Factors associated with in-hospital mortality following ICU discharge: a comprehensive review

Malcolm Elliott† RN, BN, Linda Worrall-Carter* RN, PhD, Karen Page‡ RN, DN, *St Vincent’s Centre for Nursing Research, Australian Catholic University, Melbourne, Australia †Holmesglen Institute, Melbourne, Australia ‡Clinical Care Engagement, Heart Foundation, Melbourne, Australia

Critically ill patients are admitted to the Intensive Care Unit (ICU) to reduce morbidity and mortality associated with acute illness, trauma or surgical procedures. The objective of this review is to identify key factors associated with in-hospital mortality in adult patients discharged from the ICU. A search of CINAHL, MEDLINE, PubMed and Web of Knowledge databases was performed for the period 2006-2012. Key terms were used to identify relevant literature. Inclusion criteria were research studies examining in-hospital mortality in adult patients discharged from Intensive Care, peer-reviewed studies and those published in English. Data extraction and appraisal were performed. Twenty-two studies which examined in-hospital mortality following intensive care discharge and meeting the inclusion criteria were identified. Various methodological designs were used. Key factors associated with post-Intensive Care mortality were older age, illness acuity and time of discharge. Factors associated with post-ICU mortality have changed little over the past decade. The only modifiable factor in care processes is time of ICU discharge. Research needs to identify how best to articulate modifiable risk factors and deliver care to reduce the risk of preventable mortality in patients discharged from the ICU.

INTRODUCTION

Critically ill patients are admitted to the Intensive Care Unit (ICU) to reduce morbidity and mortality associated with acute illness, trauma or surgical procedures. Up to a fifth of patients will die in the ICU. The majority survive their ICU admission to be discharged to a step-down or ward environment. Some patients though will die soon after ICU discharge, and deaths such as these are predictable and cannot be avoided. However, other deaths occurring after ICU discharge are unexpected and may be preventable with better standards of care.

Seminal research has found that one out of every five patients who died on a ward after ICU discharge was expected to survive. These patients tended to be older, have longer ICU lengths of stay and higher illness acuity scores. Researchers concluded that some of these deaths may have been avoided with a better standard of ward care. These seminal studies though important are more than a decade old and many changes to acute care processes have occurred since then.

The introduction of ICU Liaison Nurses and Medical Emergency Teams in Australia and Critical Care Outreach Teams in the United Kingdom has influenced how post-ICU care is delivered on hospital wards today. In order to reduce the incidence of short-term mortality, more information on risk factors for and determinants of post-ICU mortality are needed. It is therefore timely to conduct further review of the literature to identify factors associated with in-hospital mortality in post-ICU patients. Identifying these factors would allow the streamlining of care processes, thus reducing morbidity and mortality rates in this vulnerable patient population, as well as the associated healthcare costs.

Aim

The aim of this paper is to present a comprehensive review of current literature on in-hospital mortality in adult patients discharged from the ICU. The purpose of the review was to identify key factors associated with post-ICU mortality, rather than just describing causes of death such as malignant disease or respiratory failure.

METHODS

Search strategy

A systematic search was conducted of the electronic databases CINAHL, MEDLINE, PubMed and Web of Knowledge. A range of search terms and combinations was used: intensive OR critical care AND discharge OR transfer AND mortality OR death. The reference lists of retrieved studies were hand searched to locate further relevant studies not identified by the electronic search strategy. Inclusion and exclusion criteria were applied to aid in determining the final literature sample. Literature was included in the review if it was:

- Primary research (quantitative or qualitative) focusing on in-hospital mortality in adult patients discharged from the ICU
- Published in full text in a peer-reviewed journal, and
- Published between 2006 and 2012.

Studies on paediatric patients, cardiothoracic surgical patients and studies not reported in English were excluded. Studies on patients discharged from the ICU expected to die or made not for resuscitation were also excluded. A search for unpublished data was not conducted.

Data evaluation and synthesis

Once relevant studies were identified, data were extracted. Critical appraisal guidelines were used to critique the methodological quality of each study including design, sample size and data collection period. Research papers were read and re-read to identify aims, methods and findings. Other data extracted included ICU characteristics and study limitations.

