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The EFFECT (End-oF-liFE-CommunicaTion) Study: The Acceptability, Feasibility, and Potential Impact of Using Mortality Prediction Scores for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

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The EFFECT (**E**nd-o**F**-li**FE**-**C**ommunica**T**ion) Study:

The Acceptability, Feasibility, and Potential Impact of Using Mortality Prediction Scores for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

Shelly Orr

A dissertation submitted to the faculty of the Medical University of South Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Nursing

September, 2017

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Abstract

Purpose

The purpose of this dissertation was to determine the acceptability, feasibility, and potential impact of using Severity of Illness (SOI) mortality risk prediction scores for initiating end-of-life (EOL) goals-of-care communication in the adult Intensive Care Unit (ICU). First, an integrative review was conducted to evaluate the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU population as the basis for clinical care and provider-patient/family communication. Next, an integrative review of interventions that can guide researchers in reducing surrogate burden was conducted as the basis for conducting research that may impact surrogates of dying patients in the ICU. Finally, a mixed-methods study was conducted to determine the acceptability and feasibility of having providers use SOI mortality prediction scores for their patients as part of routine care and investigate providers' intentions to change practice related to goals-of-care communication as a result of awareness of the scores.

Problem

While healthcare teams recognize that profoundly ill patients in adult ICUs may die, many families are caught by surprise when their loved one dies in a setting with the most advanced technology and intense care available. ICU deaths account for about 20% of patient deaths in US hospitals and this rate is increasing due in part to deficiencies in EOL care communication that can compromise quality of EOL care and increase resource utilization. Previous studies suggest that communication about EOL goals-of-care is infrequent among healthcare providers, patients, and families; often occurs late in the

course of illness; and relies on family members to act as patient surrogates in discussions. Furthermore, despite advances in healthcare quality, family members remain more dissatisfied with communication in the ICU than with other aspects of care. Mechanisms for increasing the timeliness and frequency of discussions about EOL goals-of-care are needed.

Specific Aims

Aim 1. Evaluate four valid SOI instruments to determine which instrument, or combination of instruments, is the best fit for the study site, given providers' perceived feasibility of use.

Aim 2. Evaluate the acceptability and feasibility of having providers use SOI mortality prediction scores for their patients as part of routine workflow and practice.

Aim 3. Evaluate providers' intentions to change their practice related to goals-of-care communication with patients and/or their families as a result of awareness of SOI mortality prediction scores.

Design

First, an integrative review was conducted to evaluate the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU. This review provided the foundational knowledge needed in the selection of SOI systems that were used in aim 1. Next, an integrative review of interventions that can guide researchers in reducing surrogate burden was conducted. This review provided foundational knowledge needed for designing a study that may impact surrogates of dying patients in the ICU. Lastly, an explanatory mixed-methods study was conducted to

determine the acceptability and feasibility of having providers use SOI mortality

prediction scores for their patients as part of routine care and investigate providers'

intentions to change practice related to goals-of-care communication as a result of

awareness of the scores. Self-efficacy theory was used as the theoretical underpinning for

the design of this study, specifically aim 3.

Findings

Based on discrimination alone, the first integrative review found APACHE IV to

be superior, but the VA ICU, SICULA, and SOFA Max were close with 'very good'

discrimination. The second integrative review revealed six levels of intervention, from

the personal 'Direct Care of the Surrogate' to the population-based 'Legal/Regulatory'

and provided a framework to assist researchers when designing and conducting research

that involves surrogates.

The dissertation study found the use of mortality risk prediction scores as part of

routine workflow and practice to be acceptable and feasible – providers agreed to

participate, patient mortality risk were evaluated by the instrument chosen by the

providers (i.e., the Sequential Organ Failure Assessment - SOFA), and overall,

participants found use of daily mortality prediction scores possible in their setting.

However, there was some disagreement related to the use of SOFA scores as an effective

way for determining patient mortality risk. Based on themes that emerged from

interviews, providers with limited ICU experience were eager and accepting of the

mortality risk scores while those with vast experience found the scores to be an adjunct to

their own intuition; though all acknowledged the benefit of looking at daily scores or

'trends'. The most substantial of all themes identified was the need to consider SOFA

scores in relation to patient context; a number alone should not determine mortality risk and whether a goals-of-care conversation needs to occur.

Conclusion

This dissertation study found that overall, participants indicated that using mortality prediction scores as part of their daily workflow was acceptable and feasible. Use of SOFA scores for potentially increasing EOL goals-of-care conversations appears to be most beneficial for providers with limited ICU experience. Large-scale studies are needed to determine the effect of using mortality risk predictions on patient EOL outcomes.

Keywords: End-of-Life, Goals of Care, Poor Prognosis, Mortality Risk, Severity of Illness, Intensive Care, SOFA, Mixed-Methods

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Introduction

Overview

The goal of this dissertation was to determine if use of a severity of illness (SOI) scoring system, an instrument that can predict Intensive Care Unit (ICU) patient mortality risk, affects the timeliness and frequency of end-of-life (EOL) goals-of-care communication. To accomplish this, the dissertation study aimed to: 1) determine the acceptability and feasibility of having providers use SOI mortality prediction scores for their patients as part of routine care, and 2) investigate providers' intentions to change practice related to goals-of-care communication as a result of awareness of the scores.

Two integrative reviews were conducted to provide foundational knowledge needed for designing and conducting the dissertation study. First, an integrative review was conducted to evaluate the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU. This review provided the foundational knowledge needed in the selection of SOI systems that were used in aim 1 of the study. Next, an integrative review of interventions that can guide researchers in reducing surrogate burden was conducted. This review provided foundational knowledge needed for designing a study that may impact surrogates of dying patients in the ICU.

Background and Significance

While healthcare teams recognize that profoundly ill patients in adult ICUs may die, many families are caught by surprise when their loved one dies in a setting with the most advanced technology and intense care available. ICU deaths account for about 20% of patient deaths in US hospitals and this rate is increasing[1] due in part to deficiencies in EOL care communication that can compromise quality of EOL care[2] and increase

resource utilization.[3,4] Previous studies suggest that communication about EOL goals-of-care is infrequent among healthcare providers, patients, and families; often occurs late in the course of illness[5,6]; and relies on family members to act as patient surrogates in discussions.[7] Furthermore, despite advances in healthcare quality, families remain more dissatisfied with communication in the ICU than with other aspects of care.[8,9]

Increased SOI scores are associated with a significant increase in the relative risk of hospital death.[10] Uncertainties in prognosis (e.g., SOI) are a barrier to EOL communication in the ICU[11] and family meetings about EOL care can improve family satisfaction with the EOL experience.[12] However, SOI mortality risk prediction scores are not routinely calculated and there is little research examining their use for improving EOL goals-of-care communication. There are multiple valid and reliable SOI scoring systems that are available for predicting ICU mortality,[13] but there is no consensus about how or when to use them in patient care and provider-patient/family communication.

In 2014, The Institute of Medicine (IOM) called for major reform to ensure high-quality, affordable, and sustainable EOL care for Americans. One of the IOM recommendations includes enhanced provider-patient communication.[14] The high risk for mortality makes goals-of-care communication in the ICU with patients and/or their families especially important. Because patients in the ICU are commonly non-communicative during their intensive illness, their families are often relied upon to act as decision makers regarding goals-of-care, particularly EOL care. Proactive communication with the family in the ICU is of importance, especially regarding prognosis, so they can serve as the patient's surrogate for informed decision-making. Moreover, focusing on proactive family conferences earlier in the ICU course, versus

routine ICU care in which there are no standards for communication timing and frequency, can reduce psychological distress among family members and reduce prolongation of dying in the ICU.[15,16] Goals-of-care communication in the ICU is frequently used to discuss poor patient prognosis. However, previous studies suggest prediction of mortality by a treating physician is incorrect 50% of the time.[17] Confounding this uncertainty, physicians often base their assessments of prognosis on experience rather than on objective measures, and they are often unaware of patients' EOL preferences.[18] These factors, coupled with lack of communication with patients' families, can lead to prolongation of dying and prolonged use of intensive resources.[16]

Proactive communication has led to reduced symptoms of anxiety, depression, and post-traumatic stress disorder for family members who had a loved one die in the ICU.[15] Decreased resource utilization at the EOL has the potential to decrease the emotional and financial strain experienced by patients and their families.[19] Although difficult to hear, most surrogates think the ability of providers to specify numbers (i.e. ability to recover or risk of dying) would be helpful when communicating prognosis.[20] By knowing a patient's mortality risk and communicating it to the family, providers can direct care toward the patient's needs and preferences, which could enable a more positive EOL experience for the patient and their family, such as a focus on palliative care within the ICU or transfer to a more appropriate unit where family can be more present and involved in care if they wished. Furthermore, a positive EOL experience for the patient can limit moral distress experienced by nurses and physicians.[21]

Unfortunately, no evidence-based standard of care exists for EOL goals-of-care communication in adult ICUs. Mechanisms for increasing the timeliness and frequency of discussions about EOL goals-of-care are needed.[22,23]

Specific Aims

Aim 1. Evaluate four valid SOI instruments to determine which instrument, or combination of instruments, is the best fit for `the study site, given providers' perceived feasibility of use.

Aim 2. Evaluate the acceptability and feasibility of having providers use SOI mortality prediction scores for their patients as part of routine workflow and practice.

Aim 3. Evaluate providers' intentions to change their practice related to goals-of-care communication with patients and/or their families as a result of awareness of SOI mortality prediction scores.

Design and Methods

Both integrative reviews provided foundational knowledge needed for designing and conducting the dissertation study. This dissertation study used a mixed-methods explanatory design and took place in a medical-respiratory ICU (MRICU) at a large academic medical center in Richmond, Virginia. Patients are admitted to this unit for acute illnesses but commonly exhibit chronic medical conditions as well. Two medical teams provide patient care, each comprised of an attending physician, a fellow physician, and a mix of interns, residents, acute care nurse practitioners (ACNPs), and physician assistants (PAs). These teams provide care for patients throughout their ICU stay, or until the end of the provider's assigned time in the MRICU. This study was approved by the

Institutional Review Board at Virginia Commonwealth University and the Medical University of South Carolina.

To address Aim 1, attending physicians, fellow physicians, ACNPs, and PAs working in the MRICU were recruited (target N=6) for a focus group via email as they are expert providers responsible for medical care of patients admitted to the unit. Based upon the integrative review completed by the principal investigator[13] (PI) and implementation feasibility within the study setting, four SOI scoring systems (MPM III, APACHE IV, SOFA, SAPS III) were presented to the focus group participants. The PI assumed the moderator role to keep the flow of the conversation on target.[24] Participants were asked to discuss perceived feasibility of use for each SOI system. Based on discussion among the participants, the PI then requested consensus on the SOI system of choice. Participants were also asked to complete a demographic form in Research Electronic Data Capture (REDCap); descriptive statistics were used to analyze the data.

To address Aim 2, an explanatory mixed-methods approach consisting of a quantitative questionnaire (target N=12) and a qualitative follow-up interview (target N=6) were used to determine if providers could feasibly use SOI mortality prediction scores as part of their routine in the ICU and evaluate their perceptions of acceptability, feasibility, and potential impact of using the SOI scores. All MRICU fellows, residents, and intern physicians, as well as all ACNPs and PAs, were recruited on an ongoing basis via email and face-to-face for this portion of the study; attending physicians were excluded due to their short length of rotations in the ICU. The PI or research assistant (RA) calculated mortality risk percentages for MRICU patients admitted under the care of study participants for ten consecutive days, using the free web-based calculator. To

ensure consistency with the chosen system's published protocol, the PI developed a user's manual for the PI and RA to use. The PI and RA reviewed a random selection of 25% of each other's calculations to examine inter-rater reliability. Calculated scores were limited to three days per patient for feasibility purposes. Mortality risk percentages were shared with participants on a card each morning prior to team rounding. Based upon the integrative review conducted by the PI, scores lacked specific identifiers and interpretation; this was done to reduce surrogate burden related to insufficient knowledge in the instance the cards were misplaced and discovered by the surrogate. Reference cards were provided during study enrollment for providers for interpretation of the scores. Following the ten-day period, participants received a link to a REDCap questionnaire asking about acceptability and feasibility of using the SOI mortality risk prediction scores as part of their workflow and practice.[25] Results of the questionnaire were retrieved from REDCap as descriptive statistics. Additionally, participants who did not also participate in the focus group were asked to complete the same demographic form in REDCap.

To further explain the acceptability and feasibility questionnaire results and to address Aim 3, all participants who completed a questionnaire were contacted approximately one week later asking for their participation in a follow-up interview. Those agreeing to participate were scheduled for face-to-face interviews with the PI using open-ended questions. Although specific topics were covered during the interview, the PI allowed the participant's cues to determine the flow.[26] Each interview was voice recorded digitally and transcribed verbatim. A qualitative descriptive approach was used to analyze the interview data.[27,28] To accomplish this, a fluent process occurred wherein transcripts were reviewed following every 2-3 interviews; they were read repeatedly to

achieve immersion, exact words that captured key thoughts were highlighted, notes of impressions were made, and key themes were identified that emerged from the notes. As themes emerged, the PI asked for confirmation from subsequent participants. The resulting themes from all transcripts were defined and exemplars were identified. To ensure the resulting themes were credible, the PI discussed the findings with experts who were familiar with the subject under study. Lastly, final themes and exemplars were examined to help explain the results of the acceptability and feasibility questionnaire.

Theoretical Framework

Self-efficacy theory[29] was used as the theoretical underpinning for the design of this study, specifically aim 3. The PI used self-efficacy as a guiding theory when collecting data on whether awareness of mortality risk prediction scores contributed to a provider's intention to change their practice regarding the timeliness and frequency of EOL goals-of-care communication. Specifically, providers were asked about what they did with the scores they were provided and what impact, if any, they felt they could have on a patient's EOL experience in the ICU.

Self-efficacy theory provides an understanding of how individual's beliefs concerning his or her abilities can affect their own behavior.[30] Therefore, a person's motivation and performance in relation to completing a task is dependent upon how effective they believe they can be. Related to this study, a provider with high self-efficacy would believe that they are capable of positively impacting the quality of their patient's EOL and are motivated to do so. However, a provider with low self-efficacy does not believe they are capable of positively impacting the quality of their patient's EOL, and therefore, would not be motivated to put forth such effort.

Manuscripts

     Manuscript 1. An array of SOI scoring systems are available to predict mortality with no clear consensus on which system should be used for general adult ICU patients, and how the system should be integrated into daily patient care and provider-patient/family communication. This integrative review synthesized the literature that evaluated the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU population as the basis for clinical care and provider-patient/family communication. This review provided the foundational knowledge needed in the selection of SOI systems that were used for the aim 1 focus group.

     Manuscript 2. Although research is needed in the area of EOL, many people are incapable of giving consent for research during their EOL due to incapacity. Although there has been a shift in support for surrogate decision making in research, there is a need to minimize surrogate burden throughout the research trial. The purpose of this manuscript was to discuss the current state of research consent and continued enrollment for incapacitated persons through an integrative review of the literature. This review provided foundational knowledge needed for designing a study that may impact surrogates of dying patients in the ICU.

     Manuscript 3. This manuscript is a report of the findings of the dissertation research. This study evaluated the acceptability and feasibility of having providers use mortality prediction scores for their patients as part of their routine practice as well as investigated intentions to change practice, related to goals-of-care communication, as a result of awareness of the scores.

References

1. Zomorodi, M., & Bowen G. Value-behavior congruency when providing end-of-life care in the intensive care unit. J Hosp Palliat Nurs. 2010;12(5):295–302.

2. Glavan BJ, Engelberg RA, Downey L, Curtis JR. Using the medical record to evaluate the quality of end-of-life care in the intensive care unit. Crit Care Med [Internet]. 2008 Apr [cited 2014 Nov 28];36(4):1138–46. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2735216&tool=pmcentrez&rendertype=abstract

3. Quenot JP, Rigaud JP, Prin S, Barbar S, Pavon A, Hamet M, et al. Impact of an intensive communication strategy on end-of-life practices in the intensive care unit. Intensive Care Med [Internet]. 2012 Jan [cited 2014 Nov 30];38(1):145–52. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3385851&tool=pmcentrez&rendertype=abstract

4. Curtis JR, Rubenfeld GD. Improving palliative care for patients in the intensive care unit. J Palliat Med. 2005;8:840–54.

5. Curtis JR, Engelberg RA, Bensink ME, Ramsey SD. End-of-life care in the intensive care unit: Can we simultaneously increase quality and reduce costs? American Journal of Respiratory and Critical Care Medicine. 2012. p. 587–92.

6. McNeely PD, Hébert PC, Dales RE, O'Connor AM, Wells G, McKim D, et al. Deciding about mechanical ventilation in end-stage chronic obstructive pulmonary disease: How respirologists perceive their role. CMAJ. 1997;156:177–83.

7. Curtis JR, White DB. Practical guidance for evidence-based ICU family conferences. Chest [Internet]. 2008 Oct [cited 2014 Nov 30];134(4):835–43. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2628462&tool=pmcentrez&rendertype=abstract

8. Stricker KH, Kimberger O, Schmidlin K, Zwahlen M, Mohr U, Rothen HU. Family satisfaction in the intensive care unit: What makes the difference? Intensive Care Med. 2009;35(12):2051–9.

9. Heyland DK, Rocker GM, Dodek PM, Kutsogiannis DJ, Konopad E, Cook DJ, et al. Family satisfaction with care in the intensive care unit: results of a multiple center study. Crit Care Med. 2002;30(7):1413–8.

10. Knaus WA, Wagner DP, Draper EA, Zimmerman JE, Bergner M, Bastos PG, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. Chest [Internet]. 1991 Dec [cited 2014 Nov 17];100(6):1619–36. Available from: http://www.ncbi.nlm.nih.gov/pubmed/1959406

11. Kamel G, Paniagua M, Uppalapati A. Palliative Care in the Intensive Care Unit: Are Residents Well Trained to Provide Optimal Care to Critically ill Patients? Am J Hosp Palliat Care [Internet]. 2014; Available from: http://www.ncbi.nlm.nih.gov/pubmed/24879883

12. Billings JA. The End-of-Life Family Meeting in Intensive Care Part I: Indications, Outcomes, and Family Needs. J Palliat Med. 2011;14:1042–50.

13. Orr S. An Integrative Review of Severity of Illness Scoring Systems Used to Predict Mortality in the Adult Intensive Care Unit (Unpublished Journal Article). Charleston; 2015.

14. Death C on A. Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life [Internet]. Institute of Medicine; 2014 [cited 2015 Feb 8]. Available from: http://books.nap.edu/openbook.php?record_id=18748

15. Lautrette A, Darmon M, Megarbane B, Joly LM, Chevret S, Adrie C, et al. A communication strategy and brochure for relatives of patients dying in the ICU. N Engl J Med. 2007;356:469–78.

16. Lilly CM, De Meo DL, Sonna LA, Haley KJ, Massaro AF, Wallace RF, et al. An intensive communication intervention for the critically Ill. Am J Med. 2000;109:469–75.

17. Meadow W, Pohlman A, Frain L, Ren Y, Kress JP, Teuteberg W, et al. Power and limitations of daily prognostications of death in the medical intensive care unit. Crit Care Med [Internet]. 2011 Mar [cited 2014 Nov 30];39(3):474–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21150582

18. The SUPPORT Principle Investigators. A Controlled Trial to Improve Care for Seriously Ill Hospitalized Patients [Internet]. Journal of the American Medical Association. 1995. p. 1591–8. Available from: http://jama.ama-assn.org/content/274/20/1591.short

19. Khandelwal N, Curtis Randall J. Economic implications of end-of-life care in the ICU. Curr Opin Crit Care [Internet]. aDepartment of Anesthesiology and Pain Medicine bDivision of Pulmonary and Critical Care Medicine, Harborview Medical Center, University of Washington, Seattle, Washington, USA; 2014 Dec;20(6):656–61. Available from: http://proxy.library.vcu.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&AuthType=ip,url,cookie,uid&db=ccm&AN=2012785943&site=ehost-live&scope=site

20. Anderson WG, Cimino JW, Ernecoff NC, Ungar A, Shotsberger KJ, Pollice LA, et al. A multicenter study of key stakeholders' perspectives on communicating with surrogates about prognosis in intensive care units. Ann Am Thorac Soc. 2015;12(2):142–52.

21. McAndrew NS, Leske JS. A Balancing Act Experiences of Nurses and Physicians When Making End-of-Life Decisions in Intensive Care Units. Clin Nurs Res [Internet]. 2014;1054773814533791. Available from: http://cnr.sagepub.com/content/early/2014/05/22/1054773814533791%5Cnhttp://cnr.sagepub.com/content/early/2014/05/22/1054773814533791.full.pdf%5Cnhttp://www.ncbi.nlm.nih.gov/pubmed/24864319

22. Curtis JR, Engelberg RA, Bensink ME, Ramsey SD. End-of-Life Care in the Intensive Care Unit. American Thoracic Society; 2012 Dec 14 [cited 2014 Nov 14]; Available from: http://www.atsjournals.org.proxy.library.vcu.edu/doi/full/10.1164/rccm.201206-1020CP#.VGYnR8lxHhc

23. Curtis JR. Palliative and end-of-life care for patients with severe COPD. The European respiratory journal : official journal of the European Society for Clinical

           Respiratory Physiology. 2008. p. 796–803.

24. Hesse-Biber SN, Leavy P. The practice of qualitative research [Internet]. 2nd ed. Qualitative Research. Thousand Oaks, CA: Sage Publications, Inc.; 2011. 640 p. Available from: http://srmo.sagepub.com/view/qualitative-research-practice/SAGE.xml

25. Tickle-Degnen L. Nuts and bolts of conducting feasibility studies. Am J Occup Ther. 2013;67:171–6.

26. Waltz CF, Strickland OL, Lenz ER. Measurement in Nursing and Health Research [Internet]. Human Movement Science. 2010. 506 p. Available from: http://books.google.com/books?id=1xAdjkR14ocC

27. Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res. 2005;15(9):1277–88.

28. Sandelowski M. What's in a name? Qualitative description revisited. Res Nurs Heal. 2010;33(1):77–84.

29. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev. 1977;84(2):191–215.

30. Spector PE. Industrial and organizational psychology: Research and practice [Internet]. Wiley; 2012 [cited 2017 Aug 18]. 455 p. Available from: https://www.scribd.com/doc/297174972/Industrial-and-Organizational-Psychology-Research-and-Practice-6th-Edition-Paul-E-Spector

An Integrative Review of Severity of Illness Scoring Systems Used to Predict Hospital
Mortality for Patients Admitted to the Adult Intensive Care Unit

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Abstract

Introduction: Deficiencies in end-of-life communication in the adult ICU persist despite an estimated one in five patient deaths in the hospital occurring in the ICU. Discussions regarding prognosis typically are prioritized according to a patient's greater risk for mortality. An array of severity of illness (SOI) scoring systems are available to predict mortality with no clear consensus on which system should be used for general adult ICU patients, and how the system should be integrated into daily patient care and provider-patient/family communication.

Objective: This integrative review synthesizes the literature that evaluates the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU population as the basis for clinical care and provider-patient/family communication.

Methods: Using strategies specific to the integrative review method proposed by Whittemore and Knafl, a systematic search strategy was used to review and analyze the literature.

Results: A total of 969 articles were identified with seven meeting all inclusion criteria. Based on discrimination alone, this review found APACHE IV to be superior, but the VA ICU, SICULA, and SOFA Max were close with "very good" discrimination.

Conclusions: Given the differences among ICUs, until a SOI system is used with success in a respective setting, with that ICU's particular case-mix, the system's validity for that setting will remain uncertain. Future research is needed to examine the role of SOI scoring systems in the ICU for the purpose of increasing the timeliness of prognosis communication with the patient and/or family.

Introduction

An estimated 20% of patient deaths within hospitals occur in Intensive Care Units (ICU), and this trend continues to increase.[1] Due to the critical and unstable nature of most patients' illness in the ICU, frequent communication with the patient and/or family is needed regarding the patient's prognosis. However, due to the complex and fast-paced nature of the ICU, discussions regarding prognosis typically are prioritized according to a patient's greater risk for mortality.

Mortality risk is defined as the estimate of the likelihood of a patient dying while in the hospital.[2] There is evidence to suggest that providers are able to use their subjective experiences to gauge a patient's mortality risk.[3] However, because this is based on subjective experiences and not quantitative data, additionally assessing mortality risk with utilization of a score or rating that reflects a prognostic model may be beneficial. By accurately knowing a patient's mortality risk, providers may be able to direct care toward the patient's needs and preferences.

In 2014, the Institute of Medicine (IOM) called for a major reform to ensure high-quality, affordable, and sustainable end-of-life care for Americans.[4] One of their key recommendations included enhanced provider-patient communication. Although prognostic models were developed to assess ICU performance by comparing observed and risk-adjusted hospital mortality, these models can be used to guide providers, patients and families in joint decision-making.[5] Prognostic models have the ability to combine multiple characteristics related to a patient and their disease to predict a prognostic outcome.[6] An array of prognostic models are available for calculating severity of illness scores, which can be converted to a mortality risk percentage; however, there is no clear

consensus on which prognostic model should be used for general, meaning not disease specific, ICU patients, and how the model should be integrated into daily patient care and provider-patient communication. Because the term "models" as it relates to prognostication can be confusing and different terms are used to describe the models within the literature, the models reviewed will hereafter be referred to as 'severity of illness (SOI) scoring systems'. This integrative review synthesizes the literature that evaluates the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU population as the basis for clinical care and provider-patient communication.

Methods

Based on the methods proposed by Whittemore and Knafl,[7] an integrative review was completed. A systematic search of PubMed, CINAHL (EBSCOHost), Web of Science, and ProQuest Dissertations and Theses occurred in consultation with a university reference librarian. In addition, a search occurred of reference lists for the retrieved publications to identify published articles addressing SOI scoring systems, along with discussions with colleagues familiar with this literature to hand pull additional articles. The following inclusion criteria guided the search: articles written in English and addressing an adult population. Thus, mortality risks for children were not part of this review. The search was separated into two concept groups. One group encompassed the terminology used to describe "severity of illness" and another covered the terms relevant to "hospital mortality." Medical Subject Headings (MeSH) and equivalent controlled vocabulary and keywords were utilized in each database as appropriate. The initial search yielded 865 articles (Figure 1); their titles, key words, and/or abstracts were reviewed to

assess their relatedness to the inclusion criteria of general adult ICU patients within the last ten years. The decision to exclude those greater than ten years old was due to the changing landscape (i.e. increased technology and patient acuity, updates in provider practice) of the adult ICU in the previous decade. Articles also were excluded if they were a duplicate or were not related to adults (those not caught by the initial search), or if there was a more recent publication of the same work. Articles that discussed single variables as a predictor of mortality were excluded due to the variability of patients' disease etiology, presentation, and other health status; a single predictor or variable is not likely to give an adequate estimate of prognosis.[5] In addition, articles that narrowed a study to the elderly population only were excluded because of the range in age of today's ICU patients and the desire to review SOI systems applicable to the general adult population. This review of titles, abstracts, and key words resulted in 79 full texts articles. The investigator decided to exclude articles that discussed work outside of the United States (US) due to noted vast international differences in patient populations and cultural needs, along with clinical sites and administration. In addition, articles that did not discuss the specific use of a SOI scoring system and its psychometric properties were excluded, leaving seven articles for the final review.

