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These sections and past issues of RIMJ can be viewed in the Journal’s archives at http://www.rimed.org/rimedicaljournal-archives.asp.

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‘Good Initiative, Bad Judgement’

PATRICK MCGLONE, BS, MD’21

The Alpert Medical School of Brown University on September 17 announced changing selection criteria for nomination into Alpha Omega Alpha (AOA) Honor Medical Society, part of an ongoing conversation between the nation’s medical schools and the Board of Directors of AOA, attempting to make AOA nomination better represent the diversity of medical students. No longer will pre-clinical grades and National Board score be weighted into AOA nomination, which will now be based more heavily upon leadership, community engagement, scholarly activity, professionalism, and grades in the core clerkships.

The AMS Senate, as part of a broader announcement in October 2019, included this statement about the changes: “...they instead recognize that equally splendid students who are inherently disadvantaged may not fall under the older qualifications. This change will allow for students who had difficulty in their time at AMS, but still meet the standards of what AOA is meant to represent, to have the opportunity to be rightfully nominated.”

This will not be a comment about diversity, structural bias, inclusion, or exclusion. I wish to present an argument that devaluing pre-clinical exam grades in medical school is unethical and harmful to the profession. My thesis is in two parts: 1. The sum of one’s grades in medical school is a reasonable proxy for one’s effort to learn and understand the academic content of medicine, and is a reasonable proxy for one’s actual understanding of the academic content of medicine. 2. It is ethically incumbent on training physicians that they devote their greatest level of effort into understanding the academic content of medicine.

We may all agree that sitting in a classroom and taking a test is a flawed method of evaluating knowledge. There are numerous reasons why performance on multiple choice tests may not be indicative of actual level of knowledge or content mastery, including learning disabilities, test anxiety, and perhaps most concerning, structural and systemic gaps due to social factors since childhood. But, I posit that the sum of dozens of exams taken in the pre-clinical years of medical school does, in fact, have significance.

When exams of the first two years and Step 1 are taken as a whole, they make a reasonable approximation for a student’s effort at learning and achieving mastery of the academic content of medicine. I acknowledge there is room for logical disagreement with this statement. Not every student’s effort correlates one to one with test performance – these students deserve more academic support to achieve outcomes they desire. But if we cannot agree that every test taken over the first two years correlates to some measure of student effort and knowledge, then the fundamentals of medical education are broken and need to be fixed. I do not believe this to be the case.

Pass-fail curriculums and flexible standards are fantastic innovations to decrease the toxic stress of medical school and allow students the opportunity to explore passions outside of the classroom. But, at the end of the day, we are paying $63,000 in tuition alone to be taught the academic content of medicine, and this must remain the significant focus of the first two years. Community engagement, research, leadership activities, volunteerism, etc. are all amazing things which are important to the medical community – but they can all be done without incurring life-altering debt. One does not need to be paying for an Ivy League medical education in order to volunteer in the community. These activities must all be secondary to the main purpose of the pre-clinical years, which is to develop a base understanding of the academic content of medicine.

The social contract with doctors of medicine makes it incumbent upon students of the profession to learn the content of medicine to the best of their ability in order to serve their patients. We must enter medical school with this expectation, and frame our understanding of medical education around it. If we do not, this devalues the profession and is a breach of the ethical obligation into which we entered. This is not saying that every student must achieve absolute content mastery demonstrated via exams – that is obviously absurd. This is an argument that we must devote our professional effort to this goal, and that other goals are secondary to this.

We are professional students, entering a profession founded upon scholarship and the application of evidence into clinical practice in the service of improving human health. Learning the basic content of the profession to the limit of personal mastery is, in my belief, an ethical obligation and personal responsibility. If we agree that the sum of one’s test scores is a logical proxy for effort and content mastery in the first two years, then it is ethically unsound to discount these measures in the evaluation of medical students deserving honors.

Disclaimer

The opinions expressed herein are those of the author alone, and do not reflect the opinions of the Alpert Medical School, Brown University.

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3. UK  
4. Canada  
5. India  
6. Germany  
7. Spain  
8. China  
9. Japan  
10. Brazil

**AMSTERDAM, THE NETHERLANDS**

Michael E. Migliori, MD, Ophthalmologist-in-Chief at RI Hospital, and a RIMS Past President, checks RIMJ at the entrance to the Theatrum Anatomicum, below a bust of Hippocrates, at the base of the eastern turret of De Waag in Nieuwmarkt square.

De Waag, built in 1498, is Amsterdam’s only surviving gate, formerly part of the fortified city walls. It became a weigh (waag) house in 1617 and later the Surgeons Guild Hall. Its Theatrum Anatomicum (Theater of Anatomy), on the upper floor, was immortalized by Rembrandt in his painting, The Anatomy Lesson of Dr. Tulp.

The Anatomy Lesson of Dr Tulp (1632), was commissioned by the Amsterdam Surgeons Guild as a group portrait of members attending the January 16, 1632 lecture given by Dr. Nicolaes Tulp in De Waag. It was painted by Rembrandt van Rijn in 1632 when he was 25 years old, and already displaying a mastery of lifelike portraiture and the dramatic use of light and shadow.
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Updates in Critical Care Medicine: Evidence-based Practice in 2020

GERARDO P. CARINO, MD, PhD
ANDREW T. LEVINSON, MD, MPH
GUEST EDITORS

INTRODUCTION
Welcome to this issue of the Rhode Island Medical Journal titled “Updates in Critical Care Medicine,” which offers concise and comprehensive reviews on new and important issues that occur regularly in the critical care setting. Our distinguished Rhode Island colleagues, who are dedicated to improving the care and outcomes of critically ill medical patients, present the following topics:

Sepsis
Sepsis management has dramatically evolved over the last two decades. The multi-national Surviving Sepsis Campaign has driven much of the research and recommendations for sepsis care. We are fortunate that one of the campaign leaders is MITCHELL LEVY, MD, Chief of Brown’s Division of Critical Care, Pulmonary and Sleep Medicine. He and DR. JISOO LEE provide an excellent review of the most recent clinical trials related to the management of sepsis and present current recommendations for patient management.

Acute Renal Failure
Renal failure is extraordinarily common in the critically ill and has been shown to predict mortality. The correct timing for starting renal replacement in the ICU remains an unanswered question. Recent studies have attempted to better describe appropriate timing of dialysis in patients who develop renal failure. DR. KATHERINE COX, et al review some of the most important literature in the field. Of note, Rhode Island and Miriam Hospitals are sites for the current STARRT-AKI trial which aims to better address this issue.

Transfusion of red blood cells
Less may be more in the case of the transfusion of red blood cells to critically ill patients. Many patients are anemic or become anemic in the ICU setting, yet multiple studies suggest that transfusion of red blood cells may be overutilized and does not achieve desired goals. DR. CHANNING HUI, et al review data regarding red blood cell transfusions and present recommendations for appropriate transfusion triggers in the ICU.

End-of-life care in the ICU
Despite clinical advances, ICU mortality remains significant. Communicating with patients and families about a patient’s critical condition and facilitating decisions about end-of-life (EOL) are a fundamental aspect of critical care medicine. Over the last two decades there has been a significant increase in knowledge about how to best care for both patients and their families in this situation. DR. SARAH RHoads, et al review current best practices for communicating with and supporting family members and patients, as well as reducing distress during EOL. The authors also discuss the role of the evolving specialty of palliative care in the ICU.

Point-of-care ultrasound (POCUS) for patients with acute respiratory failure
Very few things have changed critical care medicine in the recent past than the advent of bedside ultrasound to answer clinical questions in real time. Initially point-of-care ultrasound (POCUS) focused on assistance with vascular access, but currently includes diagnosis of pulmonary conditions. Diagnosing the cause of patients with severe respiratory failure can be a challenging dilemma and POCUS may significantly increase diagnostic accuracy. It is now widely taught in academic critical care medicine programs such as Brown’s. DR. MOHAMMAD ARABAT, et al review key findings of lung ultrasound and the evidence for its use in diagnosing patients with dyspnea and acute respiratory failure.

Extracorporeal life support (ECLS)
Extracorporeal life support (ECLS) has been rapidly adopted for use in adult patients with severe acute respiratory failure and can help sustain patients refractory to conventional mechanical ventilator support. The Rhode Island and Hasbro Children’s Hospital ECLS program is the only one in Southern New England and has been awarded a Gold Center of Excellence by the Extracorporeal Life Support Organization. DR. COREY VENTETUOLO is the Medical Director, ECLS program, and DR. NEEL SODHA is the Surgical Director, ECMO and Mechanical Circulatory Support, at Rhode Island Hospital. They and DR. ADEEL ABBASI, et al provide an excellent state-of-the-art review about ECLS for respiratory failure.

Managing high-risk pulmonary embolism
The management of high-risk pulmonary embolism remains a rapidly evolving field in critical care medicine. Medical, interventional and surgical options can all be considered and makes decision-making quite complex. Multi-disciplinary Pulmonary Emergency Response Teams (PERTs) have been recently described as a way to assist in this complex decision-making. DR. CHRISTOPHER MULLIN is director of Rhode Island Hospital’s PERT team. He and DR. CHRISTOPHER THEROUX, et al review the recent literature and treatment options for patients with pulmonary embolism at high risk of clinical decompensation or death.
In conclusion, we very much hope you enjoy this compilation and advance your knowledge about key current topics in critical care medicine both here in Rhode Island and globally.

**Guest Editors**

Gerardo P. Carino, MD, PhD, Associate Professor of Medicine, Alpert Medical School of Brown University.

Andrew T. Levinson, MD, MPH, Assistant Professor of Medicine, Alpert Medical School of Brown University.

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Treatment of Patients with Severe Sepsis and Septic Shock: Current Evidence-Based Practices

JISOO LEE, MD; MITCHELL M. LEVY, MD, MCCM, FCCP

ABSTRACT
Sepsis remains a field of active research with many unknown and unanswered questions. Over the past few decades, advancements in sepsis management have led to improved mortality and morbidity. This article will review the current evidence-based practices of the treatment of sepsis and septic shock. It will also critically appraise some of the current controversies in sepsis management, such as fluids, steroids, early vasopressors, early goal-directed therapy and immunotherapy.

KEYWORDS: sepsis, septic shock, management, controversies

INTRODUCTION
Sepsis is a common disease entity that is associated with high morbidity and mortality. Globally, it is estimated that over 30 million people are hospitalized for sepsis every year, and sepsis may contribute to up to 5.3 million deaths every year.1 The terms systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, and septic shock were initially described through a consensus statement in the early 1990s by the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM).2 Most recently, the terms SIRS and severe sepsis were eliminated, and sepsis is now defined as “life-threatening organ dysfunction due to a dysregulated host response to infection.”3

In this review article, the concept of sepsis bundles for management of sepsis and septic shock based on evidence-based practice will be reviewed. Additionally, some of the major controversies in sepsis management will be reviewed, focusing on the roles of steroids, fluids, vasopressors, early goal-directed therapy and immunotherapy.

MANAGEMENT OF SEPSIS – THE SURVIVING SEPSIS CAMPAIGN (SSC) AND SEPSIS BUNDLE
Unfortunately, there are no specific molecular therapies that have proven to be effective in sepsis treatment. The Surviving Sepsis Campaign (SSC) was initiated in 2002 to provide guidelines for sepsis and septic shock management for clinicians with the goal to reduce mortality. The “sepsis bundles”, which have gone through multiple iterations in the SSC Guidelines, describe a selected set of interventions that are recommended to be conducted. The hour-3 bundle and hour-6 bundle highlight interventions to be completed within 3 hours and 6 hours of time of presentation, respectively. The “time of presentation” is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements severe sepsis or septic shock ascertained through chart review.

Table 1. Hour-3 and Hour-6 Bundles.
To be completed within 3 hours and 6 hours of time of presentation, respectively. The “time of presentation” is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements severe sepsis or septic shock ascertained through chart review.

