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An analysis of the risk of readmission or death following patient discharge from the intensive care unit

by

F Shaun Hosein

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

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Abstract

Introduction: The discharge of patients from the intensive care unit (ICU) to a hospital ward is a common transition of care that is associated with error and adverse events. Further identification of risk stratification tools, risk factors and overall adverse event rates may help identify high-risk patients and improve the ICU discharge process.

Methods: Ovid EMBASE, Ovid MEDLINE, CINAHL, PUBMED and Cochrane Central Register of Controlled Trials were searched from the earliest available date through March 2013, plus reference lists and citations of all studies included in the systematic review. Data were extracted on the study design, setting, population, sample size, tool and outcomes.

Results: The literature search identified 9,926 citations, of which 58 studies identifying eight tools and 41 risk factors met the inclusion criteria. Reported outcomes included ICU readmission and post-ICU mortality .We were able to determine a pooled ICU readmission rate of 6.3%(95% CI 5.5-7.2%). and post-ICU mortality rate of 7.4% (95% CI 6.6-8.2%). Pooling of identified risk factors facilitated the development of two ICU discharge meta-prediction models, which were tested in a local database yielding areas under receiver operator curves ranging from 0.72 to 0.97.

Conclusions: Eight risk stratification tools and 41 risk factors were identified from systematic review. Two meta-prediction models were developed and tested; yielding promising results, but further optimization is warranted. Although risk stratification tools may help clinician decision-making, further evaluation of the existing tools' effects on care is required prior to clinical implementation. The identification of pooled adverse event rates from systematic review is proposed to serve as ICU benchmarks, contributing to improvement of ICU quality of patient care.

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List of Symbols, Abbreviations and Nomenclature

Symbol	Definition
APACHE	Acute Physiology and Chronic Health Evaluation
AUROC	Area Under the Receiver Operating Characteristic Curve
CI	95% Confidence Interval
CVICU	Cardiovascular Intensive Care Unit
GCS	Glasgow Coma Scale
ICU	Intensive Care Unit
IOM	Institute of Medicine
LOS	Length of Stay
MET	Medical Emergency Team
MIR	Minimizing ICU Readmission Score
OR	Odds Ratio
ROC	Receiver Operator Curve
SAPS	Simplified Acute Physiology Score
SOI	Severity of Illness
SWIFT	Stability and Workload Index for Transfer Score

Chapter One: **INTRODUCTION**

The 21st century has brought many changes to the way we view health care. In a world with shrinking health care budgets and resources there has been efforts to maximize use and allocation of these limited resources. Quality of care and patient safety are areas of improvement that have a large effect on health care, and consequently on health care budgets and resources[1]. A significant proportion of hospitalized patients experience harm from adverse and avoidable events, which translates into increased health care burden and ultimately cost. Therefore, maximizing quality of care and patient safety functions to improve health care and patient wellness, as well as minimizing harm and cost burden on the health care system[2,3].

Transitions of care within the hospital have been identified as periods where patients are susceptible to harm and severe adverse events. The two largest transitions of care periods occur at discharge from the intensive care unit (ICU) and discharge from hospital. Since these processes liberate both hospital and ICU beds it is no surprise that these events are intimately linked to health care economics and resource allocation. Generally the discharge process is associated with changes to the patient's treatment team, medication and level of care[4]. Specifically at ICU discharge these changes represent a large drop in the level of care, where ICU patients are transitioned from a highly monitored ICU ward to the lower care general ward area. Since the ICU patient is critically ill and already possess a higher baseline mortality rate, it is no surprise that ICU discharge is associated with a spectrum of adverse events; ranging from death to readmission to medical emergency team activation (MET)[5,6].

In the interest of maintaining a standard of high quality care and patient safety there has been motivation to identify risk factors that are associated with increased mortality and readmission post ICU discharge[7-9]. There have also been attempts to formalize this process by developing a clinical decision-making tool, to support the ICU discharge process[10-12]. However, to date there has not been a formal systematic assessment of risk factors and clinical decision making tools associated with adverse events post ICU discharge.

The goals of this thesis are to identify risk factors and tools that are associated with ICU discharge. This information would be used to develop and improve the ICU discharge process. This knowledge would contribute to the overall improvement of health quality and minimization of patient harm within the modern ICU.

Chapter Two: **BACKGROUND**

2.1 Quality of Health Care

The Institute of Medicine (IOM) estimated that in 2009 the US health care budget was approximately 2.5 trillion dollars and growing yearly. In an already strained economy this cost burden and growth illustrates the need to control health care spending, while increasing efficiency and quality[13]. The IOM further determined that the current health care system is ineffective, and in order to increase health care quality the system requires change[14].

One of the identified areas for improvement in health care quality and safety is inefficient delivery of care that can result in adverse events and harm. The Harvard malpractice study found that adverse events occur in 3.7% of patients discharged from hospital, and approximately 1.0% of these events are avoidable. The most common adverse events were related to drug complication, wound infection and technical complications, with all of these events occurring more frequently in patients older than 64 years of age. Ultimately, the study found that overall management errors accounted for 58% of all adverse events and were, in all instances, preventable[15].

A similar Canadian study reported an overall 7.5% adverse event rate, with 36.9% being preventable, and 20.8% resulting in mortality. They calculated that these events result in an extra 1521 hospitalization days, and that management errors were the primary contributor[16]. These studies highlight the need to improve patient quality of care and safety, since this would function to not only improve healthcare; it would also reduce costs associated with inefficient care.

2.2 Adverse Events and Transitions of patient care

Adverse events are associated with transitions of patient care. Hospitalized patients undergo various transitions of care, between one service to another (such as emergency department admitting patients to the hospital), from one organization to another (hospital services discharging patients to the community) and between providers (physician's daily night and morning handover). While some transitions may be simple and the level of care continuous, some involve a significant drop in the level of care provided. This is illustrated through the discharge of a patient from the hospital or from the intensive care unit (ICU) to the general ward. Analysis of the discharge process from hospital to home has found that half the patients experience a medical error while 19-23% suffer an adverse event, primarily related to drug prescription. To improve this transition the following areas have been identified as: Physician discontinuity between hospital and the community, medication reconciliation, increased self care and social support needs, inefficient patient and physician communication[4]. Similar areas have been identified in an observational study investigating physician handover in the ICU discharge process. These results suggest that transitions from ICU to the general hospital ward are inefficient and require improvements to minimize harm[17]. ICU patients have been shown to have higher hospital mortality and lengths of stay, which illustrates a gap and warrants further quality improvement measures and research within this population[9,18].

2.3 The Intensive Care Unit Discharge process

An ICU is a specialized ward within the hospital that deals with critically ill patients. ICUs provide a higher degree of care than the general hospital ward, however, the high level of patient care does not come without high costs. In today's economy with cut backs to health care

systems and shrinking hospital budgets, an ICU bed is a scare resource, and its effective management is paramount [19,20].

The ICU discharge process has traditionally been guided by the on-duty Intensive Care specialist's (Intensivist) clinical judgment. Patients should be discharged when they are clinically stable and can safely tolerate the drop in the level of their health care provision. However, this transition is unstructured and can be associated with a spectrum of adverse events, ranging from mortality, to readmission and medical emergency team activation. These adverse events can occur from numerous factors, such as hospital-system based (ex: bed availability), patient based (ex: age) and ICU discharge process based (ex: medicine reconciliation). It has been shown that patients whom were either discharged prematurely or to an unsuitable location, both of which are factors associated with the ICU discharge process, have experienced the adverse event of ICU readmission[21,22]. Such events have shown to not only increase hospital length of stay (LOS), but also to increases in hospital mortality, and overall cost to the system[6]. It is therefore important to fully understand these factors that contribute to adverse events post-ICU discharge.

2.4 Structure of the ICU Discharge process: Risk Factors

Risk factors associated with adverse events post-ICU discharge consistently include increasing age, ICU length of stay, male gender and the presence of patient comorbid conditions[6,22-24]. A recent meta-analysis by Frost et al. identified a relationship between increasing severity of illness and the risk of readmission regardless of what point in time the measurement was taken during the ICU stay [25]. However, this meta-analysis was focused solely on the outcome of readmission and did not take into account mortality and MET team activation.

Currently there has been no attempt to systematically identify and evaluate all risk factors associated with the spectrum of adverse events post-ICU discharge.

2.5 Structure of the ICU Discharge process: Clinical Decision Making Tools

Clinical prediction rules assist with clinical decision making by functioning to suggest a diagnostic test or a particular course of treatment. They can also predict the probability of disease or a specific clinical outcome. These rules are derived from multivariate analysis and undergo rigorous validation and testing methodology before they are ready for clinical use. Standards have developed to help and guide the development of effective and high quality clinical prediction rules. These standards range from description of outcome, to description of study site, to reproducibility of results [26,27]. We however intend to employ a slightly different and novel methodology in the development of our ICU discharge rule, where the derivation of the component variables will be based on results of meta-analysis and not multivariate analysis.

Ultimately ICU discharge is a clinical decision, which should incorporate clinical information and current knowledge to produce an evidence-based decision. There are numerous tools or scores that function to aid in the clinical decision making process in specific circumstances. Classic examples of these include the Acute Physiology and Chronic Health (APACHE) scoring system[28], and the Ottawa ankle rules. The Ottawa rules were developed to address the issue of radiography in acute ankle injuries presenting to an Emergency Department[29], this rule now has now been recognized and implemented in daily clinical practice internationally[30].

There have been attempts to develop a score that can aid with ICU discharge decision-making. The Stability and Workload Index for Transfer (SWIFT) score is an ICU discharge

score that the following variables for assessment: ICU length of stay, patient admission source, Glasgow Coma Scale (GCS), partial pressure of oxygen in arterial blood [PaO_2]/ fraction of inspired oxygen [FIO_2], and nursing demand for complex respiratory care. This score was validated over a period of one year and was found to have a higher discrimination power for ICU readmission than the APACHE III score[31]. However, it has limitations in that it was developed to predict readmission but not mortality, missing half of the adverse event spectrum.

2.6 Objective

At present time there has been no formal attempt to systematically identify risk prediction tools/scores, risk factors and overall adverse event outcome rates associated with the full spectrum of adverse events post ICU discharge. Therefore the focus of this thesis will be to identify these tools, risk factors and outcome rates by conducting a systematic review. This information will then be used to derive a meta-prediction model, which will be tested in a local ICU database. This thesis will contribute to improving the efficiency and structure of the ICU discharge process by addressing the issue of improving the quality of health care provided in the modern ICU and minimizing harm to critically ill patients post ICU discharge.

Chapter Three: **METHODS**

3.1 Introduction

To better understand what is currently known about the ICU discharge structure, process and outcome we conducted a systematic review to identify: 1) tools that stratify patient risk of severe adverse events following ICU discharge, 2) risk factors that are associated with severe adverse event post-ICU discharge. We conducted a sub-analysis of systematic review results to determine overall adverse event rates post-ICU discharge. Results from systematic review served to inform the development of meta-predication models that utilized two scoring methodologies. These tools were tested within a local ICU database (TRACER) to determine overall ability to predict both readmission and mortality post-ICU discharge.

3.2 Data sources and search strategy

We conducted a systematic search of articles in Ovid EMBASE, Ovid MEDLINE, CINAHL, PUBMED, and Cochrane Central Register of Controlled Trials from inception to March 2013. Searches were performed without year or language restrictions, and used combinations of the following three groups of terms: intensive care unit, patient discharge, and severe adverse event (medical emergency team [MET] activation or ICU readmission or mortality). The search strategy for MEDLINE database is depicted in Appendix A. We also searched references in the bibliographies of retrieved articles and performed a citation search of all studies included in the systematic review (i.e. articles citing studies included in the systematic review). Search strategies were constructed with the help of an experienced information scientist (DL), and all citations were imported to an electronic database (Endnote X3, Thomson Reuters, New York, NY).

3.3 Article Selection

Two authors independently reviewed titles and abstracts (SH, SB) for all studies identified in the search, followed by full text review of articles (SH, NB) identified by either reviewer as meeting inclusion criteria. Discrepancies were resolved by discussion between the reviewers. Kappa values and their 95% confidence intervals were calculated for agreement between authors.

We selected all articles that: 1) evaluated a tool or scoring system (clinical prediction rule) designed to predict severe adverse events following patient discharge from ICU or 2) examined one or more risk factors for severe adverse events after ICU discharge. We defined a risk factor as a patient, provider or institutional characteristic that can be identified before patient discharge from ICU, and is associated with severe adverse events following patient discharge from ICU. We defined severe adverse events as any ICU readmission, mortality or medical emergency team (MET) activation during a patient's hospital stay following discharge from ICU. MET activation was defined as emergency activation of an on-call resuscitation team for hospitalized patients experiencing a life-threatening event (e.g. decreased level of conscious).

Minimum inclusion criteria were (1) articles that examined one or more risk factors for severe adverse events after ICU discharge. We defined a risk factor as a patient, provider or institutional characteristic that can be identified before patient discharge from ICU, and is associated with severe adverse events following patient discharge from ICU (2) original research describing derivation, validation or evaluation of the clinical impact of a tool that could be used at ICU discharge to identify patients at risk of adverse events, (3) the study population were adult patients (majority patients >16 years), (4) at least one adverse event (MET activation, ICU

readmission or mortality) was reported, and (5) the adverse event occurred after ICU discharge, but during the same hospitalization as the index ICU admission. We included only cohort studies and controlled trials. Case-control studies, case series, and case reports were excluded. Systematic reviews were excluded, but their reference lists were hand-searched for relevant articles. Studies examining discharge from a high dependency or step-down unit were excluded.

3.4 Data Extraction

Two reviewers independently performed data abstraction and quality assessments. We analyzed the abstracted data according to validated guidelines for narrative synthesis [32-35]. Reviewer consensus was required for inclusion of results. We extracted data describing study purpose, design, setting (country, type of ICU), sample size, study population (age, sex, illness severity), risk stratification tool (components, measurement properties), and outcomes (MET activation, ICU readmission, hospital mortality). Information extracted about risk factors included the name, definition, outcome examined, reported measures of association (odds ratios, risk ratios), their 95% confidence intervals and p-values. Study quality was evaluated using 11 pre-specified criteria: eligibility criteria described, definition of cohort timing, comorbidities reported, multivariate adjustment for potential confounders, ethics approval reported, complete follow-up, demographics described, severity of illness score reported, study duration reported, sample size calculation reported, and study limitations were reported. Studies that satisfied six or more of the criteria were classified as high quality.

3.5 Analysis of Identified Tools

Studies that identified a predictive model for ICU discharge were grouped according to outcomes measured. We compared each tool according to: model derivation and validation, operating characteristics, and individual components/variables. Pooling of quantitative data was not possible due to the limited number of evaluations of individual risk stratification tools.

3.6 Analysis of Identified Risk Factors

Due to the heterogeneity, identified risk factors were classified as broadly as possible for the purpose of frequency counts. Each risk factor was scored as to its presence in each identified study. These counts were summarized, and all risk factors that were multivariate adjusted and had a count greater than one were selected for further analysis (Appendix B). We attempted to pool estimates using a DerSimonian and Laird random effects model. Heterogeneity between studies was assessed using the I^2 statistic and a p-value<0.1 was selected as evidence of statistical heterogeneity. Pooled risk factors with 95% confidence intervals estimates that did not cross one were considered to be significant.

Analysis was conducted using Stata statistical software 11.0 (Stata Corp, College Station, Texas).

