, and monitoring of patient-specific drug therapy through collaborative practice with an interprofessional team or another health-care provider.[3] This definition encompasses the full range of pharmacist practice from the evaluation and verification of medication orders, to dispensing and assisting with administration of medications, to collaborative drug therapy management where pharmacists are authorized to select medications for identified medical conditions, adjust dosage regimens to optimize pharmacotherapy, monitor key vital signs and order laboratory tests, provide drug information, and develop and evaluate therapeutic management policies.

The paradigm for critical care pharmacy services is the 2000 Society of Critical Care Medicine (SCCM)/American College of Clinical Pharmacy position paper, which defines the fundamental, desirable, or optimal activities across clinical and nonclinical domains (Table 1).[4] Fundamental activities are services that must be provided for the safe delivery of pharmaceutical care to all patient populations; desirable activities add clinical functions necessary for the specialized care of critically ill patients; and optimal activities reflect an integrated, specialized, and dedicated model of direct patient care functions aimed at optimizing outcomes. In the interest of promoting these activities, the SCCM suggests that pharmacists are essential for the delivery of quality care to critically ill patients and recommends the integration of a dedicated, proactive, and physically present pharmacist on the ICU team as an essential component of a multidisciplinary approach to critical care.[5,6]

The remainder of this article provides a literature review of the impact of pharmacy services on safety and patient outcomes in critical care. A MEDLINE search of English-language literature was performed for January 1, 1966, to February 29, 2012, with use of the following medical subject headings: pharmacists, pharmacy service, hospital, critical care, critical illness, and ICU. All original prospective and retrospective studies, peer-reviewed guidelines, consensus statements, and review articles were evaluated for inclusion. Forty-four articles, primarily observational in design, were identified. Relevance was determined by considering the type of study, evaluation of outcomes, and consideration for bias.

Current Role and Impact of Direct Critical Care Pharmacy Services

After the publication of the SCCM/American College of Clinical Pharmacy position statement on pharmacy services in the ICU,[2] MacLaren et al[7] surveyed clinical pharmacists self-identified as practicing in an ICU to characterize the delivery of clinical pharmacy services. The respondents represented 1,084 ICUs from 382 hospitals (11.8% response rate) in the United States. At the time the survey was conducted in 2004, 62.2% of respondents attended rounds 4.4 ± 1.5 days per week. The average work week was primarily devoted to patient care (43%), followed by checking and dispensing medications (26.2%), administrative functions (12.6%), educational activities (10.9%), and scholarly responsibilities (7.3%). Fundamental services were provided for at least 75% of patient ICU days and included drug information, drug therapy evaluation, drug therapy intervention, pharmacokinetic monitoring, and informal educational activities. In general, desirable or optimal activities were provided infrequently.

Pharmacist delivery of direct, proactive, patient-centered care has been associated with both perceived and actual improvements in patient outcomes. A 2007 analysis of 2,836,991 patients across 885 hospitals showed that hospital-wide mortality rates decreased as the pharmacist-to-occupied bed ratio increased.[8] The primary factor contributing to this beneficial association was the involvement of pharmacists in the direct care of patients with activities generally deemed fundamental or desirable (Table 2). Unfortunately, despite these data, some of these services are inconsistently provided to critically ill patients. In a 2011 survey, 41 pharmacist-respondents (46% response rate) indicated that many fundamental services were provided daily, whereas others were provided only weekly.[9] Across all domains of pharmacy practice (clinical, educational, scholarly, and administrative activities), fundamental services were more commonly available than desirable or optimal services, which were provided no more than weekly. Of note, physicians working with critical care pharmacists providing direct patient care rated the perceived clinical and economic impact of fundamental services higher than that of desirable or optimal services.

Targeting Specific Therapeutic Practice Domains

These studies suggest a global improvement in care associated with the institution of direct patient care pharmacy services in the ICU. In practice, many clinical pharmacy activities are directed toward specific therapeutic practice domains where outcomes can be more clearly demonstrated and, thus, the presence of a dedicated pharmacist can be more easily justified. Therapeutic practice domains may be comprehensive but usually are focused on capturing the sickest patients or targeting certain medications, such

Table 1—*Fundamental, Desirable, and Optimal Critical Care Pharmacy Services*[2]