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<th>Hour-3 Bundle</th>
<th>Hour-6 Bundle</th>
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<tbody>
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<td>1. Measure lactate level.</td>
<td>Hour-3 Bundle elements (as seen on the left). Plus,</td>
</tr>
<tr>
<td>2. Obtain blood cultures prior to administration of antibiotics.</td>
<td>5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg</td>
</tr>
<tr>
<td>3. Administer broad-spectrum antibiotics.</td>
<td>6. In the event of persistent hypotension after initial fluid administration (MAP &lt; 65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion.</td>
</tr>
<tr>
<td>4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L.</td>
<td>7. Re-measure lactate if initial lactate elevated.</td>
</tr>
</tbody>
</table>
recommend (best practice statement) hospitals have a performance improvement program to screen for patients for sepsis. Routine microbiologic cultures including at least two sets of blood cultures should be obtained prior to starting broad-spectrum intravenous antimicrobial therapy without causing substantial delay in the therapy.

The 2018 update to the SCC guidelines describes the “hour-1 bundle” [Table 2]. This bundle consists of five bundle elements as follows: Measure lactate level; obtain blood cultures prior to administration of antibiotics; administer broad-spectrum antibiotics; rapidly administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L; and apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mm Hg. This hour-1 bundle intends to underscore the urgency to treat patients with sepsis and septic shock, combining the three-hour and six-hour bundles into a single hour to shorten the time to beginning resuscitation and management and improve outcome. Further research is warranted to assess the efficacy of hour-1 bundle implementation.

Table 2. Hour-1 Bundle.
To be completed within 1 hour of time of presentation. The “time of presentation” is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of sepsis (formerly severe sepsis) or septic shock ascertained through chart review.

<table>
<thead>
<tr>
<th>Hour-1 Bundle</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Measure lactate level. Remeasure if initial lactate is &gt;2 mmol/L.</td>
</tr>
<tr>
<td>• Obtain blood cultures prior to administration of antibiotics.</td>
</tr>
<tr>
<td>• Administer broad-spectrum antibiotics.</td>
</tr>
<tr>
<td>• Rapidly administer 30mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L</td>
</tr>
<tr>
<td>• Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65 mm Hg.</td>
</tr>
</tbody>
</table>

HOT CONTROVERSIES IN SEPSIS
There have been many hotly debated controversies in sepsis and septic shock management over the past few decades. While some have robust amount of trials with conflicting results over time, others are in need of more research. We will discuss some of the topics, including the use of steroids, fluid choice, vasopressor choice and timing, early goal-directed therapy, and immunotherapy for personalized medicine.

Steroids
Since the first randomized controlled trial published in JAMA in 1963, there have been over 40 randomized controlled trials to determine the use of corticosteroids in severe sepsis and septic shock. The 2016 SSC guidelines suggest against using intravenous corticosteroids to treat septic shock if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. However, it is suggested to use 200 mg of hydrocortisone per day if hemodynamic stability is not achievable. The most two recent trials after these guidelines showed conflicting data regarding corticosteroid use and mortality benefit in septic shock. The ADRENAL trial by Venkatesh et al. compared 200 mg of hydrocortisone per day versus placebo for 7 days in patients with septic shock undergoing mechanical ventilation, which showed no difference in 90-day mortality. The APROC-CHSS trial by Annane et al. evaluated the effect of hydrocortisone-plus-fludrocortisone therapy, drotrecogin alfa, the combination of the three drugs, or their respective placebos. This study showed that the hydrocortisone-plus-fludrocortisone therapy reduced the 90-day mortality compared to the placebo (43.0% versus 49.1%, p=0.03). The drotrecogin alfa group was not completed due to the withdrawal of the drug from the market in 2011. Regardless of the difference in the primary outcomes of mortality, both trials demonstrated that corticosteroid treatment group has a shorter time to resolution of shock compared to placebo. Although there is no systematic review and meta-analysis involving these two recent trials, the BMJ Rapid Recommendations, which is a BMJ collaboration that aims to accelerate evidence into practice, incorporated these two trials and made a weak recommendation for corticosteroids with sepsis, concluding that both steroids and no steroids are reasonable management options for refractory septic shock.

Fluids
Early fluid resuscitation is one of the key recommendations for sepsis and septic shock management, and there have been many controversies regarding the types of fluid. In the SSC guidelines, crystalloids have been recommended as the first line of fluids for resuscitation, and these are most widely available. More recently, a great deal of attention has been focused on balanced fluids. The most commonly used isotonic crystalloid, 0.9% normal saline, has high chloride concentration (154 mmol per liter) compared to human plasma (94 to 111 mmol per liter), and is thought to worsen kidney function due to the excess chloride. Unlike normal saline, balanced fluids such as lactated Ringer’s solution and Plasma-Lyte A have electrolyte compositions that are closer to that of plasma, with chloride concentration of 109 mmol per liter and 98 mmol per liter, respectively. The SPLIT trial published in 2015 compared a buffered crystalloid solution (Plasma-Lyte 148) with saline on their effect on acute kidney injury (AKI) among patients admitted to the intensive care unit. The study did not show any significant difference in the risk of AKI, the use of renal replacement therapy, or hospital mortality. However, there was a signal towards improved outcome with the buffered crystalloid solution, which prompted the need for further studies. The SMART trial published in 2018 compared balanced crystalloids...
[lactated Ringer’s solution or Plasma-Lyte A] with saline and looked at a composite of death from any cause, new renal-replacement therapy, or persistent renal dysfunction within 30 days.10 This study showed that the use of balanced crystalloids resulted in a lower rate of the composite outcome, favoring its use over saline. Most recently, a single-center, multi-crossover trial compared balanced crystalloids with saline among adults in the emergency department who were hospitalized outside an ICU.11 This study did not show any difference in the number of hospital-free days in the two groups; however, the balanced crystalloids group had less major adverse kidney events within 30 days compared to the saline group.

Other types of fluids have been studied as well. Colloids such as albumin have also been evaluated for its effect on fluid resuscitation. The SAFE trial looked at 4% albumin or normal saline for fluid resuscitation in a heterogenous population of ICU patients.12 The CRISTAL trial compared colloids [gelatins, dextrans, hydroxyethyl starches, 4% or 20% albumin] to crystalloids [isotonic or hypertonic saline or Ringer lactate solution] in critically ill patients with hypovolemic shock.13 Both the SAFE and CRISTAL trials showed no significant difference in the primary outcome of 28-day mortality.

Vaspressors
Vaspressors are one of the essential medications used in shock; however, the choice of vasopressor and the optimal timing of vasopressor initiation remain controversial. Norepinephrine is the most commonly used first-line vasoactive medication in shock, as it has shown to have lower mortality and lower risk of arrhythmias when compared with dopamine.14 Vasopressin and epinephrine are reasonable second-line agents in order to lower the amount of norepinephrine, and the use of phenylephrine does not have enough data to support its use in septic shock currently.4 The optimal timing of vasopressor initiation is unknown. Early vasopressor therapy might lead to faster achievement of the target MAP and thereby facilitate tissue perfusion. It may also prevent deleterious effects from fluid overload. However, a fine balance will need to be established as it may also be harmful to initiate vasopressor therapy when the intravascular fluid resuscitation has not been adequately achieved. This concept is currently being tested in an ongoing trial.15 The 2018 update to the SSC bundle recommends vasopressor therapy within the first hour to achieve mean arterial pressure (MAP) of 65 mm Hg or greater if blood pressure is not restored after initial fluid resuscitation of 30 mL/kg.5

Early goal-directed therapy (EGDT)
EGDT involves optimizing tissue perfusion by giving crystalloid fluid boluses to achieve central venous pressure (CVP) 8-12 mm Hg, initiating vasopressors to maintain MAP of at least 65 mm Hg, and maintaining central venous oxygen saturation [ScvO₂] at greater than 70% with red blood cell transfusion and/or dobutamine administration. In 2001, Rivers et al. showed that a significant improvement in mortality by 15% when patients with severe sepsis or septic shock were treated using six-hour EGDT compared to standard therapy.16 This study has since promoted best practice guidelines for early management of sepsis and septic shock. However, limitations of this study, including that it was a single-center trial lacking external validity, and the complexity and resourceful demand of the protocol, prompted further research. A little over a decade later, three multi-center clinical trials were published – ProCESS from the United States, ARISE from Australasia, and ProMISe from England. These trials compared protocol-based EGDT to standard therapy and all failed to show a difference in 90-day mortality.17,18,19 It is important to acknowledge that the mortality rates were lower in the newer trials compared to the Rivers et al.’s study, and there has been overall improvement in the management of initial sepsis management in the past 15 years. However, it must be concluded that mandated central lines targeting CVP and ScvO₂ are no longer supported by the current literature.

Targeted Immunotherapy
Although decades of effort and multiple, large international RCTs have been conducted on promising immunomodulatory therapeutics, all of these trials have been negative and there is no current immunotherapy that is in clinical use for sepsis and septic shock. Various agents including anti-cytokines [e.g. anti TNF-α], anti-virulence factors [e.g. monoclonal antibody against lipopolysaccharide and gram negative endotoxins], anticoagulation agents [e.g. activated protein C, antithrombin III, heparin] and immune stimulators [e.g. G-CSF] have been studied without yielding significant results.20 The heterogeneity of the patients with sepsis and septic shock, clinical trial design, variable pathways that lead to sepsis, as well as the complexity of sepsis pathophysiology, among other factors, may account for the failure of these trials. Overcoming these challenges will be crucial to advance to precision medicine and enable successful, targeted immunomodulatory therapy.

CONCLUSION
Management of sepsis and septic shock involves early interventions to achieve hemodynamic stability. Due to the heterogeneity and complexity of sepsis pathophysiology, there is no perfect therapy for sepsis that “fits for all.” However, implementation of best-practice guidelines based on evidence-based medicine has shown to improve mortality associated with sepsis and septic shock. Many elements of the guidelines remain controversial and more research is needed to address these important unanswered questions.
References


Acute Renal Failure in Critically Ill Patients: Current Evidence-Based Practices
KATHERINE COX, MD; DEBASREE BANERJEE, MD, MS

ABSTRACT
Acute kidney injury (AKI) is a common condition amongst critically ill patients in the medical intensive care unit (ICU) and is associated with increased morbidity and mortality. There are several areas of ongoing debate regarding management of AKI, specifically the initiation and timing of renal replacement therapy (RRT). In this review, we aim to concisely discuss epidemiology, current evidence with regards to optimal vascular access, timing of initiation and modality of renal replacement therapy in acute kidney injury in critically ill patients.

KEYWORDS: acute kidney injury (AKI), critically ill, renal replacement therapy (RRT)

EPIDEMIOLOGY
AKI is defined as a sudden decrease in renal function and is conventionally diagnosed utilizing the Kidney Disease: Improving Global Outcomes (KDIGO) criteria. KDIGO defines AKI as an increase in serum creatinine by ≥0.3 mg/dL within 48 hours, or an increase in serum creatinine ≥1.5 times baseline, known to have occurred within the prior seven days or urine volume <0.5 mL/kg/hr for six hours [Table 1]. Accepted alternate criteria exist and include those proposed by the Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease (RIFLE) group and criteria posed by the Acute Kidney Injury Network (AKIN) [Table 2].

AKI affects up to half of medical intensive care unit patients and is associated with increased length of ICU stay, increased hospital stay, development of chronic kidney disease and increased short-term and long-term mortality. In fact, more than 13% of critically ill patients will receive RRT within the first week of their ICU stay. Mortality rates in critically ill patients with AKI is quoted to be around 50% and is associated with a six-fold increased risk of dying in the hospital. A multinational cross-sectional study on the epidemiology of AKI in ICU patients meeting KDIGO criteria revealed an incidence of 57% with little variation in AKI occurrence and mortality between different parts of the world. Sepsis is among the most common causes of admission to the ICU and is frequently associated with AKI. The pathophysiology of AKI and sepsis is poorly understood.