3.7 Analysis of Identified Outcome Rates

The primary analysis focused on describing the rates of readmission to ICU and hospital mortality for patients discharged alive from ICU. Readmission to ICU and post-ICU mortality rates were calculated using raw event (total number of events) and study population (total

number of patients discharged alive from ICU) data from each article. Studies that did not report raw data were excluded from analysis. Authors were contacted in an attempt to gather missing data. Outcome rates were pooled using both DerSimonian and Laird random effects and Mantel-Haenszel fixed effects models.

Statistical heterogeneity was examined using the I-squared (I^2) statistic, wherein a p-value < 0.05 and an $I^2 > 50\%$ indicated the presence of heterogeneity among the included studies. To examine for potential sources of heterogeneity between studies, the analysis was repeated using stratified analyses. The pre-defined subgroups for these secondary analyses were geographic region (North America, Europe, Australasia, other), ICU type (medical-surgical, cardiovascular, other), patient characteristics (age <60 vs. ≧60 years, predicted mortality <10% vs. ≥10% according to illness severity score) and study characteristics (patients with do-not-resuscitate goals of care included, adjustment for confounding factors, duration of follow up ≤ 21 vs. >21 days, sample size < 1000 patients vs. ≥1000 patients, number of ICUs 1 vs. > 1, and composite measure of study quality).

All data analysis was conducted using Stata statistical software 11.0 (Stata Corp, College Station, Texas).

3.8 Development of a meta-tool to predict adverse events post ICU-discharge

Two predictive models from pooled systematic review risk factors were developed, a simple model and a coefficient model. There were a total of 19 risk factors that were translated to component variables; seven of these risk factors were associated both ICU readmission or post-ICU mortality, eleven were associated with ICU readmission and only one was associated with

post-ICU mortality. To deal with various severity of illness (SOI) scores in clinical practice we derived a SOI predicting > 10% mortality variable based on the pooled ORs (per point) of APACHE II, SAPS II and SOFA scores that corresponded to this mortality rate. The simple model scored the presence of each of these identified risk factors as one, with a final patient score being generated from the sum of individual patient risk factors scores. The coefficient model scored patients by multiplying the pooled beta-coefficients of the identified risk factors by the presence or value of that risk factor, deriving a final patient score from the sum of individual patient risk factor scores.

3.9 Validation of developed ICU-discharge prediction models

The TRACER database used for validation included all consecutive adult patients whom were admitted and subsequently discharged from Calgary regional Intensive Care units from the year 2002 until 2011. Patients whom died in ICU were excluded from the analysis. Only initial admission data for patients whom were readmitted was used, subsequent readmission data during hospital stay was excluded. Ethics approval was received from the University of Calgary research ethics board. The database did not contain any identifiable patient data.

Variables were generated based on demographic, physiological, and clinical data collected during ICU admission. Outcomes after a patient's first ICU discharge included ICU readmission and in-hospital death. ICU Readmission was defined as a discharge to an area that provided a lower level of care followed by a return to the ICU during the same hospital stay. A combined outcome was generated using the summation of data from the ICU readmission and post-ICU mortality variables. All outcome variables were binary coded. Odds Ratios were generated from

the TRACER database using STATA for each variable identified from meta-analysis and all three outcomes (Appendix C).

Coefficient model variables were generated from the product of meta-analysis beta-coefficients and the relevant TRACER risk factor variable. Simple model variables were generated from scoring one point for the presence of the relevant meta-analysis risk factor variable. The coefficient and simple model variables were independently summated to generate a unique variable for the respective model. These variables contained the unique score for each patient within the TRACER database, and were further analyzed with the following outcomes: ICU readmission, post-ICU mortality, and Combined outcome. Tables were created which tabulated model variables with each outcome; this data was then plotted and analyzed using linear regression techniques in STATA and Excel. Logistic regression and Receiver Operator Curve (ROC) analysis was done using STATA, where the three outcomes of ICU Readmission, Post-ICU mortality and Combined outcome were used as dependent variables.

Chapter Four: **RESULTS**

4.1 Article Screening and Selection

We initially identified 9926 articles from five databases; of these we identified 148 articles for full text review, and selected 58 articles for final inclusion (Figure 1)[7-12,15-18,28,36-82]. Common reasons for exclusion of articles during full-text review were that articles did not report original research, did not report study outcomes (MET activation, ICU readmission, hospital mortality), and were not related to ICU discharge. We achieved good inter-rater agreement for full-text review (kappa=0.84, 95% CI 0.67-1.00).

4.2 Article Characteristics and Quality

Table one summarizes the characteristics of the articles included. Year of publication ranged from 1986 to 2013. The most frequent countries of publication were the United States (n=12), Australia (n=6), United Kingdom (n=8), Canada (n=6) and Germany (n=4). The majority of studies were conducted in mixed medical/surgical ICUs (n=35), with fewer conducted in cardiac ICUs (n=7), or sole medical (n=4), or surgical ICUs (n=3). The number of patients in each study ranged from 86 to 704,963 with a total of 2,075,610 patients included in the review.

The mean age of patients was 59.65 ± 5.4 years among the 44 studies that reported a mean age. A variety of severity of illness measures were used (e.g. APACHE II, SAPS II) with some reporting median and others mean scores. Overall mortality reported among these studies was 8.2% and overall readmission was 6.4%. No studies reported medical emergency team activation as a severe adverse event.

Table two summarizes the quality of the included studies. The majority of studies included patients with do-not-resuscitate orders (n=42), used multivariable adjustment (n=49) and included only one ICU (n=33) in their data analysis. In total, 21 studies reported risk factors for ICU readmission, 25 for post-ICU mortality, and 12 for both ICU readmission and post-ICU mortality.

4.3 Description of Risk Stratification Tools

Table three describes the eight risk stratification tools identified. The Sabadell score and the tool developed by Daly *et al*. were designed to predict hospital mortality following ICU discharge. Reini *et al*. evaluated the ability of the Modified Early Warning Score (MEWS) to predict ICU readmission within 72 hours of discharge. The Stability and Workload Index for Transfer (SWIFT) score and the Frost nomogram were developed to predict ICU readmission following ICU discharge. The Minimizing ICU Readmission (MIR) score was designed to predict the combined outcome of patient death or ICU readmission seven days post-ICU discharge. Badawi and Breslow developed two tools to respectively predict readmission and mortality 48 hours post-ICU discharge. All tools except the Sabadell score incorporated between 5 and 26 variables into their risk calculation with length of ICU stay the only common variable appearing in most tools. The Sabadell score was calculated by physician judgment of patient prognosis at the time of ICU discharge using a four-point scale.

Evaluations of internal and external validity were reported for most tools. The calculated area under the receiver operating characteristic curves (AUROC) ranged from 0.66 to 0.92, with the

Badawi and Breslow mortality tool having the highest reported AUROC (0.92). The sensitivity, specificity and likelihood ratios were reported or could be calculated for all the tools except the Frost nomogram. Gajic *et al*. compared the SWIFT score to the APACHE III score (AUROC 0.75 vs. 0.62, $P < 0.01$) at the time of patient discharge from ICU. Ouanes *et al*. similarly compared the MIR score, SWIFT score and Simplified Acute Physiology Score II (AUROC 0.74 vs. 0.61 vs. 0.64).

We did not identify any studies evaluating the impact of risk prediction on processes and outcomes of care.

4.4 Risk Factor Analysis

In total we identified 788 unique risk factors with heterogeneous definitions. In order to deal with this heterogeneity we further classified these risk factors into 17 broader definitions. Figure two summarizes the number of studies in which individual risk factors were reported for either readmission or mortality. The risk factors most commonly reported in studies were severity of illness (n=52), surgical patient (n=33), out of hours discharge (n=31), age (n=26), and mechanical ventilation (n=20). All risk factors identified were reported to be associated with increased risk of readmission or mortality post-ICU discharge.

The pooled estimates for risk factors with multivariate adjusted measures of association reported in two or more studies are summarized in Tables four and five for ICU readmission and Post-ICU mortality respectively. Twenty-six risk factors were associated with ICU readmission while

15 risk factors were associated with post-ICU mortality. There were risk factors that were not significant, six were associated with ICU readmission and four were associated with post-ICU mortality. Significant risk factors associated with both ICU readmission and post-ICU mortality included APACHE II score, age, length of ICU stay and out of hours discharge. The total number of studies used to derive pooled estimates ranged from two to twelve, and included between 3,601 and 469,077 patients. Significant risk factors with the strongest association with readmission were: ICU readmission (OR 5.43 CI 5.14-5.74), gastrointestinal surgery (OR 3.39 CI 1.98–5.8), and mechanical ventilation > 24 hours (OR 3.04 CI 1.61-5.17). Significant risk factors with the strongest association with post-ICU mortality were: do not resuscitate (OR 4.99 CI 2.97-8.36), chronic liver disease (OR 2.73 CI 1.04-7.16) and sepsis (1.85 CI 1.48-2.32). The only significant risk factor reported to be associated with a reduced risk of death was cardiac surgery (OR 0.11 CI 0.06-0.19).

4.5 ICU Discharge Adverse Outcome Rate analysis

Outcome rates were pooled using fixed and random effects modeling for readmission to ICU and hospital mortality for patients discharged alive from ICU are summarized in Figure four and Figure five respectively. In patients discharged alive from ICU the fixed effect pooled rate of readmission to ICU during the same hospitalization was 5.3 readmissions per 100 patients (95% CI, 5.2 – 5.3 readmissions per 100 patient discharges), while the random effect pooled rate was 6.3 readmissions per 100 patients (95% CI, 5.5 – 7.2 readmissions per 100 patient discharges). In patients discharged alive from ICU the fixed effect pooled hospital mortality during the same hospitalization was 4.5 deaths per 100 patients (95% CI, 4.4 – 4.5 deaths per 100 patient discharges), while the random effect pooled rate was 7.4 deaths per 100 patients (95% CI, 6.6 –

8.2 deaths per 100 patient discharges). Heterogeneity was high amongst these estimates, with I^2 values ranging from 99.7 %- 99.9% and $p<0.001$ for all estimates.

The stratified pooled rates of readmission to ICU and hospital mortality for patients discharged alive from ICU are summarized in Table six according to pre-defined characteristics. The stratified analyses provided different estimates of the pooled rates of readmission to ICU and hospital mortality for patients discharged alive from ICU. This analysis was aimed at further explaining the observed heterogeneity within the overall pooled estimates, but the majority of stratifications yielded similar estimates. This is best demonstrated by the stratifications for: mean age greater than 60 years, and studies that included only one ICU unit. Examples of stratified estimates that were much lower than the overall pooled estimates were observed for the following: CVICU, North American and Australian/ New Zealand ICUs. While some stratifications yielded higher estimates: Severity of illness less than 10%, Studies with less than 1000 patients and ICU units in Europe and other regions.

4.6 Development of ICU-discharge prediction models

Two predictive models were developed from systematic review. These models were based on two scoring systems, a simple score and a score based on beta-coefficients from pooled odds ratios (Table seven). The development of these models is described in the methods section.

4.7 Validation of developed ICU-discharge prediction models

The TRACER database used contained a total of 33,293 ICU admissions, however 5538 admissions were excluded due to ICU mortality. 1661 admissions were excluded due to

readmission, since patients readmitted to ICU have a higher risk of adverse event occurrence, and represent a different population of ICU patients. This resulted in a total of 26,094 patients that were eligible for analysis. Table eight shows the overall mean characteristics of these patients, with stratification for ICU readmission (1661 patients) and post-ICU mortality (1687 patients). The overall readmission rate was 6.37% and post-ICU mortality rate was 6.47 %. Overall patients were male, had a mean age of 64.4 years, an average length of stay (LOS) of 4.9 days and a mean APACHE II score of 21.1. Patients whom were readmitted tended to be slightly younger (61.2 years), were surgical patients (38.6%) and had a longer ICU admission (8.25 days). Patients whom died in hospital post-ICU discharge were slightly older (67.7 years), had a longer ICU admission (8.68 days), and tended to be medical admissions (38.4 %).

The operationalization of the two prediction models developed from systematic review is shown in table nine. Individual component variables are identified and how they were defined within the TRACER database is reported. Some variables were directly used, such as age and APACHE II score. Other variables required some interpretation, such as postoperative acute myocardial infarction, which was defined as any patient who was coded as a surgical admission and admission diagnosis was coded as an acute myocardial infarction. All variables present were used in the coefficient model, while the simple score required further generation of a binary age and length of stay variable. Missing data is also reported and ranged from 0.1 to 12.3%, where glucose metabolism dysfunction variable was associated with the most missing data. Due to limitations of the database some risk factors were not included, such as the chronic disease risk factors. Odds ratios were calculated for all component variables (Appendix C).

Linear regression was performed to examine the relationship between the predictive models and outcomes of ICU readmission, post-ICU mortality, and combined. Figure five shows regression modeling for the simple model, where scores ranged from zero to nine, and outcomes ranged from zero to one. There is an increasing trend demonstrated for all three outcomes as the score increases. The number of patients that corresponded to each score value is also shown, where there is clustering of values from the score of one to five (1424, 5967, 7376, 4259, 2094 patients, respectively). The lowest number of patients occurred at the extremities of the scale, where a score of nine, eight and zero were respectively associated with five, 35 and 75 patients. Table 10 shows R^2 values that were associated with each model. The simple model had better values that ranged from 0.64 to 0.76, while the coefficient model had values that ranged from 0.18 to 0.54. Figure six shows similar data regarding linear regression analysis for the coefficient model with the post-ICU outcomes. The coefficient model was based on scores ranging from zero to 11 and outcomes ranging from zero to one. There is little linear trend observed for all outcomes as the score increases for the outcomes of ICU readmission and Combined. These outcomes do show some clustering around score values of four, five and six related. The outcome of post-ICU Mortality does show an initial linear association from scores zero to five, but higher scores did not continue this trend. Looking at the number of patients associated with each score value, there is a rapid increase from zero to one (404 to 14148 patients), and then a gradual decrease of patients as scores decrease. There were no patients associated with a score of ten.

Logistic regression was also done to explore the relationship between the two prediction models and the three post-ICU outcomes. Resulting beta-coefficients, pseudo-R^2 values and ORs are shown in table 10. Estimates of pseudo-R^2 for the simple model ranged from 0.11-0.16, while

the coefficient model had estimates ranging from 0.12-0.54. The highest pseudo-R^2 estimate of 0.54 was associated with the readmission outcome of the coefficient model. Beta coefficient values for the simple model ranged from 0.69-0.84, and the coefficient model had values from 0.92-2.65. Once again the highest beta-coefficient was associated with the readmission outcome of the coefficient model. The simple model had fairly modest OR, ranging from 2.00 to 2.32, with readmission having the highest estimate of 2.32 (95% CI 2.23-2.42). The beta-coefficient model produced much higher estimates, which ranged from 2.50 to 14.20, with readmission again having the highest estimate of 14.20 (95% CI 12.70-15.80). All calculated ORs were significant, with CI intervals not crossing one.

ROC analysis was conducted to further explore the relationship between the predictive models and outcomes of ICU readmission, post-ICU mortality, and Combined. Figure seven shows the ROC curves of each outcome shown in separate panels. Table 10 shows related ROC values and confidence intervals associated with this analysis. Overall the coefficient model performed better than the simple model, having area under the receiver operator curve (AUROC) values ranging from 0.75 (0.74-0.76) to 0.97(0.96-0.97). The simple model had AUROC values that ranged from 0.72 (0.71-0.74) to 0.79 (0.78-0.80). Both models best functioned to predict outcomes related to ICU readmission.