Figure 1. Literature Review Search

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┌──────────────────────────┐      ┌──────────────────────────┐
│  Records identified      │      │  Additional records      │
│  through database        │      │  identified through      │
│  searching               │      │  other sources           │
│  (n= 962)                │      │  (n= 7)                  │
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       ┌────────────────────────────────────────┐      ┌──────────────────────┐
       │  Minus duplicates;                     │      │  Records excluded     │
       │  Titles/abstracts screened             │─────▶│  (n= 786)             │
       │  (n= 865)                              │      │                       │
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       │  Full-text articles assessed for       │      │  Records excluded     │
       │  eligibility                           │─────▶│  (n= 72)              │
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       │  Studies included in                   │
       │  Integrative Review                    │
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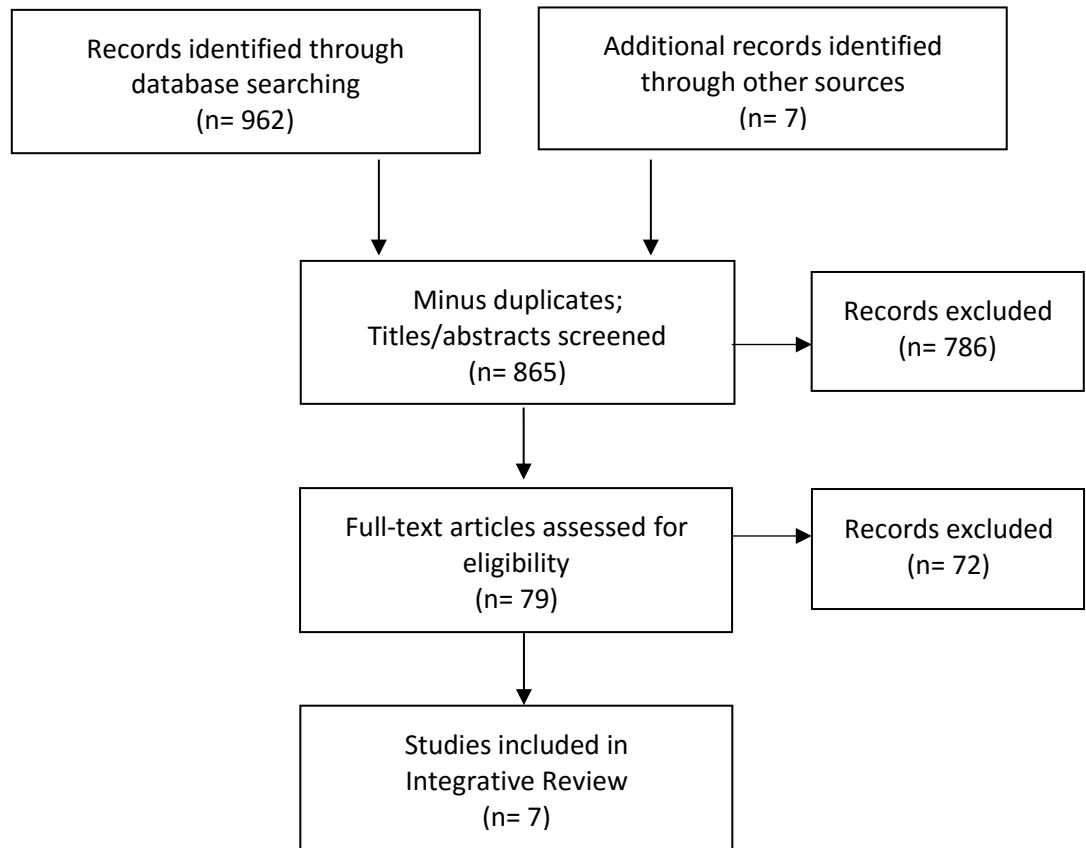
A matrix (Table 1) was used to extract data from the resulting articles.

Descriptions of the SOI scoring systems with their reported reliability, validity, and

feasibility were included, along with the determined level of evidence. This review

provides a descriptive synthesis of the literature on the psychometric properties of SOI

scoring systems that predict adult ICU patient mortality risk.

Results

Each of the seven articles included in this integrative review represented at least

one SOI scoring system used to predict mortality in adult ICU patients. Altogether, nine

SOI systems were evaluated in the review (Table 1) and those studies reported results with medium to high level evidence.[8]

Severity of Illness (SOI) Scoring Systems

The Acute Physiology and Chronic Health Evaluation (APACHE), Mortality Probability Model (MPM), and the Simplified Acute Physiology Score (SAPS) were the main SOI scoring systems discussed in the literature. Primarily due to the limited predictive ability of their older versions, updates to these systems, along with other newly developed systems, were most commonly reported and used for evaluation in the literature.

APACHE (Acute Physiology and Chronic Health Evaluation). The APACHE system was first developed in 1981 by researchers at The George Washington University Medical Center to measure severity of illness in groups of critically ill patients to compare patient outcomes, evaluate new therapies, and study ICU utilization.[9] The most current version, APACHE IV, uses physiologic data from the first 24 hours after ICU admission.[10] It incorporates 142 predictor variables, 116 admission diagnoses, and 17 physiological variables over the patient's first 24 hours in the ICU.[11] Predictor variables include age, gender, acute physiology score variables (laboratory results, vital signs, Glasgow Coma Scale (GCS)), chronic health variables, ICU admission diagnosis and source, length of stay prior to ICU admission, GCS score rescaled (or inability to assess), PaO2/FiO2 ratio, whether the patient had emergency surgery, mechanical ventilation status, and whether the patient is post-coronary artery bypass grafting (CABG), including the number of any grafts, whether an internal mammary graft was used, and whether the patient had diabetes prior to the CABG or a myocardial infarction during that

hospitalization. The APACHE II, which relies on 12 routine physiological variables, age, and previous health status,[12] remains widely used in clinical practice, primarily related to provider familiarity with the earlier version and some studies that questioned the calibration of the updated version, APACHE IV.[13]

MPM (Mortality Probability Model). The MPM system was first developed in 1985 by researchers at Baystate Medical Center to predict hospital mortality to assist with triage decisions, compare various ICUs and their utilization, and determine aggressiveness of care through communication with families.[14] The most current version, MPM III, has 16 predictor variables plus seven interaction terms that include physiological variables, chronic diagnoses, acute diagnoses, age, code status (and whether the patient has received CPR), mechanical ventilation status, and whether a medical or unscheduled surgical admit occurred.[15] The MPM III uses physiologic data from one hour before and one hour after ICU admission[10] but no initial diagnosis is needed.[16] A modified and recalibrated version of the MPM III was developed by the National Quality Forum.[17] The NQF model has 28 additional interaction terms, as well as different patient exclusions when compared to the MPM III.

SAPS (Simplified Acute Physiology Score). The SAPS system was first developed in 1984 by researchers in France to classify patients into groups of comparable probability of death to facilitate inter-ICU comparisons of treatment and management.[18] The most current version, SAPS 3, uses physiologic data collected within one hour (before or after) of ICU admission.[19] Predictor variables include age, comorbidities, pre-ICU location, pre-ICU length of stay, pre-ICU major therapeutics, reason for ICU admission, planned/unplanned admission, infection at ICU admission, surgical status, site

of surgery if applicable, GCS, laboratory results, vital signs, and ventilation/oxygenation.[19,20] A previous version, although still prominent in the literature, is SAPS II which includes only 17 variables: 12 physiology variables, age, type of admission, and three underlying disease variables.[21] The SAPS II relies on the most severe data in the first 24 hours following ICU admission. More recently, an electronic version of the SAPS 3 was developed. The eSAPS3 provides a risk adjustment score using only data available from the electronic health record.[22] For this system, some SAPS 3 variables are pulled directly from the electronic record, and other variables are adapted if the SAPS 3 item requires data that are not an exact fit with the medical record or data that must be manually reviewed. For example, the SAPS 3 variable of infection at ICU admission is adapted to diagnosis coding and antibiotic utilization and timing within the eSAPS3.

SOFA (Sequential Organ Failure Assessment). The SOFA scoring system was originally designed in 1994 by the European Society of Intensive Care Medicine as a way to quantitatively describe the degree of organ dysfunction/failure and assess the effects of new therapies for septic patients.[23] However, it was discovered that it could be applied just as well in non-septic ICU patients.[24,25] The SOFA assigns 1-4 points to the following organ systems depending on the level of organ dysfunction: circulatory, respiratory, renal, hematology, hepatic, and central nervous system.[26] Differentiations are made based on the scores used.[27] The max SOFA is the highest total SOFA measured in a pre-specified time interval, the mean SOFA is the average of all total SOFA scores in a pre-specified time interval, and the delta SOFA is the total max minus admission SOFA. Data

are typically collected upon ICU admission and throughout the ICU stay, with the most abnormal values for each day being used for scoring.[25]

VA ICU (Veterans Affairs ICU). The VA ICU system was first developed in 2005 by researchers using VA ICU patients within 17 geographically diverse regions in the US to identify differences in indicators of performance among the ICUs.[28] This risk-adjustment system uses physiologic data collected during the 24 hours surrounding ICU admission.[29] Predictor variables include age, diagnosis/procedure, operative/non-operative, comorbidities, laboratory data, and admission source. Compared to a previous version, some diagnoses designated as "other" were given specificity.[29] In addition, the ability to designate the source of admission to the ICU was added.

SICULA (Super ICU Learner Algorithm). The SICULA was developed in 2015 by researchers using patients admitted to an ICU at Beth Israel Deaconess Medical Centre, and validated with patients admitted to an ICU in France, as a method for predicating hospital mortality for patients in ICUs.[30] This is an ensemble machine learning technique that uses multiple learning algorithms using physiologic data collected within the first 24 hours after ICU admission.[30] Predictor variables include clinical data retrieved from the electronic health record (vital signs, progress notes, intravenous drip medications, fluid balances, demographics, imaging results, physician orders, laboratory results, discharge summaries, and International Classification of Disease-9 codes) and high-resolution physiological data from bedside monitors (waveforms and derived physiological measurements).

Assessing Model Performance

Health statisticians typically assess the performance of ICU SOI scoring systems to predict mortality by examining the area under the receiver operating characteristic curve (AUC) for discrimination and the Hosmer-Lemeshow (H-L) statistic for calibration.[31] The AUC is a measure of how well a SOI system differentiates between groups, for example, between survivors and non-survivors.[31] An AUC of 1 is considered perfect, 0.90-0.99 excellent, 0.80-0.89 very good, 0.70-0.79 good, 0.60-0.69 moderate, and less than 0.60 poor, with 0.5 equivalent to chance. Calibration is the correlation between the actual and predicted outcome for the entire range of risk and is considered to be good if the H-L statistic p-value is greater than 05.[32] Because the H-L statistic can be influenced by sample size, accuracy is sometimes assessed by measuring the average distance, or residual, between the observed outcome and its predicted probability for each patient.[27] The Brier score is one method for measuring accuracy by squaring the mean of the residual values, where a lower score indicates better performance. However, since the Brier score can be affected by the incidence of mortality, more recent studies have included a modified Brier's score that adjusts for this contingency; that modified score represents the percent reduction in deviation when using a specific predictive model versus assigning probability equal to the incidence rate, and a higher percentage reduction indicates better accuracy[17]. Additionally, an intercept and calibration slope (known as Cox calibration test) has been used to overcome the shortcomings of the H-L statistic.[30] In addition, a standardized mortality ratio (SMR) often is reported to indicate the observed deaths as compared to predicted mortalities; the SMR is calculated by dividing the observed mortality rate by the mean predicted mortality rate.[33]

Validity

All SOI scoring systems included within the seven articles included in the final

analysis had a minimum of "good" discrimination as determined by the AUC (> 0.70),

with the exception of SOFA when it was delineated out by systems (AUCs "moderate" at

0.655 for hepatic and 0.684 for coagulation).[27] Based on reported AUCs, the APACHE

IV had the best discrimination among all SOI systems (AUC range 0.88-0.892)[10,11,17] but

the VA ICU, SICULA, and SOFA Max were not far behind with "very good"

discrimination (AUC > 0.80).[27,29,30]

Across the nine SOI systems included, calibration was not as consistent as

discrimination. Examining the reported H-L statistics and associated alternative statistics,

four of the seven SOI scoring systems (SICULA, SOFA Max, eSAPS 3, VA ICU)

revealed adequate calibration within their single studies.[22,27,29,30] However, less than

desired calibration was discovered in others. Calibration of the APACHE IV (H-L chi-

square 219, adjusted Brier 31%) was superior to the MPM III (H-L chi-square 554,

adjusted Brier 16.1%) and NQF (H-L chi-square 760, adjusted Brier 17.8%) in one

study[17] but the APACHE IV (H-L 22.4, p= 0.01) was inferior to the MPM III (H-L 9.8,

p= 0.5) and SAPS II (H-L 18.1, p= 0.05 which also indicates poor performance) in

another.[10] An acceptable SMR was reported for the APACHE IV (1.03), MPM III (1.04),

and SAPS II (1.04) in one study but values reported indicate a higher rate of observed

deaths than actually expected.[10]

Reliability

Only two of the seven articles reported some measure of scoring index reliability.

In the study that compared the MPM III, SAPS II, and APACHE IV, auditors were used

to re-abstract data from a random sample of patients in the study to assess for interrater reliability.[10] High percentage agreement and K statistics indicated strong interrater reliability, with the exception of GCS and APACHE IV reasons for ICU admission. In the study examining the eSAPS3, percentage agreement was examined to assess for differences between the electronic and manual components of the scoring system, which revealed a discordance of 7.9% on average across all individual components.[22]

Although no reliability indicators were reported for the studies included in the systematic review of SOFA scoring systems, a third reviewer was used to resolve any differences between the two reviewers conducting the literature search.[26] Inter-observer agreement Kappa was 0.94.

Feasibility

Six of the seven articles included information on the feasibility of using various SOI scoring systems. Although manual entry of predictor variables can be time consuming (i.e. 37.3 minutes for APACHE IV)[10] and requires training for those entering the data,[10,11] many of the articles discussed the ability of computerized systems to decrease this workload[10,11,17,22,29,30] and, thus, time requirements (i.e. 1.5 minutes for APACHE IV).[17] However, the electronic system must be able to pull information automatically from the electronic health record (EHR), requires sufficient programming to guide the system in case of missing or non-valid data,[10,22,29,30] and may require the purchase of a licensed system (i.e. APACHE IV).[11] Systems such as the SAPS 3 and SICULA are available free of charge but still require a computer system capable of handling their complexities.[22,30]

Discussion

This integrative review identified nine SOI scoring systems that can be used to predict mortality for patients admitted to the adult ICU. Previous reviews have presented the development of a SOI system or compared similar systems. However, this review includes all available articles within the last ten years, including evaluations of updated and new SOI systems better suited to address the constantly changing ICU.

Validity

To compare SOI scoring systems, we often rely on reported discrimination and calibration of the systems. Good to strong discrimination was reported for all SOI systems in this review, except for SOFA when broken down into specific organ systems (some AUCs moderate).[27] However, specific organ system scores should not be used in isolation when calculating mortality risk predictions. Adequate calibration was inconsistent across studies. It is likely impossible for any system to have perfect calibration or discrimination because ICU patients can be unpredictable despite our best prognostications. Because the goal is to predict outcomes for individual patients, not to compare quality of care between ICUs, good discrimination (as reported for the SOI systems reviewed), is most important. However, we cannot negate that recalibration of all systems used to predict mortality should regularly occur to reflect current ICU practice and patient demographics.

Although the literature search was restricted to the US, a question regarding the generalizability of the findings remains. The APACHE IV, MPM III, eSAPS 3, SICULA, and VA ICU were developed with US patients,[11,15,22,29,30] but sample diversity varied greatly. APACHE IV was developed using a sample from 104 US hospitals[11] while the

SICULA sample was from only one US hospital in Boston.[30] However, the SICULA was externally validated with a sample from a hospital in France, perhaps making their findings more generalizable. SAPS 3, which provides the basis for the eSAPS 3, was developed with a sample from 5 continents, including North America.[34] This may make the eSAPS 3 more generalizable, but it is difficult to determine because their sample was restricted to 21 California hospitals.[22] Additionally, both studies using SOFA in the systematic review included in this review had samples incorporating patients from both the US and various other countries,[27] again perhaps making SOFA more generalizable. Lastly, there is no way to ascertain whether the studies in the US are generalizable to the US population due to potential selection bias. For example, the APACHE IV was developed only using hospitals with APACHE capabilities, which requires expensive software.[11] The VA ICU was developed using a sample from 42 regionally diverse ICUs but its generalizability is likely restricted due to the nature of VA patients (predominantly male and greater than 64 years old).[29]

When considering generalizability, SOI scoring system exclusions must also be considered. Many of the SOI systems (eSAPS 3, APACHE IV, NQF, MPM III) exclude repeat ICU admissions within the same hospitalization and transfers from another facility.[11,17,22] Other nuances also exist, such as the MPM III excludes acute myocardial infarction and cardiac surgery patients.[35]

Reliability

Reliability was only reported in three of the articles. However, given the complexity of SOI systems, it is understandable that consistency is not commonly examined or reported. Often times, reliability is dependent upon data abstraction for the

scoring system, such as consistency and clarity of ICU charting.[36] For example, in previous studies that examined reliability, interrater reliability was high for objective elements such as patient demographics[37] but lower for other elements that were dependent on the clinical skills of the examiner and may be influenced by the patient's medical conditions, such as GCS.[38]

Feasibility

Although all SOI scoring systems included in this review had reasonable validity and reliability (when reported), the logistics of using such systems cannot be underestimated. The feasibility of any facility staff manually entering accurate data required for SOI scores is unlikely. Manual entry of accurate and real-time data could be a barrier to feasibility. Therefore, whether hospitals can afford the software, electronic health record, and programming needed must be considered. Although automatic calculations can be done, some systems have variables that cannot be automatically populated and must be manually entered;[22] training for anyone involved with data collection can be expensive.[39] Additionally, electronically populating data may save time but can lead to errors. For example, if a patient's pulse oximeter has a poor signal, an inaccurate low number could be automatically recorded in the EHR; although the same could occur with manual entry due to human error. Although a single number may not lead to an invalid calculation, SOI scoring systems with a large number of variables could have multiple inaccuracies, likely leading to a significant under or over-prediction (more likely) in mortality risk.

Other Considerations

Among the SOI scoring systems presented in this review, data collection time points vary greatly. Some systems rely on patient data one hour before and/or one hour after ICU admission[10,34] while others collect data within or surrounding the first 24 hours after ICU admission.[11,29,30] SOFA is the only SOI system reviewed that was validated using ICU admission data and sequentially for subsequent ICU days using the most abnormal data from the previous 24 hours.[25] There is evidence to suggest that the combination of admission and daily scores may have superior prognostic performance than each instrument alone.[27] Additionally, evidence suggests that SOI systems with a large number of predictor variables being used for 24 hour data (versus within one hour) collection likely leads to better case-mix adjustment and better predictive ability.[17] However, data from within one hour of ICU admission is less likely to be affected by medical care after admission to the ICU.[10]

Limitations

Although multiple researchers reviewed this manuscript, a single reviewer was used to compile the literature which could have influenced the outcome of the review. To overcome this potential bias, specific inclusion and exclusion criteria were used and data analysis occurred using the methods specified by Whittemore and Knafl.[7] Lastly, one problematic issue in the literature is the variety of terminology used to identify SOI systems. A research librarian was used to conduct a search which included terminology used to describe "severity of illness" to reduce the risk of missing an articles due to differences in terminology.

Conclusion

This is the first known attempt at integrating a review of current SOI scoring

systems used to predict mortality for patients admitted to the adult ICU. Based on

discrimination alone, this review found the APACHE IV to be superior, but the VA ICU,

SICULA, and SOFA Max were all close behind with "very good" discrimination.

Calibration, however, was not as consistent with any of the systems reviewed. The

APACHE IV has many variables that likely overcome the potential case-mix

shortcomings, but the expense of the system, compared to other non-proprietary systems,

may be a limiting factor for some institutions. Regarding feasibility, the complexity of

the computer systems and/or programming needed for the APACHE IV, SICULA, and

VA ICU must be considered. The SOFA has far less variables and has gained recent

popularity due to its role in the updated sepsis guidelines,[40] so it is well-known to ICU

providers. Additionally, providers often prefer the ability to look at trends in data and

SOFA is the only system reviewed here that provides daily scores. Regardless, given the

differences among ICUs, until a SOI scoring system is used and calibrated in a respective

setting, the scoring system's validity for that setting will remain uncertain.

All of the SOI scoring systems included in this review proved to be valid in their

respective studies. Although we acknowledge the importance of considering the

feasibility of using a specific SOI system and the patient context in which they are used,

identifying patients at increased risk for mortality may help initiate earlier goals-of-care

discussions with patients and/or their families. Proactive communication has been shown

to reduce psychological distress among family members and reduce prolongation of

dying for patients in the ICU.[41,42] Future research is needed to examine the role of SOI

scoring systems in the ICU for this purpose.

References

1. Zomorodi, M., & Bowen G. Value-behavior congruency when providing end-of-life care in the intensive care unit. *J Hosp Palliat Nurs*. 2010;12(5):295-302.
2. Iezzoni LI, Shwartz M, Ash AS, Hughes JS, Daley J, Mackiernan YD. Severity measurement methods and judging hospital death rates for pneumonia. *Med Care*. 1996;34(1):11-28. http://www.ncbi.nlm.nih.gov/pubmed/8551809. Accessed February 8, 2015.
3. Sinuff T, Adhikari NKJ, Cook DJ, et al. Mortality predictions in the intensive care unit: comparing physicians with scoring systems. *Crit Care Med*. 2006;34:878-885. doi:10.1097/01.CCM.0000201881.58644.41.
4. Death C on A. *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life*. Institute of Medicine; 2014. http://books.nap.edu/openbook.php?record_id=18748. Accessed February 8, 2015.
5. Moons KGM, Royston P, Vergouwe Y, Grobbee DE, Altman DG. Prognosis and prognostic research: what, why, and how? *BMJ*. 2009;338(feb23_1):b375. doi:10.1136/bmj.b375.
6. Steyerberg E. *Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating*. New York, NY: Springer; 2009.
7. Whittemore R, Knafl K. The integrative review: updated methodology. *J Adv Nurs*. 2005;52(5):546-553. doi:10.1111/j.1365-2648.2005.03621.x.
8. Group OL of EW. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. *Oxford Cent Evidence-Based Med*. 2011. http://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf. Accessed February 8, 2015.
9. Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. *Crit Care Med*. 1981;9(8):591-597. doi:10.1097/00003246-198108000-00008.
10. Kuzniewicz MW, Vasilevskis EE, Lane R, et al. Variation in ICU risk-adjusted mortality: Impact of methods of assessment and potential confounders. *Chest*. 2008;133:1319-1327. doi:10.1378/chest.07-3061.
11. Zimmerman JE, Kramer AA, McNair DS, Malila FM. Acute Physiology and Chronic Health Evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. *Crit Care Med*. 2006;34:1297-1310. doi:10.1097/01.CCM.0000215112.84523.F0.
12. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818-829. doi:10.1097/00003465-198603000-00013.
13. Nassar AP, Mocelin AO, Nunes ALB, et al. Caution when using prognostic models: A prospective comparison of 3 recent prognostic models. *J Crit Care*. 2012;27(4). doi:10.1016/j.jcrc.2011.08.016.
14. Lemeshow S, Teres D, Pastides H, Avrunin JS, Steingrub JS. A method for predicting survival and mortality of ICU patients using objectively derived weights. *Crit Care Med*. 1985;13(7):519-525. doi:10.1097/00003246-198507000-00001.

15.   Higgins TL, Teres D, Copes WS, Nathanson BH, Stark M, Kramer AA. Assessing contemporary intensive care unit outcome: an updated Mortality Probability Admission Model (MPM0-III). *Crit Care Med*. 2007;35(3):827-835. doi:10.1097/01.CCM.0000257337.63529.9F.

16.   Nathanson BH, Higgins TL, Kramer AA, Copes WS, Stark M, Teres D. Subgroup mortality probability models: are they necessary for specialized intensive care units? *Crit Care Med*. 2009;37:2375-2386. doi:10.1097/CCM.0b013e3181a12851.

17.   Kramer A a, Higgins TL, Zimmerman JE. Comparison of the Mortality Probability Admission Model III, National Quality Forum, and Acute Physiology and Chronic Health Evaluation IV hospital mortality models: implications for national benchmarking*. *Crit Care Med*. 2014;42:544-553. doi:10.1097/CCM.0b013e3182a66a49.

18.   Le Gall JR, Loirat P, Alperovitch A, et al. A simplified acute physiology score for ICU patients. *Crit Care Med*. 1984;12(11):975-977. doi:10.1097/00003246-198411000-00012.

19.   Moreno RP, Metnitz PGH, Almeida E, et al. SAPS 3--From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med*. 2005;31:1345-1355. doi:10.1007/s00134-005-2763-5.

20.   Metnitz PGH, Moreno RP, Almeida E, et al. SAPS 3-From evaluation of the patient to evaluation of the intensive care unit. Part 1: Objectives, methods and cohort description. *Intensive Care Med*. 2005;31:1336-1344. doi:10.1007/s00134-005-2762-6.

21.   Le Gall J-R. A New Simplified Acute Physiology Score (SAPS II) Based on a European/North American Multicenter Study. *JAMA J Am Med Assoc*. 1993;270(24):2957. doi:10.1001/jama.1993.03510240069035.

22.   Liu V, Turk BJ, Ragins AI, Kipnis P, Escobar GJ. An electronic Simplified Acute Physiology Score-based risk adjustment score for critical illness in an integrated healthcare system. *Crit Care Med*. 2013;41:41-48. doi:10.1097/CCM.0b013e318267636e.

23.   Vincent J-L, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med*. 1996;22(7):707-710. doi:10.1007/BF01709751.

24.   Vincent JL, Ferreira F, Moreno R. Scoring systems for assessing organ dysfunction and survival. *Crit Care Clin*. 2000;16(2):353-366. http://www.ncbi.nlm.nih.gov/pubmed/10768086. Accessed April 17, 2015.

25.   Vincent JL, de Mendonça A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med*. 1998;26(11):1793-1800. http://www.ncbi.nlm.nih.gov/pubmed/9824069. Accessed March 24, 2015.

26.   Minne L, Ludikhuize J, De Jonge E, De Rooij S, Abu-Hanna A. Prognostic models for predicting mortality in elderly ICU patients: A systematic review. *Intensive Care Med*. 2011;37:1258-1268. doi:10.1007/s00134-011-2265-6.

27.   Minne L, Abu-Hanna A, de Jonge E. Evaluation of SOFA-based models for predicting mortality in the ICU: A systematic review. *Crit Care*. 2008;12:R161.

doi:10.1186/cc7160.

28.   Render ML, Kim HM, Deddens J, et al. Variation in outcomes in Veterans Affairs intensive care units with a computerized severity measure. *Crit Care Med*. 2005;33(5):930-939. doi:10.1097/01.ccm.0000162497.86229.e9.

