

The Role of Critical Care Pharmacists Beyond Intensive Care Units: A Narrative Review on Medication Management for ICU Survivors

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There is a global improvement in critical care services that leads to prolonged survival after ICU stay. This improvement has increased the demand for multidisciplinary critical care services beyond the ICU. Recently, efforts focused on the patient's quality of life after ICU discharge and family involvement in their care. Most older adults who survive an ICU stay are challenged by complex medication changes following discharge, as are their caregivers. Limited literature addresses the standard of practice for medication management and critical care pharmacists' involvement in post-ICU services. This narrative review describes the available literature that addresses medication management in post-ICU settings by critical care pharmacists and potential axes for future research. The included articles were articles published in English related to adult ICU survivors and addressed pharmacist involvement or medication management. The main findings summarize the most performed pharmacist services following ICU discharge, including medication reconciliation, full medication review, and adverse drug event preventative measures. This review concluded a lack of consensus about the standard model of post-ICU pharmacy services and the relationship of these services with long-term outcomes.

Keywords: Critical care. Follow-up clinic. Intensive care units. Pharmacist. Medication Management.

INTRODUCTION

More than 5 million patients are admitted annually to US intensive care units (ICUs) each year (SCCM, 2021a). The reported readmission rates among adult ICU survivors were 15%, 26%, and 43% at 30 days, 90 days, and one year, respectively (Hirshberg *et al.*, 2019). Global improvements in critical care services have led to prolonged survival after ICU discharge. A prospective, observational feasibility study at an academic hospital revealed that 71% of ICU patients survived hospital discharge, while 28% of survivors were seen in the post-ICU clinic (Sevin *et al.*, 2018). These statistics highlighting their effectiveness have increased the demand

for multidisciplinary critical care services and support after ICU discharge. One study found that, overall, one-year survival following ICU discharge was 42.0 %, and survival rates beyond that were comparable to those of the general population (Andersen *et al.*, 2015). Most patients who survive an ICU admission develop health-related problems due to their baseline illnesses, in addition to being in the ICU. These health-related issues are defined as post-intensive care syndrome (PICS), that starts in the ICU and persists after discharge. This syndrome can affect a patient's physical, mental, and emotional well-being. PICS is considered one of the chronic challenges for ICU survivors and their families because half of the patients never return to their baseline status (Rawal, Yadav, Kumar, 2017).

Most older adults who survive an ICU stay struggle with complex medication changes following discharge, as do their caregivers. Treatment modifications may

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include the addition of new therapies, discontinuation of some medications, failure to restart some medications, continuation of treatments not indicated after discharge, and simultaneous use of multiple drugs (polypharmacy) that are further exacerbated by PICS. Several studies have demonstrated that use of a large percentage of unnecessary medications continue following an ICU stay (Bell *et al.*, 2011).

Recently, multiple groups have tried to initiate post-ICU care services to help ICU survivors and their families. These services can range from post-ICU follow-up clinics to post-ICU recovery centers (SCCM, 2021b). The composition of ICU follow-up clinics varies widely among centers in the USA, the UK, and other countries. Typically, a clinic has an interdisciplinary team structure that includes doctors, pharmacists, nurses, social workers, and physical and occupational therapists. This structure supports ICU survivors in many aspects of health, cognition, and social, as well as therapeutic, challenges (Modrykamien, 2012). The post-ICU follow-up clinic is considered a suitable setting for medication management and adjustment.

A recent opinion paper identified and described clinical pharmacy services provided for the management of ICU survivors and the support of their caregivers in intensive care unit recovery clinics (ICU-RCs). This opinion paper emphasized several benefits that ICU recovery centers contribute, along with the required pharmacist training and credentials necessary to provide these services. The article concluded that clinical pharmacists in ICU-RCs could play a vital role in promoting education on PICS, improving medication adherence, and ensuring comprehensive medication management. Additionally, they can conduct medication reconciliation services, provide an assessment of inappropriate and appropriate medications after hospitalization, and address adverse drug events (ADEs) (Mohammad *et al.*, 2020).