Table 1. KDIGO and AKIN criteria for diagnosis of AKI

<table>
<thead>
<tr>
<th>KDIGO</th>
<th>AKIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in serum creatinine by ≥0.3 mg/dL within 48 hours or</td>
<td>Increase in serum creatinine of ≥0.3 mg/dL</td>
</tr>
<tr>
<td>Increase in serum creatinine to ≥1.5 times baseline, known to have occurred within the prior seven days</td>
<td>Increase in serum creatinine of ≥50% within 48 hours</td>
</tr>
<tr>
<td>Urine volume &lt;0.5 mL/kg/hr for six hours</td>
<td>Urine output of &lt;0.5 mL/kg/hr for &gt;6 hours</td>
</tr>
</tbody>
</table>

Table 2. KDIGO, AKIN and RIFLE staging for AKI [1,19]

<table>
<thead>
<tr>
<th>RIFLE</th>
<th>KDIGO</th>
<th>AKIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk: Increase in serum creatinine x 1.5 or decrease in GFR &gt;25% or UOP &lt;0.5 mL/kg/hr for 6-12 hours</td>
<td>Stage 1: Increase in serum creatinine of ≥0.3 mg/dL or 1.5-1.9 x baseline or UOP of &lt;0.5 mL/kg/hr for 6-12 hours</td>
<td>Stage 1: Increase in serum creatinine of ≥0.3 mg/dL or increase in serum creatinine x1.5-2.0 or UOP &lt;0.5 mL/kg/hr for 6-12 hours</td>
</tr>
<tr>
<td>Injury: Increase in serum creatinine x2 or decrease in GFR &gt;50% or UOP &lt;0.5 mL/kg/hr for 12-24 hours</td>
<td>Stage 2: Increase in serum creatinine of 2.0-2.9 x baseline or UOP &lt;0.5 mL/kg/hr for 12-24 hours</td>
<td>Stage 2: Increase in serum creatinine &gt;200-300% or UOP &lt;0.5 mL/kg/hr for 12-24 hours</td>
</tr>
<tr>
<td>Failure: Increase in serum creatinine x 3 or GFR &gt;75% or increase in serum creatinine by &gt;0.5 mg/dL if baseline creatinine is &gt;4.0 mg/dL or UOP of &lt;0.3 mL/kg/hr for &gt;24 hr or anuria for &gt;12 hours or initiation of RRT</td>
<td>Stage 3: Increase in serum creatinine of 3.0 x baseline or increase in serum creatinine to ≥4.0 mg/dL or UOP of &lt;0.3 mL/kg/hr for over 24 hours or anuria for over 12 hours or initiation of RRT</td>
<td>Stage 3: Increase in serum creatinine &gt;300% or increase in serum creatinine by &gt;0.5 mg/dL if baseline is ≥4.0 mg/dL or UOP of &lt;0.3 mL/kg/hr for &gt;24 hours or anuria for &gt;12 hours or initiation of RRT</td>
</tr>
<tr>
<td>Loss: Need for RRT for &gt;4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End Stage: Need for RRT &gt;3 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
though animal models suggest that initially, septic AKI may be caused by a combination of microvascular shunting and tubular cell stress. With resolution of sepsis, the majority of patients with AKI in the context of sepsis have renal recovery though remain at increased risk for developing chronic kidney disease.

The decision regarding whether to start RRT, optimal timing for initiation, modality used, and frequency of RRT in acutely ill patients is an area of ongoing investigation and remains controversial. Many patients will have spontaneous renal recovery and premature initiation of RRT may expose patients to risks such as complications of anticoagulation, hypotension, allergic reactions to system components, and complications of vascular access without conferring meaningful benefit.

### TIMING

It is universally accepted that urgent indications for RRT in patients with AKI include severe refractory metabolic acidosis, signs of uremia such as pericarditis or severe encephalopathy, severe refractory hyperkalemia, refractory volume overload, and certain intoxications. In the absence of these clinical scenarios, the optimal timing for initiating RRT among ICU patients remains unclear as there are poor prognostic tools to determine which patients will go on to renal recovery. Some postulate that early removal of uremic toxins and avoidance of hyperkalemia may be beneficial in patients who are critically ill, while others contest the risks of vascular access, hemodynamic effects and anticoagulation outweigh the benefits of early initiation. Three large randomized clinical trials comprise the majority of evidence in this arena (Table 3).

The ELAIN trial, published in 2016, was a randomized single center parallel group trial, which randomized 231 ICU patients with AKI to early RRT within eight hours of confirmation of KDIGO stage 2 AKI or delayed RRT which was defined as initiation of RRT within twelve hours of either KDIGO stage 3 criteria (Table 2) or absolute indications. All patients who received RRT received continuous venous hemofiltration (CVVH). The primary outcome of 90-day all-cause mortality was 39.3% in the early group when compared with 54.7% in the delayed group. They also found increased renal recovery at 90 days, a small decrease in median duration of RRT, decreased mechanical ventilation and decreased length of hospital stay in the early group. While striking, this study was limited in that it was single center, almost all patients were surgical patients, and groups were un-blinded.

Within the same year, the AKIKI trial was published. In a large multicenter, open-label randomized trial, 620 ICU patients either mechanically ventilated, or on catecholamine infusions or both, were randomized to receive either early or delayed RRT. When compared with the ELAIN trial, patients were randomized once they developed KDIGO stage 3 AKI (Table 2). The early group was randomized and treated within 6 hours of confirming KDIGO stage 3 AKI and the delayed group was treated once acute indications were met based upon laboratory abnormalities or if oliguria or anuria lasted over 72 hours after randomization. There was no significant difference in all-cause mortality at 60 days. Of note, there was a higher incidence of catheter-related bloodstream infections in the early RRT group. When compared with the ELAIN trial, these patients were mostly medical ICU patients and over 50% of patients received intermittent hemodialysis and only 30% of patients received CVVH. Also of note, half of the delayed-group patients never received RRT. Post-hoc analysis found the lowest mortality rate among patients who never underwent RRT as compared with those who underwent RRT.

More recently, the IDEAL-ICU trial was published, supporting the results of AKIKI. This was a multicenter randomized trial in which 488 ICU patients with septic shock and AKI were randomized to early initiation of RRT (within 12 hours of onset of RIFLE end-stage kidney disease) (Table 2) or delayed initiation (after 48 hours if renal function did not spontaneously recover and if no condition meeting criteria for emergent RRT developed). The primary outcome was

### Table 3. Summary of the sentinel trials regarding timing of initiation of RRT in critically ill patients with AKI.

<table>
<thead>
<tr>
<th>Clinical Study</th>
<th>Patients</th>
<th>Study design</th>
<th>N</th>
<th>Study Endpoints</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELAIN</td>
<td>Critically ill patients with AKI (KDIGO Stage 2 and higher), mostly surgical</td>
<td>Single center RCT. Early RRT (within 8 hours of KDIGO 2) versus delayed RRT (within 12 hours of KDIGO stage 3 or no initiation)</td>
<td>231</td>
<td>Mortality at 90 days after randomization</td>
<td>Early RRT compared with delayed reduced 90-day mortality</td>
</tr>
<tr>
<td>AKIKI</td>
<td>Critically ill medical patients with AKI (KDIGO stage 3)</td>
<td>Multicenter RCT. Early RRT started immediately after randomization, delayed started if patients developed urgent indications or oliguria &gt;72h</td>
<td>620</td>
<td>Overall survival at day 60</td>
<td>Mortality did not differ significantly between early and delayed strategies</td>
</tr>
<tr>
<td>IDEAL-ICU</td>
<td>Critically ill patients with early-stage septic shock and AKI (RIFLE)</td>
<td>Multicenter RCT. Early RRT within 12 hours after documentation of failure-stage AKI or delayed at 48 hours if renal recovery had not occurred</td>
<td>488</td>
<td>Death at 90 days</td>
<td>No significant difference in overall mortality at 90 days</td>
</tr>
</tbody>
</table>
The clinical practice guidelines for AKI recommend using intermittent and continuous RRT modalities as complementary therapies based on similar survival and recovery of renal function with both modalities. However, certain circumstances may favor one modality over the other. IHD may be preferable for clearance of certain toxicities as poison clearance with CRRT is 50-80% less than that achieved with intermittent modalities. CRRT, on the other hand, is recommended in patients with acute brain injury where changes in plasma solute concentration may lead to cerebral hypoperfusion. Additionally, in patients with acute hepatic failure with associated hyperammonemia and high grade encephalopathy, one multicenter cohort study suggested an association with decreased

90-day mortality and there was no statistically significant difference between the two groups. There was no significant difference in ICU days between the two groups though fewer patients in the delayed group received RRT and had more RRT free days. The trial was stopped early for futility. Again, post-hoc analysis showed the lowest mortality in patients who never received RRT. These three major trials all have important differences including number of patients and centers, differences in triggers for early or delayed RRT, and RRT modality. To add to the growing body of literature on the subject, there is an ongoing large phase three trial called STARRT-AKI, in which Rhode Island Hospital is a participating site. STARRT-AKI is including critically ill ICU patients randomized to standard RRT initiation versus accelerated RRT initiation and is due to be published at the end of 2019. A recent meta-analysis of ten randomized controlled trials suggested no additional benefit of early initiation of RRT for critically patients with AKI on 30- 60- or 90-day mortality, though studies included in the meta-analysis had a significant amount of heterogeneity with variable definitions of early versus late RRT. Overall, optimal timing remains unclear but seems to favor delayed RRT with close observation to avoid urgent or emergent indications.

ACCESS
Initial vascular access for patients newly on RRT is usually temporary as the average duration of RRT dependence for patients with AKI is less than two weeks. Historically, femoral access was thought to be associated with an increased risk of catheter-associated line infection; however, more recently a systematic review comparing the rate of catheter-associated line infections in patients with femoral, internal jugular and subclavian lines suggested that there is no significant difference between the three. One exception to this may be among obese patients with a BMI >28.4 where femoral lines have been associated with increased risk of infection. Placement of multiple catheters, longer duration, subclavian access and left internal jugular access are all associated with increased risk of development of central vein stenosis which can compromise the future use of arteriovenous fistula and graft placement in the ipsilateral extremity if needed. Tunneled cuffed catheters should be placed in patients who will require long-term RRT (until an arteriovenous fistula or graft can be used) due to the decreased rate of catheter-associated infection.

MODALITY
There are several different types of RRT available for use including intermittent hemodialysis (IHD), continuous renal replacement therapy (CRRT), peritoneal dialysis (PD), and hybrid therapies including sustained low-efficiency hemodialysis (SLED) (a combined modality where dialysis is administered for hours longer than traditional IHD with slower blood flows but still delivered on a daily basis as opposed to continuously) (Figure 1).

In a prospective randomized multicenter study including critically ill patients with acute renal failure, 60-day mortality was not different between patients who received IHD when compared with CRRT. Additionally, CRRT is associated with higher costs when compared with IHD. A recent systematic review and meta-analysis of 21 studies comparing mortality, dialysis dependence and length of stay among critically ill patients receiving CRRT, IHD or SLED for AKI did not reveal an advantage for any specific RRT modality. KDIGO practice guidelines for AKI recommend using intermittent and continuous RRT modalities as complementary therapies as studies have shown similar survival and recovery of renal function with use of both modalities. There may be certain circumstances for which a particular modality of RRT may be most beneficial. IHD may be preferable when used for clearance of certain toxicities as poison clearance with CRRT is 50-80% less than that achieved with intermittent modalities. CRRT, on the other hand, is recommended in patients with acute brain injury in whom changes in plasma solute concentration may worsen intracranial hypertension and in concert with systemic hypotension can lead to cerebral hypoperfusion. Additionally, in patients with acute hepatic failure with associated hyperammonemia and high grade encephalopathy, one multicenter cohort study suggested an association with decreased
ammonia levels and improved 21-day transplant free survival in patients who underwent CRRT as compared with no RRT and IHD. In our center, we have found that when fluid removal is the main purpose of RRT, CRRT allows for increased ultrafiltration as compared with IHD. While used more frequently in the pediatric patient population, there is a paucity of well-designed adult studies comparing the use of PD compared with other RRT modalities in AKI. One prospective, randomized, controlled trial comparing high volume PD with IHD in patients with AKI due to acute tubular necrosis found that mortality rate and renal function recovery were similar in both groups.