Pharmacy Service	Fundamental	Desirable	Optimal
Clinical activities	• Conduct medication histories • Assess suspected drug-related ICU admissions for causality • Prospectively evaluate drug therapy • Provide pharmacokinetic monitoring • Monitor therapeutic regimen for efficacy and safety • Intervene to change therapy • Evaluate parenteral nutrition orders • Document recommendations in the medical record • Provide drug information and IV compatibility data	• Determine need to continue maintenance drugs during the acute illness • Provide therapeutic management advice to patient or physician • Provide formal nutrition consultation • Respond to resuscitation events	• Assist physicians in discussions with patients and family members to help make informed decisions regarding treatment options
Educational activities	• Provide informal educational services to pharmacists or other ICU health-care professionals	• Provide didactic lectures to health-care professionals, students, residents, and fellows in critical care pharmacology and therapeutics • Train pharmacy students, residents, and fellows through experiential critical care rotations • Provide accredited continuing educational sessions	• Coordinate or direct residency or fellowship programs • Implement pharmacist and pharmacy technician training programs for personnel working in the ICU • Teach advanced cardiac life support • Educate lay groups and medical personnel in the community about the role of pharmacists as part of the multidisciplinary health-care team
Scholarly activities	• Supervise handling of investigational drugs	• Collect data • Screen patients for study enrollment • Aid in study protocol design • Aid in data analyses • Coordinate research • Aid in manuscript preparation • Disseminate case reports and practice insights	• Procure funding • Perform laboratory analyses • Disseminate results of clinical research, outcome and administrative research, or laboratory analyses
Administrative activities	• Document services provided to the ICU • Serve on ICU and pharmacy committees • Monitor and report adverse drug events to hospital committee • Conduct medication use evaluations	• Attach economic impact to services provided in the ICU • Develop and implement ICU policies and protocols	• Design new pharmacy programs for the ICU

as those highlighted by patient safety initiatives or known to cause the most serious adverse events (eg, vasoactive agents, sedatives/analgesics, electrolytes, anticoagulants, insulin). This section discusses the therapeutic and safety outcomes of focused therapeutic practice domains that incorporate clinical pharmacists. Although some of these studies did not specifically assess the direct impact of ICU pharmacists, they describe clinical pharmacy services provided to critically ill patients and, thus, represent the holistic activities of critical care pharmacists.

Antimicrobial Therapy

Critical care clinical pharmacists receive extensive training in infectious disease pharmacotherapy to complement their training in other domains of critical care practice. Moreover, the literature suggests the benefit of clinical pharmacist activity as it pertains to infectious disease pharmacotherapy in critically ill patients. In a single-centered study, the direct contribution from the clinical pharmacist through interpretation of microbiology results, review of patient records, and recommendation of antimicrobial agents was associated with a reduced time to administration of optimal antimicrobial therapy from 64.7 ± 36.8 to 39.3 ± 15.5 h ($P = .002$).[10] Additionally, deescalation of antimicrobial therapy in response to specific culture findings may reduce the emergence of antimicrobial resistance.[11] Guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America state that a clinical pharmacist with infectious disease training should be a core member of the multidisciplinary antimicrobial stewardship team.[12,13] This recommendation takes on heightened importance in the ICU, where antimicrobial

Table 2—*Specific Pharmacy Services Associated With Favorable Health-care Outcomes*[7-9]

Pharmacy Service	Annual Deaths Avoided per Hospital[a]	Level of Service	Frequency of Service in ICU,[b] %
Manage policies and protocols	29.9 ± 22.4	Desirable	95.1
Provide informal educational services	18.4 ± 14	Fundamental	92.8
Conduct medication use evaluations	5.4 ± 4.3	Fundamental	72
Attend medical rounds	54.7 ± 47.2	Fundamental to desirable	62.2[c]
Conduct medication histories	107.8 ± 87.6	Fundamental	56.9
Manage adverse drug events	23.3 ± 19.4	Fundamental	52
Respond to resuscitation events	45.8 ± 31.9	Desirable	44.6

[a]Based on data from 885 hospitals with 8,918 ± 8,292 admissions/y.
[b]Based on patient ICU days, so 100% would signify that the service was provided to every patient during each day of their ICU stay.
[c]Attend 4.4 ± 1.5 d/wk.

consumption is greater than in other inpatient care areas.

The impact of the addition of a clinical pharmacist to an antimicrobial control program was evaluated in a Veteran Affairs medical center.[14] Over a 2-year period, the pharmacist reviewed 1,329 orders for restricted and nonformulary antibiotics for appropriateness on the basis of presumed infection, culture results, formulary availability, and dosing. The pharmacist recommended changes in > 50% of orders, with most changes related to spectrum of activity, formulary substitution, or dose adjustments. These interventions were associated with shorter lengths of stay (10.8 days vs 13.2 days, $P < .001$) and decreased mortality (6.61% vs 8.28%, $P = .007$) compared with the period before the implementation of an antimicrobial control program directed by a clinical pharmacist.