Other than this recent opinion paper, literature addressing the standard of practice for medication management or critical care pharmacists' involvement in post-ICU medication services are limited. This review aims to summarize the studies that address medication management and critical care pharmacist

involvement in post-ICU settings. Articles that were published in EMBASE, MEDLINE via PubMed, and Web of Science containing the search terms "Intensive care," "Critical care," "follow-up clinic," "Survivor," "Clinical Pharmacist," and "Medication Management" were evaluated. Additional references, including abstracts and conference posters, were identified through a manual search using similar search terms. Only articles published in English related to adult ICU survivors and that directly addressed pharmacist involvement or medication management were included in this review. Studies regarding ICU survivors that evaluated cognitive, behavioral, physical, psychiatric, or ICU survivors' family or caregiving aspects were outside the scope of this review.

Current Status of Medication Management in post ICU settings

Treatment alterations can result in adverse drug effects and medication errors. A study was conducted to evaluate the rates of potentially unintentional dismissal of chronic medications following ICU admission. The study concluded that ICU admission was associated with a high number of medication discontinuations. Unintentional medication discontinuation, in addition to the inappropriate continuation of ICU-initiated medications, could result in worse long-term outcomes for ICU survivors (SCCM, 2021b).

One single-center study of 120 patients with critical illnesses reported that approximately 250 inappropriate medications were prescribed at discharge. The same study found that at least one or more of these inappropriate medications were prescribed at hospital discharge following an ICU stay (Morandi *et al.*, 2013). Medication-related problems after ICU discharge could affect ICU survivors of any age group; even younger adults are at risk due to complex ICU courses and complicated drug regimens after discharge.

The presence of pharmacists in these settings permits the early identification of medication-related problems and improves preventive health measures for ICU survivors. Data from one observational study found that 39% of patients had medication(s) stopped at the

post-ICU clinic, and 16% of patients had an adverse drug event (ADE) identified by pharmacists. Increased health-related preventive measures were also reported in ICU survivors consulted by a pharmacist; influenza vaccination was administered to 23% of the patients, and pneumococcal vaccination was administered to 4% (Stollings *et al.*, 2018).

Vanderbilt University Medical Center's post-ICU recovery clinic is among the first in the United States to address the wide variety of problems experienced by ICU survivors and to provide patients and their families with care after discharge. The Vanderbilt post-ICU clinic team applies a multidisciplinary approach with the help of critical care pharmacists, doctors, nurse practitioners, case managers, and neuropsychologists. Each team member sees the patient individually and develops a comprehensive therapeutic plan after a team conference. The goal is then communicated to the patient's primary care provider (ICU delirium, 2020).

In the United Kingdom, post-ICU clinics are scarce. One UK survey found that only 30% of surveyed institutions had ICU clinics; psychologists were present in 30% of these institutions, psychotherapy in 29%, and dietitian services were only available in 2% of facilities (Griffiths *et al.*, 2006). While pharmacists were included in US clinics, they were not included in the UK centers, even though collaboration between critical care pharmacists and health care teams has been well established for decades as a means of improving patient-related outcomes, medication safety, and cost (Richter *et al.*, 2016).

The Society of Critical Care Medicine (SCCM) has identified critical care pharmacists as essential team members in critical care services; however, little is known about the standard practice of critical care pharmacists in post-ICU clinical settings. One study that assessed the inclusion of pharmacists in post-ICU survivor care emphasized the importance of such a measure and recommended close and early post-ICU follow-up by pharmacists (Stollings *et al.*, 2018). In the THRIVE collaborator study, which included multiple international sites and multidisciplinary teams, only 4 of 15 participating centers employed pharmacists as part of the post-ICU program team (Haines *et al.*, 2019).