Chapter Five: **DISCUSSION**

5.1 Key Findings

Systematic review identified eight ICU discharge risk stratification tools evaluated in eight studies. Outcome parameters from these studies were ICU readmission, post-ICU mortality and a combination of both. All tools except the Sabadell score used patient physiological and clinical characteristics to calculate patient risk of severe adverse events following ICU discharge. The SWIFT score, Badawi and Breslow mortality tool and MIR score had the best reported operating characteristics for predicting ICU readmission, hospital mortality and the combined outcome of ICU readmission and hospital mortality, respectively. A single study compared two of the risk stratification tools. No studies reported MET activation following ICU discharge as an outcome, identifying an opportunity for evaluation in future studies.

We identified 788 risk factors associated with readmission and mortality post ICU discharge. No evaluations of risk factors associated with MET activation post –ICU discharge were identified. Multivariable adjusted estimates were reported in two or more studies for 41 risk factors allowing for pooled estimates, 26 were associated with ICU readmission, 15 were associated with post-ICU mortality, 11 were associated with both ICU readmission and mortality post ICU discharge.

We identified ICU readmission rates of 5.3 readmissions per 100 patients (95% CI, 5.2 – 5.3 readmissions per 100 patient discharges) based on fixed effects pooling and 6.3 readmissions per 100 patients (95% CI, 5.5 – 7.2 readmissions per 100 patient discharges) based on random

effects pooling. Post-ICU mortality rates were 4.5 deaths per 100 patients (95% CI, 4.4 – 4.5 deaths per 100 patient discharges) based on fixed effects pooling, and 7.4 deaths per 100 patients (95% CI, 6.6 – 8.2 deaths per 100 patient discharges) based on random effects pooling. Rates were derived from 58 studies capturing ICU data from Europe, Australia and the Americas. All associated I^2 values indicate a high degree of heterogeneity and further stratification of data did not identify any relevant clustering of data to explain heterogeneity. Both types of pooling are included to explore the differences between resulting estimates. While they both contain a high degree of heterogeneity, pooling using random effects would be more appropriate since study populations were composed of patients that were discharged from ICUs in different continents, countries, and cities. ICU clinical practice and procedures would vary at each of these geographic levels adding to the observed heterogeneity.

We developed and tested two post-ICU prediction models within a local ICU database. These models were based on risk factors and pooled odds ratios identified from systematic review, they used two unique scoring methodologies, a simple score and a score based on beta-coefficients of pooled odds ratios. Linear regression modeling for the simple score showed a relationship between the simple score and all outcomes, these relationships were not identified between the coefficient model and any outcome. ROC analysis yielded excellent AUROC values for both models, with the coefficient model out performing the simple model for prediction of all outcomes. The prediction of ICU readmission was much better than all other outcomes for both models, the simple model AUROC of 0.79 (0.78-0.80), and the coefficient model AUROC of 0.97(0.96-0.97).

5.2 Relevance to existing scientific literature

This work adds to the literature by highlighting an important gap in the science of patient care transitions from the ICU. It is unclear whether a reliable and valid risk stratification tool for patient discharge from ICU has been developed. We identified eight risk stratification tools, only two of which have been directly compared in a single study, where the MIR score had a better AUROC value than the SWIFT, although lower than those reported for the tools developed by Daly *et al*., Fernandez *et al*. and Badawi and Breslow. Furthermore, only the MIR score is designed to predict both post-ICU discharge mortality and readmission. To complicate matters it is unclear which of these two outcomes is most relevant. These data suggest that the MIR score is promising, although its use of beta coefficients to calculate patient risk will make it difficult for clinicians to use outside of a computerized algorithm. The ICU discharge readiness scores developed by Badawi and Breslow have not been compared to other tools, and their proprietary nature may make independent evaluation challenging, but their derivation and evaluation in a large number of patients and ICUs suggests promise. This work related to ICU discharge tools and scores has recently been published [83]

We have also identified new risk factors previously not reported and risk factors associated with a broader scope of adverse events than previously explored. Rosenberg et al. conducted a review in 2000 that identified severity of illness scores, fever, hypoxia, elevated respiratory rate, admission diagnosis and age as risk factors associated with readmission. The authors also found several other, risk factors including elevated pCO_2, discharge hematocrit < 30%, and positive blood culture results that were not strongly correlated or inconsistently associated with readmission. They suggested that heterogeneity of risk factor definitions limited evaluation of

studies of ICU readmission[22]. Despite the publication of additional studies since this review, heterogeneity remains an important limitation within this body of literature.

There is a lack of synthesis of published ICU benchmark rates for readmission and post-ICU mortality. ICU readmission was initially identified by Cooper et al. as an important indicator that did not associate with ICU length of stay or patient SOI, it therefore captured other complimentary aspects of hospital related performance[44]. Rosenburg et al. identified a readmission rate of 7.0% and suggested its use as a quality of care indicator[9]. We identify a similar random effect pooled rate of 7.4% that further supports the proposal that ICU readmission rate reflects a broader aspect of hospital performance. A qualitative review of ICU quality indicators identified both post ICU readmission and ICU mortality as potential ICU quality indicators. These authors further suggest further research to create and pilot test operational definitions is needed[84].

Our results provide both an operational definition and pilot testing of these definitions since our results are based on 58 studies that use retrospective data from 1479 ICUs and spans 27 years of research, which represents the population of patients discharged from ICU. We have further identified from the TRACER database an ICU readmission rate of 6.37% and a post-ICU mortality rate of 6.47%, rates that are both lower than the proposed benchmark rates. There are no studies to this date that has summarized this data using meta-analysis.

In a 2009 meta-analysis, Frost et al. pooled multiple severity of illness scores (ie. APACHE II, SAPS II) using standardized mean differences and determined increasing severity of illness to be

a significant predictor of ICU readmission. In their discussion the authors suggested more discriminating tools are necessary to specify which patients would most benefit from follow-up critical care from outreach teams[25]. Our review builds towards this goal by identifying other potentially important independent risk factors for readmission and mortality that are not included in existing tools. We further mobilize this data by developing two prediction models that have shown promising results from testing within a local ICU database. These scores can directly be used clinically in the ICU, where a threshold of acceptable ICU readmission or post-ICU mortality would be set. Using our pooled overall scores these thresholds would be 6.3% and 7.4 % for ICU readmission and post-ICU mortality. Patients considered for discharge would be scored, and scores higher than the thresholds would be flagged for having a high risk of adverse event post-ICU discharge. This information can alert and support subsequent intensivist clinical decision-making concerning ICU discharge.

There are no studies that have used results from meta-analysis to derive a meta-prediction tool. This work provides a template for development of other meta-predication tools for other processes of care, such as hospital discharge.

5.3 Limitations

There are limitations to this research. It is possible our search was not completely exhaustive, despite our search of multiple databases using a comprehensive search strategy that was developed with the help of an expert health sciences librarian. However, it is unlikely we missed important risk factors that have been frequently studied. It was challenging to obtain accurate information from some publications. One article provided no raw data and as a result

transformations of risk ratios to odds ratios were not possible[42]. Additionally, some articles did not provide clear definitions of their risk factors. This lack of consistency in data reporting and risk factor definitions limits opportunities for pooling of data despite the representation of over 1 million patients in the included studies.

We found no studies of risk factors for MET activation following discharge from ICU. This represents an important gap in the literature given the growing role of ICU Outreach services and MET to facilitate patient transfer of care from ICU to medical and surgical hospital wards and to provide rescue care for patients who clinically deteriorate.

Our search was targeted at studies examining the relationship between risk factors and post-ICU readmission and death. Nevertheless, it is unlikely that the event rates would be different. The case-mix of patients included in identified studies may not represent the broader population of discharged ICU patients. It is possible that the patients from these research studies may have higher or lower event rates than patients discharged from ICUs not participating in research. The heterogeneity observed across the studies suggests that there may not be a single universal event rate.

Not all variables from proposed post-ICU prediction models were used in testing since the relevant data were not captured within the TRACER database. The addition of these variables to the database through database linking could affect the overall functioning of the models.

5.4 Further Research

There are numerous areas that can be explored form our results; in fact we have generated more questions than answers. One area of further work that needs to be done involves further testing and optimization of the two prediction models. Linking missing component variables from other databases, such as chronic disease conditions, would potentially alter the predictive performance of the models. Once predictive models have been successfully optimized they should be comparatively tested against the other identified prediction models. Such comparative testing within the same database has not been demonstrated in the literature.

Decision-support to provide reliable and valid risk stratification for patients discharged from ICU would be valuable to health practitioners involved in the care of ICU patients, both in the ICU and in the hospital ward. The use of the tool within the ICU would guide intensivist decisions regarding resource allocation (bed allocation, ICU outreach services), and patient safety (delay or acceleration of ICU discharge). The use of a tool post-ICU discharge by the receiving physician would provide insight into the patient's overall risk of severe adverse event occurring on the ward, and allow the receiving physician to allocate further resources to improve patient care and safety. This tool could also to inform patients and families about the risk associated with ICU discharge. Currently it is unclear how risk stratification tools compare to physician clinical judgment for identifying patients at increased risk of adverse events post-ICU. Clinical estimation is often based on subjective parameters and physicians can be overconfident in their predictive abilities [85-88]. Independent risk stratification may provide clinicians with additional information to guide clinical decision-making, but further evaluation is required. To complicate

matters, patient populations can vary substantially between ICUs (for example, multisystem ICUs vs. subspecialty ICUs) suggesting that development of a tool that can be broadly applied across patient populations may be difficult [89].

It is also unknown whether implementation of a risk stratification tool can improve processes and outcomes of care for patients. Laupacis *et al*. outlined evaluation criteria for clinical prediction rules. One, the tool needs to be validated to provide evidence of reproducible accuracy. Two, the tool needs to have sufficient predictive power to provide clinicians with confidence to use the results to guide decision-making. Three, the tool needs to be actually used by clinicians (easy to use whether using memory, paper-based tool or electronic tool) to change behaviour and improve patient outcomes. Ideally, an ICU discharge risk stratification tool would forecast patient outcomes and, therefore, facilitate the delivery of safe (for example, reduce premature ICU discharge for high risk patients), effective (for example, target transition resources to high risk patients) and efficient (for example, expedite ICU discharge for low risk patients) care. The prediction models identified and developed from our research satisfy the first two evaluation criteria. Since our developed prediction models were based on meta-data and not developed from a single ICU database, they have been successfully externally validated. However, prior to implementation, an impact analysis demonstrating evidence that risk stratification changes physician behaviour and improves patient outcomes is needed [26].

There are implications to consider around the clinical use of an ICU discharge clinical tool. First, the development of the tool has been done in isolation, and there are other factors to consider within the clinical context of the overall functioning of an ICU. The most relevant issue is bed

allocation, where there are competing pressures to discharge and admit patients [90].The ICU discharge tool only affects one aspect of this process; it does not take into account patients awaiting admission to ICU. It has been shown that prolonged emergency department stay is associated with higher hospital mortality and hospital length of stay [91].

Second, the tool is largely composed of non-modifiable variables and only one modifiable variable, out of hours discharge, which leaves daytime and weekday discharge as the only option for improving a patient's discharge score. The knowledge of a patient's predicted outcome post-ICU is however still very important and useful. Further resources, such as ICU outreach follow-up can be tailored to patients with a poor predicted outcome. There have been numerous studies that have shown the effectiveness of this intervention on improving hospital outcomes [92-94].

While there are limited options for modifying a patient's risk score, there have been a few processes that affect ICU discharge that can be optimized. Medical reconciliation and physician communication at ICU discharge have been suggested as options for improvement and if optimized can provide better care to the critically ill. While these processes have not been identified in our study as specific risk factors for adverse events post-ICU discharge, they have been identified as areas to improve the ICU discharge process and patient care [95-98].

Overall there are some issues to address with the use of an ICU discharge tool within the clinical context. However, the knowledge of the risk factors that contribute to adverse outcomes post-ICU discharge is of extreme importance since furthers our basic understanding of the discharge process and critically ill patients on the whole. Most variables are available at admission to ICU,

and this prognostication is informative for not only the medical care team, but also patient's and their families [99,100]. Knowing what to expect from an ICU stay allows individuals to better understand and prepare for what events can likely occur, and can hopefully contribute to overall improved satisfaction of care [101,102]. There are numerous avenues of further research that have been identified from this body of work, all providing different aspects and knowledge about the ICU discharge process.

5.5 Conclusion

This thesis achieved four important tasks. First, it has identified eight risk stratification tools used to predict adverse events post-ICU discharge. Second, it has identified and pooled 41 risk factors that are associated with adverse events post-ICU discharge. Third, it has identified and pooled post ICU discharge adverse event estimates, and has proposed to further use these estimates as benchmarks for ICU performance. Fourth, it has successfully developed and tested two meta-prediction models for adverse events post-ICU discharge. Initial testing results were promising and further work to optimize and compare these models to the eight identified models is needed. It is important to note that these four achievements are novel, with no such work being identified within the literature. The addition of this work to the scientific literature is key to the further understanding and improvement of the ICU discharge structure, process and outcomes.