A similar impact was seen when pharmacists managed surgical antimicrobial prophylaxis.[15] A survey and database review of 242,704 Medicare surgical patients from 806 different hospitals showed that pharmacist-managed antimicrobial prophylaxis was associated with significant improvement in clinical outcomes, such as decreased surgical site infections and length of stay. Nearly 19% of the hospitals included had pharmacist-managed surgical prophylaxis. In hospitals that did not offer pharmacist-managed antimicrobial prophylaxis, annual death rates were 52% higher, with 105 excess deaths (OR, 1.54; 95% CI, 1.46-1.63; $P < .0001$); length of hospital stay was 10.2% longer, with 167,941 excess patient days ($P < .0001$); and infection complications were 34.3% higher (OR, 1.52; 95% CI, 1.40-1.66; $P < .0001$) than in those with pharmacist involvement.

Clinical pharmacists provide expertise in pharmacokinetics and pharmacodynamics essential for dosing considerations in critically ill patients.[16-18] Vancomycin and aminoglycosides are the most common drug therapies managed by a clinical pharmacist. A database review of pharmacist management of vancomycin and aminoglycosides was evaluated in a study population comprising 199,082 Medicare patients treated in 961 hospitals.[16] Hospitals with pharmacist-managed vancomycin or aminoglycoside therapies had lower mortality (17% vs 18%, $P < .0001$); shorter lengths of stay (11.56 ± 18.73 days vs 12.98 ± 18.66 days, $P < .0001$); and fewer adverse events, including hearing loss (4.6% vs 6.8%, $P < .0001$) and renal impairment (25.8% vs 34.5%, $P < .0001$). Similarly, individualized pharmacokinetic monitoring performed by a clinical pharmacist was associated with less aminoglycoside-associated nephrotoxicity compared with physician-monitored therapy in a retrospective case-control study of 2,405 patients (7.9% vs 13.2%, $P = .02$).[18]

The overall effect of a pharmacist on clinical outcomes in patients with known infections was investigated by combining data from the 2006 survey of ICU pharmacy services previously described with *International Classification of Diseases, Ninth Revision, Clinical Modification* codes and data from the Centers for Medicare & Medicaid Services.[19] Compared with ICUs with clinical pharmacists, mortality rates in ICUs that did not have clinical pharmacists were higher for nosocomial-acquired infections, community-acquired infections, and sepsis by 23.6% (386 excess deaths, $P < .001$), 16.2% (74 excess deaths, $P = .008$), and 4.8% (211 excess deaths, $P = .008$), respectively. Similarly, ICU length of stay was longer for all infection categories by 7.9% (14,248 excess days, $P < .001$), 5.9% (2,855 excess days, $P = .03$), and 8.1% (19,215 excess days, $P < .001$), respectively.

Anticoagulation Therapy

Critically ill patients requiring anticoagulation often have multiple comorbid conditions that require a delicate balance between treatment of a thromboembolism and avoidance of a detrimental bleeding event. Coupled with the need to manage these therapies in a time-sensitive manner, anticoagulation in the ICU becomes increasingly complex. Additionally, regulatory standards from the Joint Commission are placing greater importance on the safety and management of

inpatient anticoagulation.[20] As pharmacologic experts, clinical pharmacists can provide valuable services that aid in improving safety and clinical care in critically ill patients requiring anticoagulation.[21]

Clinical pharmacists often manage clinical pathways and guidelines to aid in the administration of anticoagulants in the ICU.[22] These pathways frequently empower pharmacists and nurses to independently direct anticoagulant dosage regimens under the guidance of a predefined protocol. In the case of heparin infusions in patients with DVT, such pathways reduced the time to achieve therapeutic activated partial thromboplastin time (aPTT) from a mean of 54 h before the implementation of the pathway to only 11 h after implementation.[22] Similar outcomes were documented in an 802-bed university hospital where pharmacists managed direct thrombin inhibitors for the treatment of heparin-induced thrombocytopenia.[23] The time to achieve the therapeutic aPTT was reduced by 12.5 h ($P < .001$), and the proportion of time within the therapeutic aPTT range was increased by 32% ($P < .001$).