29.   Render ML, Deddens J, Freyberg R, et al. Veterans Affairs intensive care unit risk adjustment model: validation, updating, recalibration. *Crit Care Med*. 2008;36:1031-1042. doi:10.1097/CCM.0b013e318169f290.

30.   Pirracchio R, Petersen ML, Carone M, Rigon MR, Chevret S, van der Laan MJ. Mortality prediction in intensive care units with the Super ICU Learner Algorithm (SICULA): a population-based study. *Lancet Respir Med*. 2015;3(1):42-52. doi:10.1016/S2213-2600(14)70239-5.

31.   Afessa B, Gajic O, Keegan MT. Severity of illness and organ failure assessment in adult intensive care units. *Crit Care Clin*. 2007;23(3):639-658. doi:10.1016/j.ccc.2007.05.004.

32.   Lemeshow S, Hosmer DW. A review of goodness of fit statistics for use in the development of logistic regression models. *Am J Epidemiol*. 1982;115(1):92-106. http://www.ncbi.nlm.nih.gov/pubmed/7055134. Accessed January 13, 2015.

33.   Broeck J Van Den, Kauchali S, Brestoff JR, Chhagan M. Training and Study Preparations. In: Van den Broeck J, Brestoff JR, eds. *Epidemiology: Principles and Practical Guidelines*. Vol Springer Netherlands; 2013:313-328. doi:10.1007/978-94-007-5989-3.

34.   Moreno RP, Metnitz PGH, Almeida E, et al. SAPS 3--From evaluation of the patient to evaluation of the intensive care unit. Part 2: Development of a prognostic model for hospital mortality at ICU admission. *Intensive Care Med*. 2005;31(10):1345-1355. doi:10.1007/s00134-005-2763-5.

35.   Higgins TL, Kramer A a, Nathanson BH, Copes W, Stark M, Teres D. Prospective validation of the intensive care unit admission Mortality Probability Model (MPM0-III). *Crit Care Med*. 2009;37(5):1619-1623. doi:10.1097/CCM.0b013e31819ded31.

36.   Wenner JB, Norena M, Khan N, et al. Reliability of intensive care unit admitting and comorbid diagnoses, race, elements of Acute Physiology and Chronic Health Evaluation II score, and predicted probability of mortality in an electronic intensive care unit database. *J Crit Care*. 2009;24(3):401-407. doi:10.1016/j.jcrc.2009.03.008.

37.   Chen LM, Martin CM, Morrison TL, Sibbald WJ. Interobserver variability in data collection of the APACHE II score in teaching and community hospitals. *Crit Care Med*. 1999;27(9):1999-2004. http://www.ncbi.nlm.nih.gov/pubmed/10507631. Accessed April 19, 2015.

38.   Kho ME, McDonald E, Stratford PW, Cook DJ. Interrater reliability of APACHE II scores for medical-surgical intensive care patients: a prospective blinded study. *Am J Crit Care*. 2007;16(4):378-383. http://www.ncbi.nlm.nih.gov/pubmed/17595370. Accessed April 19, 2015.

39.   Terra SM. Approach to Medical Futility in a Community Hospital: Is Use of a Prognostic Scoring System Applicable? *Internet J Allied Heal Sci Pract*. 2006;4(4). http://ijahsp.nova.edu/articles/vol4num4/terra.pdf. Accessed February 7, 2015.

40.   Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *Jama*. 2016;315(8):801-810. doi:10.1001/jama.2016.0287.

41.   Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med*. 2007;356:469-478. doi:10.1056/NEJMoa063446.

42.   Lilly CM, De Meo DL, Sonna LA, et al. An intensive communication intervention for the critically Ill. *Am J Med*. 2000;109:469-475. doi:10.1016/S0002-9343(00)00524-6.

43.   Lombardozzi K, Bible S, Eckman J, et al. Evaluation of efficiency and accuracy of a streamlined data entry process into an outcomes database. *Crit Care Med*. 2009;37(12):A370-A370. doi:http://dx.doi.org/10.1097/01.ccm.0000365439.11849.a2.

44.   Kajdacsy-Balla Amaral AC, Andrade FM, Moreno R, Artigas A, Cantraine F, Vincent JL. Use of the Sequential Organ Failure Assessment score as a severity score. *Intensive Care Med*. 2005;31:243-249. doi:10.1007/s00134-004-2528-6.

45.   Moreno R, Vincent JL, Matos R, et al. The use of maximum SOFA score to quantify organ dysfunction/failure in intensive care. Results of a prospective, multicentre study. *Intensive Care Med*. 1999;25(7):686-696. doi:10.1007/s001340050931.

Table 1. Summary of Findings

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
Comparison of the Mortality Probability Admission Model III, National Quality Forum, and Acute Physiology and Chronic Health Evaluation IV Hospital Mortality Models: Implications for National Benchmarking [17] Models: MPM III, NQF, APACHE IV	Patients from the APACHE database for ICU admissions 2008-2012. Included 99 ICUs at 47 US hospitals. However, final n= 55,304 due to missing MPM III data (55 ICUs in 38 hospitals). ICUs included medical-surgical, surgical, medical, coronary care, and neurological units. Patients with ICU readmissions, less than 18 years of age, admitted for an MI, or admitted for cardiac surgery or trauma were omitted.	Purpose: To compare the accuracy of the original MPM III, NQF modification of the MPM III (NQF Model), and APACHE IV for comparing observed and risk-adjusted hospital mortality predictions. Design: Retrospective paired analysis of day one hospital mortality predictions.	Comparison of models: APACHE IV AUC= 0.88, Hosmer-Lemeshow chi-square= 219, Adjusted Brier= 31.0%. MPM III AUC= 0.81, Hosmer-Lemeshow chi-square= 554, Adjusted Brier= 16.1%. NQF AUC= 0.80, Hosmer-Lemeshow chi-square= 760, Adjusted Brier= 17.8%.	Not Reported	Referenced Only: Manual collection of MPM III data (11.1 minutes) versus APACHE IV (37.3 minutes) per patient.[10] With electronic automated collection capability, APACHE IV data collection time is reduced (1.5 minutes).[43]	Level 3: Large study with inception cohort. Model-specific exclusions leading to exclusion of a large number of patient data.

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
Variation in ICU Risk-Adjusted Mortality: Impact of Methods of Assessment and Potential Cofounders [10] Models: SAPS II, MPM III, APACHE IV	11,300 patients that were discharged from the hospital or died after an eligible ICU admission in 25 California hospitals (with similar characteristics of all California hospitals) from 2001-2004. Patients that had missing data, were less than 18 years of age, were not admitted to an adult ICU, did not stay in the ICU for at least four hours, or experienced a burn, trauma, or a CABG were omitted.	Purpose: To compare the predictive accuracy, reliability, and data burden of existing ICU risk-adjustment models, including the MPM III, SAPS II, and APACHE IV. Design: Retrospective chart review. Cohort was randomly divided into development (60%) and validation (40%) samples. Logistic regression used to re-estimate the coefficients of the models in the development sample.	Comparison of models: MPM III AUC= 0.809, Hosmer-Lemeshow statistic= 9.8 (p=0.5), SMR= 1.04. SAPS II AUC= 0.873, Hosmer-Lemeshow statistic= 18.1 (p= 0.05), SMR= 1.04. APACHE IV AUC= 0.892, Hosmer-Lemeshow statistic= 22.4 (p= 0.01), SMR= 1.03.	Auditor re-abstracted model data from a 5% random sample of patients. Interrater reliability between data abstractor and auditor: 91.5-98.8% agreement, K statistic range 0.72-0.96 with GCS (K= 0.55) and APACHE reason for ICU admission (K=0.51) lower.	Mean manual data collection times: MPM III= 11.1 minute, SAPS II= 19.6 minutes, APACHE IV= 37.3 minutes. Manual abstraction warrants training of data collectors. Advanced system capabilities required for automated data collection from EHR.	Level 2: Study with inception cohorts and randomized division of development and validation groups.

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
Acute Physiology and Chronic Health Evaluation (APACHE) IV: Hospital Mortality Assessment for Today's Critically Ill Patients [11] Model: APACHE IV	110,558 consecutive ICU admissions 2002-2003 at 104 ICU (medical, surgical, cardiothoracic, neurologic, trauma) or coronary care units at 45 geographically diverse hospitals in the US that had APACHE III computerized data systems. Patients admitted for less than four hours, with burns, less than 16 years of age, post-transplantation (except renal and hepatic), no acute physiology score during first 24 hours of ICU admission, and those hospitalized greater than 365 days or transferred from another ICU were omitted.	Purpose: To develop and validate the APACHE IV by using predictor variables similar to the APACHE III with new variables added and different statistical modeling used. New diagnoses were added and new predictor variables included whether a patient was mechanically ventilated, whether a patient with an MI received thrombolytic therapy, adjustments for prognostic implications of GCS and Pa02/Fi02, and impact of inability to assess GCS due to sedation or paralytics. Design: Observational cohort study. Sample was randomly divided into training set (60%) and validation (40%) groups. APACHE III, versions H and I were applied to the validation data set for comparison.	Comparison among models in validation set (non-CABG surgery patients): APACHE IV SMR observed/predicted mortality= 0.997 (p= .79), AUC= 0.88, Hosmer-Lemeshow chi-square= 16.8 (p= .08). APACHE III (I) SMR observed/predicted mortality= 0.923 (p= <.001), AUC= 0.870, Hosmer-Lemeshow chi-square= 124.6 (p= <.001). APACHE III(H) SMR observed/predicted mortality= 0.799 (p= <.001), AUC= 0.868, Hosmer-Lemeshow chi-square= 635.4 (p= <.001). SMR observed/predicted for patients admitted after CABG surgery= 0.997 (chi-square= 0.002, p= .96).	Not Reported	Available on a free, public website. Dropdown options allow for relatively quick entry but complexity of variables warrants training for data collection (training manual available). Requires use of purchased APACHE system for automated collection of acute physiology score variables and laboratory data.	Level 2: Large study with inception cohorts and randomized division of training set and validation groups.

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
An Electronic Simplified Acute Physiology Score-Based Risk Adjustment Score for Critical Illness in an Integrated Healthcare System [22] Model: eSAPS3	67,889 patients at least 18 years old who had an ICU admission between January 1, 2007 and December 24, 2011 to one of 21 Kaiser Permanent North California Healthcare System facilities. Patients with a repeat ICU admission or transfer from an outside facility were excluded.	Purpose: Development and performance assessment of an electronic ICU risk adjustment score based on the SAPS 3. Design: Cohort was randomly divided into derivation (40%) and validation (60%) samples. At baseline, groups had similar characteristics. Coefficients from logistic regression in the derivation group were applied to the validation group and tested. Performance was evaluated using published SAPS 3 global and North American coefficients.	AUC= 0.80. After expanding the laboratory value retrieval window, AUC= 0.81. For the validation data set, AUC= 0.82, Hosmer-Lemeshow chi-square= 6.7 (p= .57). When limited to each hospital, AUC range= 0.77-0.85, Hosmer-Lemeshow chi-square range= 5.7-43.6. When separated by cohorts grouped per year, the Hosmer-Lemeshow chi-square was not significant for 2009 (=11.3), 2010 (=12.8), or 2011 (=6.9) using $p > 0.10$.	Manual review of 200 randomly selected ICU episodes formed by deciles of the eSAPS3 scores and assessed by percent agreement and K scores revealed discordance between electronic and manual components of SAPS 3 of 7.9% on average across all individual components.	Allows for automated extraction of data based on SAPS 3 which is nonproprietary. Requires use of EHR with data extraction capabilities. Requires adaptation of some variables that cannot be directly linked to EHR.	Level 2: Large study with inception cohorts and randomized samples within the controlled cohort.

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
Evaluation of SOFA-based Models for Predicting Mortality in the ICU: A Systematic Review [27] Model: SOFA	Two studies included patients from the US (in combination with other countries). Study one= 748 ICU patients from 40 ICUs (1 from US, 35 from Europe, 1 from Australia, 3 from South America) May 1995.[44] Study two= 1449 patients from 40 ICUs (1 from US, 35 from Europe, 1 from Australia, 3 from South America) May 1995.[45]	Purpose: To systematically review studies evaluating the performance of SOFA for predicting mortality for patients in the ICU (article n= 18). Design: Statistical performance of the model was assessed by examining the reported discrimination, calibration, and/or accuracy. Studies were included only if they were in English, were not restricted to a specific diagnosis, and were from the surgical or medical ICU populations. Quality of the studies was assessed by using a quality assessment framework for systematic reviews of prognostic studies.	Study one examined SOFA sequentially (Total Max SOFA AUC= 0.84, Hosmer-Lemeshow H p-value= 0.95, C p-value= 0.54). Study one also compared Max SOFA alone (AUC= 0.841) with Max SOFA and infection (AUC= 0.845), and Max SOFA and infection and age (AUC= 0.853). Study two examined SOFA at admission or a fixed time thereafter (AUC= 0.772) and sequentially (Total Max SOFA AUC= 0.847, Delta SOFA AUC= 0.742). Study two also evaluated individual components of SOFA. Cardiovascular AUC= 0.802, Respiratory AUC= 0.736, Hepatic AUC= 0.655, Renal AUC= 0.739, Neurological AUC= 0.727, Coagulation AUC= 0.684.	Two reviewers conducted the search and differences were resolved with inclusion of a third reviewer. Inter-observer agreement Kappa= 0.94. No reliability indicators were reported for the models included in the review.	Not reported.	Level 1: Systematic review of inception cohort studies.

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
Mortality Prediction in Intensive Care Units with the Super ICU Learner Algorithm (SICULA): A Population-Based Study [30] Model: SICULA, SAPS II, APACHE II, SOFA	All patients (n= 24,508) admitted to an ICU at Beth Israel Deaconess Medical Center in Boston 2001-2008. ICUs included medical, trauma-surgical, coronary, cardiac surgery, and medical-surgical units. Patients with greater than one ICU admission per hospital stay were omitted. Validation group: 200 randomly selected ICU patients in a Paris, France hospital 2013-2014. ICUs included medical, surgical, and trauma units.	Purpose: To determine whether the SICULA can provide a new mortality prediction algorithm for ICU patients and to compare its performance with other validated scoring systems (SAPS II, APACHE II, and SOFA). Design: A machine learning technique was used to determine if they could improve ICU mortality prediction compared with conventional methods without having to change their scoring procedures. Two sets of predictions were based on the Super Learner. The first set was based on SAPS II variables (SL1). The second set on the original, untransformed variables used in SAPS II and APACHE II (SL2= SICULA).	SOFA Score AUC= 0.71, SAPS II original version AUC= 0.78, SAPS II refitted score AUC= 0.83, APACHE II refitted score AUC= 0.82, SL1 AUC= 0.85, SL2 AUC= 0.88. Recorded versus predicted hospital mortality (Cox calibration) SOFA= 0.12, SAPS II original= 0.30, SAPS II refitted= 0.12, APACHE II refitted= 0.12, SL1= 0.12, SL2= 0.13. External validation AUC= 0.94.	Not Reported	Available online for easy access. Requires user to compile various data-fitting algorithms and to specify performance measures.	Level 2: Large study with inception cohort and randomized validation cohort.
Veterans Affairs Intensive Care Unit Risk Adjustment	All patients (n= 36,240) admitted to 30 ICUs in 15 VA hospitals July 1999-	Purpose: To further validate the VA ICU severity measure by examining its validity in	Using fixed estimates from the 1996-1997 data applied to independent data sets	Not Reported	Allows for automated extraction of data.	Level 2: Large study with inception cohorts.

Prognostic Model Reference	Research Subjects	Study Purpose/Design	Validity	Reliability	Feasibility	Level of Evidence[8]
Model: Validation, Updating, Recalibration [29] Model: VA ICU	December 2000 using a stratified sampling strategy based on hospital size and geographic location comprised cohort 1. Consecutively admitted patients October 2001-September 2004 from 62 ICUs in 42 VA hospitals in six regions that participated in a VA pilot study that measured and reported risk-adjusted outcomes comprised cohort 2. Second or later ICU admissions during the same hospitalization, those lacking arterial blood gas data, those transferred to another hospital at discharge, and those that underwent transplantation were excluded leaving n= 81,964.	two larger, diverse cohorts of VA ICUs, and comparing its prediction with the VA National Surgical Quality Improvement Plan (NSQIP= Used by the VA to assess risk-adjusted performance including 30-day mortality). Design: Retrospective data analysis from two ICU cohorts. A logistic regression model was used to predict hospital mortality in each cohort. For cohort 2, the predictor coefficients were refit after expanding the diagnostic classification and source of admission variables to update the model.	of first ICU admissions, cohort 1 AUC= 0.8744, Hosmer-Lemeshow chi-square= 72.5; cohort 2 AUC= 0.88, Hosmer-Lemeshow chi-square= 154.8. For cohort 1 patients admitted to the ICU for a second or third time during the same hospitalization, AUC= 0.827 and 0.796, Hosmer-Lemeshow chi-square= 65.2 and 44.7. For the validation set of the updated model, Brier's score= 0.06-0.07. Comparison of NSQIP and cohort 1 VA ICU data (n= 7,411) revealed VA ICU AUC= 0.83, Hosmer-Lemeshow chi-square= 63.9, SMR= 1.04; NSQIP AUC= 0.81, Hosmer-Lemeshow chi-square= 92.3, SMR= 1.15. Updated model AUC= 0.897, Hosmer-Lemeshow chi-square= 79.2.		No training is required. Requires use of EHR with data extraction capabilities.	

Supporting Surrogates of Incapacitated Individuals Throughout the Research Trial – From Initial
Consent to Study Closure and Beyond

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Abstract

Treatments are needed for medical conditions such as Alzheimer's disease and other neurocognitive disorders, head trauma, and psychiatric disorders that leave a person incapacitated, yet individuals with these conditions are often incapable of giving consent for research. Although there has been a shift in support for surrogate decision making in research, the decision to consent and agree to continued enrollment of an incapacitated person in research can place a significant amount of burden on the surrogate decision maker. The purpose of this integrative review is to discuss and critique the current state of knowledge related to interventions that can guide researchers in reducing surrogate burden throughout the research trial, from initial consent to closure of the study and beyond. 25 articles met inclusion criteria for review. Analysis of the articles revealed six levels of intervention, from the personal 'Direct Care of the Surrogate' to the population-based 'Legal/Regulatory' and provides a framework to assist researchers and other interested parties when surrogates are relied upon for decision making regarding research participation.

Keywords: Research consent, Incapacitated research, Surrogate consent, Research ethics

Introduction

Medical conditions such as end-stage Alzheimer's disease and other

neurocognitive disorders, head trauma, and psychiatric disorders that leave a person

incapacitated, or lacking the capacity to physically or mentally make decisions for

themselves (Merriam-Webster, 2017), can be devastating to the affected person and their

family. Current treatments for several of these conditions are only modestly effective in

improving cognitive function and most merely assuage symptoms; therefore, future

research is needed in these areas (Alzheimer's Association, 2017). However, the very

nature of the illness that renders a person incapacitated is the source of many ethical

issues and can preclude them from consenting to research (Kim, Appelbaum, Jeste, &

Olin, 2004). The literature indicates that persons who are incapacitated should be

excluded from research if the same research can be done with capable participants

(Griffith & Tengnah, 2010; Hoffman & Schwartz, 1998; Kim et al., 2004). However,

advancement in medical treatment can only be made if research can be conducted on

conditions that cause incapacity, and often the enrollment of participants with significant

impairments in expressive language and executive function is required (Karlawish &

Casarett, 2001; Kim et al., 2004). Incapacitated persons are considered the most

vulnerable of all research participants and the researchers are charged with following the

ethical conduct of research and sustaining their moral status while not diminishing the

incapacitated from a level of 'subjects' to one of 'objects' (Jennings, 2012).

Researchers often utilize a legally authorized representative (LAR) (also referred

to in the literature as *research surrogate*, *proxy,* or *substitute decision maker*) to provide

consent for incapacitated persons to participate in research. The process often appears to

be straightforward, yet there has been much debate in the literature regarding the use of surrogate decision makers for research consent (Macciocchi & Alves, 1997; Walters, 2009; Yarborough, 2002). The literature reveals researchers commonly express concerns that surrogates do not properly understand or are unprepared for their role as surrogate decision makers (Candilis, Wesley, & Wichman, 1993; Karlawish et al., 2009; Yarborough, 2002). Additionally, the ethical debate escalates with regard to the appropriateness of surrogate decision making for incapacitated persons if the research is considered high risk or nontherapeutic (Warren et al., 1986; Yarborough, 2002). The challenge for researchers is to develop innovative methods for consent and continued study enrollment that helps minimize burden for the surrogate decision maker. From initial surrogate consent, to engagement throughout the research process, researchers must vigilantly assess for surrogate vulnerability, not just from an ethical stance—but for the surrogate's physical, mental and emotional needs as well (Dunn et al., 2013).

Although the Belmont Report, developed decades ago, highlights respect for persons as one of the basic ethical principles guiding research involving persons who do not have the capacity to exercise their autonomy (National Commission for the protection of Human Subjects of Biomedical and Behavioral Research, 1979), there remains to be limited standards with regard to surrogate-based consent (Office for Human Research Protections (OHRP), 2009a). There are regulations related to when a surrogate can be used for consent and who that individual should be if not previously appointed, which is often governed by states (OHRP, n.d.), but specific interventions that can be used to support the surrogate during participant enrollment and throughout the research trial are limited and are provided as 'recommendations' only (OHRP, 2009a). The OHRP

recommends that Institutional Review Boards (IRBs) establish a more variable risk/benefit ratio as a requirement for approval of studies where a surrogate will be required for consent (OHRP, 2009a). The OHRP and National Institutes of Health (NIH) recommend that surrogates be educated on their roles and responsibilities during consent and throughout the study, receive communication regarding the research participant's well-being throughout the study, and inform surrogates of any new information about risks, benefits, and alternatives related to the study throughout the participant's enrollment (NIH, 2009; OHRP, 2009a). These recommendations are developed from expert opinion, likely based on their experiences. Although expert opinion is valuable, determining the outcomes of such recommendations is an area warranting further investigation.

Due to the complexities in surrogate consent for research with incapacitated persons, this integrative review synthesizes and critiques empirical and theoretical literature to provide a more comprehensive understanding of the current state of the science (Whittemore & Knafl, 2005) and provides a framework consisting of six levels of 'intervention' to assist researchers and interested parties, such as legal and policy making groups, with the surrogate consent process. The variables of interest included a review of interventions available to guide researchers in their decision making surrounding initial consent and ongoing enrollment for research involving incapacitated persons, in an attempt to minimize surrogate burden. This review evaluates the extant literature to determine: among surrogates of incapacitated persons, what are the ethically acceptable practices that can be utilized by researchers to guide enrollment and supportive involvement in research related to advancement of treatment?

Methods

Through an extensive literature review, the variables of interest were identified by asking the following questions: 1) does the article provide a description of an intervention that can guide researchers in reducing surrogate burden throughout the research study? 2) does the article report on testing the intervention and present an outcome?

To accomplish a thorough review of the pertinent literature, a medical librarian was consulted to identify appropriate databases and search strategies. A systematic search of five databases was conducted along with a search of the reference list of the retrieved publications to identify published articles addressing the topic. The database searches were conducted in PubMed, CINAHL (EBSCOHost), Web of Science, PsychInfo, and ProQuest Dissertations & Theses. The articles included were limited to those written in English and addressing an adult population. The search was limited to adults only because surrogate consent for children is not within the scope of this review. The search was broken into three concept groups. One group encompassed the terminology used to describe "competency" (competency, competence, incompetent, incompetency, mental competence), another covered the terms relevant to "informed consent" (informed consent, consenting, consent, permission), with the final keyword "research" added. Medical Subject Headings (MeSH) and equivalent controlled vocabulary and keywords were utilized in each database as appropriate. The complete search yielded 1096 articles (Figure 1).

From the total 1096 articles retrieved, a basic review of titles, key words, and/or abstracts was conducted to assess relatedness to inclusion criteria of United States (US) and surrogate consent for incapacitated person participation in research. No publication

date restrictions were imposed as discussion of surrogate consent began in the 1970's and our focus was on tracking the direction of discussion as it corresponded with regulation changes throughout the years related to human protection in research. This initial review resulted in 476 articles remaining.

Following the initial review, full text articles revealed that 426 of the resulting articles were not related to surrogate consent for incapacitated person participation in research or did not occur in the US. The 50 articles that appeared to meet the inclusion criteria of this review were reviewed in-depth to determine relevance. Although the intent of the search was to include actual interventions that had been implemented to minimize surrogate burden throughout the research study, the in-depth review revealed that only three articles met this criterion. However, many other articles reviewed suggested interventions based on lessons learned. Because these suggestions were also important to the knowledge to be gained, they too were included, leaving a total of 25 articles for the final review.

A matrix (Table 1) was used to extract data from the chosen articles. Findings from the articles were grouped according to themes identified that were consistent with the purpose of this review. Specifically, interventions and their outcomes (when available) were included. This paper is the first known attempt at reviewing interventions that can guide researchers in reducing surrogate burden throughout the research study.

Figure 1. Literature Review Search
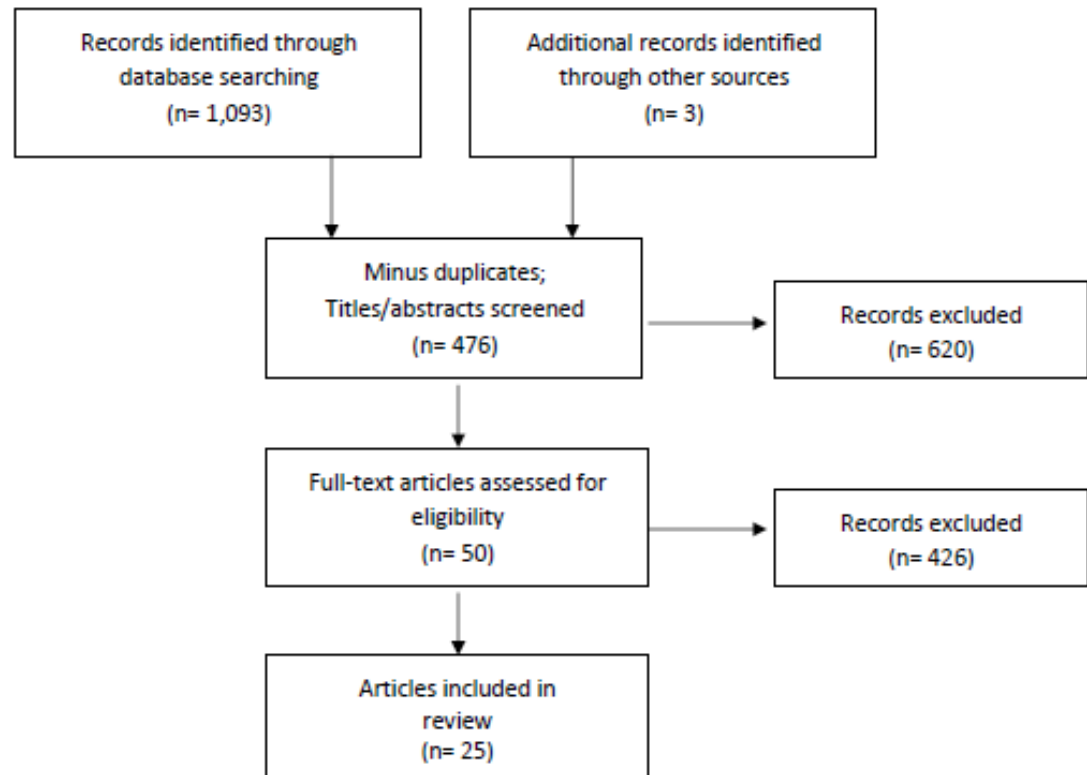
Results

All 25 of the articles included addressed at least one intervention for minimizing surrogate burden at some point during the research trial. Because most articles included did not directly test interventions, assessing the level of evidence was not applicable; even those that did test interventions were of mostly mid-level evidence because non-randomized samples were used for their rather small studies. Included articles spanned almost 30 years as the process of surrogate involvement continues to evolve with changes in both healthcare clinical practice and healthcare policy. Surrogates carry a great responsibility to decide whether or not to consent to initial enrollment and ongoing engagement for incapacitated persons (Dunn et al., 2013). Therefore, it was of interest to review interventions aimed at providing the greatest good for the person while

minimizing the physical and emotional stress experienced by the surrogate. Although few

of the articles discussed actual interventions to improve the surrogate consent process,

many of the articles presented suggested interventions based the study findings, literature

reviews, guideline development/critique, expert opinion, and case studies. In total, six

types of interventions, grouped according to themes, emerged from the review. Arranged

by the level of surrogate involvement, the literature describing each is detailed below. A

common goal of protecting those with diminished autonomy while promoting needed

research involving vulnerable populations was evident in all interventions presented.