Table 1. Characteristics of Included Studies

Study	Year	Countries	Follow-up	Type of ICU	ICU #	# of Patients	Age (Mean)	Female (%)	SOI Measure	SOI Score (Mean)	Readmission (%)	Mortality (%)	# RF
Yip	2013	Australia	34 months	Medical-Surgical	1	1446	50.2	35.7	APACHE II	19*	7.3	12.3	21
Badawi	2012	USA	ıours post-ICU discha	Mixed	402	704963	62.1	45.9	APACHE IV	47	2.5	3.1	49
Reini	2012	Sweden	30 days	Medical-Surgical	1	518	60.6	25.4	SAPS III	61*	3.7	15.5	6
Araujo	2012	Portugal	Hospital Discharge	Medical-Surgical	1	296	64.7	43.0	SAPS2	43.7	4.7	22.6	17
Brown	2012	USA	21 days	Medical-Surgical	156	196250	N/A	N/A	MPMO-III	10.9	5.4	5	13
Kramer	2012	USA	hosptial discharge	Mixed	105	263082	61.5	n/a	APACHE IV	41.3	6.3	n/a	0
Joakowaik	2012	Germany	Hospital Discharge	Cardiovascular	1	7105	69.1	30.7	EuroSCORE	9	7.8	N/A	32
Timmers	2012	Netherlands	11 years	Medical-Surgical	1	1682	58.6	33.3	Apache 2	11.1	8	N/A	14
Mahesh	2012	UK	Hospital discharge	Cardiovascular	1	6101	N/A	27.8	EuroSCORE	7.6	N/A	0.39	1
Ranzani	2012	Brazil	hosptial discharge	Medical	1	409	48.6	49	APACHE II	16	n/a	18.3	7
Laupland	2012	France	hosptial discharge	Mixed	n/a	7380	62*	39	SAPS II	40*	N/A	24	15
Ouanes	2011	France	Hospital Discharge	Medical-Surgical	4	3462	60.6	38.3	SAPS II	35.1	3.3	3.2	3
Renton	2011	Australia	Hospital discharge	Medical-Surgical	97	247103	59.9	N/A	APACHE III	47	5.5	5.3	16
Fernandez	2011	Spain	Hospital Discharge	Medical-Surgical	31	201	60.5	31	N/A	N/A	6	22	0
Kramer	2011	USA	Hospital discharge	Medical-Surgical	38	229961	N/A	44.0	N/A	N/A	6	N/A	42
Silva	2011	Brazil	Hospital Discharge	Medical-Surgical	4	600	60.7	43.3	SAPS 2	25.5	9.1	N/A	11
Fernandez	2010	Spain	Hospital discharge	Medical-Surgical	31	4132	61.5	33.6	N/A	N/A	4.6	5.9	18
Al-Subaie	2010	UK	14 days	Medical-Surgical	1	1185	60	45.1	APACHE II	16*	7	2.9	17
Utzolino	2010	Germany	Hospital discharge	Surgical	1	2558	62.1	36.4	N/A	N/A	9.7	3.1	2
Silvestre	2010	Portugal	Hospital discharge	Medical-Surgical	1	156	55	40.4	APACHE II	14.6	N/A	18.6	1
Chrusch	2009	Canada	7 days	1 medical, 1 surgery	2	8222	59.3	N/A	APACHE II	18.6	5.2	0.3	30
Litmathe	2009	Germany	Hospital discharge	Cardiovascular	1	3374	74.3	30.3	N/A	N/A	5.9	N/A	25
Gajic	2008	USA, Netherlands	7 days	Medical	1	1242	N/A	45.8	APACHE III	59.2	8.1	0.4	10
Campbell	2008	UK	Hospital discharge	Medical-Surgical	1	4376	63*	41.1	APACHE II	19*	8.8	11.2	72
Hanane	2008	USA	Hospital discharge	Medical-Surgical	3	11659	62.7	46.8	APACHE III	51.3	9.1	4.5	3
Kaben	2008	Germany	Hospital discharge	Surgical	1	2852	62	35.9	SAPS I	33.5	13.3	5.6	35
Laupland	2008	Canada	Hospital discharge	Medical-Surgical	4	17864	63.7*	26.6	APACHE II	25.1	N/A	6.7	13
Sakr	2008	Europe	60 days	N/A	198	1729	59.8	39.3	SAPS II	31.4	N/A	7.2	9
Ho	2007	Australia	Hospital discharge	Medical-Surgical	1	603	53	N/A	APACHE II	15.7	2	4.3	21
Pilcher	2007	Australia/New Zealand	Hospital discharge	Medical-Surgical	41	76690	59	N/A	APACHE III	46.3	5.3	5.8	3
Song	2007	Korea	54.4 months	N/A	1	1087	65	N/A	APACHE III	N/A	8.6	N/A	3
Alban	2006	USA	Hospital discharge	Surgical	1	10840	58.8	N/A	APACHE II	15.4	2.7	9.4	5
Mayr	2006	Austria	One year	Medical-Surgical	1	3347	59.2	28.6	SAPS II	37.6	3	4.3	5
Priestap	2006	Canada	Hospital discharge	Medical-Surgical	31	47062	61.7	40.8	APACHE II	15.1	5.3	9.3	19
Tobin	2006	Australia	Hospital discharge	Medical-Surgical	1	10963	64	35.0	APACHE II	13*	N/A	4.4	16
Fernandez	2006	Spain	Hospital discharge	Medical-Surgical	1	1159	60.2	N/A	APACHE II	20*	N/A	9.6	21
Vohra	2005	UK	Hospital discharge	Cardiovascular	1	7177	70.4	N/A	N/A	N/A	2.5	N/A	21
Azoulay	2005	France, Europe, Canada, Israel	Hospital discharge	Medical-Surgical	28	1872	60*	37.4	SAPS II	35*	N/A	10.4	39
Yoon	2004	Korea	Hospital discharge	Medical-Surgical	34	1929	55.5	35.8	APACHE III	N/A	4.1	18.8	6
Duke	2004	Australia	Hospital discharge	Medical-Surgical	1	1870	62*	N/A	APACHE II	18.5	5.1	4.9	3
Fortis	2004	Greece	Hospital discharge	Medical-Surgical	1	86	63	43.0	APACHE II	14	N/A	15.1	6
Kogan	2003	Israel	Hospital discharge	N/A	1	1613	63.5	N/A	N/A	N/A	3.3	0.4	5
Bardell	2003	Canada	Hospital discharge	Cardiovascular	1	2117	65	30.0	N/A	N/A	3.5	2.8	12
Metnitz	2003	Austria	Hospital discharge	Medical-Surgical	30	15180	62.7	39.4	N/A	N/A	5.1	N/A	7
Uusaro	2003	Finland	Hospital discharge	N/A	18	20636	N/A	N/A	SAPS II	34	11.5	N/A	2
Azoulay	2003	France	Hospital discharge	#	7	1385	65*	36.5	SAPS II	36*	N/A	10.8	5
Calafiore	2002	Italy	Hospital discharge	Cardiovascular	1	1194	N/A	18.5	N/A	N/A	1.3	0.4	4
Beck	2002	UK	Hospital discharge	Medical-Surgical	1	1654	57	38.3	APACHE II	18.3	7.6	12.6	10
Daly	2001	UK	Hospital discharge	Medical-Surgical	1	5475	N/A	30.5	APACHE II	13.7	2.6	3.7	17
Rosenberg	2001	USA	Hospital discharge	Medical	1	3310	53	66.5	APACHE III	49	9.6	2.8	9
Moreno	2001	Netherlands	Hospital discharge	N/A	48	2958	N/A	N/A	SAPS II	30.1	N/A	8.6	16
Goldfrad	2000	UK	Hospital discharge	Medical-Surgical	62	12748	58.2	N/A	APACHE II	14.7	8.3	17.1	4
Cohn	1999	USA	Hospital discharge	Cardiovascular	38	2228	65.3	32.4	N/A	N/A	5.7	9.9	10
Cooper	1999	USA	Hospital discharge	^	28	103968	63.5	48.0	APACHE III	44.3	6.1	N/A	17
Smith	1999	UK	N/A	Medical-Surgical	1	283	66	45.6	APACHE II	17*	7.8	11	1
Chen	1998	Canada	Hospital discharge	Medical-Surgical	7	5127	59.3	38.0	APACHE II	17.1	4.6	5.5	6
Rubins	1988	USA	Hospital discharge	Medical	1	229	59.9	2.2	APACHE II	10.6	13.1	3	9
Strauss	1986	USA	Hospital discharge	Medical-Surgical	1	912	50	N/A	APS	N/A	15	9.9	4

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; APS, Acute Physiology Score; ICU, Intensive Care unit; MICU, Medical Intensive Care Unit; MPMO-III, Mortality Probability Admission Model; N/A, Not Available; NICU, Neurosurgical Intensive Care Unit; RF, Risk Factor; SAPS, Simplified Acute Physiology Score; SICU, Surgical Intensive Care Unit; SIRS, Systemic Inflammatory Response Syndrome; UK, United Kingdom; USA, United States of America.

Table 2. Quality of Included Studies

Study	Year	Cohort timing	> 1 ICU	Ethics Approval Reported	Follow-up complete	Demographics described	DNR included	Comorbidities Assessed	Type of analysis	SOI Score Used	Eligibility Criteria Mentioned	Power Calculated	Study Duration Justified	Limitations discussed
Yip	2013	Retrospective	No	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Joakowaik	2013	Retrospective	No	No	Yes	Yes	No	Yes	Univariate	Yes	Yes	No	No	Yes
Badawi	2012	Retrospective	Yes	Yes	Yes	Yes	No	No	Multivariate	Yes	Yes	No	Yes	Yes
Reini	2012	Prospective	No	Yes	Yes	Yes	Yes	No	Multivariate	Yes	Yes	No	Yes	Yes
Araujo	2012	Retrospective	No	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Brown	2012	Retrospective	Yes	No	Yes	Yes	No	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Kramer	2012	retrospective	Yes	Yes	Yes	Yes	No	Yes	Univariate	Yes	Yes	No	Yes	Yes
Timmers	2012	Prospective	No	Yes	No	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Mahesh	2012	Retrospective	No	Yes	Yes	Yes	No	Yes	Unadjusted	Yes	Yes	No	No	Yes
Ranzani	2012	Retrospective	No	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Laupland	2012	Retrospective	Yes	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Ouanes	2011	Retrospective	Yes	Yes	Yes	Yes	No	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Renton	2011	Retrospective	Yes	No	Yes	No	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Fernandez	2011	Prospective	Yes	Yes	Yes	Yes	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Kramer	2011	Retrospective	Yes	Yes	No	Yes	No	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Silva	2011	Prospective	Yes	Yes	Yes	Yes	No	Yes	Multivariate	Yes	Yes	No	Yes	No
Fernandez	2010	Prospective	Yes	No	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	Yes	Yes	Yes
Al-Subaie	2010	Prospective	No	Yes	Yes	Yes	No	No	Multivariate	Yes	Yes	Yes	Yes	Yes
Utzolino	2010	Retrospective	No	No	Yes	Yes	Yes	No	Univariate	Yes	Yes	No	No	Yes
Silvestre	2010	Retrospective	No	Yes	Yes	Yes	Yes	No	ROC	Yes	Yes	No	No	Yes
Chrusch	2009	Prospective	Yes	Yes	Yes	Yes	No	No	Multivariate	Yes	Yes	No	Yes	Yes
Litmathe	2009	Retrospective	No	No	Yes	Yes	Yes	Yes	Multivariate	No	Yes	No	No	Yes
Gajic	2008	Prospective	No	Yes	Yes	Yes	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Campbell	2008	Retrospective	No	No	Yes	Yes	No	No	Multivariate	Yes	Yes	No	No	No
Hanane	2008	Retrospective	Yes	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Kaben	2008	Retrospective	No	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Laupland	2008	Prospective	Yes	Yes	N/A	Yes	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Sakr	2008	Prospective	Yes	Yes	No	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	No
Ho	2007	Prospective	No	Yes	Yes	Yes	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Pilcher	2007	Retrospective	Yes	Yes	Yes	No	Yes	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Song	2007	Retrospective	No	Yes	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Alban	2006	Prospective	No	Yes	Yes	No	Yes	No	Multivariate	Yes	Yes	No	No	No
Mayr	2006	Prospective	No	Yes	No	Yes	No	Yes	Multivariate	Yes	Yes	No	No	Yes
Priestap	2006	Retrospective	Yes	Yes	No	Yes	No	Yes	Multivariate	Yes	Yes	Yes	Yes	Yes
Tobin	2006	Retrospective	No	No	Yes	Yes	No	No	Multivariate	Yes	Yes	No	Yes	Yes
Fernandez	2006	Prospective	No	No	Yes	No	Yes	Yes	Multivariate	Yes	Yes	No	Yes	Yes
Vohra	2005	Retrospective	No	No	Yes	Yes	Yes	Yes	Multivariate	No	Yes	No	No	No
Azoulay	2005	Prospective	Yes	No	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Yoon	2004	Prospective	Yes	Yes	Yes	Yes	Yes	No	Univariate	Yes	Yes	No	No	Yes
Duke	2004	Prospective	No	Yes	Yes	No	Yes	No	Multivariate	Yes	Yes	Yes	Yes	Yes
Fortis	2004	Retrospective	No	No	Yes	Yes	Yes	No	Multivariate	No	Yes	No	No	No
Kogan	2003	Prospective	No	Yes	N/A	Yes	Yes	No	Multivariate	No	Yes	No	No	No
Bardell	2003	Retrospective	No	No	Yes	Yes	Yes	Yes	Multivariate	No	Yes	No	No	No
Metnitz	2003	Prospective	Yes	Yes	No	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	No
Uusaro	2003	Retrospective	Yes	Yes	No	No	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Azoulay	2003	Prospective	Yes	No	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	No
Calafiore	2002	Timing imprecise	No	No	Yes	Yes	Yes	Yes	Multivariate	No	Yes	No	No	No
Beck	2002	Retrospective	No	No	Yes	Yes	Yes	No	Stratification	Yes	Yes	Yes	No	No
Daly	2001	Retrospective	No	Yes	Yes	Yes	Yes	No	Multivariate	Yes	Yes	No	No	No
Rosenberg	2001	Prospective	No	No	Yes	Yes	Yes	Yes	Multivariate	Yes	Yes	Yes	No	Yes
Moreno	2001	Retrospective	Yes	No	Yes	No	Yes	No	Multivariate	Yes	Yes	No	No	No
Goldfrad	2000	Retrospective	Yes	No	Yes	Yes	Yes	Yes	Case mix	Yes	Yes	No	No	Yes
Cohn	1999	Retrospective	No	No	No	Yes	Yes	Yes	Mean comparisons	No	Yes	No	No	No
Cooper	1999	Retrospective	Yes	No	No	Yes	Yes	Yes	Multivariate	Yes	Yes	No	No	Yes
Smith	1999	Prospective	No	Yes	No	Yes	No	No	Multivariate	Yes	Yes	No	No	No
Chen	1998	Retrospective	Yes	No	No	Yes	Yes	No	Multivariate	Yes	Yes	No	No	Yes
Rubins	1988	Prospective	No	Yes	Yes	Yes	No	No	Multivariate	Yes	No	No	No	Yes
Strauss	1986	Retrospective	No	No	No	No	Yes	No	Multivariate	Yes	Yes	Yes	Yes	Yes

Abbreviations: DNR, Do Not resuscitate order; ICU, Intensive Care Unit; N/A, Not available; SOI, Severity of Illness; ROC Receiver Operating Characteristic Curves

Table 3. Identified Risk Stratification Tools

Author, Tool, Country Year	Tool Components/ Variables (Weighting/Points)	Prediction Outcome (Follow-up)	Tool Development (# patients)	Tool Validation (# patients/#ICU)	Sensitivity (%)	Specificity (%)	LR+	LR-	AUROC (95% CI)
Gajic **'SWIFT Score'** **USA, 2008**	Source of ICU admission (Other than ED: 8 pt) ICU length of stay (2 to 10 d: 1 pt, >10 d: 4 pt) Last measured PaO2/FiO2 ratio (150 to 399: 5 pt, 100 to 149: 10 pt, <100: 13 pt) GCS at ICU discharge (11 to 14: 6 pt, 8 to 10: 14 pt, <8: 24 pt) Last PaCO2 (>45 mmHg: 5 pt)	Readmission (7 days)	Multivariate (1,131)	Internal (783/1) External (708/1)	56 27	83 87	3.09 2.13	0.56 0.84	0.75 (0.70 to 0.80) 0.70 (0.64 to 0.76)
Frost **Australia, 2010**	Age (years: 0 to 8 pt) Male (2 pt) Elective admission (12 pt) Admission source (ED: 9 pt, Other hospital: 10 pt, Ward: 15 pt) APACHE II score (0 to 20 pt) ICU length of stay >7 days (17 pt) After hours discharge (4 pt) Renal failure (10 pt)	Readmission (Hospital Discharge)	Multivariate (14,952)	Internal‡ (14,952/1)	n/a	n/a	n/a	n/a	0.66 (n/a)
Reini **Sweden, 2012**	Pulse rate (0 to 3 pt) Respiratory rate (0 to 3 pt) Systolic blood pressure (0 to 3 pt) Level of consciousness (0 to 3 pt) Temperature (0 to 2 pt)	Readmission (72 hours)	Existing Score	External (518)	15δ	85δ	1.01δ	0.99δ	OR 0.98 (0.69 to 1.37)¶
Badawi **USA, 2012**	23 variables^λ	Readmission (48 hours)	Multivariate (469,967)	Internal (234,976/219)	6 to 96ψ	19 to 99ψ	1.19 to 5.72ψ	0.19 to 0.95ψ	0.71 (0.71 to 0.71)
	26 variables§	Mortality (48 hours)	Multivariate (469,967)	Internal (234,976/219)	47 to 82ψ	87 to 99ψ	6.44 to 55ψ	0.20 to 0.53ψ	0.92 (0.92 to 0.92)
Daly **United Kingdom, 2002**	β coefficients† Age per year (0.0532) Chronic Health Points (0.2501) ICU length of stay per day (0.0447) Acute Physiology points (0.1556) Cardiothoracic surgery (-2.104) Constant (-4.5821)	Mortality (Hospital Discharge)	Multivariate (5,475)	Internal (1,136/1) External (7,313/19)	74	71	2.55	0.37	0.80 (0.79 to 0.81)θ
Fernandez **'Sabadell Score'** **Spain,** **2006 and 2010**	Subjective intensive care physician scoring: Good Prognosis (0) Poor long term prognosis, >6 months (1) Poor short term prognosis, <6 months (2) Death expected within hospitalization (3)	Mortality (Hospital Discharge)	Existing Score Modified	Internal (1,521/1) External (3,587/31)	23 to 87 26 to 85	79 to 99 71 to 99	4.14 to 23 2.93 to 26	0.16 to 0.78 0.21 to 0.75	0.88 (0.84 to 0.93) 0.84 (0.81 to 0.87)
Ouanes **'MIR'** **France,** **2012**	β coefficients† SAPS II (admission) (0.017) Central venous catheter (0.74) SIRS (max) (0.61) SOFA (discharge) (0.19) Discharge at night (0.92) Constant (-5.59)	Readmission or mortality (7 days)	Multivariate (3,462)	Internal‡ (3,462/4)	50 to 96α	19 to 82α	1.19 to 2.78α	0.21 to 0.61α	0.74 (0.68 to 0.79)

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; AUROC, area under the receiver operating characteristic curves; ED, emergency department; GCS, Glasgow Coma Scale; ICU, Intensive Care unit; LR, likelihood ratio; MIR, Minimizing ICU Readmission; N/A, Not Available; SAPS, Simplified Acute Physiology Score; SIRS, Systemic Inflammatory Response Syndrome; SOFA, Sequential Organ Failure Assessment score; SWIFT, Stability and Workload Index for Transfer; USA, United States of America.