CONCLUSIONS

Acute kidney injury in acutely ill adults is associated with high morbidity and mortality and RRT remains an important part of management. Optimal criteria for and timing of initiation remain controversial though the current body of evidence favor delayed initiation with close observation to avoid urgent or emergent indications and minimize the risks of catheter related infection and intradialytic hypotension. Practice guidelines recommend using intermittent and continuous RRT modalities as complementary therapies as studies have shown similar survival and recovery of renal function in the general ICU population.

References


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Red Blood Cell Transfusions in the ICU
CHANNING HUI, DO; GRANT CAGLE, MD, MPH; GERARDO CARINO, MD, PhD

ABSTRACT
Red blood cells are commonly administered to critically ill patients, yet the desired benefit of improving oxygen delivery and overall outcome may not be achieved in many scenarios. In addition, blood products are of limited supply and there are clear risks associated with blood transfusion. Despite this, studies show that almost half of all ICU patients receiving blood transfusions do so in the setting of stable anemia, suggesting that many critically ill patients in the ICU may receive unnecessary transfusions. Critical illnesses can lead to increased rates of anemia, even without active blood loss. The benefits of transfusion in these situations are unclear. Clear indications for blood transfusions, including uncontrolled hemorrhage, symptomatic anemia, and possibly acute coronary syndrome, are met in the minority of patients receiving red blood cell transfusions. This review discusses current evidence regarding the use of red blood cell transfusions in the ICU. Two major categories are examined, transfusion in patients noted to be anemic, but not clearly actively bleeding or symptomatic, and patients with aggressive bleeding who are critically ill or require massive transfusions.

INTRODUCTION
Anemia is a common phenomenon in the ICU, with approximately 30% of patients having a hemoglobin concentration less than 10 g/dL.1 In critically ill patients, the controversy to transfuse stems from a conflict of physiological principles and the results of randomized trials. As the oxygen carrier in blood, increased hemoglobin levels theoretically increase oxygen delivery and support the patient in shock.1 However, the benefit of transfusing liberally to a higher hemoglobin concentration in non-bleeding, anemic patients is unproven, and in certain cases may be harmful. Randomized trials have demonstrated that transfusing to a lower target may have lower complication rates and decreased mortality in particular groups of patients. It remains unclear if red cell transfusions themselves are the reason for worse clinical outcomes or the result of being critically ill with anemia.

CONSEQUENCES OF ANEMIA AND EFFECTS OF TRANSFUSION
Anemia has been clearly associated with poor outcomes in many instances, including with elderly patients, acute myocardial infarction, chronic kidney disease and acute respiratory failure. The causes of anemia in the critically ill are multifactorial and include acute blood loss (including recurrent phlebotomy), poor red cell production (from nutritional deficiencies, renal insufficiency, medications or decreased bone marrow response), hemolysis or sepsis.2 Transfusions of packed red blood cells are meant to increase oxygen delivery and reduce tissue hypoxia; however, multiple studies have failed to show improvement in oxygen delivery after transfusion. This may be due to various factors associated with stored blood, including low levels of 2,3-diphosphoglycerate (which shifts the oxygen dissociation curve to the left and decreases the ability of the transfused hemoglobin to unload oxygen in the tissues), structural problems with the stored RBCs which may lead to increased aggregation or hemolysis and the inflammatory response to the transfusion.3 Attempts to mitigate some of these causes of poor oxygen delivery by using “fresh” blood [mean age 6–12 days] versus older red cells [mean age 22 days] have not shown any improvements in outcome.4,5

The risks for complications of transfusion are varied and increase with larger volume transfusion. These can vary from very minor [fever] to severe [anaphylaxis]. Due to extensive screening and testing, the risk of transferring a blood-borne infection [like HIV, hepatitis B or C] remains extremely low. Transfusion-related Lung Injury [TRALI] is an inflammatory-mediated non-cardiogenic pulmonary edema leading to hypoxia and potentially respiratory failure. It is the second leading cause [after anaphylaxis] of acute mortality due to blood transfusion.

Coagulation abnormalities are also commonly seen from RBC transfusions due to direct dilutional effects [due to a lack of coagulation factors in RBC transfusions]. Furthermore, massive transfusions can cause potentially dangerous metabolic and electrolyte abnormalities. Packed RBC units contain citrate anticoagulant that induces hypocalcemia from citrate binding to ionized calcium. Citrate itself metabolizes into bicarbonate and causes metabolic alkalosis, which can lead to hypokalemia. On the other hand,
hyperkalemia may also be noted as a result of the storage and lysis of blood products, with higher potassium levels observed when using blood stored for >12 days.  

**RBC TRANSFUSIONS IN STABLE CRITICALLY ILL PATIENTS**

Multiple studies have demonstrated increased mortality with RBC transfusion, yet rates of transfusion remain high. The CRIT Study described transfusion practices in the intensive care unit by examining 4892 critically ill patients. The mean pre-transfusion hemoglobin was 8.6 g/dL and the most common reason for transfusion was “low hemoglobin” (90% of all cases). Other clinically relevant indications, such as active bleeding and hemodynamic instability, were seen in much fewer cases of transfusion (24 and 21%, respectively). In a more recent single-center study of 10,642 ICU patients in Canada, the rate of RBC transfusions during an ICU stay was noted to be 38.3%. These data describe a high, possibly excessive rate of blood cell transfusion in the ICU and suggest that defining appropriate transfusion thresholds is an important goal.

Prospective studies establishing appropriate thresholds for transfusing red blood cells in critically ill anemic patients have trended towards a more restrictive approach. The Transfusion Requirements in Critical Care (TRICC) trial randomized non-bleeding, anemic ICU patients without active heart disease to either a “liberal” (<9 mg/dL) or “restrictive” (<7 mg/dL) transfusion trigger. The restrictive strategy showed a trend towards mortality benefit in all patients, and demonstrated a statistically significant mortality benefit in pre-determined subgroups of younger patients (<55 years old) and in less critically ill patients (APACHE II score <20). After the publication of the TRICC trial, a hemoglobin of 7 g/dL became the widely accepted and recommended threshold for transfusion in non-bleeding critically ill patients, but questions regarding applicability relating to other subgroups persisted.

In the Transfusion Requirements in Septic Shock (TRISS) study, patients with a diagnosis of septic shock were similarly assigned to two different transfusion thresholds. The comparison of transfusion thresholds of less than 7 g/dL (lower threshold) and less than 9 g/dL (higher threshold) did not show significant differences in 90-day mortality. In the subgroup analysis, patients with chronic cardiovascular disease also did not have a significant difference in relative risk of death by day 90. Another study examined patients with recent, treated acute upper-gastrointestinal bleeding, which demonstrated a higher probability of survival at six weeks if transfusions were administered at a lower threshold of 7 g/dL when compared to 9 g/dL. The primary outcome results from both trials are similar to the TRICC trial, which further support the use of a restrictive approach with blood transfusions. In both studies, patients with acute coronary syndrome (ACS) were excluded.

Anemia may worsen myocardial ischemia, induce arrhythmias, and increase infarct size during acute myocardial infarction. In patients with ACS or heart failure, anemia increases morbidity and mortality. In patients undergoing cardiac surgery, the Transfusion Requirements in Cardiac Surgery (TRICS III) trial demonstrated that a restrictive approach utilizing a hemoglobin threshold of 7.5 g/dL was noninferior to a liberal approach 9.5 g/dL. The primary outcome was a composite outcome of mortality, myocardial infarction, stroke, and new-onset renal failure requiring dialysis. Therefore, the 7.5 g/dL threshold is probably acceptable for post-cardiac surgery patients.

To our knowledge, there are no randomized trials that examine transfusion thresholds in patients with active cardiac ischemia or acute coronary syndrome. These patients have generally been excluded from randomized studies that compared transfusion thresholds. So while overall the trend with blood transfusions favors a lower threshold goal, there is no clear evidence that lower thresholds can be applied to patients with acute coronary syndrome.

**RBC TRANSFUSION IN UNSTABLE CRITICALLY ILL PATIENTS/MASSIVE TRANSFUSION**

The data discussed thus far pertains only to non-bleeding ICU patients with anemia. In the unstable, acutely hemorrhaging patient, large volumes of blood products may be necessary and restrictive transfusion triggers do not apply. The most commonly seen causes of severe acute bleeding stem from trauma, surgery, obstetrical bleeding and GI bleeding. Classic definitions of massive blood transfusion encompassed 10 units of PRBCs or a patient’s whole blood volume within 24 hours. Additional proposed definitions include three units of PRBCs within one hour and four units of total blood products within the first 30 minutes. The need to deliver blood products quickly and appropriately in the acute setting has led to the development of massive transfusion protocols.

There are several proposed methods to massive blood transfusion using different ratios of blood products. When large volumes of RBCs are delivered, dilutional coagulopathy can develop, therefore concurrent transfusion of plasma and platelets are recommended. The best available evidence for the optimal ratios of these various blood products has been described in trauma patients. The use of fresh frozen plasma (FFP), platelets, and PRBCs in a 1:1:1 ratio was compared to a group with 1:1:2 ratio in the Pragmatic, Randomized Optimal Platelet and Plasma Ratios (PROPR) trial. There was no significant difference in mortality at 24 hours or 30 days between the two groups. However, there was better hemostasis achieved in the 1:1:1 group with fewer deaths by exsanguination within 24 hours. This ratio of blood products is most commonly advocated for use as part of massive transfusion protocols and is utilized at Rhode Island Hospital’s Level I Trauma Center.
There is far less evidence to target specific massive blood transfusion ratios in the non-trauma setting, for example, in medical bleeding patients. To our knowledge, there are no randomized studies examining massive transfusions in medical patients. However, a retrospective analysis of massive transfusion in non-trauma patients examined 30-day and 48-hour mortality. Patients were stratified to higher (>1:2) or lower (<1:2) ratios of FFP to RBC, and of platelets to RBC. The investigators found no associated difference in 30-day mortality with either groups of FFP to RBC or platelets to RBC ratios. In terms of shorter term, 48-hour mortality, there was an association of decreased mortality in the higher ratio of platelet to RBC group.18 Overall, further research is necessary to better define transfusion ratios in non-trauma bleeding patients and no specific recommendations regarding massive transfusions or ratios of blood products can be made in non-trauma actively bleeding patients.

As previously discussed, administering large amounts of blood products can cause significant derangements. In trauma care, the classic lethal triad includes hypothermia, acidosis, and coagulopathy. Although the sensitivity and specificity of each of these factors to prognosis are variable, the failure to correct physiological derangements can be detrimental.19 In severe trauma, restricting surgical interventions to the minimum necessary initially has led to the term “damage control surgery” (DCS). Similarly, the term “damage control resuscitation” (DCR) entails restricting of fluids, tolerating permissive hypotension, and administering specific ratios of blood products. Active patient rewarming, and massive transfusion protocol implementation are also part of these protocols.20 The combination of DCS and DCR has shown to be associated with an improvement in 30-day survival in trauma patients and remains a potentially promising strategy in other patient groups.21

CONCLUSIONS

RBC transfusions remain a common intervention in the ICU; however, they may not result in the desired improved oxygen delivery or clinical outcomes. In the critically ill patient with exsanguination from traumatic injuries or uncontrolled bleeding, it is clear that blood products are necessary. However, in patients without active hemorrhage, the evidence suggests a more conservative approach with blood transfusions. Based on the current evidence, the transfusion threshold of 7.0 mg/dL is recommended for the majority of critically ill patients in the ICU. Patients with coronary artery disease or acute coronary syndrome may need a more liberal threshold, however, more research is necessary to elucidate the appropriate transfusion threshold for this population.