Combining the results of the 2006 survey of ICU pharmacy services with the Expanded Modified Medicare Provider Analysis and Review, mortality rates were 37% higher in ICUs without direct patient care clinical pharmacy services (OR, 1.41; 95% CI, 1.36-1.46) for patients with thromboembolic or infarction-related events.[24] ICUs without a clinical pharmacist also had a 49% greater incidence of bleeding complications (OR, 1.53; 95% CI, 1.46-1.60), which was associated with a higher likelihood for the need for blood transfusions (OR, 1.47; 95% CI, 1.28-1.69) and a greater amount of blood product administration (6.8 ± 10.4 units/patient vs 3.1 ± 2.6 units/patient, $P = .006$).

Before the requirement of an inpatient anticoagulation program, it was found that pharmacist-managed anticoagulation was associated with reductions in mortality, hospital lengths of stay, and blood transfusions.[25] Similar results were seen when a prospective evaluation of daily pharmacist-managed inpatient anticoagulation services was compared with a matched historical control group who received physician-managed anticoagulation in a 400-bed university teaching hospital.[26] Patients who received pharmacist-managed anticoagulation had a significantly shorter hospital length of stay (6.8 days vs 9.5 days, $P = .009$) and fewer supratherapeutic international normalized ratios defined as > 3.5 (27% vs 62%, $P < .001$). No differences were noted between the groups regarding international normalized ratio at discharge (2.6 vs 3.3, $P = .07$) or number of bleeding complications (6 vs 1, $P = .11$). Additionally, the pharmacist-managed patients had fewer readmission rates for bleeding or thrombosis within 1 to 3 months after discharge.

Sedation and Analgesia

Sedation and analgesia of critically ill patients is a dynamic and evolving therapeutic practice domain.[27-29] Pharmacist involvement in maintaining patient comfort has focused on adherence to clinical practice guidelines, reduction of prescribing variability, increased appropriate drug selection, and reduction of drug costs.[30-35]

Two assessments analyzed the implementation of pharmacist-driven sedation and analgesia protocols.[30,31] The implementation of a sedation scoring tool and sedation guideline with pharmacist-driven drug selection and dose adjustments of benzodiazepines and fentanyl decreased the incidence of agitation (22.4%-11%, $P < .001$) and pain (9.6%-5.9%, $P < .05$) while improving the proportion of time patients were at the goal level of sedation (17.2%-29.6%, $P < .01$).[30] In another study where clinical pharmacists concurrently evaluated all patients receiving mechanical ventilation and continuous sedation and made recommendations to adhere to the approved sedation guidelines of the institution, the intervention group (n = 78) demonstrated a shortened duration of mechanical ventilation (178 ± 178 h vs 338 ± 348 h, $P < .001$), ICU length of stay (238 ± 206 h vs 380 ± 325 h, $P = .001$), and hospital length of stay (369 ± 274 h vs 537 ± 350 h, $P = .001$) compared with a historical cohort (n = 78).[31] The daily interventions made by the clinical pharmacist during the implementation phase included adding a sedative agent (32%), discontinuing a sedative agent (20%), decreasing the sedative dose (18%), supplementing a bolus agent (11%), and adding as-needed agents (9%).

Emergency Response

Emergency response often is viewed as a component of critical care. Most critical care pharmacists receive training in advanced cardiac life support (ACLS) as well as other emergency situations such as trauma resuscitation, stroke, and ST-segment elevation myocardial infarction. This training combined with their expert knowledge of medications provides opportunities for clinical pharmacists to be valuable members of a resuscitation response team, which has been associated with reduced mortality.[8] The authors of this survey hypothesized that these findings may be partially related to improved compliance with the American Heart Association guidelines for ACLS, resulting in more rapid administration of appropriate agents and at recommended doses. The hypothesis that pharmacist participation in code response improves compliance with ACLS guidelines was investigated in 2008 by Draper and Eppert,[35] who performed a retrospective analysis of 74 consecutive in-hospital cardiac

arrests at a 350-bed community teaching hospital. In the 74 arrests, there were 650 treatment interventions. Of these, 581 (89.4%) were compliant with American Heart Association guidelines for ACLS. Significantly more of the noncompliant interventions took place during resuscitations in which a pharmacist was not present (59.3% vs 31.9%, $P = .03$). Although the investigators were unable to find a specific factor for the difference in noncompliance, they noted that the majority of discrepancies were medication related and included incorrect doses, delays in therapy, or omission of indicated medications that could be improved with routine participation by a pharmacist on the resuscitation team.