‡ Resampling using bootstrap techniques.

δ Calculated using the Modified Early Warning Score on admission to ICU of <6 vs. ≥6.

¶ Odds ratio for readmission to ICU within 72 hours of ICU discharge reported for each one point increase in the Modified Early Warning Score at the time of ICU discharge. The receiver operating characteristic curve not reported.

λ Readmission model variables: Admission characteristics (age), Elective surgery, ICU type, Admission diagnosis category, Admit source, ICU visit number, Body mass index, ICU interventions (number of lactate values in 24 hours, ICU length of stay), Last day labs, (serum bicarbonate, white blood cell count, serum creatinine, hemoglobin), Last day physiology (heart rate, respiratory rate, diastolic blood pressure, systolic blood pressure, percent oxygen, most recent Glasgow coma scale score).

ψ Range of sensitivities and specificities reported for four different thresholds of predicted readmission or mortality following ICU discharge ranging from 1% to 10%.

§ Mortality model variables: Admission characteristics (age, body mass index), Operative diagnosis (elective surgery), ICU interventions (ICU length of stay, ventilation status), Last day labs (serum lactate, serum creatinine, white blood cell count, serum glucose), Last day physiology (diastolic blood pressure, heart rate, mean arterial pressure, respiratory rate, percent oxygen saturation, most recent Glasgow coma scale score).

† β coefficients reported from multivariable regression model.

θ AUROC reported for combined data for internal and external validation cohorts.

α Range of sensitivities, specificities and likelihood ratios reported for four different thresholds of the MIR score.

Table 4. Pooled ICU Readmission Risk Factors from Systematic Review

Readmission								
Risk Factor		**# Studies**	**# Patients**	**Pooled OR**	**95% CI**		**I squared**	**p value**
APACHE II*	For each additional point	5	22281	1.06	1.02	1.12	78.6	0.009
SAPS II	For each additional point	2	250565	1.015	1.014	1.017	0	>0.001
SOFA	For each additional point	3	7760	1.08	0.967	1.2	78.5	0.174
Length of Stay	More than 3 days	3	21636	2.16	1.63	2.88	72.0	>0.001
Length of Stay	Per day	4	448923	1.038	0.987	1.092	82.2	0.147
Out of hours discharge*		7	469077	1.13	1.01	1.27	68.4	0.003
Age*	For each additional year	9	48527	1.01	1.01	1.02	80.8	>0.001
Gender	Male sex	5	39564	1.21	1.06	1.38	32.6	0.004
Mechanical Ventilation	More than 24 hours	5	209885	3.04	1.61	5.71	96.2	0.001
DNR		2	199512	0.751	0.128	4.395	97.7	0.75
Admission from ED		2	17804	1.5	1.25	1.80	0	>0.001
Acute Renal Failure	New Dialysis in ICU	2	18326	1.821	1.27	2.61	0	0.001
Readmission to ICU		2	248262	5.43	5.14	5.74	0	>0.001
Discharge to HDU/SDU		2	203307	1.36	1.29	1.43	0	>0.001
Cardiac Surgery		3	13331	1.465	0.78	2.76	93.4	0.238
Gastrointestinal Surgery		2	4534	3.39	1.98	5.8	0	>0.001
Emergent Surgery		4	208263	1.482	0.97	2.26	93.7	0.068
Post-operative Myocardial Infarction		2	10479	1.43	1.15	1.78	14.2	0.001
Co-morbidities	Any co-morbid condition	4	292695	1.3	1	1.69	98.2	0.047
Type II Diabetes		3	7672	1.6	1.22	2.08	24	0.001
Chronic Renal Failure		5	209287	1.26	1.15	1.38	0	>0.001
Cancer	Any type of cancer	2	6027	0.817	0.237	2.813	56.7	0.749
Immunosuppressive disease		2	197648	1.35	1.14	1.61	0	>0.001
Chronic Liver Disease	Cirrhosis, Hepatic failure	2	4756	2.33	1.75	3.1	0	>0.001
Chronic Respiratory Disease	COPD	3	201022	1.32	1.2	1.45	0	>0.001
Chronic Cardiovascular Disease	Hypertension, AF, CHF	5	18151	1.38	1.18	1.63	26.3	>0.001

*More than one estimate from a single study

Abbreviations: AF: Atrial Fibrillation, APACHE: Acute Physiology and Chronic Health Evaluation; CHF: Congestive Heart Failure, COPD: Chronic Obstructive Pulmonary Disease, DNR: Do Not Resuscitate, ED: Emergency Department, HDU: High Dependency Unit ICU: intensive Care Unit, SAPS: Simple Acute Physiology Score, SDU: Step-Down Unit, SOFA: Sequential Organ Failure Assessment score

Table 5. Pooled Post-ICU Mortality Risk Factors from Systematic Review

Mortality								
Risk Factor		**# Studies**	**# Patients**	**Pooled OR**	**95% CI**		**I squared**	**p value**
APACHE II*	For each additional point	6	82690	1.071	1.036	1.108	98	>0.001
APACHE III	For each additional percentage of predicted mortality	2	88349	1.04	1.034	1.047	91.4	0.001
SAPS II	For each additional point	5	16808	1.03	1.02	1.04	56.2	>0.001
SOFA	For each additional point	7	16715	1.22	1.16	1.28	58.2	>0.001
Length of Stay	For each additional day	2	9851	1.047	1.022	1.072	0	0.717
Out of hours discharge*		8	201084	1.17	0.98	1.39	71.7	0.087
Age*	For each additional year	12	83925	1.08	0.98	1.19	99.8	0.113
Gender	Male sex	4	58940	1.19	1.05	1.37	38.1	0.009
DNR		3	20424	4.99	2.97	8.36	86.8	>0.001
Admission from Ward		2	4785	1.6	0.61	4.19	90.3	0.343
Sepsis		3	10981	1.85	1.48	2.32	0	>0.001
Cardiac Surgery		2	28827	0.11	0.064	0.19	77.1	>0.001
Chronic Respiratory Disease	COPD	2	9252	1.67	1.24	2.24	5.8	0.001
Chronic Cardiovascular disease	Hypertension, AF, CHF	2	8574	3.4	0.42	27.3	73.2	0.249
Chronic Liver disease	Cirrhosis, Hepatic failure	2	3601	2.73	1.04	7.16	73.0	0.041

*More than one estimate from a single study
Abbreviations: AF: Atrial Fibrillation; APACHE: Acute Physiology and Chronic Health Evaluation; CHF: Congestive Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; DNR: Do Not Resuscitate; ED: Emergency Department; HDU: High Dependency Unit
ICU: intensive Care Unit; SAPS: Simple Acute Physiology Score; SDU: Step-Down Unit, SOFA: Sequential Organ Failure Assessment score

Table 6. Stratification of Overall Outcomes Post- ICU Discharge

	Readmission (2023336 patients)		Mortality (1225279 patients)	
	Proportion	Study (n)	Proportion	Study (n)
Overall Pooled Estimate	**0.063 (0.055 to 0.072)**	45	**0.074 (0.066 to 0.082)**	45
Geographic Region				
North America	0.069 (0.054 to 0.085)	16	0.046 (0.031 to 0.061)	12
Europe	0.062 (0.047 to 0.077)	20	0.096 (0.073 to 1.200)	24
Australia / New Zealand	0.049 (0.034 to 0.065)	4	0.057 (0.051 to 0.063)	6
Other Regions	0.061 (0.037 to 0.086)	4	0.119 (0.000 to 0.257)	3
ICU type				
Medical Surgical ICU	0.062 (0.051 to 0.072)	26	0.084 (0.072 to 0.097)	28
Cardiovascular ICU	0.044 (0.024 to 0.065)	6	0.001 (0.003 to 0.018)	4
Other ICU Type	0.077 (0.061 to 0.093)	12	0.080 (0.060 to 0.100)	13
Patient Characteristics				
SOI predicted >10% mortality	0.058 (0.049 to 0.067)	27	0.086 (0.076 to 0.096)	29
SOI predicted <10% mortality	0.090 (0.085 to 0.094)	4	0.052 (0.038 to 0.066)	13
Age <60	0.078 (0.067 to 0.089)	13	0.103 (0.083 to 0124)	13
Age>60	0.062 (0.048 to 0.076)	21	0.071 (0.061 to 0.081)	19
Study Characteristics				
DNR patients included	0.061 (0.051 to 0.071)	32	0.081 (0.067 to 0.094)	12
DNR patients excluded	0.069 (0.055 to 0.083)	12	0.065 (0.051 to 0.079)	33
High Study Quality	0.065 (0.054 to 0.077)	33	0.081 (0.072 to 0.090)	37
Low Study Quality	0.059 (0.047 to 0.070)	11	0.041 (0.025 to 0.058)	8
Adjusted for confounding factors	0.062 (0.051 to 0.072)	39	0.071 (0.066 to 0.082)	39
Not Adjusted for confounding factors	0.073 (0.067 to 0.079)	5	0.074 (0.066 to 0.082)	6
Follow-up >21 days	0.061 (0.056 to 0.066)	39	0.083 (0.072 to 0.094)	41
Follow-up <21 days	0.068 (0.017 to 0.118)	5	0.016 (0.000 to 0.082)	4
Patient number <1000	0.074 (0.053 to 0.095)	7	0.106 (0.083 to 0.128)	9
Patient number >1000	0.061 (0.055 to 0.072)	37	0.070 (0.059 to 0.081)	36
Multiple ICU study	0.049 (0.033 to 0.065)	10	0.082 (0.057 to 0.108)	10
Single ICU study	0.067 (0.059 to 0.076)	34	0.075 (0.064 to 0.087)	35

Abbreviations:DNR, Do Not Resuscitate; ICU, Intensive Care Unit; SOI, Severity of Illness;

Table 7. Proposed meta-tools and scoring

Variable	Simple Score	Coefficient Score
Previous Readmission to ICU	1	1.691939134
Gastrointestinal Surgery	1	1.220829921
Mechanical Ventilation (> 3 days)	1	1.111857515
Chronic Liver Disease	1	0.925084938
Septic Shock	1	0.615185639
Acute Renal Failure	1	0.599385801
Type II Diabetes	1	0.470003629
Admission from Emergency Department	1	0.405465108
Chronic Lung Disease	1	0.395227682
Post-operative Myocardial Infarction	1	0.357674444
Chronic Cardiovascular Diease	1	0.322083499
Discharge to HDU/SDU	1	0.3074847
Immunosuppressive disease	1	0.300104592
Chronic Renal Failure	1	0.231111721
Male	1	0.19062036
Out of hours discharge	1	0.122217633
Length of Stay (per day)	1	0.045928932
Severity of Illness Score predicting >10% mortality	1	0.042580448
Age (per yr)	1	0.009950331

Abbreviations : HDU, High Dependancy Unit; ICU, Intensive Care Unit; SDU, Step Down Unit;

Table 8. Mean Value of Characteristics for Patients within TRACER database

Characteristic	Overall (n=26094)	Readmission (n=1661)	Mortality (n=1687)
Age	64.4	61.2	67.7
Length of Stay (days)	4.90	8.25	8.68
Female (%)	35.6	35.7	43.0
APACHE II Score	21.1	21.7	23.5
Medical Admission (%)	29.7	31.0	38.4
Surgical Admission (%)	38.6	39.5	25.0
Overall Post ICU Outcome (%)	N/A	6.37	6.47

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation; ICU, Intensive Care Unit.

Table 9. Operationalized Prediction Model definitions for TRACER testing

Variables Used	Operationalized Definition	Coefficient Model	Simple Model	% missing data
Previous Readmission to ICU	Readmission variable	✓	✓	N/A
Age (per 15 yr)	ICU Demographic data	✓	> 65years old	0.21
Male	ICU Demographic data	✓	✓	0.1
Admission from Emergency Department	Admission Source data	✓	✓	0.1
Length of Stay (per day)	ICU admision and discharge dates	✓	>5 days	1.9
Severity of Illness Score predicting >10% mortality	Max admission APACHE II (>9)	✓	✓	N/A
Acute Renal Failure	CRRT or Admission definiton of ARF or Cr >150	✓	✓	4.8
Sepsis/ Infection	Admission definiton of Sepsis/ Infection	✓	✓	N/A
Glucose metabolism dysfunction	Glucose on admission >11mmol/L	✓	✓	12.3
Post-operative Myocardial Infarction	Surgical Admission + AMI	✓	✓	N/A
Gastrointestinal Surgery	Surgical Admission + GI surgery admission definition	✓	✓	N/A

Abbreviations: AMI, Acute Myocardial Infarction; APACHE, Acute Physiology and Chronic Health Evaluation; ARF, Acute Renal Failure; CR, Creatinine; CRRT, Continuous Renal Replacement Therapy; GI, Gastrointestinal; Intensive Care unit; N/A, Not Available;

Table 10. Results from Testing of Prediction Models in TRACER database

Simple Model			
Parameter	Outcome	Estimate	95% CI
Linear Regression R^2 value	Readmission	0.76	-
	Mortality	0.64	-
	Combined	0.74	-
Logistic Regression pseudo-R^2 value	Readmission	0.16	-
	Mortality	0.11	-
	Combined	0.15	-
Logistic Regression Beta Coefficient	Readmission	0.84	0.80-0.89
	Mortality	0.69	0.65-0.73
	Combined	0.79	0.76-0.83
Logistic Regression Odds Ratio (per point)	Readmission	2.32	2.23-2.42
	Mortality	2.00	1.91-2.08
	Combined	2.22	2.14-2.30
Area Under the Receiver Operator Curve	Readmission	0.79	0.78-0.80
	Mortality	0.72	0.71-0.74
	Combined	0.76	0.75-0.77
Coefficient Model			
Parameter	Outcome	Estimate	95% CI
Linear Regression R^2 value	Readmission	0.12	-
	Mortality	0.21	-
	Combined	0.57	-
Logistic Regression pseudo-R^2 value	Readmission	0.54	-
	Mortality	0.12	-
	Combined	0.33	-
Logistic Regression Beta Coefficient	Readmission	2.65	2.54-2.76
	Mortality	0.92	0.86-0.97
	Combined	1.80	1.73-1.86
Logistic Regression Odds Ratio (per point)	Readmission	14.20	12.70-15.80
	Mortality	2.50	2.37-2.63
	Combined	6.02	5.67-6.41
Area Under the Receiver Operator Curve	Readmission	0.97	0.96 – 0.97
	Mortality	0.75	0.74-0.76
	Combined	0.86	0.85-0.87