Types of Medication Management Services Post ICU

Several studies and reports have addressed the importance of comprehensive medication management following ICU discharge. Some of these studies included information about pharmacists who provided medication-related interventions. In contrast, others have a survey or scale that could be completed by a nurse or doctor in post-ICU recovery centers or clinics.

A recent study aimed to determine the prevalence of specific medication-related problems detected in patients and observed post-ICU stay (Coe *et al.*, 2020). This report focused on a pharmacy intervention program established in a post-ICU follow-up clinic. During this intervention, the researchers included patients who visited the ICU follow-up program and systematically graded each medication-related problem. The pharmacist's comprehensive medication review found 29% of drug omissions and 64% of the drug-related problems identified were classified as either moderate or major. Interestingly, the results showed that the amount of pain medication prescribed at discharge from intensive care was predictive of medication-related problems (Coe *et al.*, 2020).

Pain medications are an essential class of drugs that clinical pharmacists should review during the patient transition and, most importantly, following ICU discharge. The risk of pain medication-related side effects and adverse outcomes could be prevented by having pharmacists play integral roles in post-ICU clinics and centers. The authors concluded that pharmacist intervention and good communication of medication changes are essential in ICU recovery programs for patients and their families.

Although this study addressed the importance of pharmacist interventions in post-ICU care, the impact of these pharmacist interventions on long-term patient outcomes and whether these interventions need to be scheduled regularly or only provided once following ICU discharge remains unclear. Additionally, the pharmacoeconomic impact of pharmacists' comprehensive medication reviews in post-ICU programs needs to be addressed. Pharmacist services in the post-ICU period do not need to be limited to the recovery

center or ICU follow-up clinic; however, these services can be accessed via telephone or electronic tools.

Pharmacists can conduct comprehensive medication review and reconciliation of patients after discharge from the ICU and hospital. An electronic tool could help monitor all patient medications, specific high-risk therapies, or high-risk ICU survivors, such as immunosuppressed post-ICU patients. A quality improvement project was conducted in five ICUs at large academic centers to assess the benefits of pharmacist electronic handoff tools in reducing the rate of atypical antipsychotics (AAPs) initiated in AAP-naïve critically ill adults. The report found that the electronic handoff tool may reduce the rate of AAP continued after ICU transfer (Kram *et al.*, 2019).

There is a considerable need to investigate the impact of handoff tools for several ICU-related medications, such as stress ulcer prophylaxis, pain medications, atypical antipsychotics, and stress hyperglycemia medications. Due to the complexity of post-ICU patient cases, it is challenging to define the timeline for the critical period to apply handoff tools, but a complete medication review should be conducted physically or virtually as early as possible following ICU discharge. The medication review could detect early medication-related issues even before the patients see their primary care providers.

Potential for Pharmacist Contributions in Post-ICU Services

The role of pharmacists in transitioning patients from the ICU to general wards and from wards to home or long-term care facilities (multifaced ICU transfer) is crucial. Many medications are missed during the early transfer period, and additions and deletions are quite common throughout this critical time for vulnerable patients. The question remains whether the timing of pharmacist contributions influence long-term outcomes; however, defining the critical care pharmacist role in post-ICU settings is one crucial aspect of service initiation at any stage. This description is essential for service standardization and justification.

A prospective, observational cohort study was conducted to describe an ICU recovery center (RC)

critical care pharmacist (Stollings *et al.*, 2018). The study emphasizes various pharmacist roles, including full medication review, medication reconciliation, patient interviews, medication counseling, and resultant interventions during post-ICU follow-up. The researchers found that the pharmacist performed up to 90% of the total medication reviews. The same study found that the median number of pharmacist interventions was four, with at least one pharmacy intervention for each patient. The highest percentage of these interventions (39%) was associated with medication discontinuation in the post-ICU clinic. This study and the most recent opinion paper help identify and describe the pharmacist's role in post-ICU care, addressing its importance and its positive impact on ICU survivors (Stollings *et al.*, 2018; Mohammad *et al.*, 2020).