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Communication at the End-of-Life in the Intensive Care Unit: A Review of Evidence-Based Best Practices

SARAH RHOADS, MD; TIM AMASS, MD, ScM

ABSTRACT
This article summarizes current data and recommendations regarding the care of patients in an intensive care unit (ICU) at the end of life. Through analysis of recent literature and society guidelines, we identified three areas of focus for practitioners in order to deliver compassionate care to patients and their families at this critical time – family communication, caregiver support, and palliative care involvement. Attention to these topics during critical illness may reduce stress-related disorders in both patients and family members, as well as increase satisfaction with the care delivered.

KEYWORDS: end-of-life, family support, goals of care

INTRODUCTION
For patients who are hospitalized in an intensive care unit (ICU), there is an average mortality of 10–29% depending on age and medical condition prompting ICU admission. In comparison, overall mortality for hospitalized patients not in an intensive care unit was 2% in 2010. Navigating a patient’s end-of-life (EOL), and addressing family needs and concerns, is a crucial component of care in the ICU. A growing body of literature seeks to address how clinicians can best address these issues in a way that supports the patient’s wishes as well as the needs of their loved ones.

We will examine three primary areas of focus surrounding care around EOL - communicating with families, supporting family members/caregivers of patients and reducing distress, and involving palliative care.

COMMUNICATION WITH FAMILIES
Having a critically ill loved one in an ICU is an immensely stressful experience for families. Numerous studies have demonstrated significant residual trauma and emotional distress for caregivers following admission to the ICU, regardless of patient outcome. In order to best support families during an ICU admission, existing data supports the early and frequent use of interdisciplinary teams. While current data regarding the emotional impact of interdisciplinary team use is equivocal, there is a significant positive impact on family perceptions of care.

Regular communication with caregivers is the cornerstone of caring for patients at the end-of-life. Several studies have demonstrated the potential impact of structured discussions regarding care for critically ill patients. There should be particular emphasis on spending time addressing specific concerns and understanding the patient as an individual, including their goals and values. The Society for Critical Care Medicine (SCCM) 2017 guidelines recommend the use of the VALUE mnemonic (Figure 1) to guide discussions with families of critically ill patients. Data regarding the implementation of structured VALUE mnemonic has demonstrated decreased rates of PTSD, anxiety, and depression scores amongst family members. VALUE can help providers address family concerns appropriately and empathically.

Interestingly, the use of standardized patients to facilitate better communication skills among physicians does not appear to impact families in a positive manner, bringing into question how young physicians in training can best be prepared to discuss end-of-life care with families. Designated nurse facilitators to help ensure that communication runs smoothly and that families feel their concerns are addressed may be one way of addressing potential gaps in communication. The use and inclusion of nurse facilitators in family meetings has been associated with increased satisfaction with care.

In conducting a family meeting for a patient who is critically ill approaching end-of-life there are several important considerations. It is necessary to address both family and...
patient needs. Potential areas of miscommunication or conflicting goals should also be addressed. When meeting with families, the clinician should be mindful of the amount of time spent sharing information, as compared to families being allowed to express concerns and hopes. A demonstrable decrease in stress symptoms and an increase in family satisfaction has been shown to be directly proportional to the amount of time a family is able to speak during family meetings, as compared to time spent in which the clinician is directing communications.6,7

For critically ill and dying patients, current recommendations on addressing redirection of care encourage the family to focus on what the patient would want. However, the issue of what a patient would want does not sufficiently ground the family in the reality of the situation. For example, a family may say that their loved one would want further therapy (i.e., hemodialysis) that may not be an option. Instead, experts suggest eliciting from the family what the patient would think of their current situation, or how they would respond given their situation.8 This helps to focus a family’s attention and thought on the reality of their loved one’s illness.

**Table 1. Suggestions for Family Meeting discussions** – As referenced, this table is adapted from several references as suggestions for possible verbiage during end-of-life and difficult conversations.

<table>
<thead>
<tr>
<th>Word Choice for Family Discussions</th>
<th>Commonly Used Phrases</th>
<th>Suggestions for Rephrasing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrawing care</td>
<td>Redirecting focus of care</td>
<td></td>
</tr>
<tr>
<td>Do Not Resuscitate</td>
<td>Allow natural death</td>
<td></td>
</tr>
<tr>
<td>What do you think we should do next? OR: What do you want to do?</td>
<td>What would your [loved one] think if they were sitting here?</td>
<td></td>
</tr>
<tr>
<td>What would [loved one] want?</td>
<td>You’ve told me (or, you can tell me) about what [loved one] would think so I can help you best respect their values</td>
<td></td>
</tr>
<tr>
<td>Your [loved one] is very sick. This is what’s happening...</td>
<td>What is your understanding about what’s happening with your loved one? OR: What do you think is going on with your loved one?</td>
<td></td>
</tr>
<tr>
<td>I’m not sure what’s going to happen</td>
<td>I wish I could tell you that [loved one] will improve.</td>
<td></td>
</tr>
</tbody>
</table>

**General Principles for Family Meetings**

1. Use ‘wish’ statements when conveying concern and helping family come to terms with unrealistic goals.
2. Approach family meetings with mentality of “Hope for the best, prepare for the worst.”
3. Try to foreshadow possible outcomes and give the family an idea of what clinicians are looking for in their loved one’s course.
5. Frequently pause to assess family understanding and reactions.
6. Focus discussion around what family believes the patient’s goals are.

Attention to word choice extends to descriptions of medical interventions and changing the focus of a patient’s care. Careful attention to how messages are conveyed can help to support families and their decision-making during a stressful time, while minimizing conflict with the medical team due to lack of understanding (Table 1).

While successful communication with families should be the goal of all ICU clinicians, there are often occasions in which the clinicians’ perspective of patient care conflicts with family hopes or goals. In these situations, an ethics consultation, if available, has been shown to be helpful on multiple levels. One particular study demonstrated reduced hospital stay and life-sustaining treatments without a change in patient mortality. Perhaps more significantly, this study also demonstrated that the majority of physicians, nurses, and surrogates found the consultation to be helpful in resolving conflict as well as distress.9

**FAMILY SUPPORT & REDUCING DISTRESS**

In addition to communication, the ability of family members to be present at the bedside is crucial. The 2017 SCCM guidelines recommend that families be allowed at the bedside on an open and flexible basis, including at bedside rounds and even during resuscitation if the family so chooses. One study of families who witnessed CPR demonstrated reduced anxiety and depression symptoms than in those who were unable to witness CPR being performed on their loved ones.10 In keeping with these guidelines, the Rhode Island Hospital and Miriam Hospital Medical Intensive Care Units allow patients’ families to have unrestricted visitation with their loved ones.

Among pediatric and neonatal populations, family involvement in care has been consistently demonstrated to improve parent comfort and reduce distress. However, assessments of family needs without a concomitant change in provider approach has been associated with increased distress, indicating the need for providers to actively respond to family needs instead of merely elucidating them. Additionally, narrative writing is becoming an increasingly recognized tool for emotional support during times of stress. Among both pediatric and adult populations, there is some data to suggest that the use of regular journaling may be a useful tool for families while dealing with the stress of ICU admission. Data thus far seems to indicate a potential impact on both family satisfaction and stress scale measurements but limited utility amongst patients themselves for prevention of PTSD.13,14

There is a growing body of literature focused on mitigating the high prevalence of delirium in patients during and after being hospitalized in the intensive care unit, as well as PTSD following ICU/hospital discharge. In addition to the impact on patients, recent studies have looked at the likelihood of anxiety, depression, and PTSD symptoms...
amongst family members after a patient’s ICU stay, regardless of the patient’s ultimate outcome.15,16 There is some data that families of patients who are chronically ill, as well as patients who remain unresponsive on mechanical ventilation after 10 days, are at higher risk of developing PTSD.15
Recent work has shown flexible visitation hours in the ICU does not significantly impact patient outcomes, but have a positive impact on anxiety and depression symptoms in family members.16

A key tenant of distress reduction focuses on sharing information in a way that is meaningful to families. A communication facilitator may be a helpful way of ensuring that families understand their loved ones’ care and clinicians’ concerns.6 Programs which focus on sharing information about the ICU and the individual patient’s illness, and also follow-up with families after leaving the ICU or after discharge, can also help to smooth the transition and reduce family trauma.2

While there are ways to reduce distress while an individual is in the ICU, many recent studies have focused on interventions after a patient is discharged. For patients who survive to hospital discharge, post-ICU specific rehabilitation and follow-up clinic may help to alleviate their distress and likelihood of describing post-traumatic symptoms. There is some data to suggest that these clinics may also be helpful for families.37 In addition, support groups may be beneficial as a means of coping and processing. In an age of increased accessibility and frequent smartphone use, the use of mindfulness programs via self-directed application use may offer an interesting new approach for healthy coping on an individual basis.18

The care team in the ICU can help to reduce family distress through careful communication that follows families after patients leave the intensive care unit. Efforts to support patients’ families, particularly if there is a traumatic outcome, after their ICU stay may be beneficial in reducing longer term distress as well.

PALLIATIVE CARE

Palliative care is an often-overlooked component to responsible and patient-centered care at the end-of-life in an ICU. Current data regarding palliative care involvement has demonstrated unclear benefit of palliative care consultations in ICU patients.19 However, the integration of palliative principles can significantly lessen distress of both patients and families in the ICU.3,20

Within the ICU, individual physicians may have varying levels of comfort with palliative-based care. A specific palliative care consult may not be necessary for individual cases in which symptoms are easily managed, but this should be determined on a case-by-case basis. One recent review distinguishes between two main models for the integration of palliative care in the ICU.20 In the first model, described as the ‘consultative model,’ the focus is primarily on engaging palliative care consultants for help with symptom management, family and patient-centered care, and clear communication with the team. This may be particularly helpful with issues such as withdrawal of care and transitioning out of the ICU for patients who are at the end of life. Current SCCM guidelines recommend the early consideration of palliative care as a potential means of decreasing cost of care and length of ICU stay, although this recommendation is based on low quality evidence.2

The second model, advocated by many critical care societies as a core competency for ICU physicians, is an ‘integrative model’.20 With this approach, palliative care is a focus, rather than a consulting service. Many societies advocate for, and provide for, professional training of ICU providers in basic tenets of palliative care, and there is a small but growing subpopulation of critical care physicians who receive additional training in palliative care.

Most successful integrations of intensive and palliative care ultimately rely on both consultative and integrative models for palliative care. Clinicians who are competent and comfortable with principles of palliative care are well-positioned to effectively and empathetically communicate with families of critically ill patients as well as guide dying individuals and their families through difficult symptoms that arise. These clinicians may also be better able to recognize opportunities for further palliative care assistance through consultation, which can work synergistically with the primary team’s efforts towards palliation.

CONCLUSION

A hospitalization in an intensive care unit, particularly at the end-of-life, carries with it a high burden of patient symptoms, family distress, and difficult decisions that can manifest for many family members in the form of PTSD and depressive symptoms. These symptoms can continue months after the individual is discharged from the ICU. Three main principles for limiting distress and providing the highest quality care for those at the end of life can help guide ICU care. A focus on supporting families, limiting distress as much as possible, and appropriately directing efforts towards palliative care are crucial considerations for critically ill patients and their loved ones. Following these principles, providers can help to mitigate some of the difficulty and trauma of a stressful time and help people to feel supported and listened to during their time in the ICU.
References


Lung Ultrasound for Diagnosing Patients with Severe Dyspnea and Acute Hypoxic Respiratory Failure

MOHAMMAD ARABIAT, MD; ANDREW E. FODERARO, MD; ANDREW T. LEVINSON, MD, MPH

Abstract
Acute hypoxic respiratory failure can be caused by severe pneumonia, cardiogenic pulmonary edema (CPE), and acute respiratory distress syndrome (ARDS). Differentiating between these causes in critically ill patients can be challenging. Lung ultrasound (LUS) evaluation of acute respiratory failure has been developed and adopted only recently. LUS offers promise as a valuable clinical tool for the diagnosis and treatment of patients with severe dyspnea and acute hypoxic respiratory failure.