Reducing Adverse Drug Events

A 1999 report by the Institute of Medicine brought to light the impact of errors in health care.[36] Since that time, the health-care industry as a whole has devoted considerable time and effort to improve prevention and response to medical errors, including adverse drug events (ADEs).[37] Critically ill patients are at high risk for ADEs because of the severity of disease; organ dysfunction; and number, complexity, and duration of medications administered. Numerous published reports identified clinical pharmacists as optimal providers to identify and reduce medication errors and ADEs through medication profile review and adverse drug reaction (ADR) management and attendance during patient care rounds.[38-50] Pharmacist management of ADRs is associated with reduced mortality.[8] Specifically, increasing clinical pharmacist staffing from one to five pharmacists per 100 occupied beds was associated with a 48% decrease in ADRs.

A landmark trial by Leape et al[49] prospectively evaluated the impact of pharmacist participation during patient care rounds in the medical ICU on the rate of preventable ADEs and compared the before-and-after assessment to no such intervention in the cardiac ICU. During the 8-month study period, the presence of a pharmacist during rounds was associated with a reduction in the total number of preventable ADEs (33 vs 11.6 per 1,000 patient days, $P < .001$) and order-writing ADEs (10.4 vs 3.5 per 1,000 patient days, $P < .001$), whereas no changes occurred in the cardiac ICU. Of 366 interventions made by the pharmacist, 362 (99%) were accepted by the physicians and primarily related to the fundamental activities of order clarification (45%), drug information (25%), and alternative therapy recommendation (12%).

Identification of drug-drug or drug-disease interactions is a fundamental service of the medication profile review performed by clinical pharmacists. Prolongation of the corrected QT interval (QTc) is a serious adverse effect of certain medications. When a standardized algorithm for monitoring patients who receive QTc-prolonging medications was implemented at a tertiary academic medical center, the incidence of QTc prolongation was significantly lower in the 77 patients observed by a clinical pharmacist compared with 72 control group patients (19% vs 39%, $P = .006$).[50]

Economic Considerations

Limited information is available on the economic benefit of clinical pharmacists in the ICU. To date, most economic data justify a specific service or therapeutic intervention based on cost minimization of drugs or prevention of ADRs. It has been estimated across all hospital patients that the return on investment of a clinical pharmacist's salary is about 9:1, strictly from cost avoidance.[51,52] This ratio approaches 25:1 in the ICU, suggesting that the benefit of clinical pharmacy services may be optimized in patients in the ICU. Of note, this benefit-cost ratio may underestimate the true value of the clinical pharmacist because it does not account for a potential decreased mortality or shortened length of ICU stay.[19]

The Affordable Care Act emphasizes greater efficiency within US health-care systems.[53] Clinical pharmacists in the ICU can aid in improving the delivery of safe and efficient care to critically ill patients while reducing ADEs and medication errors. A common barrier in many institutions is securing the salary support to justify the hiring of dedicated critical care pharmacists. For example, if the support comes from the pharmacy department, these salaries detract from other departmental initiatives that may provide obvious financial and patient safety rewards (eg, hiring technicians, purchasing automated distribution systems or robotic fill devices, implementing advanced computer technologies). The economic benefit of clinical pharmacists, on the other hand, may only be realized through reduction in variable costs, such as drug expenditures and cost avoidance.[54] However, the current budgeting system used in many institutions may penalize some departments, even when the institution as a whole benefits. An example is the use of a newer, more expensive sedative agent that reduces ventilator and hospital days but at the expense of the pharmacy budget.[55] With the evolution of health-care models that promote greater efficiency and safety, increased reimbursements accrued by meeting quality metrics should be redistributed to hospital departments to offset the increased costs. In the case of most hospital pharmacy departments, the fixed budget must be delicately balanced by optimizing drug therapies to improve patient outcomes while dedicating clinical pharmacist personnel to support patient care services

and by maintaining a positive return on investment. For this reason, critical care physician and nurse champions are essential in promoting resources needed for the clinical pharmacist because they may advocate for these roles on the basis of improved patient care, safety, and clinical outcomes. These partnerships, in collaboration with pharmacy administration, may garner support from hospital executives and help to define the roles and responsibilities of the clinical pharmacist so that expectations are realized.