One of the essential aspects of patient care that has not been adequately addressed is how to identify which ICU survivors are among the highest-risk groups for medication issues and which post-ICU patients might benefit the most from critical care pharmacist interventions in the post-ICU period. Moreover, it is unclear whether the most benefit to ICU survivors came from the critical care pharmacist during the early post-ICU period when they were not seeing their primary care physicians or later in the post-ICU period when seeing their providers.

Facilitators and Barriers for Post-ICU pharmacist contribution

As previously described, pharmacists could play a significant role in post-ICU survivor medication management; however, they face many barriers. A survey conducted on ICU-RC pharmacists described their roles, perceived barriers, and facilitators. Pharmacists report that comprehensive medication review is the primary activity they perform along with medication reconciliation. In addition, ICU-RC pharmacists state that incorporation in the post-ICU clinic workflow and support from other healthcare providers are the primary facilitators (Coe *et al.*, 2020).

The method used to communicate medication interventions during the post-ICU period is a cornerstone

for facilitating proper medication management with other healthcare providers. A study has reported that pharmacists communicated with other healthcare providers in the post-ICU recovery clinic via face-to-face interactions, case conferences, e-mails, documentation in electronic medical records (EMRs), and telephone calls (Stollings *et al.*, 2018).

Communication between critical care pharmacists, other healthcare providers, and ICU survivors could be improved. Several applications and platforms could be utilized to conduct comprehensive medication reviews for ICU survivors. Virtual communication can replace traditional means of communication, a shift that has already begun in response to the COVID-19 pandemic, as many in-person clinical services have transitioned to virtual tools. Still, more research is needed to evaluate the effectiveness of utilizing virtual tools in post-ICU medication review clinics for ICU survivors.

Pharmacists report a lack of dedicated time and inadequate billing for services as the main barriers to their participation in post-ICU patient care (Coe *et al.*, 2020). It is crucial for decision-makers and stakeholders to further prioritize the establishment of appropriate billing strategies for post-ICU pharmacy services, as timing and billing are ongoing issues for pharmacists. However, it is unclear if medication management services

conducted by other healthcare team members who have billing privileges are equally effective as medication management services undertaken by pharmacists. In addition, researchers did not investigate whether other pharmacists, such as ambulatory care pharmacists, could conduct medication management in post-ICU centers.

Several factors might justify the presence of a specialized critical care pharmacist in such services. These include knowledge of the patients' ICU admission history, familiarity with common omissions and unintentional continuations of ICU-related medications, and consistent care during the transition period, especially if the same ICU pharmacist is also working in the post-ICU clinic.

A review of which medications are required after ICU discharge is crucial in preventing medication duplications and unnecessary medication continuation, thereby avoiding adverse outcomes. A comprehensive medication review should be considered one of the critical services provided to any discharged ICU survivor. Pharmacists should utilize a standardized list of questions to assess medication use, dosages, side effects, and adherence in post-ICU settings.

A summary of the literature related to pharmacist contributions or medication reviews for post-ICU survivors is included at the end of the paper in Table I.

TABLE I - Summary of the literature related to pharmacist contributions or medication review for post-ICU survivors

Study	Year	Study Design	Participants	Objective	Pharmacist Involvement	Medication Review	Interventions	Conclusion
Crocker <i>et al.</i>	2003	Descriptive study	101 post-ICU patients seen in the clinic	To describe the experience of a multidisciplinary clinic	No	Yes 30 minutes are spent with the doctor to review medications	Visit to ICU and referral to specialist. Interventions included drug reconciliation, physical therapy, and occupational therapy assistance	This service has been extremely valuable to patients and their care and has helped staff understand the needs of patients once they have left intensive care.