1. Direct Care of Surrogate Interventions

Surrogates, whether family, friends or legal representatives of persons who lack

decisional capacity, are asked routinely to make decisions about involvement in clinical

research. Researchers used questionnaire items and open-ended questions to assess how

surrogates for persons with advanced dementia made decisions regarding research

enrollment (Dunn et al., 2013). By answering questions regarding hypothetical clinical

trials, researchers were able to gain knowledge regarding the difficulty (physically,

emotionally, logistically) for surrogates of honoring the wishes of the person while

maintaining their own quality of life. Suggested interventions based on these findings

included incorporating respite care and ongoing education for the surrogates into research

protocols (Dunn et al., 2013).

Caring for individuals who are incapacitated can take a physical and mental toll

on surrogates if they are also the primary caregiver. However, caregivers that enroll

persons in research studies may have less distress from caregiver tasks, perhaps due to

the time allowed to take a break from caregiver duties when study-related activities are

occurring, although there is no published data to support this inclination (Karlawish &

Casarett, 2001). However, for others, having to drive the participant to a study site may

be more burdensome. If so, it is suggested that the research team could drive to the

location of the person to lessen the travel burden (Karlawish & Casarett, 2001).

2. Advance Directive Interventions

While Advance Directives (AD) may outline end-of-life preferences, these

documents rarely address involvement in clinical research. Currently in the US, specific

regulations regarding advance directives for research are lacking (OHRP, 2009b).

Perhaps this is in part due to varying views regarding 'advance directives for research'

which is either a special document specifying this preference, or a statement of this

preference within a general advance directive. Those who favor the promotion of advance

directives for research consent ascertain these directives provide a means for a competent

person to exercise his or her right to consent to research participation after their

competence is lost (Buller, 2015).

For states that allow people to designate a surrogate for consent to treatment in the

case of their incapacity, the designation could also be extended to consent to research

(Appelbaum, 2002; Berg, 1996; Fletcher, Dommel, & Cowell, 1985; Kapp, 1994; Miller,

1982; Sachs, 1994; Wendler, Martinez, Fairclough, Sunderland, & Emanuel, 2002). The

most prominent suggestion is for advance directives to validate consent for studies that

have minimal risk with some benefit (Appelbaum, 2002). However, a study that

conducted phone interviews to examine the attitudes of healthy individuals with a family

history of Alzheimer's disease who had participated in clinical research found that some

individuals would consent to research that offers no potential for medical benefit

(Wendler et al., 2002). However, others ascertain that incapacitated persons should be able to participate in research with more than a minimal risk as long as they have an advance directive indicating their willingness to be enrolled in such studies (Berg, 1996; Sachs, 1994). Because allowing persons to make specific authorizations within their advance directive for research would protect autonomy to the greatest extent, researchers could identify persons who have progressive diseases and encourage them to complete advance directives for research with specific authorizations while they are still competent (Miller, 1982). However, others studying dementia assert that advance directives for research are unlikely to be effective because only a minority of people complete advance directives for treatment decisions, a likely indicator of how many would contemplate the unpleasant thought of developing dementia and participating in research (Kim & Kieburtz, 2006).

Healthy adult individuals with a family history of Alzheimer's disease that participated in a study by Wendler et. al. (2002) (n= 246) were assessed regarding their attitudes surrounding safeguards for research which included incapacitated persons. Participants indicated advance directives for research should not be automatically regarded as definitive. Eighty percent of the respondents for the study indicated that it would be acceptable if their surrogate enrolled them in research that had potential medical benefits even when their advance directive specified no research participation. Karlawish et al. (2009) found similar results in a study that explored older adult participants' views on granting surrogates leeway to override decisions about research participation once the person became incapacitated. The results of this study support a recommendation to grant surrogate leeway over advance consent for research. Noting that

advance directives may be outdated, an ethics committee position statement from almost 20 years ago also recommends that surrogates should be allowed to refuse or enroll persons into research studies because they believe their decision is based on the best interests for the person, even if that decision contradicts with the person's advance directive (Sachs, 1998). However, another older working group recommendation from Maryland's Policy Initiative argues surrogate consent should not be sufficient when there is no direct medical benefit but greater than minimal risk (Hoffman & Schwartz, 1998).

3. Enhanced Communication Interventions

Surrogates routinely make decisions without any knowledge of preferences and may struggle between what they think is best for an incapacitated person versus what they believe the person wanted (Howe, 2012). Sometimes termed 'substituted judgment', this action is based on essentially extrapolated knowledge of what the 'impaired' person's values and beliefs would support; some authorities believe this is morally unsound and care should focus on what is in the person's best interest (Torke, Alexander, & Lantos, 2008). Even though the opportunity is not always possible, for persons with deteriorating diseases such as Alzheimer's, emphasis is placed on communication prior to the person deteriorating to an incapacitated state (Howe, 2012). Based on public support of surrogate decision makers, Howe (2012) recommends a psychiatrist taking the initiative to encourage discussions between individuals and surrogates regarding future research desires as soon as a person is diagnosed with a deteriorating disease.

Demonstrating the length of time 'substituted judgment' has been debated, Warren et al. (1986) examined the basis for surrogate decision making by questioning surrogates regarding whether they would consent to the person's participation in a study

involving minimal risk. Of the 55 surrogates who believed the person would refuse enrollment consent, 17 gave consent *in opposition to the individual's indications*. Based on these findings and respect for autonomy, a recommendation was made to have investigators ask surrogates specifically whether they think the individual would have consented to the study had the person been competent. Based on a response of "no," the recommendation includes disqualifying the person from participation even if the surrogate is willing to consent.

Surrogates of intensive care unit (ICU) patients often experience stress due to the critical nature of the patient's condition; asking them to consent for their loved one's participation in research likely adds additional stressors (Shelton, Freeman, Fish, Bachman, & Richardson, 2015). In an attempt to alleviate some of these stressors, researchers developed a computer-based education module to see if they could increase surrogate understanding of the process of informed consent for genomics research. Their intervention was effective as evidenced by greater understanding of the informed consent process in the experimental group in comparison to the control group which received a basic consent form to review (Shelton et al., 2015). The results of this study support the addition of computer-based education modules to conventional approaches for obtaining informed consent from surrogates in the ICU.

In addressing the ethical challenges of clinical trials that involve persons with dementia, Karlawish and Casarett (2001) acknowledged the need to ensure that individuals and/or their surrogates receive feedback about the results of the research. By communicating the benefits of their participation, surrogates can feel more comfortable with their decision to consent to enrollment and ongoing participation. They recommend

that individuals, and in the case of incapacitated individuals, their surrogates, should receive feedback about what intervention the individual received and what the overall results were (Karlawish & Casarett, 2001).

4. Expert Consultant Interventions

A proposal to facilitate surrogate consent suggests that health care institutions could appoint surrogates or even 'referees' to represent the patient's best interest. Wendler and Prassad (2001) compared four US and two international guidelines that proposed safeguards for adults who are unable to consent. Based on their comparison of points of consensus and differences, they presented six core safeguards for research with those unable to consent. One safeguard included a recommendation for "consent monitors" to be utilized when the research involves greater than minimal risk. Consent monitor use is intended to ensure enrollment is consistent with the individual's preferences and interests which can decrease the surrogate's burden related to decision-making (Wendler & Prasad, 2001).

In a study that examined policies and guidelines used by Alzheimer's disease researchers pertaining to research involving cognitively impaired individuals, the need for ethical advice was discovered (Cahill & Wichman, 2000). A recommended intervention was to include in policy the need for a representative from the bioethics committee to be available to consult any time in which the investigator, Institutional Review Board, or surrogate desired ethical consultation (Cahill & Wichman, 2000).

5. Institutional Review Board (IRB) Interventions

The IRB is an institutional body charged with the duty to oversee all aspects of research that could put an individual at risk especially 'additional safeguards [for]

mentally disabled persons … [and] outlines precise requirements for the consent process, including when consent is provided by an LAR [legally authorized representative]' (Association for the Accreditation of Human Research Protection Programs (AAHRPP), 2014). Although standard requirements include consent for research prior to accessing medical records to determine individual eligibility, approaching surrogates for consent prior to ensuring eligibility may add undue stress. Following completion of a study with individuals with dementia in the nursing home setting that resulted in a protocol for informed consent and assent, researchers recommended obtaining an IRB waiver to access records to assess inclusion-exclusion criteria to ensure only surrogates of eligible persons were contacted (Batchelor-Aselage, Amella, Zapka, Mueller, & Beck, 2014).

Institutional review boards are charged with analyzing the risks and benefits of proposed research studies (Kim et al., 2004). One recommendation calls for IRBs to have a more stringent risk-benefit analysis if there is a proposal that calls for surrogate consent (Kim et al., 2004). This is an attempt to employ additional safeguards to protect the interest of incapacitated persons.

The consent process may be too much of an emotional strain for surrogates at the time research needs to begin in the cases of acute illness leading to an person's incapacity (Fost & Robertson, 1980). Institutional review boards have been asked to review research projects in which investigators asked for omission of consent for research involving critically ill individuals due to the foreseen stress on the surrogate (Fost & Robertson, 1980). Although the IRB is focused on protection of individuals enrolled in the study, they did adopt a compromise position in which surrogates would be informed at the time of admission that the incapacitated person would be entered into a research study, but

they would not receive explicit study details until later. The intervention was developed

to allow for "deferred consent" in which the investigator was responsible for obtaining

informed consent from the surrogate within 48 hours. In another study, the argument for

"deferred consent" was related more to the desire to uphold the best interest of the

individual when research was available for severe head injury and no surrogate was

readily available (Prentice et al., 1994). The authors suggested that the ability to

participate in limited interventions for severe head injury could bring relief to the

surrogate. For this study, the IRB and US Food and Drug Administration (FDA)

promoted a framework that required documentation of efforts to initially and

continuously contact the surrogate. Once contacted, the surrogate had the ability to

withdraw the incapacitated individual from the study.

Karlawash et al. (2002) surveyed Alzheimer's disease investigators to determine

how their sites conducted the informed consent process. Although specific information

was not provided, four of the 39 sites reported assessment of surrogate decision-making

capacity in their IRB approved consent procedures. Because of the survey results,

Karlawash et al. (2002) recommended examining whether the materials used to

summarize a study for enrollment recruitment affected surrogate comprehension and

satisfaction with the recruitment and consent process. In cases of complicated research

studies involving high risks, the authors suggested the IRB could require investigators to

take additional steps to ensure surrogate decision maker's comprehension (Berg, 1996).

For example, they could require employment of a neutral educator to assist the surrogate.

Adults with severe traumatic brain injury (TBI) are likely to exhibit a loss of

decision-making capacity (Pape, Jaffe, Savage, Collins, & Warden, 2004). However,

unlike other deteriorating diseases, persons with TBI may gain decision-making capacity following the acute phase of their injury. A study examining the legal and ethical components of TBI research recognized the need for continued assessment of individual decision-making capacity following initial research approval by a surrogate (Pape et al., 2004). Following a review of IRB feedback, weekly consciousness screening and determination of decision-making capacity were added to research procedures involving individuals with TBI that required surrogate consent for research (Pape et al., 2004). Upon return of the individual's capacity, the surrogate could be relieved of their decision-making responsibilities.

Kapp (1994) discussed potential surrogate decision-making mechanisms following an analysis of legal and ethical concerns regarding Alzheimer's disease. Based on safeguards needed to protect the vulnerable population of individuals with advanced Alzheimer's disease, a recommended intervention of heightened IRB involvement in the protocol approval process was set forth (Kapp, 1994). Specifically, building in an extra level of scientific and methodological review to verify an acceptable risk/benefit ratio was suggested along with additional monitoring if a surrogate was utilized for consent.

6. Legal/Regulatory Interventions

Professional groups interested in promoting research on vulnerable populations advocate for rules that permit the enrollment of incapacitated patients in appropriate research missions (Appelbaum, 2002). Appelbaum (2002) suggested a mandate requiring all states have a statute authorizing surrogate consent to research to decrease the burden of surrogate decision-making.

Stocking, Hougham, Baron, and Sachs (2003) sought the opinions of experienced researchers involved in Alzheimer's disease research to examine their thoughts on if additional regulations would provide enhanced protection of research participants. To their surprise, the results of the survey revealed that half of the participants did not perceive that having a standardized surrogate selection process (when not indicated by the individual prior to their incapacitated state) would enhance participant protection. However, since nearly an equal number of participants perceived a standardized surrogate as a means of increased protection, the study researchers hypothesized that the mixed feedback was a result of possible added workload that would result from utilization of the regulation.

Synthesis

This review covers almost four decades of studies and reviews that make recommendations about six lenses through which the consenting and continued enrollment processes for incapacitated persons could be viewed. Two are focused on the personal level – direct care of the surrogate; eleven are focused on advance directives and how they might relate to research participation; four address the process of enhanced communication with the surrogate; two advocate for the role of experts; eight are centered on the role of the IRB for the protection of human 'subjects'; and finally, two are centered on proposed legal/regulatory changes.

The limitation seen throughout the literature is that many of these interventions are recommendations only; few have actually been tested. Additionally, there are a few recommendations from regulators for supporting surrogates (Office for Human Research Protections, 2009a) but the results of this review further concede that few outcomes of

these recommendations have been reported. Therefore, do we really know the interventions being recommended are effective at supporting surrogates throughout the research trial? Because researchers are all trained on the principles of human subject protection and the surrogate is an extension of the 'subject,' it is likely that researchers are already following some of these recommendations but not reporting outcomes related to their interventions.

Advance directive interventions are complicated by the fact that relatively few people complete advance directives. Although the rate of completion has increased over the last decade, more current estimates still indicate that less than 30 percent of Americans have advance directives (Black, 2010). Furthermore, even when directives are present, they contain little information regarding the desires of the person to participate in research (Kim et al., 2013). These findings are coupled with evidence that even high-quality directives do not improve accuracy in the surrogates' ability to predict the preferences of the incapacitated person (Ditto et al., 2001; Kim et al., 2013).

Issues may not be related to the effectiveness of surrogate consent but may be rooted in the problems with inconsistencies in the consent process and ongoing engagement to minimize surrogate burden throughout the research trial. The quality and support given to the surrogate, rather than the risk of the study, emerges as the ethically fundamental consideration in deciding whether to enroll incapacitated persons in research (Yarborough, 2002).

Recommendations for Research

Most of the articles discovered in this review are greater than a decade old, with some as old as almost four decades. Given the emerging research in areas involving those

with potentially diminished capacity, the need to revisit ways in which we can support surrogates during research trials involving incapacitated individuals is needed. For example, as life expectancy has expanded, new types of gene-altering techniques (i.e. CRISPR/Cas 9) are being studied in those with neurodegenerative disorders (Yan, Tu, Li, & Li, 2017).

One of the primary principles in the Belmont Report includes beneficence in which persons should be protected from harm and efforts to secure their well-being are made (Biomedical & Behavioral Research MD., 1978). While great efforts have been made to ensure this ethical principle for individuals eligible for research participation is respected, it behooves us to treat surrogate decision-makers in the same respect by securing their well-being through interventions accounted for in research protocols. There is a need to identify effective interventions to minimize surrogate burden; this review is only a starting point. The interventions found through this review to help minimize surrogate burden provide a framework for researchers to consider when designing studies that likely involve surrogate decision-making, but the interventions need to be further tested and the framework further developed.

Initiatives towards this goal would be a noteworthy contribution to the evidence that will be necessary to expand opportunities for the participation of incapacitated persons in research. Expanding research opportunities for persons with end stage Alzheimer's disease and other neurocognitive disorders, head trauma, severe stroke, and psychiatric disorders has the potential to make scientific progress in the prevention and treatment of these diseases.

References

AAHRPP. (2014). Tip Sheet 26: Reviewing Research Involving Adult Participants with Diminished Functional Abilities Related to Capacity to Consent, *20037*(202). Retrieved from file:///C:/Users/user/Downloads/Tip_Sheet_26_Reviewing_Research_Involving_Adult_Participants_with_Diminished_Functional_Abilities.pdf

Alzheimer's Association. (2017). Treatment Ho. Retrieved from http://www.alz.org/research/science/alzheimers_treatment_horizon.asp

Batchelor-Aselage, M., Amella, E., Zapka, J., Mueller, M., & Beck, C. (2014). Research with dementia patients in the nursing home setting: a protocol for informed consent and assent. *IRB*, *36*(2), 14–20.

Berg, J. W. (1996). Legal and ethical complexities of consent with cognitively impaired research subjects: proposed guidelines. *J Law Med Ethics*, *24*(1), 18–35.

Biomedical, N. C. for the P. of H. S. of, & Behavioral Research MD., B. (1978). *The Belmont report: Ethical principles and guidelines for the protection of human subjects of research*. ERIC Clearinghouse.

Black, K. (2010). Promoting Advance Care Planning Through the National Healthcare Decisions Day Initiative. *Journal of Social Work in End-Of-Life & Palliative Care*, *6*(1–2), 11–26. http://doi.org/10.1080/15524256.2010.489220

Buller, T. (2015). Advance consent, critical interests and dementia research. *Journal of Medical Ethics*, *41*(8), 701–7. http://doi.org/10.1136/medethics-2014-102024

Candilis, P. J., Wesley, R. W., & Wichman, A. (1993). A survey of researchers using a consent policy for cognitively impaired human research subjects. *IRB*, *15*(6), 1–4.

Ditto, P. H., Danks, J. H., Smucker, W. D., Bookwala, J., Coppola, K. M., Dresser, R., … Zyzanski, S. (2001). Advance directives as acts of communication: a randomized controlled trial. *Archives of Internal Medicine*, *161*(3), 421–430. http://doi.org/10.1001/archinte.161.3.421

Dunn, L. B., Fisher, S. R., Hantke, M., Appelbaum, P. S., Dohan, D., Young, J. P., & Roberts, L. W. (2013). "Thinking about it for somebody else": Alzheimer's disease research and proxy decision makers' translation of ethical principles into practice. *Am J Geriatr Psychiatry*, *21*(4), 337–345. http://doi.org/10.1016/j.jagp.2012.11.01410.1097/JGP.0b013e31824362ca

Griffith, R., & Tengnah, C. (2010). Safeguarding research subjects who lack decision-making capacity. *Br J Community Nurs*, *15*(10), 508-509-512.

Hoffman J.D., D. E. and S. (1998). Symposium: "Conducting Medical Research on the Decisionally Impaired" Article: Proxy to Participation of the Decisionally Impaired in Medical Research--Maryland's Policy Initiative. *Journal of Health Care Law & Policy*.

Jennings, B. (2012). The Ethics of Meaning in Dementia Care.

Karlawish, J. H., & Casarett, D. (2001). Addressing the ethical challenges of clinical trials that involve patients with dementia. *J Geriatr Psychiatry Neurol*, *14*(4), 222–228.

Karlawish, J., Rubright, J., Casarett, D., Cary, M., Ten Have, T., & Sankar, P. (2009). Older adults' attitudes toward enrollment of non-competent subjects participating in Alzheimer's research. *Am J Psychiatry*, *166*(2), 182–188.

http://doi.org/10.1176/appi.ajp.2008.08050645

Kim, S. Y., Appelbaum, P. S., Jeste, D. V, & Olin, J. T. (2004). Proxy and surrogate consent in geriatric neuropsychiatric research: update and recommendations. *Am J Psychiatry*, *161*(5), 797–806.

Kim, S. Y., Kim, H. M., Ryan, K. A., Appelbaum, P. S., Knopman, D. S., Damschroder, L., & De Vries, R. (2013). How important is "accuracy" of surrogate decision-making for research participation? *PLoS One*, *8*(1), e54790. http://doi.org/10.1371/journal.pone.0054790

Macciocchi, S., & Alves, W. (1997). Ethical considerations in neuroclinical trials. *Neurosurgical Review*, *20*(3), 161–170. http://doi.org/10.1007/BF01105559

Merriam-Webster. (2017). Incapacitate | Definition of Incapacitate by Merriam-Webster. Retrieved August 15, 2017, from https://www.merriam-webster.com/dictionary/incapacitate

National Commission for the protection of Human Subjects of Biomedical and Behavioral Research. (1979). The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. *Federal Register*, *44*, 23192–23197. http://doi.org/10.1089/blr.1993.12.868

National Institutes of Health. (2009). Research Involving Individuals with Questionable Capacity to Consent: Points to Consider. Retrieved August 16, 2017, from https://grants.nih.gov/grants/policy/questionablecapacity.htm

OCEBM Levels of Evidence Working. (2011). *Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence*. *Oxford Centre for Evidence-Based Medicine*. Retrieved from http://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf

Office for Human Research Protections. (n.d.). Informed Consent FAQs | HHS.gov. Retrieved August 17, 2017, from https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/informed-consent/index.html

Office for Human Research Protections. (2009a). Attachment: Recommendations Regarding Research Involving | HHS.gov. Retrieved August 15, 2017, from https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2009-july-15-letter-attachment/

Office for Human Research Protections. (2009b). Code of Federal Regulations: Title 45, Part 46. Retrieved August 16, 2017, from https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

Sachs, G. A. (1994). Advance consent for dementia research. *Alzheimer Dis Assoc Disord*, *8*(Suppl. 4), 19–27.

Sachs, G. A. (1998). Informed consent for research on human subjects with dementia. AGS Ethics Committee. American Geriatrics Society. *Journal of the American Geriatrics Society*, *46*(10), 1308–10. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9777917

Shelton, A. K., Freeman, B. D., Fish, A. F., Bachman, J. A., & Richardson, L. I. (2015). A computer-based education intervention to enhance surrogates' informed consent for genomics research. *American Journal of Critical Care : An Official Publication, American Association of Critical-Care Nurses*, *24*(2), 148–55. http://doi.org/10.4037/ajcc2015983

Torke, A. M., Alexander, G. C., & Lantos, J. (2008). Substituted judgment: The

limitations of autonomy in surrogate decision making. *Journal of General Internal Medicine*. http://doi.org/10.1007/s11606-008-0688-8

Walters, T. P. (2009). The Mental Capacity Act--a balance between protection and liberty. *Br J Nurs*, *18*(9), 555–558.

Warren, J. W., Sobal, J., Tenney, J. H., Hoopes, J. M., Damron, D., Levenson, S., … Muncie Jr., H. L. (1986). Informed consent by proxy. An issue in research with elderly patients. *N Engl J Med*, *315*(18), 1124–1128. http://doi.org/10.1056/nejm198610303151804

Whittemore, R., & Knafl, K. (2005). The integrative review: updated methodology. *J Adv Nurs*, *52*(5), 546–553. http://doi.org/10.1111/j.1365-2648.2005.03621.x

Yan, S., Tu, Z., Li, S., & Li, X.-J. (2017). Use of CRISPR/Cas9 to model brain diseases. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. http://doi.org/10.1016/j.pnpbp.2017.04.003

Yarborough, M. (2002). Adults are not big children: examining surrogate consent to research using adults with dementia. *Camb Q Healthc Ethics*, *11*(2), 160–168.