Limitations to the Existing Literature

The literature reviewed herein is limited by a lack of robust, prospective, randomized trials and consists primarily of database, retrospective cohort, and preintervention/postintervention study designs. Given the inability to control for factors such as therapeutic advancements in critical care medicine and the increasing heterogeneity of patients over time, it is difficult to attribute the results reported in the literature solely to clinical pharmacist service in intensive care. Moreover, there exists a likely possibility of publication bias in favor of positive results that challenge a robust interpretation and application of study results. Additionally, there are few data on the impact of desirable or optimal clinical pharmacy services, such as education, scholarship, and committee service, in addition to pharmacotherapy management. Future studies should focus on quantifying clinical pharmacist contributions to clinical care in blocked study design to control for the aforementioned variations.

Conclusions

Critical care pharmacists are pharmacotherapy experts and offer unique skills and insight into the care of critically ill patients. Patient safety and clinical outcomes are enhanced when clinical pharmacists participate proactively as a member of the multidisciplinary ICU team. The focused assessment by the clinical pharmacist to concentrate on the sickest patients or specific therapeutic practice domains, such as antimicrobial management, anticoagulation, sedation and analgesia, and emergency response, may help to fiscally justify their services. However, the true yield may be realized in the comprehensive application of their skills to all critically ill patients by delivering safe, efficient, and rational pharmacotherapy while potentially contributing to reducing drug expenditures. In an era focused on improving health-care efficiency, clinical pharmacists positively contribute to the overall delivery of care for critically ill patients. Future research should focus on the contributions of clinical pharmacists as members of interdisciplinary ICU or rapid response teams to measure prospectively the effects of critical care clinical pharmacist personnel allocation on patient outcomes and related metrics.

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References

1. Dasta JF. Critical care. *Ann Pharmacother*. 2006;40(4):736-737.
2. The definition of clinical pharmacy. American College of Clinical Pharmacy website. http://www.accp.com/docs/positions/commentaries/Clinpharmdefnfinal.pdf. Accessed November 23, 2012.
3. Scope of contemporary pharmacy practice: roles, responsibilities, and functions of pharmacists and pharmacy technicians. Council on Credentialing in Pharmacy website. http://www.pharmacycredentialing.org/Contemporary_Pharmacy_Practice.pdf. Accessed November 23, 2012.
4. Rudis MI, Brandl KM; Society of Critical Care Medicine and American College of Clinical Pharmacy Task Force on Critical Care Pharmacy Services. Position paper on critical care pharmacy services. *Crit Care Med*. 2000;28(11):3746-3750.
5. Haupt MT, Bekes CE, Brilli RJ, et al; Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Guidelines on critical care services and personnel: recommendations based on a system of categorization of three levels of care. *Crit Care Med*. 2003;31(11):2677-2683.
6. Brilli RJ, Spevetz A, Branson RD, et al; American College of Critical Care Medicine Task Force on Models of Critical Care Delivery; American College of Critical Care Medicine Guidelines for the Definition of an Intensivist and the Practice of Critical Care Medicine. Critical care delivery in the intensive care unit: defining clinical roles and the best practice model. *Crit Care Med*. 2001;29(10):2007-2019.
7. MacLaren R, Devlin JW, Martin SJ, Dasta JF, Rudis MI, Bond CA. Critical care pharmacy services in United States hospitals. *Ann Pharmacother*. 2006;40(4):612-618.
8. Bond CA, Raehl CL. Clinical pharmacy services, pharmacy staffing, and hospital mortality rates. *Pharmacotherapy*. 2007;27(4):481-493.
9. MacLaren R, Brett McQueen R, Campbell J. Clinical and financial impact of pharmacy services in the intensive care unit: pharmacist and prescriber perceptions. *Pharmacotherapy*. 2013;33(4):401-410.
10. Carver PL, Lin SW, DePestel DD, Newton DW. Impact of mecA gene testing and intervention by infectious disease clinical pharmacists on time to optimal antimicrobial therapy for *Staphylococcus aureus* bacteremia at a University Hospital. *J Clin Microbiol*. 2008;46(7):2381-2383.
11. Kuper KM, Septimus EJ. Health-care-associated infections: the legislative perspective and the pharmacist's role. *Am J Health Syst Pharm*. 2009;66(5):488-494.
12. Dellit TH, Owens RC, McGowan JE Jr, et al; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;44(2):159-177.
13. ASHP statement on the pharmacist's role in antimicrobial stewardship and infection prevention and control. *Am J Health Syst Pharm*. 2010;67(7):575-577.