Keywords: lung ultrasound, point-of-care ultrasound, pneumonia, cardiogenic pulmonary edema (CPE), acute respiratory distress syndrome (ARDS)

Introduction
Acute respiratory failure is a common problem encountered on a daily basis caring for critically ill patients. While diagnostic imaging is commonly obtained in order to reach a diagnosis in a timely manner in the critically ill patient, some of the imaging techniques, including computed tomography (CT) and routine chest radiography (CXR), have significant drawbacks. These drawbacks include cost, radiation exposure, and the need for transportation across the hospital.

The increasing availability of point-of-care ultrasound equipment as well as technical expertise has opened a door into new areas of bedside diagnostics. Although lung ultrasound (LUS) is unlikely to replace commonly used imaging modalities, it has become a valuable tool in the care of the critically ill patients. LUS performed by the physician taking care of the patient allows for the direct correlation of imaging findings to the clinical presentation.

LUS has been shown to significantly reduce the number of chest radiographs and CT scans obtained in the ICU. In addition, lung ultrasound has been shown to maintain diagnostic accuracy in differentiating various causes of acute respiratory failure, including pneumothorax, lung consolidation, and alveolar-interstitial syndrome.

Basic Lung Ultrasound
Air is a strong ultrasound beam reflector. Lung ultrasound depends on artifacts in the detection of different lung pathologies. The high frequency linear transducer (5–12 MHz) can be used to detect the pleural line and the lung parenchyma immediately below the pleural line. The low frequency microconvex or convex transducers (2–5 MHz) can be used to visualize the pleural line as well as deeper lung parenchyma. Current techniques for performing complete lung scanning using standard point-of-care ultrasound machines and transducers can be learned quickly and specific methods and protocols are well described in the literature. Which transducer is best for lung ultrasound is currently controversial.

Normal Lung Ultrasound Findings
Normal LUS findings include the Bat sign, lung sliding, A-lines, and B-lines. The Bat sign occurs when, as the probe is placed longitudinally, the pleural line can be visualized as a horizontal hyper-echoic line between the two adjacent ribs (Figures 1 and 2).

A-lines are horizontal single or multiple hyperechoic lines parallel to the pleural line. The pleural line is visualized as a horizontal hyperechoic line at the top of the image. This is the area where lung sliding can be seen on real-time imaging.
ultrasound beam. These lines represent repetitive reverberation artifacts of the pleura. Visualizing A-line confirms the presence of air, which can be alveolar or pleural in location [Figure 2].

Lung sliding is the movement of the parietal pleura against the visceral pleura. The absence of lung sliding can be the result of pleural separation from pneumothorax, or pleural adhesions due to lung pleurodesis or fibrotic lung disease, as well as non-vented lung from right main stem intubation or collapse.

**Figure 2.** “Bat sign” and A-lines: The bat sign is formed by the pleural line between the two adjacent ribs with hypoechoic areas below the ribs due to rib-shadow artifact. A-lines, seen below the pleural line, are horizontal single or multiple hyperechoic lines that are parallel to the pleural line and perpendicular to the ultrasound beam. These lines represent repetitive reverberation artifacts of the pleura. They are a normal finding in healthy lung.

B-Lines are vertical hyperechoic lines that originate from the interface of the pleura, extend down to the bottom of the screen and move with lung sliding while effacing A-lines. Although the presence of two or less B-lines in a single view can be normal, they can also represent a pathologic process including a filling process of the interlobular septa, often seen in acute cardiogenic pulmonary edema, acute respiratory distress syndrome (ARDS), pneumonia and pulmonary fibrosis among others [Figure 3]. These abnormal findings usually are represented by a higher number of B-lines in each ultrasound window view.

**LUNG ULTRASOUND FEATURES OF PNEUMOTHORAX**

There are a variety of LUS findings associated with pneumothorax. The visualization of lung sliding accurately rules out pneumothorax at the site of the transducer, but its absence does not necessarily confirm it. In addition, the point at which the two pleural linings detach from each other is called the “lung point.” The identification of a lung point is a 100% specific for pneumothorax and 66% sensitive. Finally, as B-line arise from the visceral pleura, the appearance of even a single B-line rules out pneumothorax at the site of the transducer.

**ULTRASOUND FEATURES OF SEVERE PNEUMONIA AND PULMONARY EDEMA**

Lung ultrasound continues to grow as a tool for the evaluation of respiratory failure, including for the evaluation of common causes of dyspnea such as pneumonia and pulmonary edema. As discussed above, the normal lung findings include lung sliding, A-lines, and a small number of B-lines. When utilizing LUS to diagnose pneumonia and pulmonary edema, it is important to consider the etiologies for respiratory failure in these conditions. Predominant findings found on LUS in patients with severe pneumonia and pulmonary edema include alveolar filling and interstitial or septal abnormalities.

Findings in severe pneumonia on LUS include translobar alveolar consolidation (sonographic hepatization of the lung [Figure 4]), nontranslobar alveolar consolidation (shred or fractal sign), sonographic air bronchograms, alveolar-interstitial syndrome (AIS), and lung pulse.

Translobar and nontranslobar pneumonia vary with the extent of disease. Translobar alveolar consolidation of the lung [sonographic hepatization of the lung] represents consolidation of an entire lobe or more [Figure 4]. Nontranslobar alveolar consolidation (shred or fractal sign) represents less extensive pneumonia involving a localized area or sub-segment of a lobe of the lung [Figure 5]. The differences in location and extent of consolidation result in unique ultrasound findings. With translobar pneumonia, sonographic...
hepatization is apparent, which represents acoustic impedance to ultrasound waves due to alveolar filling from inflammatory exudates, which gives an appearance similar to that of the liver. The less extensive nontranslobar pneumonia has areas of alveolar filling adjacent to areas of normal aerated lung. The LUS findings of hypochogetic regions separated by an irregular line from normal lung findings result in the “shred” sign. The stark difference between hypoechogetic and normal areas create a linear abnormality which can resemble a shredded piece of paper, which is why it is termed the shred sign.8

Other findings of pneumonia on ultrasound can be found in both trans and nontranslobar pneumonia. Sonographic air bronchograms appear similar to those seen on other radiographic techniques (Figure 6), including chest computed tomography scans. The air-filled bronchi become visible due to surrounding alveolar filling. Another finding which can be seen, especially in early pneumonia, is Alvedar Institial Syndrome (AIS), which is interstitial edema, represented by B lines (Figure 7).

Combining the above findings with a history of infectious respiratory symptoms is suggestive of pneumonia. There are multiple studies that have shown LUS to be comparable or even more accurate than chest X-ray in diagnosing pneumonia when compared to computed tomography as the gold standard.9

The other major cause of respiratory failure which can be...
evaluated by LUS is left-sided heart failure with resultant pulmonary edema. Using the common LUS findings of A lines and B lines can help to differentiate pulmonary edema from normal aerated lung. Left-heart failure results in a combination of interstitial and septal edema, alveolar filling, and pleural effusions related to increased hydrostatic pressure. 10

The LUS findings that are predominate in pulmonary edema are >2 B-lines in multiple lung fields. These B-lines are generally vertical, well defined, and extend from the pleural line with movement with lung sliding. 11

**DIAGNOSING ETIOLOGIES OF SEVERE DYSPNEA WITH LUS**

Acute dyspnea, especially in patients with comorbidities, is an extremely challenging clinical diagnosis to make, even for the experienced clinician. Multiple studies have found that chest radiograph, clinical examination, and the use of N-terminal pro-brain-type natriuretic peptide for differentiating between various etiologies of dyspnea are often quite inaccurate, with corresponding sensitivities of 50–60%. Treating patients for multiple possible causes (aka “triple therapy,” giving diuretics, antibiotics, and steroids) can be quite costly for the healthcare system as a whole and have significant negative side effects for individual patients.

Differentiating cardiogenic from non-cardiogenic pulmonary edema can be especially diagnostically challenging. Multiple studies have shown that brain-type natriuretic peptide (BNP), NT-proBNP, chest radiograph, and common physical examination findings are inaccurate for identifying and excluding patients with CPE, with sensitivities and specificities ranging from 50% to 60%. 12 In addition, meta-analyses show that BNP is inconclusive for ruling out acute CPE. 13

LUS has been recently shown to be a very useful tool in helping to diagnose the etiology of dyspnea in non-critically ill patients. In one recent study of 152 patients admitted to a medical floor with a diagnosis of dyspnea, a definitive diagnosis was made by blinded reviewers of all available clinical evidence. Lung US and pro-BNP levels were obtained on admission and at 48 hours. The study found that Lung US findings (8 or more B-lines on LUS) was significantly better then utilizing BNP to diagnose CHF as the cause of dyspnea in patients admitted to the medical floor. 14 Another recent study in internal medicine patients examined 150 patients also admitted to the medical wards with acute dyspnea. Utilizing a blinded reviewer with access to the complete medical record as the “gold standard”, the study examined the predictive value of LUS findings compared to clinical exam and CXR findings alone to differentiate respiratory and cardiogenic etiologies for the patient’s dyspnea. The authors concluded that LUS greatly improved the accuracy of the clinical diagnosis of patients admitted to the general wards with acute dyspnea. The study also found that LUS diagnostic accuracy for the diagnosis of pneumonia was better than chest X-ray. 15 A recent systematic review also found that lung ultrasound using B-lines had high sensitivity and specificity in the diagnosis of acute cardiogenic pulmonary edema. 11

Finally, a study in emergency department patients presenting with acute dyspnea found that LUS combined with point-of-care cardiac ultrasound was more sensitive for the diagnosis of heart failure; however, a standard evaluation without LUS was better in the diagnosis of COPD/asthma and PE. 16

**DIFFERENTIATING SEVERE PNEUMONIA, CARDIOGENIC PULMONARY EDEMA, AND ARDS WITH LUS**

Differentiating between severe pneumonia, CPE, and ARDS remains a diagnostic challenge in critically ill patients. LUS has been shown in many studies to have better predictive value than usual clinical practice in differentiating the causes of acute respiratory failure. 11, 14, 15, 17

Identification of pleural effusions on ultrasound can help differentiate CPE from ARDS. At the bedside, the use of ultrasound is more sensitive than chest radiograph for this identification. 18 The ultrasound finding of bilateral pleural effusions, especially if they are large, can be a rapid and effective diagnostic tool and in combination with interstitial syndrome can be suggestive of CPE from left-sided heart failure.

Specifically with regard to ARDS, the currently widely used Berlin definition requires 3 central criteria: “[1] Occurrence within 1 week of a known clinical insult or new or worsening respiratory symptoms; [2] bilateral opacities on chest imaging not fully explained by effusions, lobar/lung collapse, or nodules; and [3] respiratory failure not fully explained by cardiac failure or fluid overload, and need objective assessment (e.g., echocardiography) to exclude hydrostatic edema if no risk factor present.” Imaging to fulfill the second criterion is traditionally by CT scan and/or chest radiograph. 19, 20

Specific findings on LUS, such as bilateral opacities not fully explained by effusions, lobar or lung collapse, or nodules, may suggest the diagnosis of ARDS. 21 Other findings suggestive of ARDS include multiple bilateral lung regions with 2 or more B lines or bilateral consolidations.