RESULTS

Online searches identified 1566 publications relating to the review topic. When the inclusion criteria were applied to
Table 1. Studies examining post-ICU mortality

<table>
<thead>
<tr>
<th>Author</th>
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<th>Design</th>
<th>Sample</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Utzolino et al.</td>
<td>20-bed surgical ICU in Germany</td>
<td>To assess if unplanned ICU discharge correlates with a worse outcome</td>
<td>Retrospective analysis</td>
<td>2558 ICU discharges during 1 year</td>
<td>2% of daytime ICU discharges and 3% of night time discharges died on the ward.</td>
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<td>Mortality rate increased by 4% in readmissions for each year of age (p&lt;0.05; OR for death 1.04 for each year of age).</td>
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<td>Readmission correlates with a higher risk of death.</td>
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<td>Singh et al.</td>
<td>20-bed Australian ICU</td>
<td>To assess effect of after-hours ICU discharge on in-hospital mortality</td>
<td>Observational cohort study</td>
<td>2300 patients admitted to ICU during 3-year period</td>
<td>34.7% of patients were discharged after hours; crude mortality of these patients was 13.7% vs 10.1% in patients not discharged after hours.</td>
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<td>After-hours discharge was associated with a higher risk of in-hospital mortality (OR 1.38; p&lt;0.05).</td>
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<tr>
<td>Braber &amp; van Zanten</td>
<td>12-bed medical-surgical ICU in the Netherlands</td>
<td>To study characteristics of patients dying in hospital after ICU discharge</td>
<td>Retrospective cohort study</td>
<td>405 ICU patients</td>
<td>10.3% of post-ICU patients died in hospital. Independent predictors of post-ICU death were: age (mean 73.9 years), number of co-morbidities (mean 1.05), ICU length of stay (mean 9.8 days), APACHE II score (mean 21).</td>
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<tr>
<td>Al-Subaie et al.</td>
<td>17 bed medical-surgical ICU in British university teaching hospital</td>
<td>To assess the value of CRP as a predictor of ICU readmission and post-ICU death</td>
<td>Prospective observational study</td>
<td>1185 ICU discharges during 12 month period</td>
<td>2.9% of post-ICU patients died unexpectedly. These patients were older (76 vs 59 yrs; p&lt;0.001) and had a higher APACHE II score (21 vs 15; p&lt;0.001).</td>
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<tr>
<td>Martinez et al.</td>
<td>26-bed medical-surgical ICU in 700-bed Spanish teaching hospital</td>
<td>To assess relationship between tracheostomy tube in situ at ICU discharge and hospital mortality</td>
<td>Prospective observational cohort study</td>
<td>118 patients tracheostomised in ICU</td>
<td>Ward mortality was 19% overall; 11% in decannulated patients and 26% with tracheostomy tube in situ. Three factors were significantly associated with ward mortality: lack of decannulation before ICU discharge (OR 0.14, 95% CI 0.03–0.83, p=0.03), body mass index &gt; 30 kg/m² (OR 5.81, p=0.03), tenacious sputum at ICU discharge (OR 7.27, p=0.05).</td>
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<tr>
<td>Chrusch et al.</td>
<td>Single ICU in Canadian tertiary hospital</td>
<td>To determine whether a lack of ICU beds was leading to premature ICU discharge and subsequent death</td>
<td>Prospective cohort study</td>
<td>10,185 ICU admissions during 8-year period</td>
<td>5.5% of patients experienced an adverse event (readmission, death) within 7 days of ICU discharge. Adjusted risk factors for post-ICU death or readmission included: age &gt; 35 years (OR 1.46), APACHE II score of 20–29 (OR 2.16), ICU length of stay 3–10 days (OR 1.72, 95% CI 1.35–2.18) and no ICU vacancy at the time of discharge (OR 1.16).</td>
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<tr>
<td>Bagshaw et al.</td>
<td>57 Australian and New Zealand ICUs</td>
<td>To assess rate, characteristics and outcomes of very old patients (&gt;80 yrs) admitted to ICU</td>
<td>Retrospective analysis of prospectively collected data</td>
<td>15,640 ICU admissions over 6-year period</td>
<td>Crude in-hospital mortality rate was higher for patients aged &gt; 80 years (24% vs 13%, p&lt;0.001). Factors associated with hospital mortality were: age &gt; 80 years (OR 5.4), medical admission (OR 2.58, p&lt;0.001), and ICU length of stay (per day) (OR 1.17, p&lt;0.001).</td>
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<tr>
<td>Sakr et al.</td>
<td>198 ICUs in 24 European countries</td>
<td>To investigate predictors of post-ICU mortality</td>
<td>Sub-analysis of data collected from larger study</td>
<td>3147 patients admitted to ICU</td>
<td>In-hospital mortality rate 4%; of these 20% died on first day after ICU discharge. Non-survivors were: older (70 years + 12.5 vs 59 + 18 years, p&lt;0.001), had higher incidence of cancer (8.8% vs 1.5%, p&lt;0.001) and cirrhosis (8.8% vs 2.7%, p&lt;0.001), had greater SAPS II (45.5 + 14.7 vs 30.3 + 13, p&lt;0.001) and SOFA scores (4.6 + 3.1 vs 2.5 + 2.1, p&lt;0.001), and were more likely to be admitted for medical than surgical reasons (68% vs 48.6%, p&lt;0.001).</td>
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<tr>
<td>Laupland et al.</td>
<td>All ICUs in one Canadian health region.</td>
<td>To determine whether patients admitted to ICU on evenings or weekends have increased mortality rates.</td>
<td>Inception cohort design</td>
<td>20,466 ICU admissions</td>
<td>26% of patients were discharged on weekends; 41% at night and/or weekend. Post-ICU mortality rate 6%. The crude risk for post-ICU death was lowest in late morning and early afternoon and then increased gradually until midnight. Increased crude mortality rates were associated with discharge at night versus day time (12% vs 5%, p&lt;0.0001).</td>
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### Table 1. Studies examining post-ICU mortality (continued)