Table 1. Summary of Findings

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Appelbaum, P. S. (2002). Involving decisionally impaired subjects in research: The need for legislation. *American Journal of Geriatric Psychiatry, 10*(2), 120-124.	To provide a position statement regarding a need for legislation for involving decisionally impaired subjects in research.	N/A	Advance Directive Legal/Regulatory	Suggested: For states with statutes authorizing surrogate consent to treatment, the power they convey should be extended to research consent. Suggested: States without statutes authorizing surrogate consent to research that presents minimal risk with some benefit should develop them.	N/A: Position Statement
Batchelor-Aselage, M., Amella, E., Zapka, J., Mueller, M., & Beck, C. (2014). Research with dementia patients in the nursing home setting: A protocol for informed consent and assent. *IRB: Ethics and Human Research, 36*(2), 14-20.	To describe the implementation of a consent protocol that can be used when recruiting participants that are decisionally incapacitated.	N/A	Institutional Review Board	Suggested: Obtain IRB approval to access medical records for patients to determine recruitment eligibility prior to contacting the representatives of persons with dementia. This limits contacting surrogates of patients that are not eligible.	N/A: Protocol Development

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Berg, J. W. (1996). Legal and ethical complexities of consent with cognitively impaired research subjects: Proposed guidelines. *Journal of Law, Medicine & Ethics, 24*(1), 18-35.	To examine the historical evolution of constraints on human experimentation and explore the contours of surrogate decision making.	N/A	Advance Directive Institutional Review Board	Suggested: Allow competent subjects to consent in advance and designate a surrogate for future research participation purposes once the subject is no longer competent. Suggested: Allow incompetent subjects to enroll in greater than minimal risk studies as long as their advance consent indicated this designation. However, allow the surrogate to withdrawal the subject from the research if they believe the subject would have withdrawn themselves. Surrogate: In cases of complicated research studies, the IRB might require investigators to employ neutral educators to ensure surrogate comprehension of the study.	N/A: Guideline Proposal
Cahill, M., & Wichman, A. (2000). Research involving persons with cognitive impairments: Results of a survey of Alzheimer disease	To assess policies or guidelines used by Alzheimer's Disease Centers with regard to research involving cognitively impaired subjects.	N/A	Expert Consultant	Suggested: A representative from the bioethics committee should be available to consult in any situation in which the principle investigator, IRB, or surrogate desires further ethical advice.	N/A: Policy/Guideline Review

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
research centers in the United States. *Alzheimer Disease and Associated Disorders, 14*(1), 2-27.					
Dunn, L. B., Fisher, S. R., Hantke, M., Appelbaum, P. S., Dohan, D., Young, J. P., & Roberts, L. W. (2013). "Thinking about it for somebody else": Alzheimer's disease research and proxy decision makers' translation of ethical principles into practice. *American Journal of Geriatric Psychiatry, 21*(4), 337-345.	To examine whether and to what degree surrogates differentiate between consenting dementia patients for research based on "substituted judgment" or based on the patient's best interests.	Interviewed 40 surrogate decision makers to assess their different approaches to decision making for the patient.	Direct Care of Surrogate	Suggested: Offer services to help make the research participation more convenient and rewarding for the participant and surrogate. Services include respite care, transportation, education, etc. Incorporate these services into the research protocol.	Level 3: Non-random Sample
Fletcher, J. C., Dommel, F. W., & Cowell, D. D. (1985). A trial policy for the intramural programs of the National Institutes of Health: Consent to research with impaired	Describe a trial policy for the consent process with impaired human subjects for the intramural research programs of the	Trial of a policy for the intramural research of the NIH.	Advance Directive	Actual: Policy that incorporates Durable Power of Attorney (DPA) appointment by a prospective research subject, determination of when the DPA should be used, and DPA ability to approve the incapable subject's enrollment into a	N/A: Policy Development

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
human subjects. *IRB: Ethics and Human Research, 7*(6), 1-6.	National Institute of Health (NIH).			study with no more than minimal risk.	
Fost, N., & Robertson, J. (1980). Deferring consent with incompetent patients in an intensive care unit. *IRB: Ethics and Human Research, 2*(7), 5-6.	To describe instances when "deferred consent" may be an applicable approach for enrolling incompetent patients in the intensive care unit (ICU) into research studies.	N/A	Institutional Review Board	Suggested: Allow for "deferred consent" for research involving incompetent subjects in the ICU. Surrogates would be notified that an experimental procedure was being used but requests for surrogate consent would be deferred until 48 hours after the start of the study.	N/A: Case Study
Hoffmann, D. E., & Schwartz, J. (1998). Proxy consent to participation of the decisionally impaired in medical research -- Maryland's policy initiative. *Journal of Health Care Law & Policy, 1*(1), 123-153.	To provide working group recommendations regarding surrogate consent for participation of the decisionally impaired in medical research.	N/A	Advance Directive	Suggested: In the absence of direct medical benefit with increased risk, relying on the surrogate's "substituted judgment" should not be enough to approve enrollment of a decisionally impaired subject in research.	N/A: Policy Development
Howe, E. (2012). Informed consent, participation in research, and the Alzheimer's patient.	To discuss the ethical issues of informed consent and participation in	N/A	Enhanced Communication	Suggested: Encourage patients with Alzheimer's disease to discuss their future wishes as fully as possible with their chosen surrogate decision	N/A: Expert Commentary

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Innovations in Clinical Neuroscience, 9(5-6), 47-51.	research involving Alzheimer's patients.			maker before they enter a research study.	
Kapp, M. B. (1994). Proxy decision making in Alzheimer disease research: Durable powers of attorney, guardianship, and other alternatives. *Alzheimer Disease and Associated Disorders, 8*(4), 28-37.	To discuss potential surrogate decision-making mechanisms regarding research participation in light of ethical and legal concerns.	N/A	Advance Directive Institutional Review Board	Suggested: Heightened IRB involvement for research protocols contemplating the use of dementia patients. This would include an extra level of review to verify an acceptable risk/benefit ratio. Suggested: Encourage individuals in early stages of Alzheimer's disease (or before) to complete an advance directive where they indicate a surrogate to make future research participation decisions for them. The individuals should communicate their values and preferences to their chosen surrogate.	N/A: Framework Development
Karlawish, J. H., & Casarett, D. (2001). Addressing the ethical challenges of clinical trials that involve patients with dementia. *Journal of Geriatric*	To determine whether and how patients' cognitive impairments and the caregiving experience impact on their decision making	N/A	Direct Care of Surrogate Enhanced Communication	Suggested: Minimize travel to the study site by having the research team make home visits. Suggested: Research protocol to include ensuring that the subject (and/or surrogate) receive	N/A: Literature Review

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Psychiatry and Neurology, 14, 222-228.	and what kinds of research justify research risks.			feedback about the intervention that the subject received and the results of the study.	
Karlawish, J. H., Knopman, D., Clark, C. M., Morris, J. C., Marson, D., Whitehouse, P. J., & Kawas, C. H (2002). Informed consent for Alzheimer's disease clinical trials: A survey of clinical investigators. *IRB: Ethics and Human Research, 24*(5), 1-5.	To better understand the process of informed consent for Alzheimer's disease (AD) clinical trials.	Surveyed 39 AD clinical research sites.	Institutional Review Board	Suggested: Assess caregiver decision-making capacity. Already used at 4 sites that responded to survey. Suggested: Test whether materials used to describe study for enrollment purposes enhance caregiver comprehension and satisfaction with recruitment and informed consent process.	Level 3: Non-random Sample
Karlawish, J., Rubright, J., Casarett, D., Cary, M., Have, T. T., & Sankar, P. (2009). Older adults' attitudes toward enrollment of non-competent subjects participating in Alzheimer's research. *American Journal of*	To explore older persons' attitudes about enrolling non-competent patients with Alzheimer's disease in research without presenting any potential benefit to participants.	Interviewed 538 subjects greater than 65 years old to assess their perception of research with non-competent patients.	Advance Directive	Suggested: Grant surrogate leeway over advance consent. This includes enrollment of non-competent patients in research on the patient's disease even if that research will not benefit the study participant's health but might benefit others instead.	Level 3: Non-random Sample

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Psychiatry, 166(2), 182-188.					
Kim, S. Y., Appelbaum, P. S., Jeste, D. V., & Olin, J. T. (2004). Proxy and surrogate consent in geriatric neuropsychiatric research: Update and recommendations. *American Journal of Psychiatry, 161*(5), 797-806.	To discuss, critique, and provide recommendations for clear legal and regulatory policy for research involving decisionally incapable adults.	N/A	Institutional Review Board	Suggested: For studies that involve no benefit for the subject, a more conservative risk-benefit analysis is required. Suggested: IRBs have a more stringent risk-benefit analysis if there is a proposal that calls for surrogate consent.	N/A: Policy Development
Kim, S. Y., & Kieburtz, K. (2006). Appointing a proxy for research consent after one develops dementia. *Neurology, 66*, 1298-1299.	To review the current literature related to appointing a surrogate for research consent for patients with dementia.	N/A	Advance Directive	Suggested: Consider alternatives to relying on advance directives to indicate research preferences or designate a surrogate because only a minority of persons complete an advance directive even for treatment decisions.	N/A: Literature Review
Miller, B. L. (1982). Autonomy and Proxy Consent. *IRB: Ethics and Human Research, 4*(10), 1-8.	To determine whether, and if so to what extent, surrogate consent is consistent with the right to autonomy.	N/A	Advance Directive	Suggested: Advance directives for research purposes should be used by those with capacity to express their research participation preferences before they lose decisional capacity.	N/A: Concept Analysis

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Pape, T. L., Jaffe, N. O., Savage, T., Collins, E., & Warden, D. (2004). Unresolved legal and ethical issues in research of adults with severe traumatic brain injury: Analysis of a ongoing protocol. *Journal of Rehabilitation Research & Development, 41*(2), 155-174.	To identify, define, and clarify the unresolved legal and ethical issues regarding research involving adults with traumatic brain injury (TBI).	N/A	Institutional Review Board	Actual: Procedure for defining and determining lack of capacity and return to capacity was incorporated into research procedures involving subjects with TBI. Weekly "consciousness screening" and "determination of decision-making capacity" placed in consenting procedures of research study.	N/A: Protocol Analysis
Prentice, E. D., Antonson, L., Leibrock, L. G., Prabhu, V. C., Kelso, T. K., & Sears, T. D. (1994). An update on the PEG-SOD study involving incompetent subjects: FDA permits an exception to informed consent requirements. *IRB: Ethics and Human Research, 16*(1/2), 16-18.	To describe the IRB approval algorithm for use in a randomized control trial to investigate a treatment for severe closed head injury.	N/A	Institutional Review Board	Suggested: Allow for "deferred consent" for research involving subjects with severe closed head injury. Algorithm includes attempts to identify the patient, contact their surrogate, obtain retrospective consent from the surrogate, withdrawal from study if surrogate refuses to consent.	N/A: Protocol Development

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
Sachs, G. A. (1994). Advance consent for dementia research. *Alzheimer Disease and Associated Disorders, 8*(4), 19-27.	Examine dementia research issues and the advance consent model.	N/A	Advance Directive	Suggested: Designation of surrogate for research decision-making could be a part of the advance consent process, with or without specific guidelines regarding what decisions that surrogate should later make. Suggested: Advance consent for research could be in the form of a written document or conversations with an individual. Should not require a formal advance directive for dementia research to take place.	N/A: Model Analysis
Sachs, G. A. (1998). Informed consent for research on human subjects with dementia: AGS ethics committee position statement. *Journal of American Geriatric Society, 46*(10), 1308-1310.	To provide position statements regarding informed consent for dementia research.	N/A	Advance Directive	Suggested: Advance directives for research purposes should be used by those with capacity to express their research participation preferences before they lose decisional capacity. These preferences should be respected in the future. Suggested: Limit research that does not provide direct benefit to the subject but exposes them to more than minimal risk to those subjects with an advance directive indicating their	N/A: Position Statement

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
				willingness to be enrolled in such studies. Suggested: Allow surrogates to refuse to enroll subjects or to withdraw a subject from an ongoing study because they believe the study is not in the best interests of the subject, even if that decision goes against the subject's advance directive.	
Shelton, A.K., Freeman, B.D., Fish, A.F., Bachman, J.A., & Richardson, L.I. (2015). A computer-based intervention to enhance surrogates' informed consent for genomics research. American Journal of Critical Care, 24(2), 148-155.	To examine the effectiveness of a computer-based education module on surrogates' understanding of the informed consent process for genomics research.	Provided an education module to experimental group (n= 65), then compared their test results on informed consent with control group (n= 69).	Enhanced Communication	Actual: Add computer-based education modules to conventional approaches for obtaining informed consent from surrogates in the ICU. Module in this study included information on the essential elements of informed consent, surrogate consent, research in general, and genomics research.	Level 2: Randomized Study
Stocking, C. B., Hougham, G. W., Baron, A. R., & Sachs, G. A. (2003). Are the rules for research with subjects with dementia	To examine the recommended additional protections for persons with dementia included in clinical research.	Surveyed 38 research authors regarding consent	Legal/Regulatory	Suggested: Having a standardized surrogate selection process when not indicated by the patient prior to their incapacitated state. Survey revealed roughly half of	Level 3: Non-random Sample

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
changing? *Neurology, 61*, 1649-1651.		procedures and trial risks.		participants perceived a standardized surrogate as a means of increased patient protection - Study researchers hypothesize the mixed feedback was a result of potential added workload that would result.	
Warren, J. W., Sobal, J., Tenney, J. H., Hoopes, J. M., Damrom, D., …… Muncie, H. L. (1986). Informed consent by proxy: An issue in research with elderly patients. *The New England Journal of Medicine, 315*(18), 1124-1128.	To study the decisions of surrogates regarding whether to permit incompetent patient's participation in a study involving minimal risk.	Interviewed 151 surrogates for their perspective using a standardized questionnaire	Enhanced Communication	Suggested: Patient should be excluded from study participation if the surrogate answers "no" when asked whether they think the patient would consent to the study if he or she were competent, even if the surrogate is willing to consent.	Level 3: Non-random Sample
Wendler, D., Martinez, R. A., Fairclough, D., Sunderland, T., & Emanuel, E. (2002). Views of potential subjects towards proposed regulations for clinical research with adults unable to	To assess healthy individuals' attitudes toward proposed safeguards related to the consent process for research with adults unable to consent.	Interviewed 246 individuals to assess their attitudes towards proposed safeguards	Advance Directive	Suggested: Incorporate statements about individuals' research preferences on clinical advance directives. This may also prompt individuals to discuss their preferences with their families. Suggested: Allow surrogates to override the preferences	Level 3: Non-random Sample

Author, Date, Title	Purpose	Study Design	Intervention Type	Intervention	Level of Evidence (OCEBM Levels of Evidence, 2011)
consent. *American Journal of Psychiatry, 159*(4), 585-591.				specified in an advance directive regarding research if it is in the best interest of the patient.	
Wendler, D., & Prasad, K. (2001). Core safeguards for clinical research with adults who are unable to consent. *Annals of Internal Medicine, 135*(7), 514-523.	To compare safeguards for clinical research with adults who unable to consent to compare points of consensus and differences.	N/A	Expert Consultant	Suggested: Utilize "consent monitors" when the research involves greater than minimal risk. Consent monitor use is intended to ensure enrollment is consistent with the patient's preferences and interests.	N/A: Guidelines Comparison

The EFFECT (**E**nd-o**F**-li**FE**-**C**ommunica**T**ion) Study:

The Acceptability, Feasibility, and Potential Impact of Using Mortality Prediction Scores

for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

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Abstract

Background- Uncertainties in prognosis remain a barrier to end-of-life (EOL) communication in the adult intensive care unit (ICU). Providers often base assessments of prognosis on experience rather than on objective measures, and may be unaware of patients' wishes regarding EOL care. These factors may lead to prolonged dying and over-use of intensive resources. Mechanisms for increasing the accuracy and timeliness of EOL care goal communication are needed.

Objective- This study evaluated 1) the acceptability and feasibility of providers' use of patient mortality prediction scores as part of routine practice, and 2) providers' intentions to change practice, related to goals-of-care communication, as a result of awareness of the scores.

Method- An explanatory mixed-methods approach was used. Using the Sequential Organ Failure Assessment (SOFA), mortality prediction scores were provided to ICU providers (n=12) for patients admitted (n=145) under their care for ten consecutive days. Subsequently, the providers completed a questionnaire regarding the acceptability and feasibility of using the scores as part of their workflow and practice. Follow-up interviews (n= 7) were used to further understand questionnaire responses and gain insight into providers' perceptions regarding EOL practice changes as a result of having the scores readily available.

Results- Overall, use of mortality risk prediction scores as part of routine workflow and practice was found to be acceptable and feasible – providers agreed to participate, patient

mortality risk were evaluated, and overall, participants found use of daily mortality prediction scores possible in their setting. However, there was some disagreement related to the use of SOFA scores as an effective way for determining patient mortality risk. Based on themes that emerged from interviews, providers with limited ICU experience were eager and accepting of the mortality risk scores while those with vast experience found the scores to be an adjunct to their own intuition; though all acknowledged the benefit of looking at daily scores or 'trends'. The most substantial of all themes identified was the need to consider SOFA scores in relation to patient context; a number alone should not determine mortality risk and whether a goals-of-care conversation needs to occur.

Discussion- Overall, participants indicated that using mortality prediction scores as part of their daily workflow was acceptable and feasible. Use of SOFA scores for potentially increasing EOL goals-of-care conversations appears to be most beneficial for providers with limited ICU experience. Large-scale studies are needed to determine the effect of using mortality risk predictions on patient EOL outcomes.

Key Words: Poor Prognosis, Mortality Risk, Intensive Care, End-of-Life, Goals of Care, Severity of Illness, SOFA

Introduction

While healthcare teams recognize that profoundly ill patients in adult intensive care units (ICUs) may die, many families are caught by surprise when their loved one dies in a setting with the most advanced technology and intense care available. ICU deaths account for about 20% of patient deaths in US hospitals and this rate is increasing[1] due in part to deficiencies in end-of-life (EOL) care communication that can compromise quality of EOL care[2] and increase resource utilization.[3,4] Previous studies suggest that communication about EOL goals-of-care is infrequent among healthcare providers, patients, and families; often occurs late in the course of illness[5,6]; and relies on family members to act as patient surrogates in discussions.[7] Furthermore, despite advances in healthcare quality, family members remain more dissatisfied with communication in the ICU than with other aspects of care.[8,9]

Increased severity of illness (SOI) scores are associated with a significant increase in the relative risk of hospital death.[10] Family meetings about EOL care can improve family satisfaction with the EOL experience;[11] however, uncertainties in prognosis (e.g., SOI) are a barrier to EOL communication in the ICU.[12] SOI mortality risk prediction scores are not routinely calculated and there is little research examining their use for improving EOL goals-of-care communication. There are multiple valid and reliable SOI scoring systems that are available for predicting ICU mortality,[13] but there is no clear consensus about how or when to use them in patient care and provider-patient/family communication.

Unfortunately, no evidence-based standard of care exists for EOL goals-of-care communication in adult ICUs. Mechanisms for increasing the timeliness and frequency of

discussions about EOL goals-of-care are needed.[14,15] As an initial step in addressing this gap, this study aimed to determine the acceptability, feasibility, and potential impact of using SOI mortality risk prediction scores for initiating EOL goals-of-care communication in the adult ICU.

The specific aims of this study were to:

1. Evaluate four valid SOI instruments to determine which instrument, or combination of instruments, was the best fit for the study site, given providers' perceived feasibility of use.

2. Evaluate the acceptability and feasibility of having providers use SOI mortality prediction scores for their patients as part of routine workflow and practice.

3. Evaluate providers' intentions to change their practice related to goals-of-care communication with patients and/or their families as a result of awareness of SOI mortality prediction scores.

Methods

This study used a mixed-methods explanatory design and took place in a medical-respiratory ICU (MRICU) at a large academic medical center in Richmond, Virginia. Patients are admitted to this unit for acute illnesses but commonly exhibit chronic medical conditions as well. Two medical teams provide patient care, each comprised of an attending physician, a fellow physician, and a mix of interns, residents, acute care nurse practitioners (ACNPs), and physician assistants (PAs). These teams provide care for patients throughout their ICU stay, or until the end of the provider's assigned time in the MRICU. This study was approved by the Institutional Review Board at Virginia Commonwealth University and the Medical University of South Carolina.

To address Aim 1, attending physicians, fellow physicians, ACNPs, and PAs working in the MRICU were recruited (target N=6) for a focus group via email as they are expert providers responsible for medical care of patients admitted to the unit. Based upon an integrative review completed by the principal investigator[13] (PI) and implementation feasibility within the study setting, four SOI scoring systems (MPM III, APACHE IV, SOFA, SAPS III) were presented to the focus group participants. The PI assumed the moderator role to keep the flow of the conversation on target.[16] Following a brief introduction about the purpose of the group, participants were asked to discuss perceived feasibility of use for each SOI system. Based on discussion among the participants, the PI then requested consensus on the SOI system of choice. Participants were also asked to complete a demographic form in Research Electronic Data Capture (REDCap). Descriptive statistics were used to analyze the demographic data.

To address Aim 2, an explanatory mixed-methods approach consisting of a quantitative questionnaire (target N=12) and a qualitative follow-up interview (target N=6) were used to determine if providers could feasibly use SOI mortality prediction scores as part of their routine in the ICU and evaluate their perceptions of acceptability, feasibility, and potential impact of using the SOI scores. All MRICU fellows, residents, and intern physicians, as well as all ACNPs and PAs, were recruited on an ongoing basis via email and face-to-face for this portion of the study; attending physicians were excluded due to their short length of rotations in the ICU. The PI or research assistant (RA) calculated mortality risk percentages for MRICU patients admitted under the care of study participants for ten consecutive days, using the free web-based calculator available to the public. To ensure consistency and congruency with the chosen system's

published protocol, the PI developed a user's manual for the PI and RA to use. The PI and RA reviewed a random selection of 25% of each other's calculations to examine inter-rater reliability. Calculated scores were limited to three days per patient for feasibility purposes. Mortality risk percentages were shared with participants on a card each morning prior to team rounding. Laminated reference cards were provided during study enrollment for interpretation of the scores. Following the ten-day period, participants received a link to a REDCap questionnaire (Figure 1) asking about acceptability and feasibility of using the SOI mortality risk prediction scores as part of their workflow and practice.[17] Results of the questionnaire were retrieved from REDCap as descriptive statistics. Additionally, participants who did not also participate in the focus group were asked to complete the same demographic form in REDCap.

To further explain the acceptability and feasibility questionnaire results and to address Aim 3, all participants who received scores and completed a questionnaire were contacted approximately one week later asking for their participation in a follow-up interview. Those agreeing to participate were scheduled for face-to-face interviews with the PI in a private setting using open-ended questions. Although specific topics were covered during the interview (Figure 2), the PI allowed the interview to move freely from topic to topic, allowing the participant's cues to determine the flow.[18] Each interview was voice recorded digitally and transcribed verbatim. A qualitative descriptive approach was used to analyze the interview data.[19,20] To accomplish this, a fluent process occurred wherein transcripts were reviewed following every 2-3 interviews; they were read repeatedly to achieve immersion, exact words that captured key thoughts were highlighted, notes of impressions were made in the margins, and key themes were

identified that emerged from the notes. As these themes emerged, the PI asked for confirmation from subsequent participants. The resulting themes from all transcripts were defined and exemplars were identified. To ensure the resulting themes were credible, the PI discussed the findings with experts who were familiar with the subject under study. Lastly, final themes and exemplars were examined to help explain the results of the acceptability and feasibility questionnaire.

Results

Participant Characteristics

The age of all participants combined ranged from 26-51, with a majority being female (60%) and white (93%). However, there was greater diversity in discipline of practice with a total of four ACNPs, one PA, and ten physicians (four interns, two residents, two fellows, and two attendings) participating (total n=15). Additionally, there was diversity in years of practice in the ICU setting and previous EOL experience (Table 1).

Table 1. Study Participant Demographics

Variable	Statistic
Gender	
Female	60% (9/15)
Male	40% (6/15)
Race	
American Indian or Alaska Native	0%
Asian	6.7% (1/15)
Black or African American	0%
Native Hawaiian or Other Pacific Islander	0%
White	93.3% (14/15)
Other	0%
Health Discipline	
Acute Care Nurse Practitioner	26.7% (4/15)
Physician Assistant	6.7% (1/15)
Physician	66.7% (10/15)
Intern	40% (4/10)
Resident	20% (2/10)
Fellow	20% (2/10)
Attending	20% (2/10)
Years of Practice in an ICU Setting	
Less than one year	26.7% (4/15)
One year	0% (0/15)
Two years	6.7% (1/15)
Three years	26.7% (4/15)
Four years	13.3% (2/15)
Greater than four years	26.7% (4/15)
Previous Experience with EOL	
None	6.7% (1/15)
Personal (i.e. loss of someone close to you)	60% (9/15)
Professional	73.3% (11/15)
Coursework on EOL care	45.5% (5/11)
Hands-on experience with patients during their EOL	81.8% (9/11)

Focus Group

Two ACNPs, two attending physicians, and one fellow physician participated in

the exploratory SOI instrument selection focus group (n=5); an additional ACNP was

unable to attend due to scheduling conflicts. Following discussion, the Sequential Organ

Failure Assessment (SOFA) was chosen by the group as the most feasible to use for the

study site given its free and easy online access, limited number of variables required,

ability to provide admission and daily scores, and increasing use (and therefore,

recognition among providers) due to its role in the updated sepsis guidelines.[21] SOFA

assigns 1-4 points to the following organ systems depending on the level of organ

dysfunction: circulatory, respiratory, renal, hematologic, hepatic, and central nervous

system.[22] Data required for the calculation are typically collected upon ICU admission,

and daily thereafter throughout the ICU stay, with the most abnormal values for each day

being used for scoring.[23]

Acceptability and Feasibility Questionnaire

Two of the ACNPs who participated in the focus group also participated in the

second phase of the study. These ACNPs, along with two additional ACNPs, one PA,

four interns, two residents, and one fellow physician (total n=12) received SOI mortality

risk prediction scores (total n= 145) for ten days for patients admitted under their care.

Scores were calculated for 70 patients total with an average of 2.1 daily scores provided

per patient; some patients were transferred out of the unit or died which prohibited a full

three days of calculations. Additionally, some providers simultaneously enrolled in the

study cared for the same patients allowing for concurrent score calculations. Patient

census was higher than expected during the study period, which enabled participants to

have greater exposure to the SOI scores than originally expected. On average,

participants received scores for 2.6 patients per day. When reviewing a random sample of

each other's calculations, there were two SOFA scores in which the PI and RA had

conflicting calculations; these were resolved by a simultaneous review of the various

SOFA variables. Questionnaire data (Figure 3) revealed that overall, participants found use of SOI mortality prediction scores for their patients as part of routine workflow and practice to be acceptable and feasible. However, there was some disagreement, particularly related to the use of the scores as an effective way for determining patient mortality risk that warranted exploration.

The PI and RA spent an average of 12 minutes per patient to calculate SOFA scores using the online calculator available (http://clincalc.com/icumortality/sofa.aspx); with the additional time required to check 25% of each other's calculations, the total time spent by the PI and RA in calculating scores was approximately 20 hours. Additionally, calculations required early arrival to the unit so scores could be calculated prior to team rounding each morning.

Face-to-Face Interviews

Seven of twelve participants who received daily SOI scores participated in a follow-up interview. A summary of participant responses follows, organized according to main themes that correspond with the purpose of this study, then divided into subthemes, identified throughout the transcriptions:

Effects on clinical decision-making

Context. The most substantial of all themes identified, participants reported the need to consider SOFA scores in relation to patient context. Respondents suggested that a number alone should not determine mortality risk and whether a goals-of-care conversation should occur, as there could be contextual issues related to the score being elevated. The following example illustrates this theme:

There was a patient, for example, that was kind of middle of the road, so probably

around a 50% mortality risk, but they had a procedure done and they were

intubated and were put on 100% [oxygen on the ventilator]. They were bronched

or something.

Level of experience. Participants with limited ICU experience (less than one

year), either personally or professionally, were eager and accepting of SOI mortality risk

prediction scores provided for them. This was due to the ability of SOFA scores to detect

nuances that they did not always see in the clinical picture alone and because they

experienced instances where SOFA scores they received that differed from their

subjective assessment were more accurate. Additionally, those with less experience

indicated that high mortality risk scores pushed them to have earlier goals-of-care

conversations than they would have had if they not had the score. The following

examples illustrate this theme:

One time when I should have trusted it and didn't, we had one patient who we had

jump one day in his score and the only thing that really changed was that his

bilirubin had gone up. I was like I don't know, he was still pretty well and then of

course that ended up not going very well.

It allowed me to take a moment and be like I think we should have that talk

instead of waiting a day or two to see what happened kind of.

In contrast, participants with vast EOL experiences found the scores to confirm their own

judgment or intuition. Because the scores matched their subjective assessments, the

scores were trusted and provided a level of confidence to coincide with their thoughts;

however, some participants said they might distrust the scores if they differed drastically

from their assessment using their typical strategies (i.e. trends in labs and vitals and previous experiences with similar diagnoses). Additionally, those with more experience voiced concerns that although those with less experience could benefit from having the scores, they might be reckless with the results by not considering the whole picture and change their level of care or have premature goals-of-care conversations.

Trends. All participants spoke of the value of looking at trends in data to examine the 'big picture'; an admission SOI score alone would not be as helpful as it simply provides a 'snapshot.' Participants were able to follow trends in daily scores and indicated that they followed the trends as a way for determining whether treatment interventions were useful or not.