One study found significantly increased diagnostic accuracy for ARDS using LUS as the imaging modality compared with chest radiograph, when thoracic CT scan was used as the gold standard.22 Another study that compared chest radiograph and LUS found they were both equally useful in the identification of ARDS using the Berlin definition, although LUS was more accurate in predicting mortality. 23

**CONCLUSION**

Diagnosing the cause of acute respiratory failure in a critically ill patient can often be quite challenging, even for skilled providers. LUS is rapidly being adopted as a complementary tool in the identification and treatment of acute respiratory failure.
modality to conventional thoracic imaging techniques for critically ill patients with dyspnea or acute hypoxic respiratory failure. LUS can help elucidate rapidly the etiologies of acute respiratory failure and severe dyspnea. There is growing evidence for the use of LUS to help differentiate cardiogenic pulmonary edema, ARDS, and pneumonia.

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Extracorporeal Life Support in Adults with Acute Respiratory Failure: Current Evidence-Based Practices
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ABSTRACT
There has been rapid adoption of extracorporeal life support (ECLS) in adult patients with severe acute respiratory failure. Extracorporeal membrane oxygenation (ECMO) is used to rescue patients with severe hypoxic and hypercapnic respiratory failure refractory to optimal therapy and extracorporeal carbon dioxide removal (ECCO₂R) supports hypercapnic respiratory failure and allows very low tidal volume ventilation to minimize the risk of ventilator-induced lung injury. Currently over 3,000 cases of ECLS (ECMO and ECCO₂R) in adults with respiratory failure are reported annually to the Extracorporeal Life Support Organization registry. Advances in the care of patients with acute respiratory distress syndrome, technological innovations in extracorporeal circuitry, and insights from modern clinical trials of ECLS have led to favorable outcomes and a renewed interest in the use of this technology. Significant gaps in knowledge about best practices remain, however. This review will summarize indications for respiratory support in adults, current evidence available from clinical trials and our institution’s experience with adult respiratory ECLS.

KEYWORDS: extracorporeal life support, extracorporeal membrane oxygenation, extracorporeal carbon dioxide removal, acute respiratory distress syndrome, low tidal volume ventilation

INTRODUCTION
The first adult successfully supported with extracorporeal life support (ECLS) was a patient with acute respiratory failure in 1972.¹ Two consecutive negative trials failed to show a benefit of extracorporeal membrane oxygenation (ECMO) or extracorporeal carbon dioxide removal (ECCO₂R) over mechanical ventilation in adults with severe respiratory failure, dampening enthusiasm for the use of ECLS in adults.²³ Widespread adoption of ECLS for acute respiratory failure in adults did not occur until the 2009 influenza A (H1N1) pandemic, which coincided with publication of the Conventional Ventilation or ECMO for Severe Adult Respiratory Failure (CESAR) trial.⁴ Consequently ECLS (including ECMO and ECCO₂R) has been rapidly integrated into the management algorithm of adult patients with acute respiratory failure, most commonly acute respiratory distress syndrome (ARDS). Over 3,000 cases are reported annually to the Extracorporeal Life Support Organization (ELSO). Common respiratory indications for adults in cases reported to ELSO include ARDS, bacterial and viral pneumonia.

We will review common respiratory indications for ECLS and discuss three modern randomized trials that have compared ECLS to standard therapy in patients with severe ARDS: the CESAR trial, the ECMO to Rescue Lung Injury in Severe ARDS (EOLIA) trial and the Xtravent trial. The Strategy of Ultra-Protective lung ventilation with Extracorporeal CO₂ Removal for New-Onset moderate to Severe ARDS (SUPERNOVA) trial, a feasibility trial of ECCO₂R support to achieve very low tidal volume ventilation (LTVV) for moderate ARDS will also be highlighted.⁴⁻⁷ Finally, we will present our institution’s experience using ECLS in the management of adult patients with acute respiratory failure.

INDICATIONS
The goal of ECLS in acute respiratory failure is to permit lung rest while maintaining adequate gas exchange and oxygen delivery as a bridge to recovery or as a bridge to destination with transplantation. The use of ECLS to reduce the injurious effects of positive pressure mechanical ventilation is the greatest potential of this technology. A LTVV strategy that targets a tidal volume of 6 mL/kg of ideal body weight and plateau pressures < 30 cm H₂O improves outcomes in ARDS.⁸ However even higher plateau pressures (i.e., < 30 cm H₂O) in patients with severe ARDS increases the risk of mortality, suggesting there may be no safe plateau pressure limit.⁹ An aggressive strategy to protect the lungs on ECLS in which airway pressures and alveolar overdistention are minimized may therefore be beneficial.

The degree of respiratory support and configuration of ECLS used is determined by the severity of the patient’s respiratory failure and the primary gas exchange abnormality. In patients with isolated respiratory failure that do not require concurrent hemodynamic support, veno-venous (VV-) ECMO is the most common configuration used. In VV-ECMO, blood is drained from a central vein, passed through a blood pump and oxygenator and then returned to a central vein. Lower flow ECCO₂R (which requires smaller
cannulae with target flows of 10–20 mL/kg/min compared to flows of 60–80 mL/kg/min in ECMO) can be used to support adult patients with less severe respiratory failure including hypercapnic respiratory failure from airways exacerbations. ECCO₂R can also be used to support very LTVV (< 6 mL/kg) strategies to maintain plateau pressures below 30 cm H₂O in ARDS and to overcome permissive hypercapnia. In patients supported with ECCO₂R, blood is drained via a central vein and passed through a blood pump and oxygenator before it is returned to the venous system; an arteriovenous (AV) configuration which drains blood from an artery and uses the patient’s systemic blood pressure gradient without a blood pump may also be used.¹⁰ Dual lumen cannulas, which offer single site cannulation to increase mobility, are available for both ECMO and ECCO₂R.

The most common indication for respiratory support in adults reported to the ELSO registry remains ARDS. Respiratory support can be considered for all patients with a treatable underlying condition resulting in refractory hypoxemic or hypercapnic respiratory failure despite optimal care, massive air-leak syndromes, or as a bridge to transplantation. In all four ‘modern’ trials of ECLS discussed here, patients on mechanical ventilation for 7 days or longer were excluded. While the ideal timing to consider ECLS after the initiation of mechanical ventilation remains unclear, prolonged mechanical ventilation is an independent predictor of in-hospital mortality.¹¹ The Respiratory ECMO Survival Prediction (RESP) Score is a validated risk assessment tool created to guide candidate evaluation for ECMO in adults with acute respiratory failure. In addition to younger age and the presence of single organ failure, patients supported with ECMO within 48 hours of initiation of mechanical ventilation had the most favorable outcomes while those supported after 7 days had a significantly higher mortality. Our institution’s practice is to consider ECLS if a patient has not reached optimal ventilator targets after LTVV, early paralytic, and (in appropriate cases) a trial of proning and ideally within 48–72 hours of mechanical ventilation.⁸,¹²,¹³

MODERN ECLS TRIALS
Early randomized trials of ECMO and ECCO₂R for acute respiratory failure in adults with severe ARDS showed no benefit of ECLS.²,³ These trials were problematic in their design, their execution, and limited by the available ECLS technology and prevailing clinical practices at the time. The last two decades have been marked by advances in extracorporeal technology including miniaturized, heparin-coated circuits, more durable solid hollow fiber oxygenators that are less prone to shear stress, and dual lumen cannulas. General medical care and ventilator strategies in patients with ARDS have also evolved. For these reasons, there has been a renewed interest in ECLS clinical trials.

ECMO TRIALS
The first modern trial of ECLS for acute respiratory failure in adults with severe ARDS, the single-center CESAR trial, was similar in design to an earlier successful trial in neonates.⁴,¹⁴,¹⁵ CESAR enrolled 180 adults with severe ARDS randomized to conventional mechanical ventilation versus transfer to a highly experienced ECMO center. Once transferred, subjects in the ECMO group were managed using a standardized ARDS protocol including lung protective LTVV, diuresis and prone positioning. If a subject did not improve within twelve hours they were cannulated for VV-ECMO. CESAR demonstrated that subjects in the ECMO group had a significantly higher composite of survival without severe disability at six months compared to the control group, 63% versus 47% respectively [RR 0.69, 95% CI 0.55–0.97, p = 0.03]. Of note, only 75% of subjects transferred for ECMO actually received it. The major criticism of CESAR is that the management of subjects in the conventional mechanical ventilation arm was not standardized and those in the intervention arm who were transferred for ECMO were more likely to receive LTVV for longer periods of time. The CESAR trial demonstrated that care at an ECMO-center including a standardized ARDS protocol may improve outcomes in ARDS. Experience from this pragmatic trial guided the design of the EOLIA trial. Published in 2018, EOLIA was the first international, multicenter randomized trial of ECLS for acute respiratory failure in adults with severe ARDS.⁵ Adults with severe ARDS were randomized to VV-ECMO and very LTVV versus standardized LTVV. To account for the ethical quandary of potentially withholding a life-saving therapy within the control group, the study design permitted crossover to ECMO for patients in the control group with refractory hypoxemia. Unlike in the CESAR trial, subjects in both arms were treated with a standardized lung protective ARDS protocol including adjunctive therapies such as inhaled nitric oxide, prone positioning and recruitment maneuvers. The primary end point was 60-day mortality. After enrolling 249 subjects the trial was terminated early for statistical futility after the preplanned fourth interim analysis. While the ECMO group had a lower 60-day mortality compared to the control group [35% versus 46% respectively], this difference was not statistically significant [RR 0.76, 95% CI 0.55–1.04, p = 0.09]. Given the high crossover rate (28%), the trial would not have achieved a statistically significant difference in the primary outcome between the two groups, defined a priori as an absolute reduction in mortality of 20% in favor of ECMO. It should be noted that at the time of crossover the 35 subjects in the control group were extremely ill. With rescue ECMO, 15 (43%) of these crossover subjects survived. Taking this into account, there was a significant reduction in the relative risk of treatment failure defined as death by 60 days in the ECMO group, crossover to ECMO or death in the control group [RR 0.62,
95% CI 0.47–0.82, p < 0.001), a predefined key secondary end point. While EOLIA was a negative trial, it is difficult to draw definitive conclusions given these results. A post-hoc Bayesian analysis found it highly probable that ECMO reduced mortality in EOLIA.\textsuperscript{16} Taken together, these results suggest that ECMO is effective but the size of the benefit and the risk/benefit ratio in individual candidates is yet to be defined.

**ECCO\textsubscript{R} TRIALS**

Xtravent is the first modern trial of ECCO\textsubscript{R} for acute respiratory failure in adults with ARDS. In this multicenter trial, 79 adult patients with ARDS were randomized to pumpless ECCO\textsubscript{R} and very LTVV (3 mL/kg) versus standardized LTVV (6 mL/kg).\textsuperscript{6} Patients with significant hemodynamic instability were excluded. The results of this trial published in 2013 revealed that very LTVV with ECCO\textsubscript{R} was feasible and safe. The ECCO\textsubscript{R} group had higher 28- and 60-day ventilator-free days (the primary endpoint) compared to the control group but the difference was not clinically nor statistically significant, 10.0 ± 8 days versus 9.3 ± 9 days (p = 0.78) at 28 days and 33.2 ± 20 days versus 29.2 ± 21 days (p = 0.469) at 60 days respectively. While Xtravent is a negative study, subjects in this trial were not as ill as those in the CESAR and EOLIA trials and the overall mortality was only 16.5%. In a post-hoc analysis of sicker patients (PaO\textsubscript{2}/FiO\textsubscript{2} ≤ 150), subjects in the ECCO\textsubscript{R} group had a significantly higher number of ventilator-free days at 60-days (40.9 ± 12.8 versus 28.2 ± 16.4, p = 0.03).