<table>
<thead>
<tr>
<th>Author</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Ho et al.24</td>
<td>22-bed ICU in Australian university hospital</td>
<td>To assess ability of clinical markers to predict ICU-discharge mortality</td>
<td>Prospective cohort study</td>
<td>603 consecutive ICU patients who survived their first admission</td>
<td>4.3% of post-ICU patients died in hospital; most deaths occurred within 2 weeks (mode 1 day, median 8.5 days). High CRP concentrations at ICU discharge were associated with in-hospital mortality (OR 1.09, p=0.001).</td>
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<tr>
<td>Fernandez et al.25</td>
<td>16-bed medical-surgical ICU</td>
<td>To determine the effect of ICU discharge with a tracheostomy on ward mortality</td>
<td>Retrospective cohort study</td>
<td>936 patients discharged from ICU</td>
<td>13.9% of patients were discharged with a tracheostomy; ward mortality was higher than those without a tracheostomy (26 vs 7%, p&lt;0.001). Three factors were associated with ward mortality in multivariate analysis: age (OR 1.03, p=0.009), tracheostomy in situ (OR 2.2, p=0.01) and Sabadell score of 1 or higher (OR 4.6, p=0.001).</td>
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<tr>
<td>Campbell et al.3</td>
<td>Single ICU in Scotland</td>
<td>To identify post-ICU patients at risk of death or readmission</td>
<td>Secondary analysis of clinical audit data</td>
<td>6208 admissions to ICU during 10-year period</td>
<td>11.2% of patients died in hospital after ICU discharge. Risk factors for post-ICU mortality included: increasing age (70 vs 59 years, OR 1.04, p&lt;0.001), days in hospital before ICU admission (2 vs 1; OR 1.03, p&lt;0.001), APACHE II (22 vs 17; OR 1.09, p&lt;0.001), and CPR in 23 hours before ICU admission (OR 1.98, p&lt;0.001).</td>
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<tr>
<td>Pilcher et al.26</td>
<td>ICUs in 40 Australian and New Zealand hospitals</td>
<td>To determine prevalence, trends and effect on patient outcomes of ICU discharge time</td>
<td>Retrospective analysis of data routinely recorded on ICU admission</td>
<td>76,690 ICU discharges</td>
<td>Post-ICU mortality rate 5.8%. After-hours discharges occurred in 18.2% of patients; mortality in these patients was higher than daytime discharges (8% vs 5.3%, p&lt;0.0001). In multivariate analysis, factors associated with mortality were after-hours discharge (OR 1.42, p&lt;0.0001) and emergency admission to ICU (OR 1.53, p&lt;0.001).</td>
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<tr>
<td>Obel et al.27</td>
<td>Single ICU in Danish university hospital</td>
<td>To assess whether weekend ICU discharge is associated with mortality</td>
<td>Prospective, observational cohort study</td>
<td>783 patients admitted to ICU during 5-year period</td>
<td>Medical ICU patients discharged early in the weekends had increased mortality risk (adjusted OR 1.43).</td>
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<tr>
<td>Litton et al.28</td>
<td>22-bed multidisciplinary ICU of university hospital</td>
<td>To assess ability of clinical markers to predict in-hospital mortality post-ICU</td>
<td>Nested case-control study</td>
<td>1272 who survived their ICU admission</td>
<td>2.3% of ICU discharges died unexpectedly in hospital. CRP level at ICU discharge was associated with mortality.</td>
</tr>
<tr>
<td>Clec'h et al.29</td>
<td>12 French medical or surgical ICUs</td>
<td>To examine link between tracheostomy insertion in ICU and post-ICU mortality</td>
<td>Prospective, observational cohort study</td>
<td>177 patients who had a tracheostomy inserted whilst in ICU</td>