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Cuthbertson <i>et al.</i>	2009	A pragmatic, nonblinded, multi-center, randomized controlled trial	286 patients ages ≥ 18 years recruited after discharge from intensive care	Nurse led intensive care follow-up programs (involve medications review) versus standard care follow-up programs	No (nurse)	Yes Review of current drug therapy within 9 months (97%) Changes to current medications within 9 months (2%)	To test the hypothesis that nurse-led follow-up programs are effective and cost effective in improving quality of life after discharge from intensive care	A nurse led intensive care follow-up programs showed no evidence of being effective or cost effective in improving patients' quality of life in the year after discharge from intensive care.
Bell <i>et al.</i>	2011	A population-based cohort study	3963 patients aged 66 years or older using at least 1 of 5 long-term medications	To evaluate rates of potentially unintentional discontinuation of medications following hospital or ICU admission	No	Yes The highest rate of medication discontinuation occurred in the antiplatelet or anticoagulant agent group (19.4%)	Rates of medication discontinuation were compared across three groups: patients admitted to the ICU, patients hospitalized without ICU admission, and non-hospitalized patients (controls)	Patients with chronic diseases were at risk for potentially unintentional discontinuation after hospital admission. Admission to the ICU was generally associated with an even higher risk of medication discontinuation.
Morandi <i>et al.</i>	2013	Prospective cohort study	120 patients ≥ 60 years old who survived an ICU hospitalization	To determine types of PIMs and AIMs, which PIMs are most likely to be considered AIMs, and risk factors for PIMs and AIMs in elderly ICU survivors at hospital discharge. * potentially (PIMs) and inappropriate medications (AIMs).	Yes	Yes The number of pre-admission PIMs ($P < .001$), at hospital discharge	PIMs were defined according to published criteria; AIMs were adjudicated by a multidisciplinary panel. Medication lists were abstracted at the time of preadmission, ward admission, Intensive Care Unit (ICU) admission, ICU discharge, and hospital discharge	Certain types of PIMs, which are commonly initiated in the ICU, are more frequently considered inappropriate upon clinical review. Efforts to reduce AIMs in elderly ICU survivors should target these specific classes of medications.

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Khan <i>et al.</i>	2015	Descriptive study	53 patients ≥ 18 years of age, admitted to ICU, and either spent ≥ 48 hours on mechanical ventilation or had delirium for ≥ 48 hours	Evaluation by the interdisciplinary team (intensive care physician, nurse, and social worker) and the creation of a personalized care plan, including cognitive exercises, self-management training manuals, pharmacological and nonpharmacological prescriptions, and proactive referrals to community resources, neuropsychologists, and physical rehabilitation services	No	Yes	To share experience of implementing the collaborative critical care model and its patient characteristics	Patients who participated in 3 visits showed better physical performance in the 6-minute Walk Test and better leg strength over time. There were improvements in scores on anxiety, depression, and PTS scores.
Stollings <i>et al.</i>	2018	A prospective, observational cohort study conducted in ICU recovery center	All adults referred to the ICU-RC at an academic tertiary care center (Vanderbilt University Medical Center)	To describe the role of an ICU-RC critical care pharmacist in identifying and treating medication-related problems among ICU survivors	Yes	Yes 39% patients had medication(s) stopped at the clinic appointment, and (32%) patients had new medication(s) started. The pharmacist identified (16%) patients who had an adverse drug event (ADE)	The pharmacist completed a full medication review, including medication reconciliation, patient interview, medication counseling, and resultant interventions, during the ICU-RC appointment.	Use of a critical care pharmacist resulted in the identification and treatment of multiple medication-related problems in an ICU-RC as well as implementation of preventive measures.