More than mortality prediction. Most participants also described benefits of using SOFA beyond, but related to, mortality risk. Considering the individual system scores within the SOFA calculation was beneficial in identifying specific areas in which additional intervention might or might not be beneficial. This theme is related to 'context' too in that individual components of SOFA can provide context for what body system is causing an increase in mortality risk. Additionally, two of the participants mentioned the idea of using SOFA scores on the general floors; with the intent to look at scores before transfer to an ICU to prevent an ICU admission if not in alignment with the patient's goals-of-care.

Feasibility and acceptability.

Approval of SOFA. All of the participants indicated they were at least somewhat familiar with SOFA. Participants also specified their acceptance of SOFA to be used in calculating SOI scores and its benefit over tools that calculate admission scores only.

However, the importance of educating users of the scores was highlighted since it could 'fall into the hands of' a less-experienced provider. Suggestions were made to provide SOFA scores in the electronic health record (EHR) that required users to click on it to learn the score's conversion to a mortality risk prediction percentage and individual system scores.

Time as a consideration. Many participants acknowledged the time required for someone to calculate SOFA scores and indicated they would not be able to perform the calculations daily. Suggestions were made to have SOFA scores auto-generated in the EHR. The following example illustrates this theme:

> *Being provided the score was a great thing because I did not feel like I had the*
> *time to calculate myself on my patients.*

Promising opportunity. Most participants revealed they were excited about their participation in the study, appreciated getting the scores each day, and looked forward to seeing how the results of the study might change current practice. The following example illustrates this theme:

> *It was awesome.*

EOL care planning and practice.

'Fixing' everyone. Most of the physician participants spoke of their desire to 'fix' everyone, that despite the realization that a patient was likely going to die, moving away from curing was extremely difficult; 'facing reality' as one participant indicated. This was in contrast to reports from two ACNPs who highlighted their years of bedside nursing as the likely key to their ability to move from 'curing to caring' with those 'very sick' patients early in the course of their admission. Overall, however, participants with

more experience expressed that despite the difficulty, they are already having conversations with families about poor prognosis on a consistent basis. However, although the scores gave them confidence in their assessment of the patient's risk, they did not change the frequency of goals-of-care conversations for them.

Communication with patient/family. Many participants indicated that sensitivity is needed when discussing mortality risk with patients and/or their families. A few participants emphasized that numbers should not be reported to families as they can distract them and provide false reassurance. Additionally, they indicated that communication with family about patient prognosis could positively affect the EOL care provided. The following example illustrates this theme:

> *A couple of times I couldn't talk because we had family around and I didn't bring it [mortality risk score] up when family were around. That would be more like a family meeting kind of situation.*

Collaboration with team. Many participants indicated that they discussed their SOFA scores with the interdisciplinary team during daily rounds and the discussion was well received by the team. This gave them the opportunity to talk with their peers about different treatment or care options that could impact on the patient's trajectory. Additionally, many indicated their approval of having the scores be a formal part of daily rounds. The following example illustrates this theme:

> *I think it was generally well received. The people seemed open to it.*
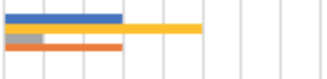
Looking at the Big Picture. A couple of the participants contributed the idea that our focus should be beyond the ICU admission; instead it should be on the patient's quality of life even after their ICU stay. They highlighted the need to have goals-of-care

conversations with all patients with chronic disease regardless of whether their risk for

mortality during that hospitalization was low.

Explanatory Connections

        Resulting themes and corresponding exemplars helped to better understand results

of the acceptability and feasibility questionnaire (Figure 3).

Figure 3. Connected Quantitative and Qualitative Findings

Discussion

Increasing the timeliness of EOL goals-of-care communication in the adult ICU is warranted to ensure care is in alignment with the wishes of the patient. In addition to the benefits for the patient, proactive communication reduces anxiety, depression, and post-traumatic stress disorder for family members whose loved one dies in the ICU.[24] Furthermore, decreasing EOL resource utilization may decrease emotional and financial strain experienced by patients and families.[25]

Implementation of future studies using mortality risk scores in the ICU may fail if provider perceptions of their use is not considered first.[26] This study found SOFA to be a feasible and acceptable tool for calculating mortality risk prediction scores; it was easy to use, widely accepted and trusted, and should be considered for use in future studies in this area of research. Overall, participants indicated that using mortality prediction scores as part of their daily workflow was acceptable and feasible. However, interview data indicated that context must not be forgotten when doing so; scores alone should not be used to initiate EOL goals-of-care communication without first considering what contributed to the score. In addition, without integrating SOFA scoring into the EHR, the feasibility of its use in clinical practice will likely be low due to limited time for providers to calculate the scores themselves.

The use of SOFA mortality risk scores for potentially increasing EOL goals-of-care conversations appears to be most beneficial for providers with limited ICU experience. This may result from their limited intuition gained thus far in the setting. Because more experienced providers indicated that the scores only provided confidence in their ability to perform accurate subjective assessments of patient mortality risk, it does

not seem that the scores will increase their probability of meeting with patients and families earlier. According to their reports, these conversations are already occurring; an effort for which these providers should be commended. This could be in part due to the chronic nature of MRICU patients and frequency of EOL occurrences in that unit. However, it warrants further investigation to learn what would happen if the scores became part of their everyday evaluation and they were able to witness scores actually predicting outcomes.

This study is the first known attempt at examining the acceptability and feasibility of using SOI mortality risk scores for initiating EOL goals-of-care communication. Although successful in meeting the objectives of the study, difficulties experienced are worth mentioning. Recruitment for Aim 2 work took longer than expected. Although a few providers responded to the recruitment email within one week, face-to-face time was required for recruitment of the remaining participants. One month was required to obtain the targeted number of participants. A fear of time available to participate during their busy ICU rotation was the noted barrier; however, when participants learned they would not have to calculate the scores themselves, many agreed to participate immediately. Additionally, although the target number of participants recruited for Aim 3 follow-up interviews was exceeded, it took two months to get all participants scheduled for their interviews due to their busy schedules.

The single ICU used for this study may limit the generalizability to other types of ICUs. Additionally, the small nature of this study provides acceptability and feasibility information only and further limits generalizability. However, the information learned

may guide future large-scale studies needed to determine the effect of using mortality risk predictions on patient EOL outcomes.

Conclusion

The use of mortality risk prediction scores as part of routine workflow and practice for ICU providers was found to be acceptable and feasible and positively impact some providers' intentions to change practice, related to goals-of-care communication, as a result of awareness of the scores. Large-scale studies are needed to determine the effect of using mortality risk predictions on patient EOL outcomes.

References

1.   Zomorodi, M., & Bowen G. Value-behavior congruency when providing end-of-life care in the intensive care unit. *J Hosp Palliat Nurs*. 2010;12(5):295-302.
2.   Glavan BJ, Engelberg RA, Downey L, Curtis JR. Using the medical record to evaluate the quality of end-of-life care in the intensive care unit. *Crit Care Med*. 2008;36(4):1138-1146. doi:10.1097/CCM.0b013e318168f301.
3.   Quenot JP, Rigaud JP, Prin S, et al. Impact of an intensive communication strategy on end-of-life practices in the intensive care unit. *Intensive Care Med*. 2012;38(1):145-152. doi:10.1007/s00134-011-2405-z.
4.   Curtis JR, Rubenfeld GD. Improving palliative care for patients in the intensive care unit. *J Palliat Med*. 2005;8:840-854. doi:10.1089/jpm.2005.8.840.
5.   Curtis JR, Engelberg RA, Bensink ME, Ramsey SD. End-of-life care in the intensive care unit: Can we simultaneously increase quality and reduce costs? *Am J Respir Crit Care Med*. 2012;186:587-592. doi:10.1164/rccm.201206-1020CP.
6.   McNeely PD, Hébert PC, Dales RE, et al. Deciding about mechanical ventilation in end-stage chronic obstructive pulmonary disease: How respirologists perceive their role. *CMAJ*. 1997;156:177-183.
7.   Curtis JR, White DB. Practical guidance for evidence-based ICU family conferences. *Chest*. 2008;134(4):835-843. doi:10.1378/chest.08-0235.
8.   Stricker KH, Kimberger O, Schmidlin K, Zwahlen M, Mohr U, Rothen HU. Family satisfaction in the intensive care unit: What makes the difference? *Intensive Care Med*. 2009;35(12):2051-2059. doi:10.1007/s00134-009-1611-4.
9.   Heyland DK, Rocker GM, Dodek PM, et al. Family satisfaction with care in the intensive care unit: results of a multiple center study. *Crit Care Med*. 2002;30(7):1413-1418. doi:10.1097/00003246-200207000-00002.
10. Knaus WA, Wagner DP, Draper EA, et al. The APACHE III prognostic system. Risk prediction of hospital mortality for critically ill hospitalized adults. *Chest*. 1991;100(6):1619-1636. http://www.ncbi.nlm.nih.gov/pubmed/1959406. Accessed November 17, 2014.
11. Kamel G, Paniagua M, Uppalapati A. Palliative Care in the Intensive Care Unit: Are Residents Well Trained to Provide Optimal Care to Critically ill Patients? *Am J Hosp Palliat Care*. 2014. doi:10.1177/1049909114536979.
12. Billings JA. The End-of-Life Family Meeting in Intensive Care Part I: Indications, Outcomes, and Family Needs. *J Palliat Med*. 2011;14:1042-1050. doi:10.1089/jpm.2011.0038.
13. Orr S. *An Integrative Review of Severity of Illness Scoring Systems Used to Predict Mortality in the Adult Intensive Care Unit (Unpublished Journal Article)*. Charleston; 2015.
14. Curtis JR, Engelberg RA, Bensink ME, Ramsey SD. End-of-Life Care in the Intensive Care Unit. December 2012. http://www.atsjournals.org.proxy.library.vcu.edu/doi/full/10.1164/rccm.201206-1020CP#.VGYnR8lxHhc. Accessed November 14, 2014.
15. Curtis JR. Palliative and end-of-life care for patients with severe COPD. *Eur Respir J Off J Eur Soc Clin Respir Physiol*. 2008;32(3):796-803. doi:10.1183/09031936.00126107.

16.   Hesse-Biber SN, Leavy P. *The Practice of Qualitative Research*. Vol 337. 2nd ed. Thousand Oaks, CA: Sage Publications, Inc.; 2011. doi:10.4135/9781848608191.

17.   Tickle-Degnen L. Nuts and bolts of conducting feasibility studies. *Am J Occup Ther*. 2013;67:171-176. doi:10.5014/ajot.2013.006270.

18.   Waltz CF, Strickland OL, Lenz ER. *Measurement in Nursing and Health Research*. Vol 22. 2010. doi:10.1016/j.humov.2004.02.004.

19.   Hsieh H-F, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277-1288. doi:10.1177/1049732305276687.

20.   Sandelowski M. What's in a name? Qualitative description revisited. *Res Nurs Heal*. 2010;33(1):77-84. doi:10.1002/nur.20362.

21.   Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *Jama*. 2016;315(8):801-810. doi:10.1001/jama.2016.0287.

22.   Minne L, Ludikhuize J, De Jonge E, De Rooij S, Abu-Hanna A. Prognostic models for predicting mortality in elderly ICU patients: A systematic review. *Intensive Care Med*. 2011;37:1258-1268. doi:10.1007/s00134-011-2265-6.

23.   Vincent JL, de Mendonça A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med*. 1998;26(11):1793-1800. http://www.ncbi.nlm.nih.gov/pubmed/9824069. Accessed March 24, 2015.

24.   Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med*. 2007;356:469-478. doi:10.1056/NEJMoa063446.

25.   Khandelwal N, Curtis Randall J. Economic implications of end-of-life care in the ICU. *Curr Opin Crit Care*. 2014;20(6):656-661. doi:10.1097/MCC.0000000000000147.

26.   Ayala GX, Elder JP. Qualitative methods to ensure acceptability of behavioral and social interventions to the target population. *J Public Health Dent*. 2011;71(SUPPL. 1). doi:10.1111/j.1752-7325.2011.00241.x.

Figure 1. REDCap Questionnaire: Acceptability and Feasibility of Using SOI Instrument

Below are seven questions that relate to your use of the severity of illness (SOI) prediction instrument(s) used for predicting mortality risk for patients in the adult intensive care unit (ICU). The principal investigator for this study is interested in learning more about your experience using SOI scores in your routine practice. There are no right or wrong answers to the following statements. Your answers will remain anonymous and will be compiled with others participating in this study to help gather data needed for future studies.

Please check the box beside the answer that best describes your agreement or disagreement with the statement.

1. I clearly understood what the SOI mortality prediction score meant.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

2. I trust that the SOI mortality prediction scores that were provided to me were accurate.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

3. I had enough time to incorporate the SOI mortality prediction score into the plan of care for my patients.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

4. It is appropriate for me to know an accurate prediction of my patient's mortality risk.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

5. Knowing my patient's SOI mortality prediction score made me think about the prognosis more.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

6. Using SOI mortality prediction scores is an effective way for determining my patient's mortality risk.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

7. I believe it would be beneficial to use the results of SOI mortality prediction calculations on a daily basis.

   __1- Strongly disagree   __2- Disagree   __3-Neither agree or disagree   __4-Agree   __5-Strongly agree

Figure 2. Topics for Focused Interviews

1. Tell me about any experience you have had with patients during the end of life.

2. What data, if any, do you currently use to guide your end-of-life care practice?

3. A few weeks ago, you were provided with Severity of Illness (SOI) mortality

   prediction scores for your patients. How did you feel about that? Specifically tell me

   about:

   a. what made you trust or distrust the score

   b. why you thought being provided with the score was a good thing or a bad thing

   c. what you did with the information

   d. how you think the scores could be incorporated into your daily routine as a

      provider

   e. any ways in which it may have changed your thinking about your patient's

      prognosis

4. Tell me about any ways your practice may have changed regarding communication

   with patients and/or families about EOL goals-of-care since your experience with

   using SOI mortality prediction scores. If your practice has not changed, tell me about

   any intentions you have for changing (or not) based on the experience with the SOI

   scores.

5. When caring for an ICU patient with a high risk for mortality, tell me about your

   perceived ability to impact their EOL experience?

Summary

This dissertation has provided evidence for the feasibility, acceptability, and preliminary impact of using Severity of Illness (SOI) mortality prediction scores for initiating end-of-life (EOL) goals-of-care communication in the adult Intensive Care Unit (ICU).

Overview of Manuscripts

This dissertation includes three manuscripts:

An integrative review of severity of illness scoring systems used to predict hospital mortality for patients admitted to the adult intensive care unit. This integrative review synthesizes the literature that evaluates the psychometric properties of existing SOI scoring systems and their ability to predict mortality in the adult ICU population as the basis for clinical care and provider-patient/family communication. A total of 969 articles were identified with seven meeting all inclusion criteria. Based on discrimination alone, this review found APACHE IV to be superior, but the VA ICU, SICULA, and SOFA Max were close with 'very good' discrimination. This review provided the foundational knowledge needed in the selection of SOI systems that were used for the aim 1 focus group. Based on the findings from this review and implementation feasibility within the study setting, four SOI scoring systems (MPM III, APACHE IV, SOFA, SAPS III) were presented to the focus group participants; SOFA was ultimately chosen and was used for the study examining the feasibility and acceptability of using mortality risk scores in the ICU as the basis for EOL communication.

Supporting surrogates of incapacitated individuals throughout the research trial – From initial consent to study closure and beyond. This integrative review discusses and critiques the current state of knowledge related to interventions that can guide researchers in reducing surrogate burden throughout the research trial. A total of 25 articles met inclusion criteria for review. Analysis of the articles revealed six levels of intervention, from the personal 'Direct Care of the Surrogate' to the population-based 'Legal/Regulatory' and provides a framework to assist researchers and other interested parties when surrogates are relied upon for decision making regarding research participation. This review provided foundational knowledge needed when designing the dissertation study. Knowledge gained from this review led to decisions on how SOI scores would be reported to providers in aim 2. Specifically, a design was used that protected surrogates from unnecessary burden during the study.

The EFFECT study: The acceptability, feasibility, and potential impact of using mortality prediction scores for initiating end-of-life goals of care communication in the adult intensive care unit. This manuscript details the dissertation study. This mixed-methods study evaluated 1) the acceptability and feasibility of providers' use of patient mortality prediction scores as part of routine practice, and 2) providers' intentions to change practice, related to goals-of-care communication, as a result of awareness of the scores. Overall, use of mortality risk prediction scores as part of routine workflow and practice was found to be acceptable and feasible – providers agreed to participate, patient mortality risk were evaluated, and overall, participants found use of daily mortality prediction scores possible in their setting. However, there was some disagreement related to the use of SOFA scores as an effective way for

determining patient mortality risk. Based on themes that emerged from interviews, providers with limited ICU experience were eager and accepting of the mortality risk scores while those with vast experience found the scores to be an adjunct to their own intuition; though all acknowledged the benefit of looking at daily scores or 'trends'. The most substantial of all themes identified was the need to consider SOFA scores in relation to patient context; a number alone should not determine mortality risk and whether a goals-of-care conversation needs to occur. Use of SOFA scores for potentially increasing EOL goals-of-care conversations appears to be most beneficial for providers with limited ICU experience.

Limitations and Lessons Learned

This dissertation is the first known attempt at examining the acceptability and feasibility of using SOI mortality risk scores for initiating EOL goals-of-care communication. Although successful in meeting the objectives of the study, difficulties experienced are worth mentioning. Recruitment for Aim 2 took longer than expected. Although a few providers responded to the recruitment email within one week, face-to-face time was required for recruitment of the remaining participants. One month was required to obtain the targeted number of participants. A fear of time available to participate during their busy ICU rotation was the noted barrier; however, when participants learned they would not have to calculate the scores themselves, many agreed to participate immediately. Additionally, although the target number of participants recruited for Aim 3 follow-up interviews was exceeded, it took two months to get all participants scheduled for their interviews due to their busy schedules.

The results of the study indicated that providers found use of SOI scores to be acceptable and feasible. However, the time required for the principal investigator (PI) to calculate daily scores should be highlighted. Many participants acknowledged the time required for someone to calculate Sequential Organ Failure Assessment (SOFA) scores and indicated they would not be able to perform the calculations daily. Therefore, without integrating SOFA scoring into the electronic health record (EHR), the feasibility of its use in clinical practice will likely be low due to limited time for providers to calculate the scores themselves.

The single ICU used for this study may limit the generalizability to other types of ICUs. Additionally, the small nature of this study provided acceptability and feasibility information only and further limits generalizability. However, the information learned may guide future large-scale studies needed to determine the effect of using mortality risk predictions on patient EOL outcomes.

Importance of Theory

For this dissertation, self-efficacy theory[1] provided an understanding of how study providers' beliefs concerning his or her abilities affected their own behavior.[2] Using self-efficacy as the theoretical underpinning, providers with high self-efficacy believe that they are capable of positively impacting the quality of their patient's EOL and are motivated to do so. However, providers with low self-efficacy do not believe they are capable of positively impacting the quality of their patient's EOL, and therefore, are not motivated to put forth such effort. In future intervention studies that build on the results of this study, the PI will use self-efficacy theory to guide changes in

interdisciplinary team members' behaviors regarding EOL goals-of-care communication and thus test this theory in a new domain.

Research Trajectory

There are several areas for future research based on this dissertation work. The ultimate goal is to design interventions aimed at improving the quality of dying and death experienced by patients in the adult ICU. This initial study provides crucial foundational knowledge related to the acceptability and feasibility of using mortality risk scores for initiating EOL goals-of-care communication. Next steps will involve use of SOFA mortality risk scores on a larger scale to examine its effect on timeliness and frequency of EOL goals-of-care communication. Furthermore, determining the impact of earlier and more frequent communication on the patient's quality of dying and death is of interest.

Contribution of Research

The results of this dissertation point to several implications for research. The integrative review examining SOI mortality risk scoring systems validates the use of multiple SOI systems for predicting ICU mortality that can be incorporated into research even beyond their use for initiating EOL goals-of-care communication. Additionally, the integrative review examining interventions used for reducing surrogate burden throughout the research trial provides a framework that any researcher can consider when designing studies that includes incapacitated persons as potential participants.

Findings from this current work also lead to implications for clinical care. The dissertation study found the use of mortality risk prediction scores by ICU providers to be acceptable and feasible. Furthermore, explanatory follow-up interviews uncovered some preliminary positive outcomes of using the daily SOFA scores; some providers reported

the scores encouraged them to have earlier EOL goals-of-care communication with families. Current deficiencies in EOL care communication can compromise quality of EOL care[3] and increase resource utilization.[4,5] Although future work that builds upon the results of this study is needed, the implications may have the ability to help form standards for EOL communication in the adult ICU so these inadequacies can be addressed.

References

1. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. Psychol Rev. 1977;84(2):191–215.

2. Spector PE. Industrial and organizational psychology: Research and practice [Internet]. Wiley; 2012 [cited 2017 Aug 18]. 455 p. Available from: https://www.scribd.com/doc/297174972/Industrial-and-Organizational-Psychology-Research-and-Practice-6th-Edition-Paul-E-Spector

3. Glavan BJ, Engelberg RA, Downey L, Curtis JR. Using the medical record to evaluate the quality of end-of-life care in the intensive care unit. Crit Care Med [Internet]. 2008 Apr [cited 2014 Nov 28];36(4):1138–46. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2735216&tool=pmcentrez&rendertype=abstract

4. Quenot JP, Rigaud JP, Prin S, Barbar S, Pavon A, Hamet M, et al. Impact of an intensive communication strategy on end-of-life practices in the intensive care unit. Intensive Care Med [Internet]. 2012 Jan [cited 2014 Nov 30];38(1):145–52. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3385851&tool=pmcentrez&rendertype=abstract

5. Curtis JR, Rubenfeld GD. Improving palliative care for patients in the intensive care unit. J Palliat Med. 2005;8:840–54.

Appendix A: VCU IRB Approval Letter

VCU   Michelle L Orr <mlorr@vcu.edu>

Notification: IRB HM20007357 Orr - IRB Correspondence
1 message

IRBPANELA@vcu.edu <IRBPANELA@vcu.edu>   Tue, Jun 21, 2016 at 10:14 AM
Reply-To: IRBPANELA@vcu.edu
To: mlorr@vcu.edu

VIRGINIA COMMONWEALTH UNIVERSITY

VCU   Make it real.

Office of Research
Office of Research Subjects Protection
BioTechnology Research Park
800 East Leigh Stree, Suite 3000
P.O. Box 980568
Richmond, Virginia 23298-0568

(804) 828-0868
Fax: (804) 827-1448

TO: Michelle Orr
        Amy Heineman
CC:

FROM: VCU IRB Panel A

RE: Michelle Orr ; IRB HM20007357   The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality
        Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

On 6/15/2016, the referenced research study was **approved** by expedited review according to 45 CFR 46.110 by VCU IRB Panel A. This
study is approved under Expedited categories 5, 6, and 7.

The information found in the electronic version of this study's smart form and uploaded documents now represents the currently approved
study, documents, informed consent process, and HIPAA pathway (if applicable). You may access this information by clicking the Study
Number above.

The reliance agreement with the Medical University of South Carolina (MUSC) is not yet complete. Please follow all requirements set by
MUSC and complete the agreement.

This approval expires on 5/31/2017. Federal Regulations/VCU Policy and Procedures require continuing review prior to continuation of
approval past that date. Continuing Review notices will be sent to you prior to the scheduled review.

If you have any questions, please contact the Office of Research Subjects Protection (ORSP) or the IRB reviewer(s) assigned to this study.

The reviewer(s) assigned to your study will be listed in the History tab and on the study workspace. Click on their name to see their contact
information.

Attachment – Conditions of Approval

Conditions of Approval:

In order to comply with federal regulations, industry standards, and the terms of this approval, the investigator must (as applicable):

1. Conduct the research as described in and required by the Protocol.
2. Obtain informed consent from all subjects without coercion or undue influence, and provide the potential subject sufficient opportunity
   to consider whether or not to participate (unless Waiver of Consent is specifically approved or research is exempt).
3. Document informed consent using only the most recently dated consent form bearing the VCU IRB "APPROVED" stamp (unless
   Waiver of Consent is specifically approved).
4. Provide non-English speaking patients with a translation of the approved Consent Form in the research participant's first language.
   The Panel must approve the translated version.
5. Obtain prior approval from VCU IRB before implementing any changes whatsoever in the approved protocol or consent form, unless
   such changes are necessary to protect the safety of human research participants (e.g., permanent/temporary change of PI, addition
   of performance/collaborative sites, request to include newly incarcerated participants or participants that are wards of the state,
   addition/deletion of participant groups, etc.). Any departure from these approved documents must be reported to the VCU IRB
   immediately as an Unanticipated Problem (see #7).

6. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.
7. Report Unanticipated Problems (UPs), including protocol deviations, following the VCU IRB requirements and timelines detailed in VCU IRB WPP VIII-7:
8. Obtain prior approval from the VCU IRB before use of any advertisement or other material for recruitment of research participants.
9. Promptly report and/or respond to all inquiries by the VCU IRB concerning the conduct of the approved research when so requested.
10. All protocols that administer acute medical treatment to human research participants must have an emergency preparedness plan. Please refer to VCU guidance on http://www.research.vcu.edu/irb/guidance.htm.
11. The VCU IRBs operate under the regulatory authorities as described within:

a. U.S. Department of Health and Human Services Title 45 CFR 46, Subparts A, B, C, and D (for all research, regardless of source of funding) and related guidance documents.

b. U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.

c. Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

Appendix B: MUSC IRB Approval Letter

Institutional Review Board for Human Research (IRB)
Office of Research Integrity (ORI)
Medical University of South Carolina

Harborview Office Tower
19 Hagood Ave., Suite 601, MSC857
Charleston, SC 29425-8570
Federal Wide Assurance # 1888

Pro00057095 entitled:
The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

Submitted by: **Michelle Orr**
Department: **Medical University of South Carolina**
Sponsor: **American Nurses Foundation**

The MUSC IRB agreed to rely on Virginia Commonwealth University IRB for the review and continuing oversight for its human subjects research for this study.

Facilitated Review Acceptance Date: July 12, 2016

Type: Facilitated Review

IRB Manager - Medical University of South Carolina
Stacey C. Goretzka, CIP*

Statement of Principal Investigator:

As previously signed and certified, I understand that approval of this research involving human subjects is contingent upon my agreement:

1. To report to the Institutional Review Board for Human Research (IRB) any adverse events or research related injuries which might occur in relation to the human research. I have read and will comply with IRB reporting requirements for adverse events.
2. To submit in writing for prior IRB approval any alterations to the plan of human research.
3. To submit timely continuing review reports of this research as requested by the IRB.
4. To maintain copies of all pertinent information related to the research activities in this project, including copies of informed consent agreements obtained from all participants.
5. To notify the IRB immediately upon the termination of this project, and/or the departure of the principal investigator from this Institution and the project.

Electronic Signature: This document has been electronically signed by the IRB Chairman through the HSSC eIRB Submission System authorizing IRB approval for this study as described in this letter.