Abbreviations: CI, Confidence interval

Figure 1. Study Flow

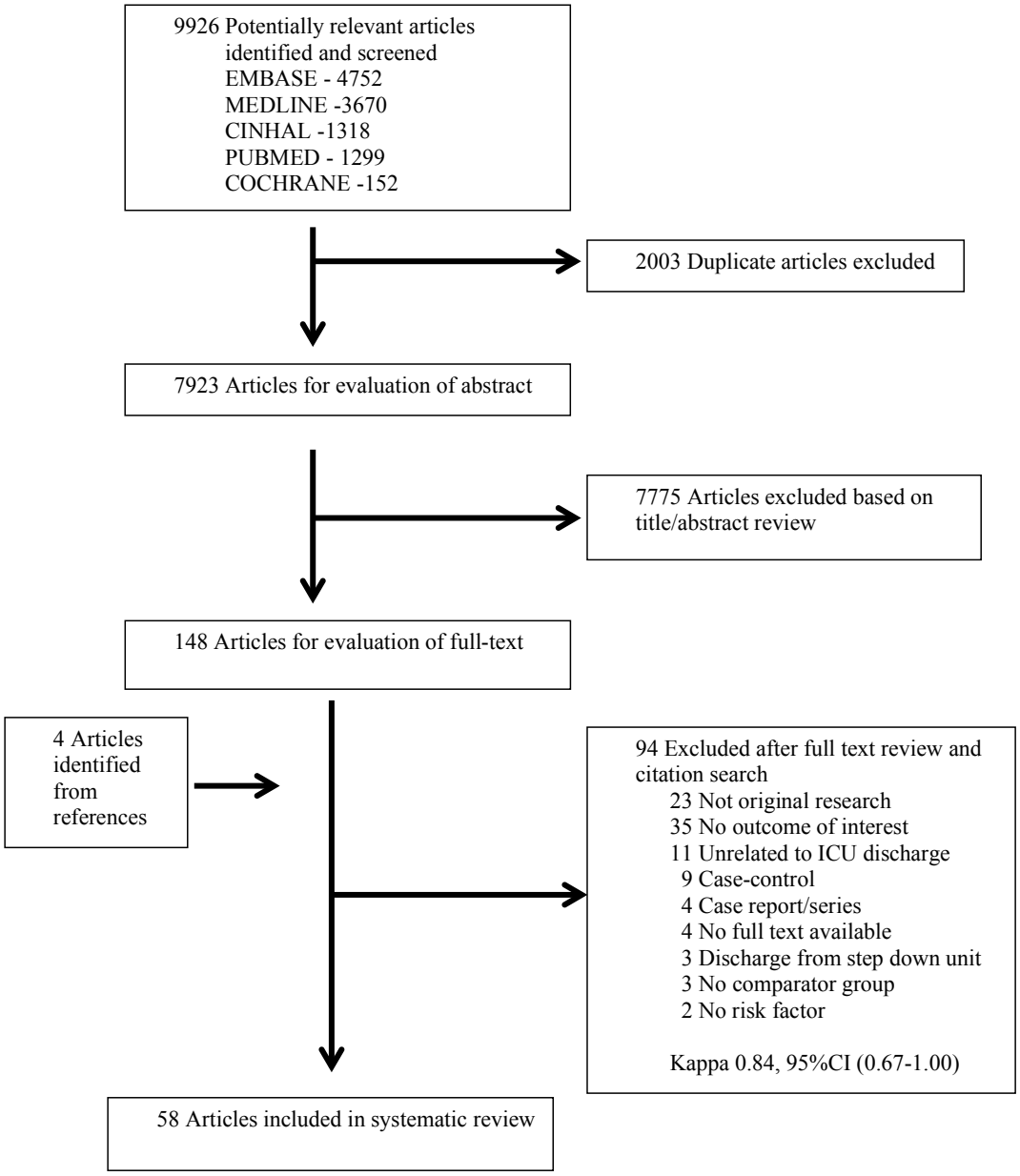


Figure 2. Semi-Qualitative Analysis of Post-ICU Discharge Risk Factors

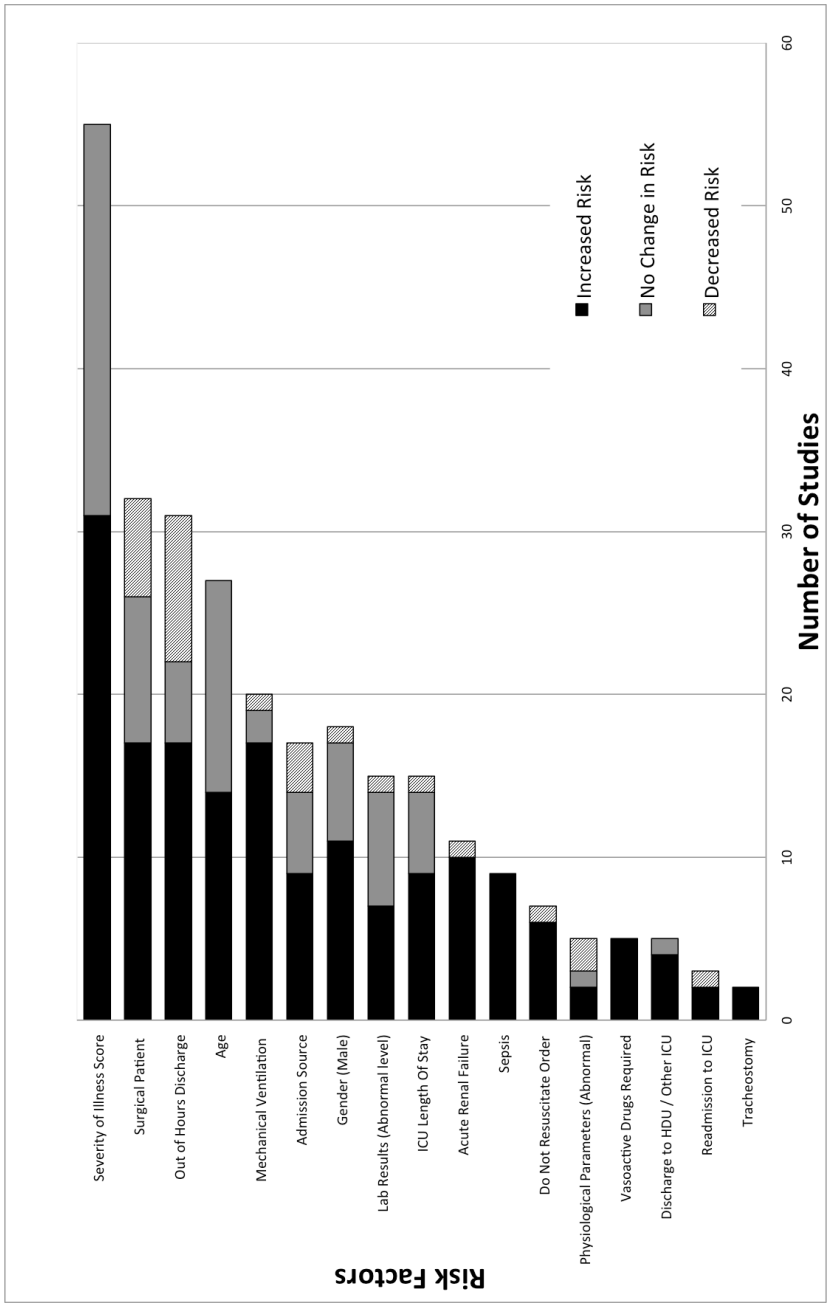
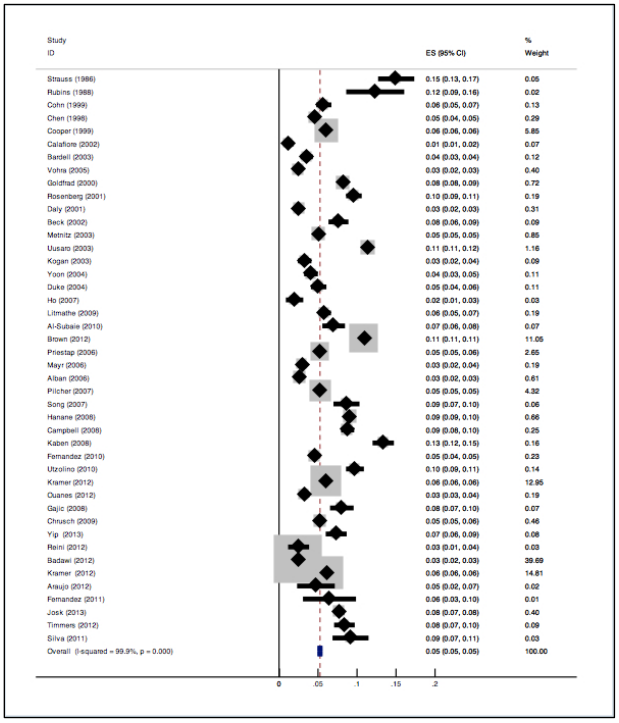


Figure 3. Post-ICU Discharge Readmission Proportion Outcome

Fixed Effect model 0.053 (0.053 – 0.054)



B) Random Effect model 0.063 (0.055 – 0.072)

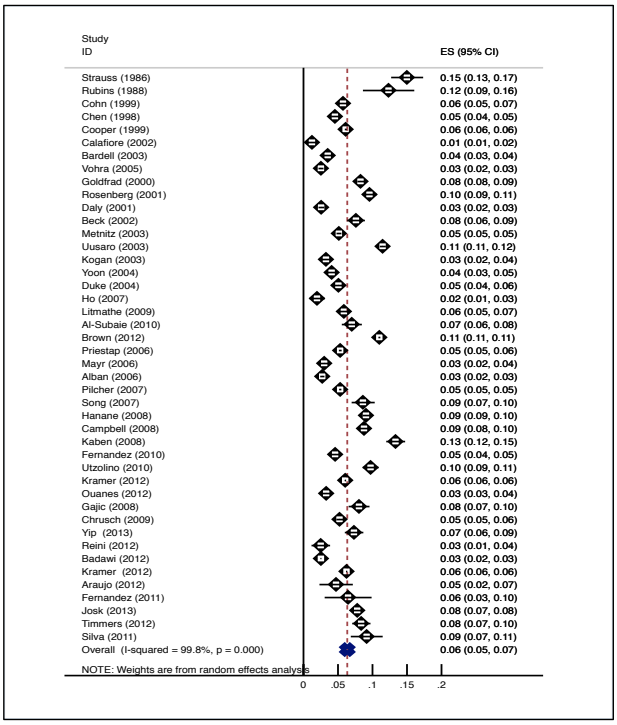
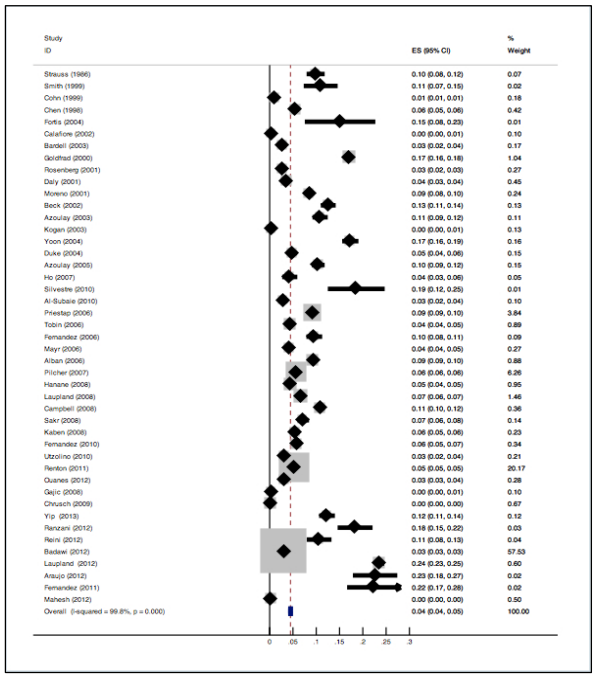


Figure 4. Post-ICU Discharge Mortality Proportion Outcome

A) Fixed Effect model 0.045 (0.044 – 0.045)



B) Random Effect model 0.074 (0.066 – 0.082)

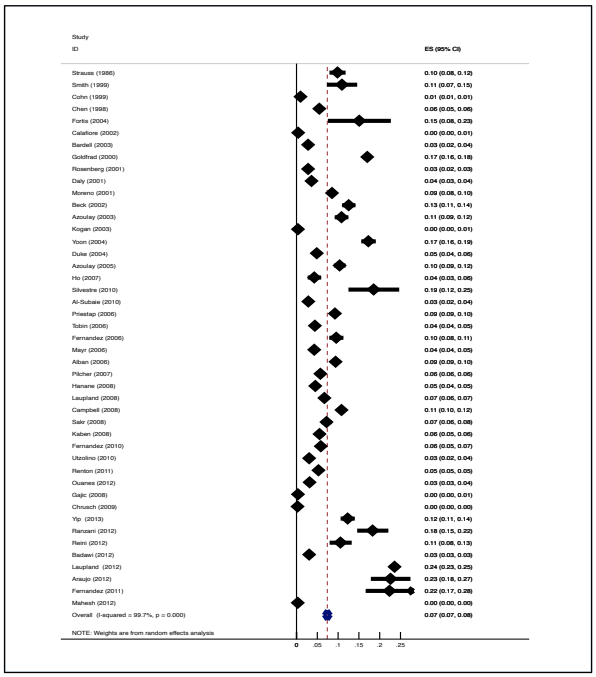
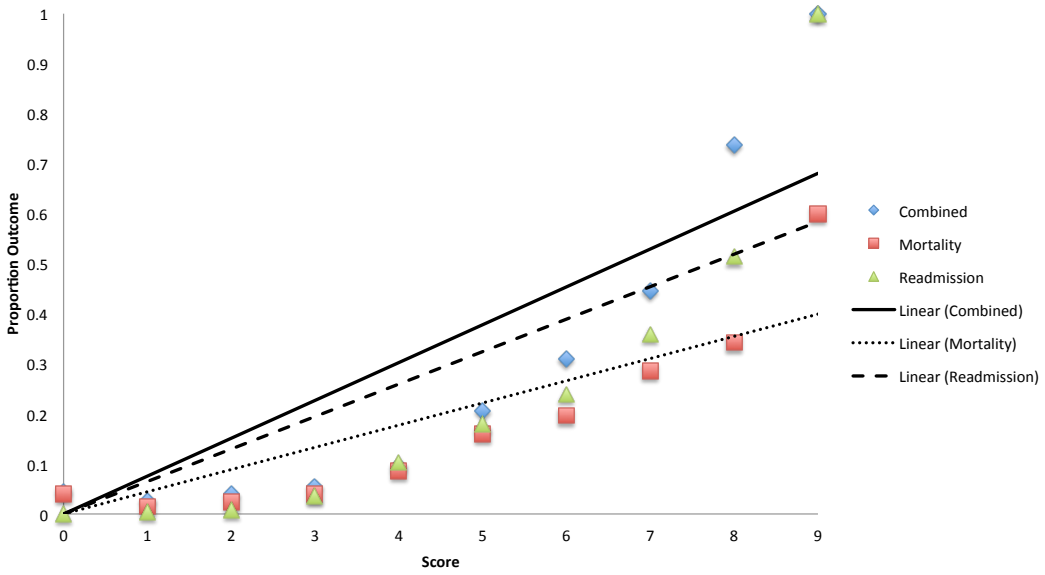
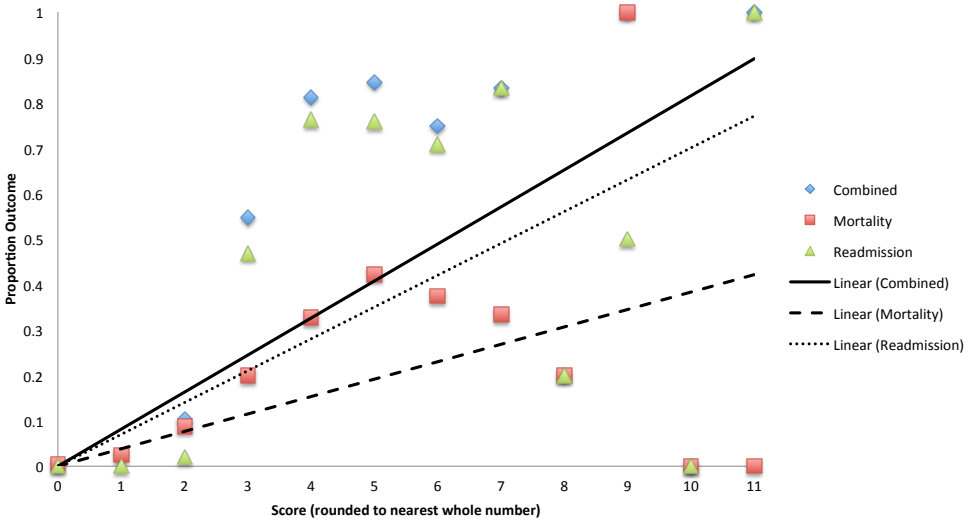