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Kram <i>et al.</i>	2018	This single-center, pre-post quality improvement study	358 patients, who were at least 18 years of age, and admitted to an adult ICU (medical, surgical, cardiothoracic surgery, neurosciences, and cardiac) with an AAP ordered while in the ICU	To evaluate whether a pharmacist-initiated electronic handoff tool can reduce the overall, and potentially inappropriate hospital discharge prescribing rate of atypical antipsychotics (AAP) initiated in AAP-naïve critically ill adults.	Yes	Yes (AAP only) The proportion of ICU survivors with an AAP continued at the time of ICU transfer to the floor was reduced post intervention. (78.7% vs 66.7%, P=.012).	The intervention included the following: Upon order verification or recognition of an AAP initiated in the ICU in an AAP-naïve patient, the ICU clinical pharmacist generated an electronic handoff that flagged this medication for daily follow-up	A pharmacy-initiated electronic handoff tool may reduce the proportion of AAP-naïve ICU survivors with an AAP continued at the time of ICU transfer
Sevin <i>et al.</i>	2018	A prospective, observational feasibility study	Eligible patients were critically ill adults ≥18 years old with one or more risk factors for the development of PIC	Referred patients were followed by an ICU-RC coordinator (this role was performed at various times by a nurse practitioner, case manager, or clinical pharmacist) throughout their hospital stay and then offered an appointment.	Yes	Yes The median number of pharmacy interventions, was 4 per patient	To describe the design and initial implementation of an Intensive Care Unit Recovery Center (ICU-RC) in the United States	An ICU-RC identified a high prevalence of cognitive impairment, anxiety, depression, physical debility, lifestyle changes, and medication-related problems warranting intervention. Whether an ICU-RC can improve ICU recovery in the US should be investigated in a systematic way.
Coe <i>et al.</i>	2020	Cross-sectional study	9 ICU recovery center pharmacists	To describe ICU recovery clinic pharmacists' activities, roles, and perceived barriers and facilitators to practicing in ICU recovery clinics across different institutions	Yes	Yes Seven (78%) pharmacists always performed medication reconciliation and a comprehensive medication review in each patient visit.	15 survey questions	The ICU recovery clinic pharmacists address ICU survivors' medication-related needs by providing direct patient care in collaboration within the interdisciplinary ICU recovery clinic setting. Strategies to mitigate a pharmacist's barriers to practicing in ICU recovery clinics, such as lack of dedicated time and inability to adequately bill for pharmacist services

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Haines <i>et al.</i>	2019	Qualitative inquiry via SCCM focus group	Participants were recruited from the in-person meetings of the THRIVE collaborative sites for follow-up clinics	To identify the key mechanisms that clinicians perceive improve care in ICU	Yes	No	A semi-structured interview guide was used with prompting questions.	The follow-up of patients and families in post-ICU care settings was perceived to improve care within the ICU via five key mechanisms.

CONCLUSION AND FUTURE PERSPECTIVES

The most frequently performed pharmacist services following ICU discharge are medication reconciliation, full medication review, and adverse drug event preventative measures. This narrative review concluded that there is a lack of consensus regarding the standard model of post-ICU pharmacy services and the proper timing for providing such services. With the expansion of post-ICU clinics and the increase in ICU survivor numbers, it is imperative to standardize the role of critical care pharmacists in post-ICU settings.

This narrative review was limited in some aspects: the selection criteria for inclusion of the articles in this review may not have been comprehensively specified, leading to inherent bias in article selection, in addition to a sparsity of available literature, the heterogeneity of the relevant studies, and different outcome parameters. Various practice models are challenging when attempting to conduct a validated review to address specific outcomes; therefore, a systematic review or meta-analysis would be valuable for accurately evaluating the consequences of these services.

The role of critical care pharmacists in post-ICU recovery centers or clinics could be extended to administrative and scholarly activities. Pharmacists should be involved in developing policies and procedures for medication reviews and workflows, developing post-ICU clinic infrastructure, and conducting clinical studies in post-ICU settings. Future research should expand the literature by evaluating the timing and standard practice

model for these services, billing issues, and provider status. Furthermore, the economic benefits of these services and their relationship with improved long-term outcomes, including readmission rate and quality of life, needs to be addressed.

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