14. Gentry CA, Greenfield RA, Slater LN, Wack M, Huycke MM. Outcomes of an antimicrobial control program in a teaching hospital. *Am J Health Syst Pharm*. 2000;57(3):268-274.
15. Bond CA, Raehl CL. Clinical and economic outcomes of pharmacist-managed antimicrobial prophylaxis in surgical patients. *Am J Health Syst Pharm*. 2007;64(18):1935-1942.
16. Bond CA, Raehl CL. Clinical and economic outcomes of pharmacist-managed aminoglycoside or vancomycin therapy. *Am J Health Syst Pharm*. 2005;62(15):1596-1605.
17. Wade WE, McCall CY. Pharmacist-managed aminoglycoside therapy in combination with a beta-lactam agent in the treatment of nosocomial pneumonia in critically ill patients. *Pharmacotherapy*. 1995;15(2):216-219.
18. Streetman DS, Nafziger AN, Destache CJ, Bertino AS Jr. Individualized pharmacokinetic monitoring results in less aminoglycoside-associated nephrotoxicity and fewer associated costs. *Pharmacotherapy*. 2001;21(4):443-451.
19. MacLaren R, Bond CA, Martin SJ, Fike D. Clinical and economic outcomes of involving pharmacists in the direct care of critically ill patients with infections. *Crit Care Med*. 2008;36(12):3184-3189.
20. National patient safety goals effective January 1, 2012. The Joint Commission website. http://www.jointcommission.org/assets/1/6/2013_CAH_NPSG_final_10-23.pdf. Accessed January 5, 2013.
21. Dobesh PP, Phillips KW, Haines ST. Improving the use of anticoagulant therapies in acutely ill medical patients. *Am J Health Syst Pharm*. 2008;65(15 suppl 7):S5-S12.
22. Petitta A. Assessing the value of pharmacists' health-system wide services: clinical pathways and treatment guidelines. *Pharmacotherapy*. 2000;20(10 pt 2):327S-332S.
23. To L, Schillig JM, Desmet BD, Kuriakose P, Szandzik EG, Kalus JS. Impact of a pharmacist-directed anticoagulation service on the quality and safety of heparin-induced thrombocytopenia management. *Ann Pharmacother*. 2011;45:195-200.
24. MacLaren R, Bond CA. Effects of pharmacist participation in intensive care units on clinical and economic outcomes of critically ill patients with thromboembolic or infarction-related events. *Pharmacotherapy*. 2009;29(7):761-768.
25. Bond CA, Raehl CL. Pharmacist-provided anticoagulation management in United States hospitals: death rates, length of stay, Medicare charges, bleeding complications, and transfusions. *Pharmacotherapy*. 2004;24(8):953-963.
26. Dager WE, Branch JM, King JH, et al. Optimization of inpatient warfarin therapy: impact of daily consultation by a pharmacist-managed anticoagulation service. *Ann Pharmacother*. 2000;34(5):567-572.
27. Jacobi J, Fraser GL, Coursin DB, et al; Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists (ASHP), American College of Chest Physicians. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med*. 2002;30(1):119-141.
28. Kress JP, Pohlman AS, O'Connor MF, Hall JB. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. *N Engl J Med*. 2000;342(20):1471-1477.
29. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet*. 2008;371(9607):126-134.
30. MacLaren R, Plamondon J, Ramsay K, Rocker G, Patrick W, Hall R. A prospective evaluation of empiric versus protocol-based sedation and analgesia. *Pharmacotherapy*. 2000;20(6):662-672.
31. Marshall J, Finn CA, Theodore AC. Impact of a clinical pharmacist-enforced intensive care unit sedation protocol on duration of mechanical ventilation and hospital stay. *Crit Care Med*. 2008;36(2):427-433.
32. Devlin JW, Holbrook AM, Fuller HD. The effect of ICU sedation guidelines and pharmacist interventions on clinical outcomes and drug cost. *Ann Pharmacother*. 1997;31(6):689-695.
33. Devlin JW, Nasraway SA Jr. Reversing oversedation in the intensive care unit: the role of pharmacists in energizing guideline efforts and overcoming protocol fatigue. *Crit Care Med*. 2008;36(2):626-628.
34. Forni A, Skehan N, Hartman CA, et al. Evaluation of the impact of a tele-ICU pharmacist on the management of sedation in critically ill mechanically ventilated patients. *Ann Pharmacother*. 2010;44(3):432-438.
35. Draper HM, Eppert JA. Association of pharmacist presence on compliance with advanced cardiac life support guidelines during in-hospital cardiac arrest. *Ann Pharmacother*. 2008;42(4):469-474.
36. To err is human: building a safer health system. Institute of Medicine website. http://www.iom.edu/~/media/Files/Report%20Files/1999/To-Err-is-Human/To%20Err%20is%20Human%201999%20%20report%20brief.pdf. Accessed November 23, 2012.
37. Landrigan CP, Parry GJ, Bones CB, Hackbarth AD, Goldmann DA, Sharek PJ. Temporal trends in rates of patient harm resulting from medical care. *N Engl J Med*. 2010;363(22):2124-2134.
38. Bertsche T, Mayer Y, Stahl R, Hoppe-Tichy T, Encke J, Haefeli WE. Prevention of intravenous drug incompatibilities in an intensive care unit. *Am J Health Syst Pharm*. 2008;65(19):1834-1840.
39. Brown JN, Barnes CL, Beasley B, Cisneros R, Pound M, Herring C. Effect of pharmacists on medication errors in an emergency department. *Am J Health Syst Pharm*. 2008;65(4):330-333.
40. Calabrese AD, Erstad BL, Brandl K, Barletta JF, Kane SL, Sherman DS. Medication administration errors in adult patients in the ICU. *Intensive Care Med*. 2001;27(10):1592-1598.
41. Klopotowska JE, Kuiper R, van Kan HJ, et al. On-ward participation of a hospital pharmacist in a Dutch intensive care unit reduces prescribing errors and related patient harm: an intervention study. *Crit Care*. 2010;14(5):R174.
42. Kopp BJ, Mrsan M, Erstad BL, Duby JJ. Cost implications of and potential adverse events prevented by interventions of a critical care pharmacist. *Am J Health Syst Pharm*. 2007;64(23):2483-2487.
43. Rivkin A, Yin H. Evaluation of the role of the critical care pharmacist in identifying and avoiding or minimizing significant drug-drug interactions in medical intensive care patients. *J Crit Care*. 2011;26(1):104.e1-104.e6.
44. Weant KA, Humphries RL, Hite K, Armitstead JA. Effect of emergency medicine pharmacists on medication-error reporting in an emergency department. *Am J Health Syst Pharm*. 2010;67(21):1851-1855.
45. Valentin A, Capuzzo M, Guidet B, et al; Research Group on Quality Improvement of the European Society of Intensive Care Medicine (ESICM); Sentinel Events Evaluation (SEE) Study Investigators. Errors in administration of parenteral drugs in intensive care units: multinational prospective study. *BMJ*. 2009;338:b814.
46. Vasileff HM, Whitten LE, Pink JA, Goldsworthy SJ, Angley MT. The effect on medication errors of pharmacists charting medication in an emergency department. *Pharm World Sci*. 2009;31(3):373-379.