Figure 5. Linear Regression Analysis of Simple-Model



Score	0	1	2	3	4	5	6	7	8	9
Patients (n)	75	1424	5967	7376	4259	2094	809	231	35	5

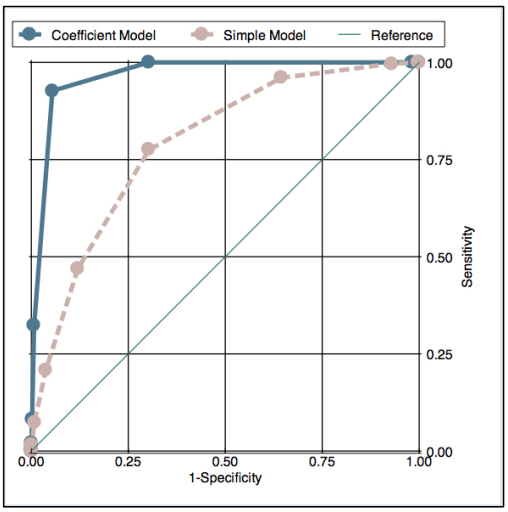
Figure 6. Linear Regression Analysis of Coefficient-Model



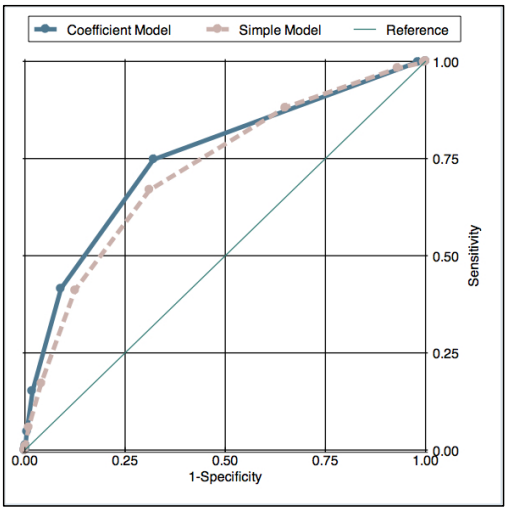
Score	0	1	2	3	4	5	6	7	8	9	10	11
Patients (n)	404	14148	5278	1852	452	116	24	12	5	4	0	1

Figure 7. TRACER Receiver Operating Curve Analysis of Prediction Models

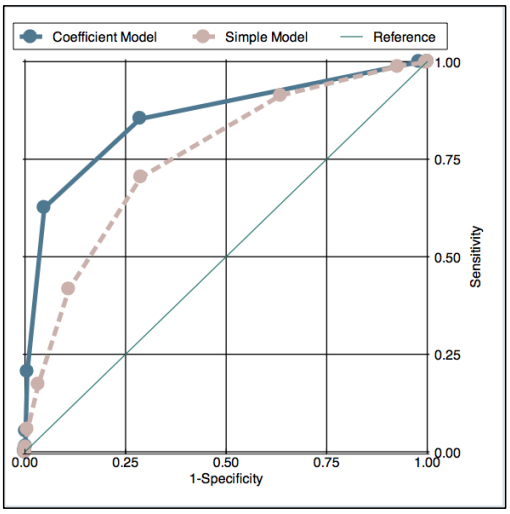
A) Readmission



B) Mortality



C) Readmission or Mortality



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APPENDIX A: SAMPLE SEARCH STRATEGY

1. exp Intensive Care Units/
2. exp Intensive Care/ or exp Critical Care/
3. exp Critical Illness/
4. special care unit.tw.
5. close attention unit.tw.
6. intensive care department.tw.
7. intensive care units.tw.
8. respiratory care unit.tw.
9. intensive care.tw.
10. critical care.tw.
11. icu.tw.
12. icu.tw.
13. exp Patient Discharge/
14. exp Patient Transfer/
15. (patient adj5 discharg*).tw.
16. (discharg* adj5 planning).tw.
17. patient dumping.tw.
18. intrahospital transfer.tw.
19. discharge.tw.
20. exp Patient Readmission/
21. exp Patient Readmission/
22. Readmission.tw.
23. (Patient adj5 readm*).tw.
24. (Unit adj8 readm*).tw.
25. (Unplan* adj5 adm*).tw.
26. exp Hospital Mortality/ or exp Mortality/
27. death rate*.tw.
28. mortality determinant.tw.
29. differential mortalit*.tw.
30. age-specific death rates.tw.

31. mortality decline.tw.
32. premature mortality.tw.
33. case fatality rate.tw.
34. in-hospital mortal*.tw.
35. inhospital mortal*.tw.
36. hospital mortal*.tw.
37. exp Death, Sudden/
38. exp Death, Sudden, Cardiac/
39. exp Hospital Rapid Response Team/
40. rapid response team.tw.
41. cardiac crash team.tw.
42. code team*.tw.
43. team code.tw.
44. medical emergency team.tw.
45. medical care team.tw.
46. health care team.tw.
47. healthcare team.tw.
48. exp Cardiopulmonary Resuscitation/
49. Code blue.tw.
50. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
51. 13 or 14 or 15 or 16 or 17 or 18 or 19
52. (unplan* adj5 admi*).tw.
53. 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 48 or 49 or 52
54. 50 and 51 and 53

APPENDIX B: LIST OF RISK FACTORS WITH MULTIVARIATE ESTIMATES

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Fernandez 2006	APACHE II	Per point	1159	1.01			1.00	1.03
Campbell 2008	APACHE II	Per point	4376	1.06			1.04	1.08
Laupland 2008	APACHE II	Per point	17864	1.06			1.05	1.07
Priestap 2006	APACHE II	Per point	47062	1.10			1.09	1.10
Tobin 2006	APACHE II	Per point	10963	1.14			1.12	1.16
Campbell 2008	APACHE II	Per point	4376		1.03		1.01	1.05
Fortis 2004	APACHE II	Per point	86		1.03		0.23	4.68
Frost 2010	APACHE II	Per point	14952		1.20		1.07	1.23
Timmers 2012	APACHE II	Per point	1682		1.02		0.97	1.07
Al-Subaie 2010	APACHE II	Per point at A/D	1185			1.06	1.02	1.10
Chursch 2008	APACHE II	Per point	8222			2.69*		
Yip 2013	APACHE II	Per 10% inc in mortality	1446		1.04		0.94	1.17
Hanane 2008	APACHE III	Predicted mortality	11659	1.04			1.04	1.05
Pilcher 2007	APACHE III	Predicted mortality	76690	1.04			1.04	1.04
Kaben 2008	SAPS II	Per point at A/D	2852	1.02			1.01	1.04
Sakr 2008	SAPS II	Per point	1729	1.04			1.03	1.06
Laupland 2012	SAPS II	Per point	7380	1.03			1.02	1.03
Azoulay 2004	SAPS II	Per point	1385	1.16			1.02	1.31
Renton 2011	SAPS II	Per point	247103		1.02		1.01	1.02
Ouanes 2011	SAPS II	Per point	3462			1.02	1.01	1.03
Azoulay 2003	SOFA	Per point at D/C	1385	1.11			1.03	1.18
Laupland 2012	SOFA	Per point at D/C	7380	1.19			1.14	1.23
Reini 2012	SOFA	Per point	518	1.32			1.23	1.41
Ranzani 2012	SOFA	Per point	409	1.22			1.06	1.41
Moreno 2001	SOFA	Per point	2958	1.30			1.10	1.53
Kaben 2008	SOFA	Per point	2852		1.03		0.99	1.17
Ho 2007	SOFA	Change in SOFA	603	1.30			1.08	1.57
Ouanes 2011	SOFA	Per point	3462			1.20	1.10	1.30
Yip 2013	SOFA	Per point at D/C	1446		1.01		0.92	1.11
Fortis 2004	TISS-28	>14 vs <8	86	3.861			1.39	10.70
Fortis 2004	TISS-28	8-13 vs <8	86	1.197			1.05	1.38
Campbell 2008	TISS-76	Per point at D/C	4376	1.01			1.00	1.02
Campbell 2008	TISS-76	Per point at D/C	4376		1.01		1.00	1.02
Reini 2012	SAPS III	per point	518	1.09			1.07	1.11
Timmers 2012	SAPS III	per point	1682		1.00		0.97	1.03

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Hanane 2008	Out of hours Discharge	Nighttime	11659	1.05			0.64	1.70
Goldfrad 2000	Out of hours Discharge	Nighttime	12748	1.18			0.90	1.56
Laupland 2008	Out of hours Discharge	Nighttime	17864	1.20			1.01	1.41
Priestap 2006	Out of hours Discharge	Nighttime	47062	1.22			1.10	1.36
Pilcher 2007	Out of hours Discharge	Nighttime	76690	1.42			1.32	1.52
Tobin 2006	Out of hours Discharge	Nighttime	10963	1.63			1.37	3.18
Laupland 2012	Out of hours Discharge	Nighttime	7380	1.54			1.12	2.11
Duke 2004	Out of hours Discharge	Nighttime	1870	1.7*			1.03	2.90
Kaben 2008	Out of hours Discharge	Nighttime	2852		0.98		0.74	1.22
Beck 2002	Out of hours Discharge	Nighttime	1654		1.7		1.28	2.25
Yip 2013	Out of hours Discharge	Nighttime	1446		0.69		0.42	1.12
Ouanes 2011	Out of hours Discharge	Nighttime	3462			2.50	1.30	4.90
Brown 2012	Out of hours Discharge	Nighttime	196202		1.20		1.05	1.37
Chursch 2009	Out of hours Discharge	Nighttime	8222			0.69*	0.43	1.11
Uusaro 2003	Out of hours Discharge	Out of hours	20636	0.89			0.73	1.07
Renton 2011	Out of hours Discharge	Out of hours	247103		1.13		1.08	1.19
Frost 2010	Out of hours Discharge	Out of hours	14952		1.20		1.04	1.36
Laupland 2008	Out of hours Discharge	Out of hours	17864	1.09			0.81	1.47

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Kaben 2008	Out of hours Discharge	Out of hours	2852		0.94		0.76	1.16
Laupland 2008	Out of hours Discharge	Weekend	17864	0.81			0.67	0.98
Uusaro 2003	Out of hours Discharge	Weekend	20636	1.11			0.93	1.31
Kaben 2008	Out of hours Discharge	Weekend	2852		0.84		0.61	1.34
Laupland 2008	Out of hours Discharge	Weekend Nightime	17864	1.35			1.05	1.73
Laupland 2012	Out of hours Discharge	Weekend	7380	1.26			0.80	2.00
Laupland 2012	Out of hours Discharge	Weekend	7380	1.41			0.84	2.35
Laupland 2012	Weekday discharge	Thursday	7380	0.80			0.53	1.21
Laupland 2012	Weekday discharge	Wed	7380	0.91			0.60	1.36
Laupland 2012	Weekday discharge	Tuesday	7380	0.99			0.66	1.48
Laupland 2012	Weekday discharge	Friday	7380	1.45			1.01	2.10
Azoulay 2004	Age	per year	1872	1.02			1.01	1.03
Campbell 2008	Age	per year	4376	1.03			1.02	1.04
Ho 2007	Age	per year	603	1.03			0.99	1.06
Priestap 2006	Age	per year	47062	1.04			1.04	1.05
Sakr 2008	Age	per year	1729	1.04			1.02	1.06
Uusaro 2003	Age	per year	20636	1.04			1.01	1.07
Fernandez 2006	Age	per year	1159	1.05			1.03	1.07
Fortis 2004	Age	per year	86	1.054			1.00	1.11
Daly 2001	Age	per year	5475	1.70			1.68	1.72
Campbell 2008	Age	per year	4376		1.01		0.99	1.02
Chen 1998	Age	per year	5127		1.01		1.00	1.02
Frost 2010	Age	per year	14 952		1.01		1.00	1.01
Metniz 2003	Age	per year	15180		1.01		1.00	1.01
Kaben 2008	Age	per year	2852		1.01		1.00	1.02
Laupland 2008	Age	per year	17864		1.03		1.03	1.04
Al-Subaie 2010	Age	per year	1185			1.02	1.01	1.04
Ranzani 2012	Age	per year	409	1.04			1.02	1.05
Reini 2012	Age	per year	518	1.06			1.04	1.08