<td>Tracheostomy was associated with increased post-ICU mortality when left in situ (Model 1: OR 3.73, p=0.008; Model 2: OR 4.63, p=0.003).</td>
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<tr>
<td>Chen et al.30</td>
<td>Medical ICU in Taiwanese tertiary hospital</td>
<td>To examine the effects of severity of illness at ICU discharge on post-ICU mortality</td>
<td>Prospective observational study</td>
<td>203 patients discharged from ICU</td>
<td>In-hospital mortality 19%. Two independent risk factors for post-ICU mortality: discharge APACHE II score (OR 1.17, p&lt;0.0001) and male gender (OR 3.24, p=0.015).</td>
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<tr>
<td>Tobin &amp; Santamarina31</td>
<td>Single ICU in Australian tertiary referral hospital</td>
<td>To examine ICU discharge patterns and impact of discharge time on mortality</td>
<td>Retrospective cohort study</td>
<td>10,903 patients discharged from ICU</td>
<td>In-hospital mortality 4.5%; 25% of deaths occurred within 3 days of discharge. Mortality after ICU discharge was increased by: higher APACHE II score, admission to ICU from ward or operating theatre, and discharge during afternoon and night shift.</td>
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<tr>
<td>Rellos et al.32</td>
<td>General ICU in Greek tertiary hospital</td>
<td>To compare outcomes of oldest ICU patients (&gt; 90) with younger patients</td>
<td>Prospective cohort study</td>
<td>5505 consecutive ICU admissions</td>
<td>1.1% of patients were aged &gt;70; in-hospital mortality was 40% (vs 8.9%). APACHE II score was independently associated with in-hospital mortality.</td>
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<tr>
<td>Priestap et al.33</td>
<td>31 Canadian hospitals</td>
<td>To determine impact of night time ICU discharge on post-ICU mortality</td>
<td>Multicentre retrospective observational cohort study</td>
<td>47,062 discharges from ICU to wards</td>
<td>10.1% of patients were discharged at night (9pm or later). OR of death for patients discharged at night was 1.35 (p&lt;0.05). Mortality risk was increased 1.22 fold for night discharges (p&lt;0.05).</td>
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<tr>
<td>Mayr et al.34</td>
<td>12-bed ICU in tertiary hospital in Austria</td>
<td>To evaluate causes of post-ICU in-hospital mortality.</td>
<td>Prospective cohort study</td>
<td>3700 ICU admissions</td>
<td>In-hospital post-ICU mortality was 4.3%; those patients had longer ICU length of stay. Most common causes of in-hospital post-ICU deaths were malignant tumour disease and chronic cardiovascular disease.</td>
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<tr>
<td>Alban et al35</td>
<td>20-bed surgical ICU in tertiary hospital</td>
<td>To determine whether severity-adjusted outcomes are impacted by ICU readmission</td>
<td>Prospective observational study</td>
<td>10,840 patients admitted to ICU</td>
<td>Readmission rate 2.73%; these patients had higher APACHE II scores on day of discharge. ICU readmission significantly increased the risk of death beyond that predicted by APACHE II and SAPS scores.</td>
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</table>
the titles and abstracts, 126 were deemed relevant. Once inclusion and exclusion criteria were applied 22 studies were identified for review. Table 1 presents a summary of these. All reviewed studies used quantitative methods including prospective cohort and retrospective observational designs. The mean sample size was 10,040 with a range of 118 to 76,690 patients. Where reported, study findings are listed in Table 1 as odds ratios (ORs).