Facilitated Review   8/21/2017

Appendix C: VCU IRB Continued Approval Letter

VCU   Michelle L Orr <mlorr@vcu.edu>

Notification: IRB HM20007357_CR1 Orr - IRB Correspondence
1 message

IRBPANELA@vcu.edu <IRBPANELA@vcu.edu>   Mon, May 8, 2017 at 3:04 PM
Reply-To: IRBPANELA@vcu.edu
To: mlorr@vcu.edu

VCU
Office of Research and Innovation

Office of Research and Innovation
Office of Research Subjects Protection
BioTechnology Research Park
800 East Leigh Street, Suite 3000
Box 980568
Richmond, Virginia 23298-0568

(804) 828-0868
Fax: (804) 827-1448

TO: Michelle Orr

CC: Amy Heineman

FROM: IRB Panel A

RE: Michelle Orr ; IRB HM20007357_CR1   The Acceptability, Feasibility, and Potential Impact of
        Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care
        Communication in the Adult Intensive Care Unit

On 5/8/2017, this research study was *approved for continuation* by expedited review according to 45 CFR 46.108(b) and 45 CFR
46.109(e) and 45 CFR 46.110 by VCU IRB Panel A. This study is approved under Expedited categories 5, 6, and 7.

The information found in the electronic version of this study's smart form and uploaded documents now represents the currently approved
study, documents, informed consent process, and HIPAA pathway (if applicable). Please see instruction box below for details on viewing
the approved study.

This approval expires on 4/30/2018, Federal Regulations/VCU Policy and Procedures require continuing review prior to continuation of
approval past that date. Continuing Review notices will be sent to you prior to the scheduled review.

If you have any questions, please contact the Office of Research Subjects Protection (ORSP) or the IRB reviewer(s) assigned to this
study. The reviewer(s) assigned to your continuing review will be listed in the History tab and on the continuing review workspace. Click
on their name to see their contact information.

Attachment – Conditions of Approval

Conditions of Approval:

In order to comply with federal regulations, industry standards, and the terms of this approval, the investigator must (as applicable):

1. Conduct the research as described in and required by the Protocol.

2. Obtain informed consent from all subjects without coercion or undue influence, and provide the potential subject sufficient opportunity
to consider whether or not to participate (unless Waiver of Consent is specifically approved or research is exempt).

3. Document informed consent using only the most recently dated consent form bearing the VCU IRB "APPROVED" stamp (unless Waiver of Consent is specifically approved).

4. Provide non-English speaking patients with a translation of the approved Consent Form in the research participant's first language. The Panel must approve the translated version.

5. Obtain prior approval from VCU IRB before implementing any changes whatsoever in the approved protocol or consent form, unless such changes are necessary to protect the safety of human research participants (e.g., permanent/temporary change of PI, addition of performance/collaborative sites, request to include newly incarcerated participants or participants that are wards of the state, addition/deletion of participant groups, etc.). Any departure from these approved documents must be reported to the VCU IRB immediately as an Unanticipated Problem (see #7).

6. Monitor all problems (anticipated and unanticipated) associated with risk to research participants or others.

7. Report Unanticipated Problems (UPs), including protocol deviations, following the VCU IRB requirements and timelines detailed in VCU IRB WPP VII-6):

8. Obtain prior approval from the VCU IRB before use of any advertisement or other material for recruitment of research participants.

9. Promptly report and/or respond to all inquiries by the VCU IRB concerning the conduct of the approved research when so requested.

10. All protocols that administer acute medical treatment to human research participants must have an emergency preparedness plan. Please refer to VCU guidance on http://www.research.vcu.edu/irb/guidance.htm.

11. The VCU IRBs operate under the regulatory authorities as described within:
a) U.S. Department of Health and Human Services Title 45 CFR 46, Subparts A, B, C, and D (for all research, regardless of source of funding) and related guidance documents.
b) U.S. Food and Drug Administration Chapter I of Title 21 CFR 50 and 56 (for FDA regulated research only) and related guidance documents.
c) Commonwealth of Virginia Code of Virginia 32.1 Chapter 5.1 Human Research (for all research).

Conditions of Approval (version 010507)

Appendix D: IAA Agreement – VCU & MUSC

IRB Authorization Agreement

The purpose of this agreement is to document the relationship between:

VIRGINIA COMMONWEALTH UNIVERSITY (Institution A)
OHRP Federalwide Assurance (FWA) #: 00005287

and

MEDICAL UNIVERSITY OF SOUTH CAROLINA (Institution B)
OHRP Federalwide Assurance (FWA) #: 00001888

This agreement authorizes *Institution B* to rely upon *Institution A* for IRB review of the following research.

IRB Number: HM20007375
Title of Study: "The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit"
Principal Investigator at Institution A: Michelle (Shelly) Orr, MSN, RN, CNE
Principal Investigator at Institution B: Michelle (Shelly) Orr, MSN, RN, CNE

The following terms are agreed upon by all parties and attested to by signature below:

Institution A Responsibilities:

1. Maintain an FWA with OHRP and maintain IRB registration with both OHRP and the FDA, as applicable.
2. The membership of the IRB(s) will meet applicable federal regulations and human subject protection requirements of the FWA.
3. Make available to Institution B, the Institution A policies and procedures.
4. Conduct reviews of initial, continuing, and amendment submissions; unanticipated problem reports; DSMB reports; and any other documentation submitted by the Principal Investigator.
5. For federally funded studies, determine that the proposed research is consistent with the federal award.
6. Maintain and make accessible to Institution B the IRB application, protocol reviews, letters to Principal Investigators, approvals and disapprovals, and approved informed consent documents upon request or provided through the principal investigator.
7. The Institution A IRB will perform those determinations required by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its implementing regulations with respect to the mechanism for permitting the use and disclosure of Protected Health Information (PHI).
8. Investigate and manage any event that appears to rise to the level of an unanticipated problem involving risks to subjects or others and/or serious or continuing noncompliance.
9. Notify Institution B promptly if a determination of serious or continuing noncompliance is found, and the corrective actions deemed necessary by the IRB. Institution A may request that Institution B conduct its own investigation and report back to Institution A.
10. If Institution A determines that an event must be reported to oversight entities, such as ORHP and FDA, it will notify Institution B in advance and provide the opportunity for Institution B to review and comment on the report before it is sent.

11. Notify Institution B promptly if it decides to suspend, disapprove, or terminate a study covered by this agreement.
12. Notify Institution B Investigators of any lapses of approval.
13. Maintain a post approval monitoring program to ensure compliance with IRB approved protocols and adherence to regulatory requirements.
14. Provide a mechanism for research subjects enrolled at Institution B to address concerns or ask questions pertaining to the rights of research subjects.
15. Notify institution B of any correspondence regarding this study to or from the FDA, OHRP and /or other regulatory agency.

Institution B Responsibilities

1. Maintain a Federal Wide Assurance (FWA) and human research protection program as required by the DHHS OHRP.
2. Educate and train its investigators to perform research in compliance with human subjects' protection regulations.
3. Provide Institution A with information pertaining to any specific requirements of local laws, regulations, policies, standards or other factors applicable to the conduct of research.
4. Ensure that resources are adequate to carry out the research planned to take place at Institution B.
5. Ensure that the investigators and other personnel at Institution B who are involved in the study are appropriately qualified and meet the relying site's standards for eligibility to conduct research. This includes, but is not limited to, having the required professional staff appointments, credentialing, insurance coverage, and background checks for their assigned role in the study.
6. Notify Institution A of any special local considerations that must be considered during IRB review.
7. Maintain policies and procedures to address Conflicts of Interest in research that comply with DHHS regulations. Ensure that Institution B investigators and study personnel disclose financial interests according to Institution B policy. Ensure that conflicts of interest are reviewed and a management plan is implemented, if required by Institution B policy. Provide all management plans to Institution A IRB for review. Ensure compliance of all management plans related to the study. If Institution B does not maintain policies and procedures compliant with DHHS requirements, ensure that all research personnel identified as Conflict of Interest Investigators complete Institution A financial interest disclosure requirements; cooperate with Institution A in the development of management plans, if applicable; and adhere to any associated management plans.
8. If Institution B chooses to provide its own HIPAA Authorization, Institution B will ensure that the Authorization explicitly permits PHI to be used and shared by and with Institution A and all participating study sites and their investigators as necessary for conducting, reviewing, and overseeing all studies.
9. Remain independently responsible for its own HIPAA compliance and obligations in connection with research covered under this Agreement other than the initial determinations regarding mechanisms for use and disclosure of PHI.
10. Perform local review by other local ancillary committee reviews as applicable per Institution B policies, such as radiation safety or pharmacy. Provide any relevant results of the reviews that may impact the conduct of this study as part of the information provided to Institution A.
11. Assure that research activities at Institution B are not initiated until IRB approval is obtained.
12. Notify Institution A within twenty-four hours of becoming aware of a suspension or restriction of an Institution B investigator or other personnel involved in research.
13. Maintain policies and procedures for dealing with injuries to human research subjects and share these policies and procedures with Institution A as requested. To the extent of its own policies, Institution B

will provide or arrange for treatment of injuries to human subjects, if any, that may result from study-related procedures that occur at Institution B. This agreement does not preclude the institutions from making other arrangements between or among them at the outset of a specific study to allocate differently the responsibility for costs associated with injuries to human subjects that might occur in the course of the study.

14. Ensure a mechanism exists by which complaints about research can be made by local study subjects or others. Promptly report such complaints to Institution A if they meet the criteria of a potential unanticipated problem as defined by Institution A policies.
15. Cooperate with and use all reasonable efforts to ensure Institution B investigators' cooperation with any inquiry by Institution A post approval monitoring requests relating to the study.
16. *Inform Institution A if the site plans to no longer rely upon Institution A for IRB review.*
17. Notify institution A of any correspondence regarding this study to or from the FDA, OHRP and /or other regulatory agency.

Institution A Investigator Responsibilities

1. Ensure all Institution B research personnel designated as Conflict of Interest Investigators complete Institution A financial interest disclosure requirements unless the Institution B personnel will adhere to Institution B conflict of interest policies that are compliant with DHHS requirements.
2. Promptly provide Institution B PI with:
   a. Current approved protocol and consent documents;
   b. Approved modifications, amendments or changes to research protocols; and
   c. Approval of continuing reviews and reviews of unanticipated problems;
3. Notify Institution B PI of standards and guidelines for reporting any post approval events such as adverse events, subject injuries, unanticipated problems, and protocol violations. Collect reports from Institution B of any unanticipated problems, deviations, suspensions and terminations, non-compliance, subject complaints, and submit such reports to the Institution A IRB per reporting requirements.
4. Notify Institution B investigator promptly of any unanticipated problems involving risks to subjects or others as determined by the IRB of record.
5. Collect required information from Institution B necessary for completing continuing review submissions.
6. Notify Institution B investigator promptly about any lapses of approval. Forward to the Institution A IRB any request from the Institution B investigator for continuation of a specific research subject on a protocol during a lapsed period of approval.

Institution B Investigator Responsibilities

1. Provide Institution A with:
   a. The list of research personnel engaged in the conduct of research;
   b. Evidence of training for all engaged research personnel, including the investigator; and
   c. Any other information required for IRB review.
2. Assure that all research activities at Institution B are not initiated until all IRB and funding-related requirements are completed.
3. Conduct protocols and obtain informed consent as approved by the IRB and in compliance with Institution A policies and procedures and all relevant federal, state, and local regulations for human subjects research.

4. Provide any information requested by Institution A that may be necessary for the continuing review process. This may include information regarding subject recruitment, summary of all enrolled subjects, screen failures, minor violations, and all other information needed for continuing review.
5. Notify Institution A within five days of becoming aware of potential unanticipated problems involving risk to subjects or others or of serious or continuing non-compliance.
6. If at any time IRB approval lapses, cease all human subjects research work related to the expired protocol. Notify Institution A of any subjects who are already enrolled who may be harmed if research ceases.
7. Promptly cooperate with any investigations of serious or continuing non-compliance or unanticipated problems.
8. Promptly cooperate with any post approval monitoring conducted by Institution A. Such cooperation will include, but is not limited to, providing research records and related information and meeting with institutional research representatives upon request.
9. Maintain records of all research and related activities for at least six years, and longer if required by law, following completion of research.
10. Cooperate with Institution A in reporting and resolving any conflicts of interest reported by Institution B identified conflict of interest investigators, including but not limited to entering into management plans, as required by Institution A.
11. Promptly respond to requests for information from Institution A.

The Officials signing below agree that <u>Medical University of South Carolina</u> *may rely on the* <u>Virginia Commonwealth University IRB</u> *under the terms of this agreement.*

- *This Agreement will become effective upon the date of the last signature below. The Agreement will remain in effect until such time that any institution provides a 30 day written notice of amendment or termination to the other institution.*
- *This document must be kept on file at both institutions and provided to the Department of Health and Human Services Office of Human Research Protections, upon request.*

Virginia Commonwealth University Signatory Official
I agree and accept the responsibilities under this agreement as outlined above:

FWA Institutional Official (or
designee) Signature: _____ Date: _____

Name: Francis L. Macrina, Ph.D.   Title: Vice President for Research

Address: 800 East Leigh Street, Suite 3000   Phone: 804-827-2262

Richmond, VA 23298

Virginia Commonwealth University Principal Investigator
I agree and accept the responsibilities under this agreement as outlined above:

PI Signature: _Michelle Jr. Orr_____ Date: 6|22|16

Name: Michelle (Shelly) Orr   Title: Clinical Assistant Professor

Address: 2911 Esnora Lane   Phone: 804-221-5159

Church Road, VA 23833

Medical University of South Carolina Signatory Official
I agree and accept the responsibilities under this agreement as outlined above:

FWA Institutional Official (or
designee) Signature: _____ Date: _____

Name: Kathleen T. Brady, MD, PhD   Title: Vice President for Research
                                                    843-792-5205
Address: 125 Doughty St.   Phone:

Charleston, SC 29425

Medical University of South Carolina Principal Investigator
I agree and accept the responsibilities under this agreement as outlined above:

PI Signature: _Michelle J. Orr_____ Date: 6|22|16

Name: Michelle (Shelly) Orr   Title: PhD Student, MUSC College of Nursing

Address: 2911 Esnora Lane   Phone: 804-221-5159

Church Road, VA 23833

Appendix E: Focus Group Recruitment Email

We are looking for participants for a research study regarding the acceptability, feasibility, and potential impact of using a severity of illness (SOI) mortality prediction instrument for initiating end-of-life goals-of-care communication in the adult intensive care unit. You are being asked to participate in this study because you are a provider in the Medical-Respiratory Intensive Care Unit (MRICU) that is responsible for total patient care, including prognosis.

Prior to asking providers to use SOI scores in their everyday practice to examine its impact, we need help with determining which instrument, or combination of instruments, is best for use in the MRICU, given your perceived feasibility of its use. In this arm of the study, you will be asked to participate in a focus group with five other MRICU providers (MD, NP, PA combination). In the focus group, you will be given a table that compares all four potential instruments and will be asked to discuss your perceived feasibility of using each instrument and rank them in order of preference. The focus group is anticipated to last less than two hours. The focus group will be audio recorded as a backup and the audio file will be stored in a secure web-based data capture system. In addition, all study participants will be asked to complete an online demographic form that consists of items related to age, race/ethnicity, gender, health discipline, years of practice, and previous experience with end-of-life care. Demographic data will only be used for descriptive purposes when describing the results of the study. All data collected will be kept confidential.

You may not get any direct benefit from this study, but the information we learn from people in this study may help us design standards for communication with patients and their families during the patient's end-of-life in the ICU. Participants will be compensated for their time with a meal during the focus group.

If you are interested in participating in this study, please contact the principal investigator, either by email or phone. We appreciate your consideration in partaking in this important study.

Shelly Orr, MSN, RN, CNE
Clinical Assistant Professor, VCU School of Nursing
Principal Investigator
Phone: (804) 221-5159
Email: mlorr@vcu.edu

Appendix F: Focus Group Consent Form

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

VCU IRB NO.: HM20007357
If any information contained in this consent form is not clear, please ask the study staff to explain any information that you do not fully understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

PURPOSE OF THE STUDY
The purpose of this research study is to find out if patient mortality prediction scores can and should be used as a part of your routine workflow and practice as a healthcare provider.

You are being asked to participate in this study because you are a provider in the Medical-Respiratory Intensive Care Unit (MRICU) that is responsible for total patient care, including prognosis.

DESCRIPTION OF THE STUDY AND YOUR INVOLVEMENT
If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered and understand what will happen to you.

In this initial phase of the study, you will be asked to participate in a focus group with five other MRICU providers to evaluate four mortality prediction instruments to determine which instrument, or combination of instruments, is best for the MRICU. Participants will be given a table that compares four available instruments and will be asked to discuss perceived usability of each instrument. Participants will be asked to verbally provide ranking scores for the instruments. The length of the focus group is anticipated to be approximately two hours. The focus group will be audio recorded in case further analysis related to rankings needs to occur and the audio files will only be retrievable only by the Principal investigator (PI) or research assistant (RA). The PI will notify all participants via email which instrument(s) were selected. If there are any participant concerns, an additional focus group will be held to reach consensus. In addition, all study participants will be asked to complete an online demographic form that consists of items related to age, race/ethnicity, gender, health discipline, years of practice, and previous experience with end-of-life care. Demographic data will only be used for descriptive purposes when describing the results of the study.

Significant new findings developed during the course of the research that may relate to your willingness to continue participation will be provided to you.

RISKS AND DISCOMFORTS
Sometimes talking about patient mortality risk causes people to become upset. You do not have to talk about anything you do not want to talk about, and you may choose to leave the focus group at any time. If you become upset, the study staff will give you names of counselors to contact so you can get help in dealing with these issues. Also, because your time as a provider is already limited, the time required to participate in this study may make you feel overwhelmed. Although the time required to participate is minimal, you may choose to leave the study at any time.

BENEFITS TO YOU AND OTHERS
You may not get any direct benefit from this study, but, the information we learn from people in this study may help us design standards for communication with patients and their families during the patient's end-of-life in the ICU.

COSTS
There are no costs for participating in this study other than the time you will spend partaking in the focus group discussion.

PAYMENT FOR PARTICIPATION
You will receive a meal during the focus group meeting.

ALTERNATIVES
The only alternative for this study is not to participate.

CONFIDENTIALITY
Potentially identifiable information about you will consist of demographics and audio recordings. Data is being collected only for research purposes.

A secure web-based data capture system will be used to collect demographic data, as well as store audio recordings. The audio recording will be deleted once transcription occurs and no names will be recorded. Your data will be identified by ID numbers, not names or other identifiers, and stored separately from research data in a locked research area. All personal identifying information will be kept in password-protected files and these files will be deleted one year after completion of the study. Consent forms will be destroyed three years after study completion. Study data, without identifiers, will be kept indefinitely on a password-protected computer. Access to all data will be limited to study personnel.

We will not tell anyone the responses you give us; however, information from the study and the consent form signed by you may be looked at or copied for research or legal purposes, or by Virginia Commonwealth University. Personal

information about you might be shared with or copied by authorized officials of the Department of Health and Human Services or other federal regulatory bodies.

What we find from this study may be presented at meetings or published in papers, but your name will not ever be used in these presentations or papers.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
You do not have to participate in this study. If you choose to participate, you may stop at any time without any penalty. You may also choose not to answer particular questions that are asked in the study.
Your participation in this study may be stopped at any time by the study staff without your consent. The reasons might include:
- the study staff thinks it is necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

QUESTIONS
If you have any questions, complaints, or concerns about your participation in this research, contact:

> **Shelly Orr, MSN, RN, CNE**
> **Principal Investigator**
> **Phone: (804) 221-5159**
> **Email: mlorr@vcu.edu**

The researcher/study staff named above is the best person(s) to call for questions about your participation in this study.

If you have any general questions about your rights as a participant in this or any other research, you may contact:

> Office of Research
> Virginia Commonwealth University
> 800 East Leigh Street, Suite 3000
> P.O. Box 980568
> Richmond, VA 23298
> Telephone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk with someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

CONSENT
I have been given the chance to read this consent form. I understand the information about this study. Questions that I wanted to ask about the study have been answered. My signature says that I am willing to participate in this study. I will receive a copy of the consent form once I have agreed to participate.

_____
Participant name (Printed)   Participant signature   Date

_____
Name of Person Conducting Informed Consent Discussion (Printed)

_____
Signature of Person Conducting Informed Consent Discussion   Date

_____
Principal Investigator Signature (if different from above)   Date

Appendix G: Demographic Information Questionnaire Email

Thank you for your participation in the study ***The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit*** (VCU IRB NO.: HM20007357).

As part of your participation in this study, we are asking that you complete a demographic questionnaire. Your answers will be kept confidential and available to the study staff only. Your answers will be combined with others and used when reporting the descriptive results of the study.

If you have any questions or concerns about this questionnaire, contact:
Shelly Orr, MSN, RN, CNE, Principal Investigator
Phone: (804) 221-5159
Email: mlorr@vcu.edu

Please complete the questionnaire within the next week by clicking on the following link. **Insert REDCap Link Here*

Appendix H: Participant Demographic Data Form (REDCap)

Age	Health Discipline
Age at last birthday: _____ years	__ Acute Care Nurse Practitioner (ACNP) __ Physician Assistant (PA) __ Physician __Intern __Resident __Fellow __Attending
Gender	**Years of Practice in this Discipline**
__ Male __ Female	Years in your profession: _____ years If less than one year, specify months in your profession: _____ months
Race/Ethnicity	**Previous Experience with End-of-Life (EOL)**
__ American Indian or Alaska Native __ Asian __ Black or African American __ Hispanic or Latino __ Native Hawaiian or Other Pacific Islander __ White __ Other	__ None __ Personal (i.e. loss of someone close to you) __ Professional __ Coursework on EOL care __ Hands-on experience with patients during their EOL (including training in palliative care) __ Other – Please specify: _____

Appendix I: Focus Group Principal Investigator Guide

1. The purpose of this focus group is to have you all evaluate four valid severity of illness (SOI) instruments, used to calculate patient mortality risk, to determine which instrument, or combination of instruments, is the best fit for use in the MRICU, given your perceived feasibility of use as providers in the unit. As the Principal Investigator of this study, I will assume the moderator role of this focus group to keep the flow of the conversation on target.

   *A copy of the table that compares the four SOI instruments (Appendix B) is distributed to all focus group participants.

2. Questions for the focus group:
   a. How practical/feasible is the use of the MPM III in the MRICU?
   b. How practical/feasible is the use of the APACHE IV in the MRICU?
   c. How practical/feasible is the use of the SOFA in the MRICU?
   d. How practical/feasible is the use of the SAPS III in the MRICU?
   e. What are your preferences regarding an admission score only versus an admission score plus a daily score (i.e. SOFA)?
   f. Provide ranking scores for the instruments (if needed).

3. The PI will notify all participants via email which instrument(s) were selected. If there are any participant concerns, an additional focus group will be held to reach consensus.

Appendix J: Focus Group SOI Instrument Comparison Table

Severity of Illness (SOI) Instrument	About the Instrument….
Mortality Probability Admission Model (MPMo III)	Has 16 predictor variables plus seven interaction terms that include physiological variables, chronic diagnoses, acute diagnoses, age, code status (and whether the patient has received CPR), mechanical ventilation status, and whether a medical or unscheduled surgical admit occurred (Higgins et al., 2007a). Estimates mortality probability at hospital discharge using data obtained at the time of or within 1 hour of ICU admission; values are assumed to be normal when measurements have not been obtained (Higgins et al., 2009). Excludes certain patient subsets, including cardiac surgery, myocardial infarction, burn, less 18 years old, and ICU readmissions (Higgins et al., 2009). Because data are collected at ICU arrival, may be less potential for the score to be influenced by care received after admission to the ICU (Kuzniewicz et al., 2008). 74,578 patient records from Project IMPACT ICUs (135 ICUs at 98 hospitals including mostly US, but 3 were Canada and 1 Brazil) were used for development of instrument; 50,307 patient records were used for validation (AUROC= 0.823; H-L statistic= 11.62, p= 0.31) (Higgins et al., 2007b). MPMo III not readily available online, but the MPM II is. The MPMo III takes around 11 minutes to manually abstract required data, requiring yes/no answers only (Kuzniewicz et al., 2008). However, this does not account for analysis time requirements. Cerner supports collection of variables used by the MPMo III and markets it's use (Kramer, Higgins, & Zimmerman, 2014).
Acute Physiology and Chronic Health Evaluation (APACHE IV)	Incorporates 142 predictor variables, 116 admission diagnoses, and 17 physiological variables (Zimmerman, Kramer, McNair, & Malila, 2006). Predictor variables include age, acute physiology score variables (labs, vital signs, GCS, chronic health variables, ICU admission diagnosis and source, length of stay prior to ICU admission, GCS score rescaled, and PaO2/FiO2 ratio. Also entered into the system are data on whether the patient had emergency surgery, mechanical ventilation, or an inability to assess GCS. Also collected are data on gender, whether the patient is post-coronary artery bypass grafting (CABG), number of any grafts, whether an internal mammary graft was used, and whether the patient had diabetes prior to the CABG or an MI during that hospitalization. Uses physiologic data from the first 24 hours after ICU admission (Kuzniewicz et al., 2008). Scores based on worse measurements for each component on ICU day 1 (Zimmerman et al., 2006).

Severity of Illness (SOI) Instrument	About the Instrument….
	Initially validated in a study consisting of a non-randomized observational cohort of 131,618 consecutive patients admitted to 104 ICUs in 45 US hospitals (AUROC= 0.88; H-L statistic= 16.8, p= 0.8) (Zimmerman et al., 2006). Only patients excluded were those with burns, those admitted for less than 4 hours, less than 16 years old, or those admitted after transplant operations (except for renal and hepatic transplants). Only included first ICU admission and excluded ICU transfer patients (Zimmerman et al., 2006). ICU locations were diverse across US, teaching versus non-teaching, number of beds, and type (medical, trauma, cardiac, neuro) (Zimmerman et al., 2006).
	Publically accessible web-based option calculates predicted mortality when variables are manually entered (Zimmerman et al., 2006).
	Training manual is available and reliability can be enhanced by auto collection of variables through EHR (Zimmerman et al., 2006).
	Cerner owns the registered trademark for APACHE and markets the APACHE IV instrument (Kramer et al., 2014). Require purchase of APACHE system to be automatically calculated in Cerner.
Sequential Organ Failure Assessment (SOFA)	Assigns 1-4 points to the following organ systems depending on the level of organ dysfunction: circulatory, respiratory, renal, hematology, hepatic, and central nervous system (Minne, Ludikhuize, De Jonge, De Rooij, & Abu-Hanna, 2011). Differentiations are made based on the scores used (Minne et al., 2008). The total max SOFA is the sum of the highest scores per individual organ system during the entire ICU stay. The max SOFA is the highest total SOFA measured in a pre-specified time interval, and the mean SOFA is the average of all total SOFA scores in the pre-specified time interval. The delta SOFA is the total max minus admission SOFA. Data are typically collected upon ICU admission and throughout the ICU stay, with the most abnormal values for each day being recorded (Vincent et al., 1998).
	Admission scores calculated using the most abnormal values from the first 24 hours after ICU admission (Minne et al., 2008).
	In a systematic review published in 2008, the highest AUC's were reported for max SOFA (0.792-0.922) and total max SOFA (0.69-0.921) and the lowest AUC's for delta SOFA (0.51-0.828). The H-L statistics for total max SOFA (0.33-0.95) were superior to delta and mean SOFAs (all being <0.05). Many studies combined SOFA with other models (APACHE II, SAPS II) which resulted in improved performance and discrimination compared to the models alone (Minne et al., 2008).
	Web-based option calculates predicted mortality when variables are manually entered.