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Timmers 2012	Age	per year	1682		1.01		1.00	1.03
Yip 2013	Age	per year	1446		1.00		0.99	1.02
Fortis 2004	Male		86	0.230			0.05	1.15
Priestap 2006	Male		47062	1.17			1.10	1.26
Campbell 2008	Male		4376	1.23			0.98	1.54
Laupland 2012	Male		7380	1.30			1.02	1.65
Frost 2010	Male		14952		1.10		0.95	1.25
Litmathe 2009	Male		3374		1.30		0.70	1.90
Metniz 2003	Male		15180		1.36		1.17	1.59
Campbell 2008	Male		4376		1.38		0.96	1.99
Chursch 2009	Male		8222			1.01*	0.82	1.24
Timmers 2012	Male		1682		0.97		0.66	1.42
Yip 2013	Female		1446		0.75		0.47	1.18
Campbell 2008	LOS	per day	4376	1.04			1.00	1.09
Daly 2001	LOS	per day	5475	1.05			1.02	1.08
Renton 2011	LOS	per day	247103		1.02		1.02	1.02
Campbell 2008	LOS	per day	4376		1.05		1.00	1.10
Gajic 2008	LOS	per day	1242		1.44		1.14	1.87
Brown 2012	LOS	per day	196202		1.00		0.91	1.09
Rosenburg 2001	LOS	> 7days	3310		1.40		0.97	2.03
Litmathe 2009	LOS	> 3 days	3374		2.10		1.40	2.60
Joakowaik 2013	LOS	>3 days	7105		3.61		2.35	5.62
Frost 2010	LOS	> 7days	14952		2.20		1.85	2.56
Chursch 2009	LOS	LOS>10 days vs.<3 days	8222			2.22*		
Chursch 2009	LOS	LOS 3-10days vs.<3 days	8222			1.72*		
Campbell 2008	Respiratory Support	Days of MV	4376	0.97			0.92	1.03
Campbell 2008	Respiratory Support	Days of MV	4376		0.96		0.91	1.02
Kaben 2008	Respiratory Support	Days of MV	2852		1.02		1.05	0.98
Brown 2012	Respiratory Support	Days of MV	196202		1.12		1.02	1.23
Metniz 2003	Respiratory Support	MV last day ICU	15180		3.00		3.89	2.31
Gajic 2008	Respiratory Support	MV or not	1242		2.149		1.01	4.58
Litmathe 2009	Respiratory Support	> 24 hours MV	3374		3.20		2.20	4.50
Song 2007	Respiratory Support	> 5 days MV	1087		7.86		2.38	26.00
Bardell 2003	Respiratory Support	> 24 hours MV	2117		10.52		6.18	17.91
Joakowaik 2013	Respiratory Support	MV	7105		1.58		1.27	1.91
Metniz 2003	Respiratory Support	MV last day ICU	15180		1.72		2.06	1.43

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Timmers 2012	Respiratory Support	MV	1682		1.79		1.03	3.11
Joakowaik 2013	Respiratory Support	MV	7105		2.39		1.93	2.90
Tobin 2006	Cardiac surgery		10963	0.08	28827.00		0.05	0.13
Laupland 2008	Cardiac surgery		17864	0.14			0.11	0.17
Litmathe 2009	Cardiac surgery		3374		2.90		2.10	3.70
Kaben 2008	Cardiac surgery		2852		0.71		0.44	1.15
Joakowaik 2013	Cardiac surgery		7105		1.41		1.21	1.65
Daly 2001	Cardiac surgery		5475	0.12			-0.41	0.65
Chursch 2009	Cardiac surgery		8222			0.4*	0.07	0.23
Priestap 2006	ER Admission	ER Admission	47062	0.62	123752.00		0.57	0.67
Pilcher 2007	ER Admission	ER Admission	76690	1.53			1.40	1.68
Kaben 2008	ER Admission	ER Admission	2852	17804.00	1.51		0.59	3.84
Frost 2010	ER Admission	ER Admission	14952		1.50		1.27	1.83
Kramer 2011	ER Admission	ER Admission	229961		0.88		x	x
Azoulay 2004	Infection	Hospital-acquired infection	1872	1.65	3601.00		1.14	2.37
Sakr 2008	Infection	Sepsis	1729	2.30			1.51	3.49
Kaben 2008	Infection	Sepsis	2852		1.18		0.73	1.90
Chursch 2009	Infection	Sepsis	8222			1.66*		
Laupland 2012	Infection	Sepsis	7380	1.76			1.20	2.56
Song 2007	Renal failure	CRRT	1087	3.61			1.10	11.90
Litmathe 2009	Renal failure	CRRT	3374	18326.00	2.20		1.00	3.10
Frost 2010	Renal failure		14952		1.60		0.97	2.47
Kramer 2011	Renal failure	CRRT	229961		1.17			
Kramer 2011	GCS	A/D GCS 3 to 6 vs 15	229961		0.88			
Kramer 2011	GCS	A/D GCS 7 to 10 vs 15	229961		0.91			
Kramer 2011	GCS	A/D GCS 11 to 14 vs 15	229961		1.02			
Kramer 2011	GCS	D/C GCS 3 to 6 vs 15	229961		0.49			
Kramer 2011	GCS	D/C GCS 7 to 10 vs 15	229961		0.79			
Kramer 2011	GCS	D/C GCS 11 to 14 vs 15	229961		1.11			
Gajic 2008	GCS	Discharge GCS	1242	0.81			0.75	0.88
Azoulay 2003	DNR		1385	9.64	13044.00		5.75	16.16
Hanane 2008	DNR		11659	3.28			2.65	4.06
Rosenburg 2001	DNR		3310		0.30		0.26	0.72
Brown 2012	DNR		196202		1.82		1.53	2.17
Duke 2004	DNR		1870	5.1*			2.20	12.00
Laupland 2012	DNR		7380	4.55			3.34	6.20

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Kaben 2008	Transfer from another hospital		2852	6162.00	0.60		0.47	3.05
Rosenburg 2001	Transfer from another hospital		3310		1.70		1.30	2.30
Priestap 2006	Transfer from another hospital		47062	0.61			0.52	0.72
Kramer2011	Transfer from another hospital		229961		1.28			
Litmathe 2009	Diabetes	Diabetes	3374	6226.00	1.50		1.00	1.70
Kaben 2008	Diabetes	Diabetes	2852		1.47		0.99	2.16
Kramer 2011	Diabetes	Diabetes	229961		1.03			
Yip 2013	Diabetes		1446		2.97		1.33	6.65
Fernandez 2010	Readmission		1159	5.7			3.70	8.80
Renton 2011	Readmission		247103	5.43			5.14	5.74
Brown 2012	Emergent Surgery	Emergent Surgery	196202		1.10		1.01	1.21
Litmathe 2009	Emergent Surgery	Surgical reexploration	3374		2.70		1.50	3.70
Timmers 2012	Emergent Surgery	Emergency vs elective surgery	1682		0.89		0.54	1.47
Joakowaik 2013	Emergent Surgery	Surgical re-exploration	7105		2.02		1.65	2.41
Brown 2012	Chronic Renal Failure		196202		1.24		1.10	1.39
Kaben 2008	Chronic Renal Failure		2852		1.17		0.72	1.91
Timmers 2012	Chronic Renal Failure		1682		0.63		0.17	2.49
Joakowaik 2013	Chronic Renal Failure		7105		1.32		1.12	1.53
Yip 2013	Chronic Renal Failure		1446		0.89		0.33	2.42
Brown 2012	Discharge to HDU/step down unit		196202		1.37		1.29	1.44
Joakowaik 2013	Discharge to HDU/step down unit		7105		1.29		1.09	1.44
Yip 2013	Cancer	Leukemia/myeloma	1446		0.56		0.06	4.90
Yip 2013	Cancer	Lymphoma	1446		0.02		0.01	9.90
Yip 2013	Cancer	Metastatic ca	1446		2.87		0.59	13.90

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Kaben 2008	Cancer	Cancer	2852		1.05		0.63	1.76
Sakr 2008	Cancer	Hematologic cancer	1729	3.70			1.52	9.10
Laupland 2012	Cardiovascular Disease	Cardiovascular Disease	7380	1.50			1.04	2.16
Calafiore 2002	Cardiovascular Disease	CHF	1194	13.5			1.50	121.50
Yip 2013	Cardiovascular Disease	Chronic CVD	1446		1.23		0.67	2.29
Litmathe 2009	Cardiovascular Disease	AF	3374		1.70		1.20	1.90
Litmathe 2009	Cardiovascular Disease	Arterial hypertension	3374		1.10		0.80	1.50
Kaben 2008	Cardiovascular Disease	Chronic heart failure	2852		1.13		0.43	2.94
Joakowaik 2013	Cardiovascular Disease	Pulmonary hypertension	7105		1.37		1.16	1.63
Araujo 2012	Co-morbidities	Charlson score (per point)	296	1.20			1.10	1.40
Ranzani 2012	Co-morbidities	Comorbidity	409	1.29			1.03	1.63
Timmers 2012	Co-morbidities	Comorbitiy	1682		1.47		0.85	2.54
Silva 2011	Co-morbidities	Comorbitiy	600		2.97		1.23	7.22
Rosenburg 2001	Co-morbidities	Comorbidity	3310		1.02		1.01	1.03
Renton	Co-morbidities	Comorbidity	247103		1.37		1.31	1.44
Laupland 2012	Chronic Respiratory Disease	Respiratory Disease	7380	1.53			1.11	2.10
Azoulay 2004	Chronic Respiratory Disease	Chronic Respiratory failure	1872	2.18			1.20	3.93
Yip 2013	Chronic Respiratory Disease	Respiratory Disease	1446		1.03		0.42	2.54
Brown 2012	Chronic Respiratory Disease	COPD	196202		1.31		1.19	1.44
Litmathe 2009	Chronic Respiratory Disease		3374		1.60		1.10	2.30
Campbell 2008	Admission from ward		4376		1.02		1.01	1.02
Campbell 2008	Admission from ward		4376	1.02			1.01	1.03

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Ranzani 2012	Admission from ward		409	2.75			1.50	5.02
Timmers 2012	Gastrointestinal Surgery		1682		4.21		2.04	8.70
Kaben 2008	Gastrointestinal Surgery		2852		2.60		1.17	5.80
Yip 2013	Chronic liver disease	Cirrhosis	1446		1.36		0.38	4.86
Rosenburg 2001	Chronic liver disease		3310		2.40		1.83	3.30
Sakr 2008	Chronic liver disease	Cirrhosis	1729	4.70			2.07	10.92
Azoulay 2004	Chronic liver disease	Cirrhosis	1872	1.75			1.00	3.11
Yip 2013	Chronic liver disease	Hepatic Failure	1446		0.02		0.01	10.00
Yip 2013	Immunosuppresive disease	HIV	1446		0.02		0.01	10.00
Yip 2013	Immunosuppresive disease	Immunosuppressive Treatment	1446		0.82		0.23	3.00
Yip 2013	Immunosuppresive disease		1446		2.32		0.25	21.50
Brown 2012	Immunosuppresive disease		196202		1.35		1.14	1.61
Azoulay 2004	Immunosuppresive disease	Immunosuppression	1872	1.82			1.28	2.58
Litmathe 2009	Postoperative myocardial infarction		3374		1.30		1.00	1.70
Joakowaik 2013	Postoperative myocardial infarction		7105		1.63		1.17	2.19
Araujo 2012	C-reactive protein	≥6 mg/dL	296	2.80			1.40	5.70
Ranzani 2012	C-reactive protein	reduction <25%	409	2.70			1.39	5.29
Ho 2007	C-reactive protein	per 10mg/L	603	1.09			1.03	1.16
Azoulay 2005	Trauma		1872	0.85			0.29	2.48
Kaben 2008	Trauma		2852		0.79		0.32	1.92
Chursch 2009	Trauma		8222			0.95*		
Yip 2013	General Surgery		1446		1.10		0.66	1.83
Timmers 2012	General Surgery		1682		1.23		0.46	3.31
Mayr 2006	General Surgery		3347	5.09			3.20	8.20
Timmers 2012	Vascular Surgery		1682		2.91		1.39	6.11
Chursch 2009	Vascular Surgery		8222			0.83*		

Author	Risk Factor	Risk Factor Definition	Patients (#)	Mortality	Readmission	Combined	Lower CI	Upper CI
Timmers 2012	Type of admission	Active treatment	1682		3.96		2.12	7.39
Timmers 2012	Type of admission	High risk monitoring	1682		2.56		1.60	4.09
Ranzani 2012	Shock		409	2.59			1.26	5.36
Calafiore 2002	Shock	Vasoactive drugs	1194		9.6			
Al-Subaie 2010	Shock	Vasoactive drugs	1185					
Azoulay 2004	Shock	Shock	1872		1.46			
Fernandez 2010	Shock	Vasoactive drugs	1159		2.3			
Fernandez 2006	Shock	Vasoactive drugs	1159		2.5			
Ranzani 2012	Hemoglobin at D/C		409	0.78			0.66	0.91
Yip 2013	Esinophenia at D/C		1446		2.50		1.38	4.50
Timmers 2012	Oncological Surgery		1682		2.48		1.16	5.33
Joakowaik 2013	Reintubation		7105		2.01		1.53	2.67
Chursch 2009	Gastrointestinal Disease		8222			2.55*	1.54	4.25
Laupland 2012	Gastrointestinal Disease		7380	1.83			1.30	2.56
Araujo 2012	Tracheostomy		296	3.80			1.80	8.30
Fernandez 2011	Tracheostomy		201				0.30	1.20
Ho 2007	White Cell count		603	1.04			0.98	1.09
Yip 2013	White Cell count		1446		0.99		0.95	1.04

*Estimate of Relative Risk

Combined is an outcome comprising of both ICU readmission and post-ICU Mortality

Abbreviations: A/D, Admission; D/C, Discharge

APPENDIX C: ODDS RATIO ESTIMATES FROM TRACER DATABASE

Combined Readmission and Mortality					
Variable	# outcome	# patients	proportion	OR	95% CI
Female	1134	9277	0.122	1.22	1.12 - 1.32
Male	1724	16777	0.103	0.82	0.76 - 0.89
Admission from Emergency Dept.	736	6395	0.115	1.07	0.98-1.17
SOI >10% mortality	2773	24896	0.111	1.54	1.24-1.94
Sepsis/ Infection	581	3949	0.147	1.5	1.36-1.66
Glucose dysfunction	728	5181	0.141	1.46	1.33-1.6
Postsurgery AMI	4	31	0.129	1.2	0.3-3.46
GI Surgery	34	141	0.241	2.6	1.71-3.86
Acute Renal Failure	707	3106	0.228	2.95	2.68-3.25
age >65	614	10139	0.061	1.86	1.72-2.01
LOS > 5days	318	6088	0.052	2.58	2.38-2.8
Readmission					
Variable	# outcome	# patients	proportion	OR	95% CI
Female	723	9277	0.078	1.00	0.9-1.11
Male	1067	16777	0.064	1.00	0.9-1.11
Admission from Emergency Dept.	349	6395	0.055	0.81	0.71-0.91
SOI >10% mortality	1597	24896	0.064	1.21	0.94-1.6
Sepsis/ Infection	285	3949	0.072	1.17	1.03-1.34
Glucose dysfunction	409	5181	0.079	1.33	1.18-1.5
Postsurgery AMI	2	31	0.065	1.01	0.12-4.01
GI Surgery	23	141	0.163	2.89	1.76-4.57
Acute Renal Failure	365	3106	0.118	2.28	2.01-2.58
age >65	811	11139	0.073	1.3	1.18-1.44
LOS > 5days	743	7088	0.105	2.31	2.08-2.56
Mortality					
Variable	# outcome	# patients	proportion	OR	95% CI
Female	723	9277	0.078	1.39	1.26-1.54
Male	962	16777	0.057	0.72	0.65-0.8
Admission from Emergency Dept.	480	6395	0.075	1.24	1.11-1.39
SOI >10% mortality	1655	24896	0.066	2.59	1.82-3.82
Sepsis/ Infection	407	3949	0.103	1.87	1.66-2.11
Glucose dysfunction	447	5181	0.086	1.54	1.37-1.73
Postsurgery AMI	3	31	0.097	1.55	0.30-5.03
GI Surgery	15	141	0.106	1.73	0.94-2.97
Acute Renal Failure	491	3106	0.158	3.59	3.19-4.03
age >65	1083	11139	0.097	2.56	2.31-2.84
LOS > 5days	836	7088	0.118	2.85	2.58-3.16
ICU Readmission	485	1661	0.292	7.97	7.05-9.01

Abbreviations: AMI, Acute Myocardial Infarction; CI, Confidence Interval; GI, Gastrointestinal; Intensive Care unit; LOS, Length of Stay; SOI, Severity of Illness;