**Study findings**

Post-ICU mortality rates in 18 studies ranged between 2 and 12% of all patients (average 5.95%). Four studies reported higher rates. Two studies,1,21,31 focused on patients aged over 80 years, reported mortality rates of 24 and 40%. In addition, a high mortality rate of 19% was reported in a small study22 (n=203) of patients discharged from the ICU with a tracheostomy, and in a study26 conducted in a medical ICU, with non-surgical, non-cardiac and non-neurological patients.

**Age**

The patient's age was significantly associated with post-ICU mortality in nine studies.1,2,11,20,21,22,24,25,28,31,33 Age groups identified were age greater than 35 years, 70 years and 80 years.20,21 In three studies comparing survivors and non-survivors, patients who died following ICU discharge were older than survivors: 73 versus 60 years; 70 versus 58 years22; and 65 versus 52 years.24

**Illness severity**

Illness severity was significantly associated with post-ICU mortality in 11 studies.1,13,18,20,21,22,24,28,30–33 Scoring systems used were APACHE II, Simplified Acute Physiology Score (SAPS) and Sequential Organ Failure Assessment (SOFA). For each of these scoring systems, a higher score was associated with a greater risk of mortality.

**Discharge time**

Time of ICU discharge was significantly associated with post-ICU mortality in six studies.17,23,26,27,31,33 Higher mortality rates were associated with discharge from the ICU in the evenings and at night time after hours. This involved ICU discharge between 6pm and 7am. Discharge from the ICU during the 'early weekend', Friday and Saturday, was associated with post-ICU mortality in one study.21

**Other factors**

Other factors were found to be significantly associated with post-ICU mortality but only in single studies.25,28,31,33 These factors were: male gender, emergency ICU admission, admission from a general ward, mean white cell count, mean CRP concentration, requiring renal replacement therapy during ICU stay, mechanical ventilation greater than 96 hours, requiring parenteral nutrition or vasoactive drugs, being discharged from the ICU at time of no vacancy, and body mass index greater than 30 kg/m².

**DISCUSSION**

Clinical outcomes research tends to focus endpoints that are considered important for patients and society; survival is the primary endpoint. A clinical outcome such as mortality is also easy to define and measure using empirical methods. Mortality following ICU discharge is a quality indicator and frequently an anticipated event. The sudden death of post-ICU patients who are expected to survive for example represents a waste of valuable healthcare resources and a missed opportunity to save a life. Safety and quality must be care priorities in discharged patients. However, post-ICU patients often have complex care needs which may be difficult to provide in a ward environment, resulting in poor outcomes. In part this may be because inexperienced nurses and doctors struggle to provide the necessary complex care. Up to a third of patients for example will experience an adverse event after ICU discharge. Half of these events may be preventable with better standards of ward care.

Despite recent changes in acute care processes such as the introduction of ICU Liaison Nurses and Critical Care Outreach Teams, factors associated with post-ICU mortality have changed little over time. In the time since seminal research10,39,44 was conducted, the need to better support ward patients with complex needs has been recognised. ICU Liaison Nurses and Critical Care Outreach teams have evolved in part to help meet the needs of these challenging patients. A recent study44 for example demonstrated the positive impact of ICU Liaison Nurses in preventing adverse events in post-ICU patients. Research36 has also found that Outreach Teams can improve hospital mortality. However, none of the 22 studies in this review mentioned whether support roles such as Liaison Nurses and Outreach Teams existed in the study hospitals. Some researchers speculated that Outreach teams may influence the quality of care before ICU admission and thus post-ICU outcomes, but this was not an empirical finding.

Whilst this review has similar findings to seminal research,9,10,39,44 limited research focus has been given to potentially modifiable factors. One such factor is the time of ICU discharge. Research26,31 indicates that after hours ICU discharge is becoming more common. This may reflect an increasing demand for ICU beds or a lack of ward beds when an ICU patient is ready for discharge.46 In one study31 half of night-time ICU discharges were preceded or followed by another admission, suggesting intense pressure for beds. A time of ICU discharge is the only modifiable factor identified which is associated with post-ICU mortality. This is key for future research and clinical care.