Severity of Illness (SOI) Instrument	About the Instrument….
Simplified Acute Physiology Score (SAPS III)	Predictor variables for this model include age, comorbidities, pre-ICU location, pre-ICU length of stay, pre-ICU major therapeutics, reason for ICU admission, planned/unplanned admission, infection at ICU admission, surgical status, site of surgery if applicable, GCS, total bilirubin, body temperature, creatinine, heart rate, leukocytes, pH, platelets, systolic blood pressure, and ventilation/oxygenation with scores ranging from 0-217 (Metnitz et al., 2005; Moreno et al., 2005).

Data are collected within one hour of ICU admission in an attempt to dissociate evaluation of the patient from evaluation of the ICU; Data collected within one hour of ICU admission provides probability of death during hospitalization.

Any data not available assumed normal (Moreno et al., 2005).

Developed with data from 19,577 ICU patients in 35 countries (AUROC= 0.848; H-L statistic= 14.29, p= 0.16) (Moreno et al., 2005).

Can be computed manually or integrated into a computerized data retrieval system. Requires adaptation of some variables that cannot be directly linked to EHR (Moreno et al., 2005). |

Appendix K: Acceptability & Feasibility Questionnaire and Follow-Up Interview Recruitment Email

We are looking for participants for a research study examining whether patient mortality prediction scores can and should be used as a part of routine workflow and practice as a healthcare provider. You are being asked to participate in this study because you are, or will soon be, a provider in the Medical-Respiratory Intensive Care Unit (MRICU) that is responsible for total patient care, including prognosis.

In this study, you will be asked to receive mortality prediction scores for your patients for 10 consecutive days (scores provided by the study investigator or assistant on a note card), and complete a seven-item online questionnaire about your experience afterwards. The questionnaire is expected to take less than ten minutes to complete and will ask about your experience with the mortality prediction scores, such as whether you understood what the score meant and whether you thought knowing the score was beneficial. Following completion of the questionnaire, you will be contacted to ask for your additional participation in a follow-up interview. If you choose to do so, you will be asked to partake in an individual face-to-face interview with the study's investigator. The interview is expected to take less than one hour and will ask about your experience with the mortality prediction scores and how your practice may or may not have changed as a result of knowing those scores. The interviews will be audio recorded so we are sure to get everyone's ideas, but no names will be recorded on the tape. In addition, all study participants will be asked to complete an online demographic form that consists of items related to age, race/ethnicity, gender, health discipline, years of practice, and previous experience with end-of-life care. Demographic data will only be used for descriptive purposes when describing the results of the study. All data collected will be kept confidential.

You may not get any direct benefit from this study, but the information we learn from people in this study may help us design standards for communication with patients and their families during the patient's end-of-life in the ICU. Participants will be compensated for their time with gift cards for Au Bon Pain Café Bakery.

If you are interested in participating in this study, please contact the principal investigator, either by email or phone. We appreciate your consideration in partaking in this important study.

Shelly Orr, MSN, RN, CNE
Clinical Assistant Professor, VCU School of Nursing
Principal Investigator
Phone: (804) 221-5159
Email: mlorr@vcu.edu

Appendix L: Acceptability & Feasibility Questionnaire and Follow-Up Interview Consent Form

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE: The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit

VCU IRB NO.: HM20007357
If any information contained in this consent form is not clear, please ask the study staff to explain any information that you do not fully understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

PURPOSE OF THE STUDY
The purpose of this research study is to find out if patient mortality prediction scores can and should be used as a part of your routine workflow and practice as a healthcare provider.

You are being asked to participate in this study because you are a provider in the Medical-Respiratory Intensive Care Unit (MRICU) that is responsible for total patient care, including prognosis.

DESCRIPTION OF THE STUDY AND YOUR INVOLVEMENT
If you decide to be in this research study, you will be asked to sign this consent form after you have had all your questions answered and understand what will happen to you.

In this study, you will be asked to receive mortality prediction scores for your patients for 10 consecutive days. The scores will be provided to you by the study investigator or assistant on a note card each morning before interdisciplinary rounds. To protect patient confidentiality, the note cards will only have patient room numbers and mortality prediction scores on them and you will be asked to place them in the shredder box before leaving the unit at the end of the day. To help you with interpretation of the score, a reference card will be provided to you upon study enrollment. Following the ten days, you will then be asked to complete a seven-item online questionnaire about your experience. The questionnaire is expected to take less than ten minutes to complete and will ask about your experience with the morality prediction scores, such as whether you understood what the score meant and whether you thought knowing the score was beneficial. Following completion of the questionnaire, you will be contacted to ask for your additional participation in a follow-up interview. If you choose to do so, you will be asked to partake in an individual face-to-face interview with the study's investigator. The interview is expected to take less than one hour and will ask about your experience with the mortality prediction scores and how your

practice may or may not have changed as a result of knowing those scores. The interviews will be tape recorded so we are sure to get everyone's ideas, but no names will be recorded on the tape. In addition, all study participants will be asked to complete an online demographic form that consists of items related to age, race/ethnicity, gender, health discipline, years of practice, and previous experience with end-of-life care. Demographic data will only be used for descriptive purposes when describing the results of the study.

Significant new findings developed during the course of the research that may relate to your willingness to continue participation will be provided to you.

RISKS AND DISCOMFORTS
Sometimes talking about patient mortality risk causes people to become upset. You do not have to talk about anything you do not want to talk about, and you may choose not to answer questions or leave the interview at any time. If you become upset, the study staff will give you names of counselors to contact so you can get help in dealing with these issues. Also, because your time as a provider is already limited, the time required to participate in this study may make you feel overwhelmed. Although the time required to participate is minimal, you may choose to leave the study at any time.

BENEFITS TO YOU AND OTHERS
You may not get any direct benefit from this study, but, the information we learn from people in this study may help us design standards for communication with patients and their families during the patient's end-of-life in the ICU.

COSTS
There are no costs for participating in this study other than the time you will spend filling out questionnaires and partaking in an interview.

PAYMENT FOR PARTICIPATION
You will receive a $25.00 gift card for Au Bon Pain Café Bakery for completing the demographic form and questionnaire. If you chose to also participate in the follow-up interview, you will receive an additional $25.00 gift card for Au Bon Pain. The study's investigator or assistant upon participation completion will provide gift cards.

ALTERNATIVES
The only alternative for this study is not to participate.

CONFIDENTIALITY
Potentially identifiable information about you will consist of demographics, questionnaire responses, and interview notes and recordings. Data is being collected only for research purposes.

A secure web-based data capture system will be used to collect demographic and questionnaire data, as well as store interview recordings and transcriptions. Interview audio recordings will be deleted once transcription occurs and no

names will be recorded. Your data will be identified by ID numbers, not names or other identifiers, and stored separately from research data in a locked research area. All personal identifying information will be kept in password-protected files and these files will be deleted one year after completion of the study. Consent forms will be destroyed three years after study completion. Study data, without identifiers, will be kept indefinitely on a password-protected computer. Access to all data will be limited to study personnel.

We will not tell anyone the answers you give us; however, information from the study and the consent form signed by you may be looked at or copied for research or legal purposes, or by Virginia Commonwealth University. Personal information about you might be shared with or copied by authorized officials of the Department of Health and Human Services or other federal regulatory bodies.

What we find from this study may be presented at meetings or published in papers, but your name will not ever be used in these presentations or papers.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
You do not have to participate in this study. If you choose to participate, you may stop at any time without any penalty. You may also choose not to answer particular questions that are asked in the study.

Your participation in this study may be stopped at any time by the study staff without your consent. The reasons might include:
- the study staff thinks it necessary for your health or safety;
- you have not followed study instructions;
- the sponsor has stopped the study; or
- administrative reasons require your withdrawal.

QUESTIONS
If you have any questions, complaints, or concerns about your participation in this research, contact:

> **Shelly Orr, MSN, RN, CNE**
> **Principal Investigator**
> **Phone: (804) 221-5159**
> **Email: mlorr@vcu.edu**

The researcher/study staff named above is the best person(s) to call for questions about your participation in this study.

If you have any general questions about your rights as a participant in this or any other research, you may contact:

Office of Research
Virginia Commonwealth University
800 East Leigh Street, Suite 3000
P.O. Box 980568
Richmond, VA 23298
Telephone: (804) 827-2157

Contact this number to ask general questions, to obtain information or offer input, and to express concerns or complaints about research. You may also call this number if you cannot reach the research team or if you wish to talk with someone else. General information about participation in research studies can also be found at http://www.research.vcu.edu/irb/volunteers.htm.

CONSENT
I have been given the chance to read this consent form. I understand the information about this study. Questions that I wanted to ask about the study have been answered. My signature says that I am willing to participate in this study. I will receive a copy of the consent form once I have agreed to participate.

_____

Participant name (Printed)   Participant signature   Date

_____

Name of Person Conducting Informed Consent Discussion (Printed)

_____

Signature of Person Conducting Informed Consent Discussion   Date

_____

Principal Investigator Signature (if different from above)   Date

Appendix M: EFFECT Study Badge Buddy for Participants Receiving SOI Mortality Risk Scores

VCU School of Nursing
VIRGINIA COMMONWEALTH UNIVERSITY

EFFECT Study (**E**nd-o**F**-li**FE**-**C**ommunica**T**ion)

How do I use the Sequential Organ Failure Assessment (SOFA) score that's been reported to me?

SOFA is a mortality prediction tool that assigns points depending on the level of organ dysfunction

Scores are calculated using the most abnormal values from the previous 24 hours; values are obtained from the EHR

SOFA scores can be converted to an estimate of mortality risk – This is the % that's been reported to you for patients admitted under your care

For questions about the EFFECT Study, contact the PI, Shelly Orr (804-221-5159; mlorr@vcu.edu)

Appendix N: SOFA SOI Instrument- Online Calculator
(http://clincalc.com/icumortality/sofa.aspx)

SOFA Calculator

Sequential Organ Failure Assessment (SOFA) severity of illness score for hospital mortality

ClinCalc.com » Critical Care » Sequential Organ Failure Assessment (SOFA) Calculator

Use the *worst* value for each physiological variable within the past 24 hours.

Respiration	
FiO_2	[ ] %
PaO_2	[ ] mmHg
Mechanical ventilation	No / Yes

Coagulation	
Platelets	[ ] $x10^3/mm^3$

Liver	
Bilirubin	[ ] mg/dL

Neurological	
Glasgow coma score	[ ]

Cardiovascular	
MAP	[ ] mmHg
Vasopressors	No / Yes

Renal	
Creatinine	[ ] mg/dL
Urine output	Greater than 500 mL/day

Reset   Calculate

Appendix O: Calculating SOFA Scores User's Manual

Calculating SOFA Scores User's Manual

EFFECT Study Important Reminders

- Research manual and box of SOFA score notecards are kept in MRICU locker room (locker room entrance code is 1350), locker number 002, lock code 2**
- Date and SOFA scores must be entered into REDCap – Leave as "unverified" so we can double check some of the scores for reliability purposes
- Patient room numbers and %s should be recorded on orange notecard and handed directly to participating providers before rounds (8:30am for both teams)
- If any providers are not present for the day they're slated to receive scores, place back in notecard box until they return but be sure it includes their participant number so we can keep track of who it should be given to upon their return (this likely mostly applies to nurse practitioners or physician assistant)
- Direct the providers to place the orange cards in the shredder when they're done – At the very least, at the end of the day
- Participant tracking sheet is kept in the research manual (in locker) and should be used to record patient room number & MRN as well as which participant SOFA score was provided to
- FYI….
  - Providers have been given "badge buddies" so they have information on what SOFA scores represent
  - Following 10 days of scores, providers will be sent a link to a questionnaire regarding their experience with the scores; Gift cards will be distributed once they complete the questionnaire
- Please call Shelly directly with any questions or concerns (804-221-5159), day or night

SOFA Score Calculations

Basic Information:
- You need to be logged into Cerner and SOFA calculator online (http://clincalc.com/icumortality/sofa.aspx)
- SOFA is calculated using the WORST values from the previous 24 hours; Be sure to change your date/time in Cerner search bar to capture this within each screen
- Additionally, if there is less than 24 hours of data available, the 1st day of scores should not be calculated until the following morning
- Scores will only be calculated 3 times for applicable patients –
  1) MRICU admission day-- Day 1
  2) Admission plus one day-- Day 2
  3) Admission plus two days-- Day 3
- Admissions are determined by the admission log at the front desk & board in MD work room

FiO2—

In iView, click on Vital Signs

Right click on the gray bar and set your time parameters
 for "Last 24 Hours"

Obtain "Fi02 actual" and enter as Fi02 in calculator; If room air or given as liters instead in Cerner as "O2 flow rate", use conversion chart to obtain Fi02 to enter into calculator (NOTE: greatest value should be recorded)

Oxygen Flow Rate Conversion to Fi02:

Oxygen FLOW RATE in liters/min	Fi02 – Fraction of Inspired Oxygen Value
0 (no oxygen, just room air)	20%
1 L/min	24%
2 L/min	28%
3 L/min	32%
4 L/min	36%
5 L/min	40%
6 L/min	44%
7 L/min	48%
8 L/min	52%
9 L/min	56%
10 L/min	60%
11 L/min	64%
12 L/min	68%
13 L/min	72%
14 L/min	76%
15 L/min	80%

3

PaO2

Look in Results, Lab Results Tab, Anesthesia Laboratory heading, usually at the very top of the results section

Right click on gray bar and specify date range from exactly 24 hours previous to date and time of calculation to current date/time
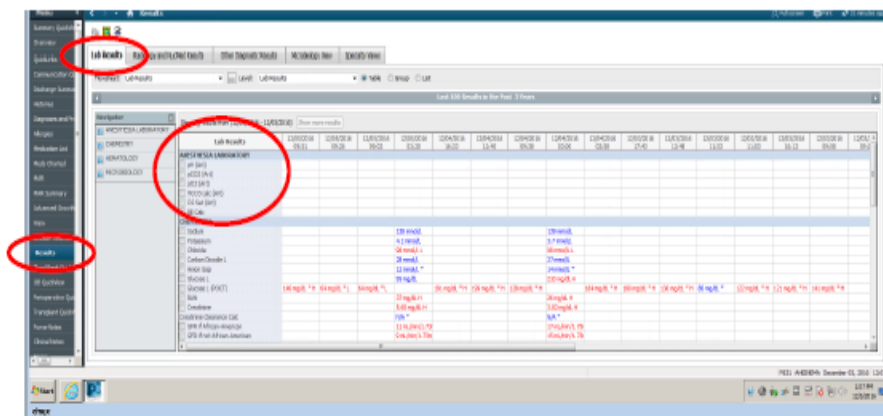
Obtain "p02" from Arterial blood gas and enter as Pa02 in calculator

*** Ensure value is from an arterial blood gas, it will state (Art) or (Ven)

If venous or no lab result is available, look at "Sp02" in iView under Vital Signs and use conversion chart to enter Pa02 in calculator (NOTE: lowest value should be recorded)

SO_2 (%)	PaO_2 (mmHg)
80	44
81	45
82	46
83	47
84	49
85	50
86	52
87	53
88	55
89	57
90	60
91	62
92	65
93	69
94	73
95	79
96	86
97	96
98	112
99	145

Mechanical Ventilation—

In iView, click on Vital Signs

Set your time parameters for "Last 24 Hours"

Look at "Oxygen delivery device" – Select yes/no for mechanical ventilation in calculator

Platelets--

Look in Results, Lab Results Tab, Look for the heading Hematology

Set your time parameters for date range from exactly 24 hours previous to date and time of calculation to current date/time

Platelets is about halfway down the list, labelled PLT. If no result is available, enter "200" as platelets in calculator (NOTE: lowest value should be recorded).
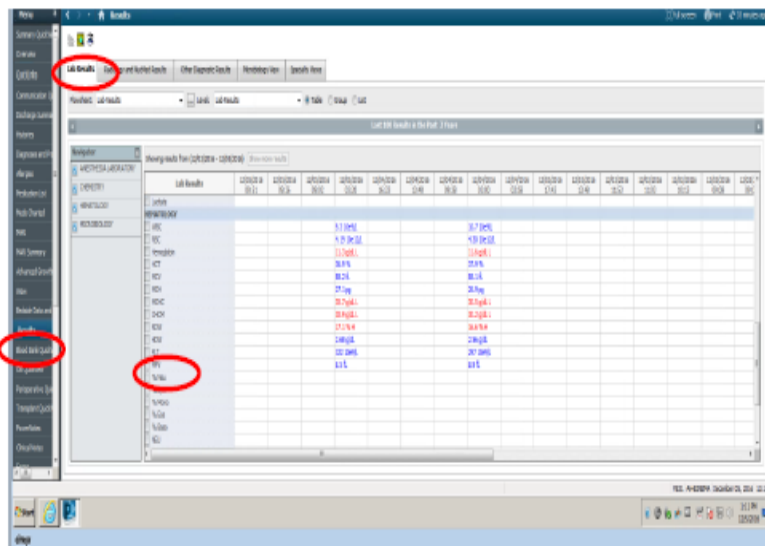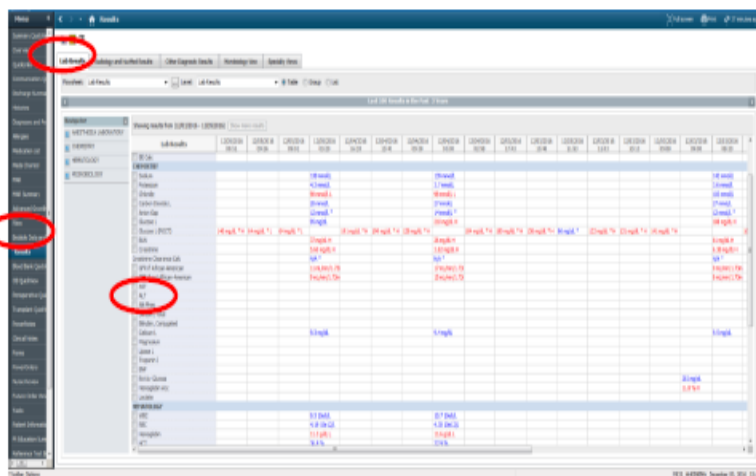

Bilirubin—

Look in Results, Lab Results Tab, Chemistry heading

Set your time parameters for date range from exactly 24 hours previous to date and time of calculation to current date/time
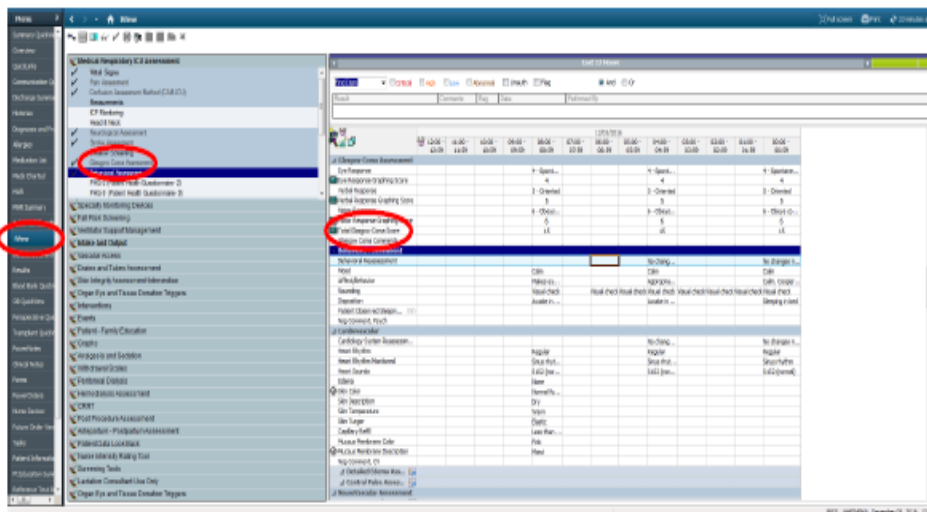
Enter the highest value for Bilirubin, Total. If no result is available, enter "1" as bilirubin in calculator (NOTE: greatest value should be recorded)

Glasgow coma score—

In iView, set your time parameters for "Last 24 Hours"

Under Medical Respiratory ICU Assessment, scroll down the list until you see "Total Glasgow Coma Scale" (NOTE: lowest value should be recorded)
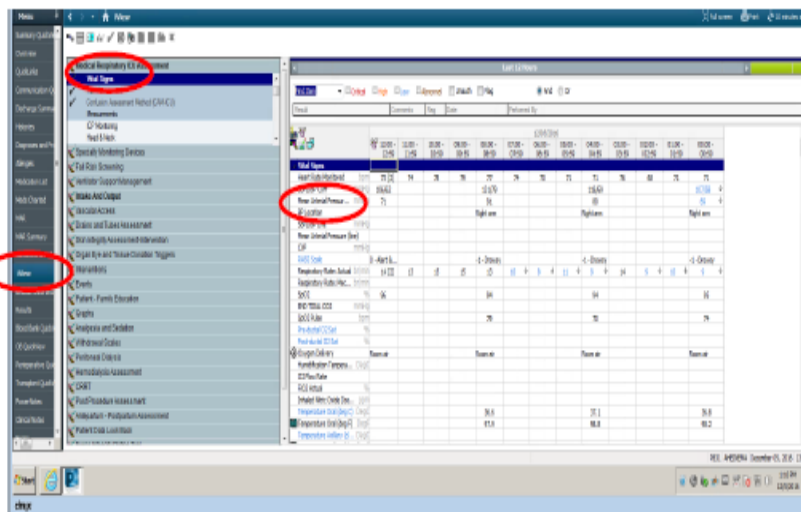

MAP—Mean Arterial Pressure

In iView, click on Vital Signs

Set your time parameters for "Last 24 Hours" (NOTE: lowest value should be recorded)

Just below the documented Blood Pressure SBD/DBP Cuff is "Mean Arterial Pressure"

7

Vasopressors--

In iView, click on Intake and Output

Set your time parameters for "Last 24 Hours"

Look at "Continuous Drips" to determine whether the patient is on any vasopressors (dopamine, dobutamine, epinephrine, norepinephrine)

Select yes/no for vasopressors in calculator

If patient is on Norepinephrine, enter the highest ml/hr from the last 24 hours as the mcg/min in calculator (It is nearly a 1:1 conversion from ml to mcg/min for 16mg in 250ml concentration bag)

If patient is on Dopamine, Dobutamine, or Epinephrine, use online calculator to convert ml/hr recorded to mcgs based on concentration of bag

***If required, obtain patient weight from Overview in the menu on the far left of cerner, and enter as weight in calculator; select kg or lbs as appropriate
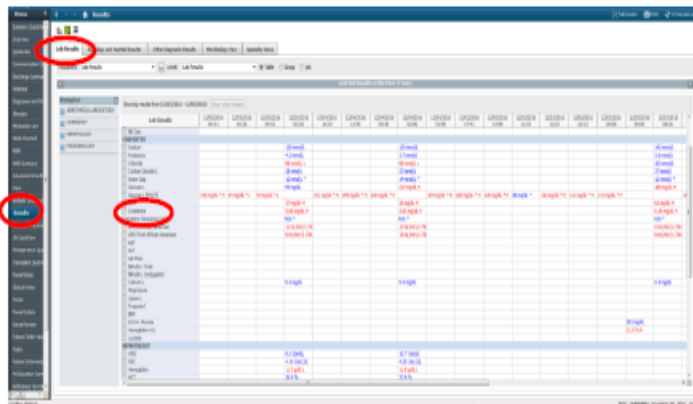
Creatinine--

Look in Results, Lab Results Tab, Chemistry heading

Set your time parameters for date range from exactly 24 hours previous to date and time of calculation to current date/time

Enter the highest creatinine for the last 24 hours. If no result is available, enter "1" as creatinine in calculator (NOTE: greatest value should be recorded)
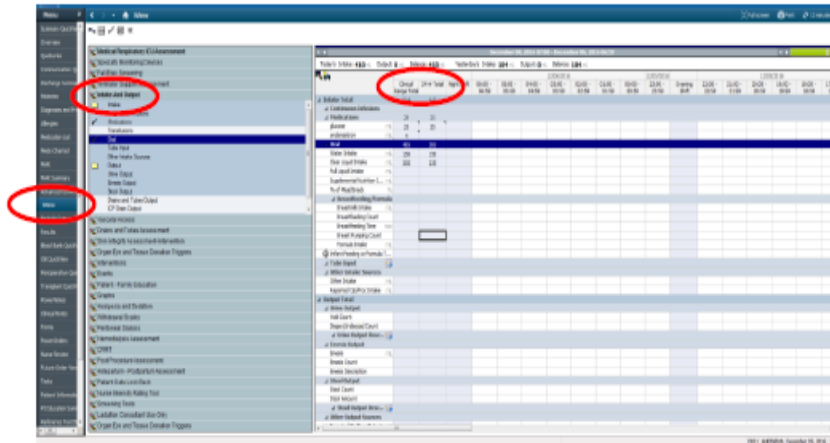

Urine Output—

In iView, click on Intake and Output

Set your time parameters for date range from exactly 24 hours previous to date and time of calculation to current date/time

Under "Clinical Range Total", obtain "Urine output" and select appropriate choice for urine output in calculator

Appendix P: Daily Cards Provided to Participants Receiving SOFA Mortality Risk Scores

Participant:

	Date:	Date:	Date:
For: _____	_____ %	_____ %	_____ %
For: _____	_____ %	_____ %	_____ %
For: _____	_____ %	_____ %	_____ %
For: _____	_____ %	_____ %	_____ %

Appendix Q: Acceptability & Feasibility Questionnaire Reminder Email

Thank you for your participation in the study ***The Acceptability, Feasibility, and Potential Impact of Using a Severity of Illness Mortality Prediction Instrument for Initiating End-of-Life Goals of Care Communication in the Adult Intensive Care Unit*** (VCU IRB NO.: HM20007357).

For the previous 10 days, you have received mortality prediction scores for your patients in the Medical Respiratory ICU (MRICU). Following your experience with these scores, you are now being asked to complete a seven-item online questionnaire about your experience. The questionnaire is expected to take less than ten minutes to complete. Following completion of the questionnaire, you will receive compensation for your participation and you will be contacted to ask for your additional participation in a follow-up interview.
Please remember that data is being collected for research purposes only and no responses will be linked to your identifying information. A secure web-based data capture system is being used to collect the questionnaire data.

If you have any questions or concerns about this questionnaire, contact:
Shelly Orr, MSN, RN, CNE, Principal Investigator
Phone: (804) 221-5159
Email: mlorr@vcu.edu

Please complete the questionnaire within the next week by clicking on the following link. **Insert REDCap Link Here*