47. Viktil KK, Blix HS. The impact of clinical pharmacists on drug-related problems and clinical outcomes. *Basic Clin Pharmacol Toxicol*. 2008;102(3):275-280.
48. Bond CA, Raehl CL, Franke T. Clinical pharmacy services, hospital pharmacy staffing, and medication errors in United States hospitals. *Pharmacotherapy*. 2002;22(2):134-147.
49. Leape LL, Cullen DJ, Clapp MD, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA*. 1999;282(3):267-270.
50. Ng TM, Bell AM, Hong C, et al. Pharmacist monitoring of QTc interval-prolonging medications in critically ill medical patients: a pilot study. *Ann Pharmacother*. 2008;42(4):475-482.
51. Schumock GT, Meek PD, Ploetz PA, Vermeulen LC; The Publications Committee of the American College of Clinical Pharmacy. Economic evaluations of clinical pharmacy services—1988-1995. *Pharmacotherapy*. 1996;16(6):1188-1208.
52. Schumock GT, Butler MG, Meek PD, Vermeulen LC, Arondekar BV, Bauman JL; 2002 Task Force on Economic Evaluation of Clinical Pharmacy Services of the American College of Clinical Pharmacy. Evidence of the economic benefit of clinical pharmacy services: 1996-2000. *Pharmacotherapy*. 2003;23(1):113-132.
53. Emanuel E, Tanden N, Altman S, et al. A systemic approach to containing health care spending. *N Engl J Med*. 2012;367(10):949-954.
54. Rauh SS, Wadsworth EB, Weeks WB, Weinstein JN. The savings illusion—why clinical quality improvement fails to deliver bottom-line results. *N Engl J Med*. 2011;365(26):e48.
55. Dasta JF, Kane-Gill SL, Pencina M, et al. A cost-minimization analysis of dexmedetomidine compared with midazolam for long-term sedation in the intensive care unit. *Crit Care Med*. 2010;38(2):497-503.