ICU discharge decision-making is often based on demand for ICU beds rather than patient readiness.47 When faced with an urgent bed shortage, ICU staff are often forced to discharge the patient who is doing the best, even though he or she may not be doing particularly well. In one hospital,16 this was a frequent problem. A study48 of 55 Swiss ICU found marked heterogeneity in ICU discharge practices; less than a quarter of the responding ICU used written discharge guidelines. This suggests an absence of evidence-based guidelines on ICU discharge.

The reviewed studies which demonstrated a relationship between after-hours discharge and mortality were not able to identify specific causes of mortality. However, numerous reasons were speculated: inconsistency in care after hours, inferior medical care on the receiving ward, less surveillance on the ward, lower nurse:patient ratios, lower doctor:patient ratios, and less immediate access to experienced medical staff. Older research44 speculated similar reasons. One study46 demonstrated lower mortality rates for ICU patients discharged to a high dependency unit compared with those discharged directly to the ward environment. Research8,39 also found that higher nursing dependence at
the time of ICU discharge is associated with a worse outcome. The factors speculated to be associated with after-hours ICU discharge and mortality may therefore be worth investigating.

A possible explanation for the similar findings of this review and seminal research is that research has not attempted to explore the influence of potentially modifiable factors such as organisational structure on post-ICU mortality. For example, research has demonstrated a relationship between patient outcomes and nurse-patient ratios and staff educational levels. A relationship has also been demonstrated between patient mortality and the characteristics of the healthcare environment, such as staffing levels. The impact of factors such as these on post-ICU mortality needs exploration. A method of facilitating this is the use of an accident causation model.

Researchers and psychologists examining industrial errors have developed theoretical and conceptual models to help analyse error causation. Conceptual frameworks such as these facilitate the examination of adverse events and enable outcomes to be linked to the existing body of knowledge. Reason’s accident causation model for example proposes that within complex systems multiple layers or barriers exist to prevent accidents but these barriers contain weaknesses. Identifying these weaknesses is a step towards accident prevention.

Accident causation models such as Reason’s and Donabedian’s structure/process/outcome model promote the analysis of factors associated with accidents to help identify where remedial action should focus. Using these models allows factors associated with clinical adverse events to be categorised into either patient, clinician or system factors. Some researchers acknowledged they did not consider the impact of potentially relevant organisational factors such as ICU bed occupancy and level of ward care on post-ICU mortality. Others speculated that inadequate clinical handover or poor appraisal of patient needs may compromise the quality of ongoing care after ICU discharge; but these were not substantiated by research. Failing to identify the underlying causes of an adverse event does little to prevent the event from recurring. Future research on post-ICU adverse events may therefore benefit from the guidance of an accident causation model.

Practice implications

The findings of this review suggest that patients should not be discharged from the ICU after hours. If an older patient whose acute illness has not completely resolved is discharged after hours, their mortality risk is increased considerably. Whilst after hours ICU discharges should be avoided, resource limitations such as a shortage of ICU beds may prevent this. If a patient is discharged from the ICU after hours, staff on the receiving ward should be aware of the significant risk increase. Such patients may be best managed with the ongoing input of ICU staff and other support services such as ICU Liaison Nurses and Outreach Teams.

Limitations

This review has some limitations. A number of studies had methodological weaknesses such as a retrospective or single site design, small sample sizes and short data collection periods. There was a lack of homogeneity in the research methods used and patient characteristics. Some studies for example used prospective data collection methods whilst others used retrospective methods. The research was conducted in different types of ICUs including medical and surgical, hence the differing patient characteristics. These differences prevented a full systematic review being conducted. Some studies though published since 2006, presented data that were over ten years old. Furthermore only English language publications were included in the review, limiting the generalisability of the findings to many countries.

CONCLUSIONS AND RECOMMENDATIONS

This review has identified key factors associated with in-hospital mortality following ICU discharge. Given the high costs associated with providing intensive care, preventable death must be avoided in patients expected to survive following ICU discharge. Patients at greatest risk of post-ICU mortality need to be targeted so that processes of care can be streamlined. Future research needs to identify modifiable factors within care process, to reduce the incidence of preventable in-hospital mortality following ICU discharge.

REFERENCES