The recently published SUPERNOVA trial is the largest international, multicenter feasibility and safety trial to date of ECCO\textsubscript{R} and very LTVV (4 mL/kg and plateau pressures ≤ 25 cm H\textsubscript{2}O) for acute respiratory failure in adults with moderate ARDS. SUPERNOVA enrolled 95 patients with moderate ARDS expected to require mechanical ventilation for more than 24 hours into this single-arm trial. In the first 24 hours, sedation and paralysis was used to maintain LTVV. After initiation of ECCO\textsubscript{R}, the tidal volume was lowered incrementally from 6 mL/kg to 4 mL/kg, while titrating the positive end-expiratory pressure to maintain target plateau pressures of 23–25 cm H\textsubscript{2}O. The primary outcome, very LTVV without a rise in PaCO\textsubscript{2} > 20% above baseline and an arterial pH > 7.30 at 8 hours, was achieved in 78% subjects while 82% achieved these goals at 24 hours. Subjects were supported on ECCO\textsubscript{R} for a mean of 5 days (range of 3–8 days) with an in-hospital survival of 62%. Adverse events occurred in 39% of subjects with two serious adverse events attributed to ECCO\textsubscript{R}. Like the Xtravent trial, this trial showed that ECCO\textsubscript{R} and very LTVV for acute respiratory failure in adults with moderate ARDS is feasible. The randomized portion of the SUPERNOVA trial will help determine if a strategy to protect the lungs from ventilator-induced lung injury using ECCO\textsubscript{R} and very LTVV is beneficial over conventional LTVV in ARDS. A similar randomized trial, the ongoing pRotective vEntilation with veno-venous lung assistT in respiratory failure (REST) trial will also address this question by randomizing adults with moderate ARDS (PaO\textsubscript{2}/FiO\textsubscript{2} < 150 mm Hg) to ECCO\textsubscript{R} and very LTVV (3 mL/kg or less and a plateau pressure ≤ 25 cm H\textsubscript{2}O) versus LTVV alone.\textsuperscript{17} The primary outcome of the REST trial is mortality at 90-days following randomization (NCT02654327).

**LOCAL EXPERIENCE**

The Lifespan ECLS program was started in 2010 with the first adult patient supported for acute respiratory failure the same year. It has been recognized as a Gold Center of Excellence by ELSO since 2015 and is the only ECLS center in Southern New England. Mirroring a global trend, acute respiratory failure is no longer the most common indication for ECLS in adults in our region. To date, 162 patients have been treated with ECLS, including 107 adults, of whom 57 were supported for acute respiratory failure. The overall survival to discharge or transfer in this subset of patients was 66%, while 75% of patients survived ECLS, comparable to similar-sized ECMO-centers. Rhode Island Hospital is one of the U.S. sites of the international, multicenter VENT-AVOID trial, the first randomized trial of ECCO\textsubscript{R} in chronic obstructive pulmonary disease (COPD), which compares ventilator free days at day 60 in patients with severe COPD exacerbations randomized to ECCO\textsubscript{R} versus standard of care (NCT03255057).

**SUMMARY**

ECLS has been widely adopted to rescue adult patients with refractory respiratory failure and support patients with respiratory failure to minimize ventilator-induced lung injury. Two modern randomized trials suggest a possible benefit of rescue ECMO in adults with severe ARDS, while the role of ECCO\textsubscript{R} and very LTVV in patients with moderate ARDS remains unclear based on current evidence.\textsuperscript{4,6} While significant questions remain regarding patient selection, optimal care strategies, and cost effectiveness, this potentially life-saving therapy is best deployed by centers who are expert in its use.
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ABSTRACT
Acute pulmonary embolism (PE) causes significant morbidity and mortality, particularly for patients with subsequent right ventricular (RV) dysfunction. Once diagnosed, risk stratification is imperative for therapeutic decision making and centers on evaluation of RV function. Treatment includes supportive care, systemic anticoagulation, and consideration of reperfusion therapy. In addition to systemic anticoagulation, patients with high-risk PE should receive reperfusion therapy, typically with systemic thrombolysis. The role of reperfusion therapies, which include catheter-based interventions, systemic thrombolysis, and surgical embolectomy, are controversial in the management of intermediate risk PE. Catheter directed thrombolysis (CDT) can be considered in certain intermediate risk patients although prospective, comparative data for its use are lacking. Surgical or catheter embolectomy are viable treatment options for high-risk patients in whom reperfusion therapy is warranted but who have absolute contraindications to thrombolysis. Further research is needed to better elucidate which patients with PE would most benefit from advanced reperfusion therapies.

KEYWORDS: pulmonary embolism, catheter-directed thrombolysis, systemic thrombolysis

INTRODUCTION
Pulmonary embolism (PE) is both common and a significant cause of morbidity and mortality worldwide. There are an estimated 900,000 cases of venous thromboembolism (VTE) every year in the United States. Although mortality from acute PE is reported to be as high as 100,000 per year, this is likely to be an underestimate, given that approximately 25% of patients with PE present with sudden death. There is also a 10–30% mortality rate within one month of acute PE diagnosis. Acute PE is a common indication for intensive care unit (ICU) admission and is associated with high short-term mortality. As such, an understanding of diagnosis, risk stratification, and treatment of acute PE is paramount for critical care physicians.

DIAGNOSIS AND RISK STRATIFICATION
The diagnosis of acute PE can be challenging, and diagnostic algorithms have been proposed. According to all current diagnostic algorithms, contrast-enhanced chest computed tomography angiography (CTA) is the preferred imaging modality for diagnosis of acute PE. Once acute PE is diagnosed, risk stratification is essential to guide treatment decisions. In general, risk stratification for acute PE incorporates several factors, including clinical appearance, vital signs, validated PE risk scores, and right ventricular (RV) function assessed by imaging modalities and cardiac biomarkers. Figure 1 demonstrates a risk stratification algorithm used by the Pulmonary Embolism Response Team at Rhode Island Hospital. The initial step in risk stratification is to assess for shock or hemodynamic instability, defined as a systolic blood pressure less than 90mmHg for more than 15 minutes or a need for vasopressors. Acute PE that causes hemodynamic instability is referred to as massive PE or high-risk PE, and warrants immediate consideration of reperfusion therapies. In acute PE patients who present without shock or hemodynamic instability, multimodal risk stratification is used to identify patients at low and intermediate risk.

The Pulmonary Embolism Severity Index (PESI) and simplified PESI (sPESI) are validated clinical scores used to predict 30-day mortality in acute PE. Patients with PESI class III-VI or sPESI ≥1 (see Figure 1), or who have signs of RV dysfunction on CTA or echocardiography, or elevated cardiac biomarkers [Brain natriuretic peptide or BNP and troponin above the normal lab values] have intermediate risk, or sub-massive PE. These patients can be sub-classified into intermediate-low and intermediate-high risk, the latter defined by the presence of RV dysfunction by both imaging and biomarkers. Patients with PESI class I-II or sPESI=0 are classified as low risk, indicating a low likelihood of mortality, and are unlikely to be encountered in the ICU setting. In addition to informing treatment decisions, risk stratification can be helpful in assessing the need for ICU level of care.
Once the diagnosis of acute PE is made, treatment focuses on supportive care, systemic anticoagulation, and consideration of reperfusion therapy. Unless there are contraindications, systemic anticoagulation should be started after the diagnosis of acute PE is established. For higher risk patients, intravenous unfractionated heparin is typically the preferred agent as its pharmacokinetics allow the ability to stop if thrombolysis or interventional procedures are indicated. In addition to anticoagulation, hemodynamic and respiratory support should be provided. Clinicians should be extremely cautious with intravenous volume expansion as this may worsen right ventricular function and precipitate rapid clinical decompensation. Pulmonary Embolism Response Teams (PERT) can be activated for intermediate or high risk PE, or in any case where there is uncertainty about diagnosis or optimal treatment strategy.

**SYSTEMIC THROMBOLYSIS**

Systemic thrombolysis is well established for the management of high risk or massive PE. Thrombolytics reduce pulmonary artery resistance and pressure, and in hemodynamically unstable patients decrease mortality. \(^4\) Guidelines routinely recommend systemic thrombolysis for patients with massive PE without contraindications to thrombolytics. \(^4\) The use of systemic thrombolysis for intermediate-risk PE remains controversial. \(^4\) This question was addressed in the Pulmonary Embolism Thrombolysis (PEITHO) trial, a multicenter, randomized, double-blind, placebo-controlled trial that is the largest trial to examine systemic thrombolysis in intermediate-risk PE. \(^10\) In this study, 1006 acute PE patients [symptoms less than 15 days] were randomized to receive either unfractionated heparin alone or in conjunction with...
with tenecteplase. PE was confirmed by VQ scan, CTA, or pulmonary angiogram, and right ventricular dysfunction confirmed by echocardiogram or CTA and elevated troponin. At seven days, the tenecteplase group had a significant decrease in a composite endpoint of all-cause mortality and hemodynamic decompensation (2.6% vs 5.6%; p=0.02), although there was no difference in mortality. The incidence of extracranial bleeding [6.3% vs 1.2%, p<0.001] and stroke [2.4% vs 0.2%, p=0.003] were higher in patients that received tenecteplase compared to heparin alone, suggesting an unfavorable risk-benefit ratio for the use of systemic thrombolysis for hemodynamically stable PE with RV dysfunction. Subsequent meta-analyses have shown that systemic thrombolysis reduces overall mortality but is associated with a higher risk of fatal or intracranial hemorrhage. Reduced dose thrombolytics have been studied in small trials, but this is also not recommended for routine use in intermediate-risk PE. In the PEITHO study, 23 patients in the heparin alone group required open-label thrombolysis after randomization. Only 2 of these patients died, suggesting, as is our current clinical practice, a role for close observation of patients with intermediate-risk PE, and consideration of the use of rescue systemic thrombolysis if clinical deterioration subsequently occurs. Further study is needed in this particular area as sample size is a limiting factor.

**Catheter-Based Interventions**

Several catheter-based interventions are currently available for the treatment of acute PE. These broadly fit into two categories: catheter directed thrombolysis (CDT) and catheter embolectomy. The two are currently proposed for use in intermediate-high risk patients who are at risk for clinical deterioration based on vital signs, severity of RV dysfunction, tissue perfusion, and/or gas exchange, and who have absolute or relative contraindications to or failed response to systemic thrombolysis. CDT uses imaging guidance to place an infusion catheter to the site of the clot in order to locally deliver low-dose thrombolytics over the course of several hours. The thrombolytic dose is significantly lower than what is administered systemically. Depending on the specific device used, this can be accompanied by low-power, high-frequency ultrasound, which is referred to as ultrasound-assisted catheter-directed thrombolysis (UACDT). There is only one prospective, randomized trial comparing CDT to anticoagulation alone for the management of acute PE. The ULTIMA trial randomized 59 patients with acute main or lower lobe PE and a transesophageal echocardiogram RV/LV ratio >1.0 to receive either unfractionated heparin alone or with a UACDT regimen of 10 to 20mg recombinant tissue plasminogen activator (tPA) over 15 hours. Compared to the heparin alone group, the UACDT group had a greater decrease in mean RV/LV ratio from baseline to 24 hours, although at 90 days there was no difference in RV/LV ratio improvement. Another retrospective, comparative study found no difference in echocardiographic RV/LV ratio at 30 days between patients who received CDT compared to anticoagulation alone. Although these and other non-comparative studies have shown that CDT improves RV function and PA pressures in the short term, it remains unclear if CDT confers any meaningful long-term benefit. The only patient that died in the ULTIMA study was in the heparin-alone group. Pooled mortality estimates from studies for CDT are similar to the mortality estimates of the anticoagulation groups of the larger studies of systemic thrombolysis in intermediate risk PE. While these may represent slightly different patient populations, it seems unlikely that CDT carries a mortality benefit. The rate of bleeding complications for UACDT are likely less than that of systemic thrombolysis, but more than that of systemic anticoagulation alone. It is our opinion that prospective, randomized trials with more meaningful or validated clinical outcomes are necessary before CDT can be used routinely for intermediate-risk PE. In our clinical practice, CDT is considered on a case-by-case basis and is reserved for patients with high likelihood of clinical decompensation. It is possible that improvement in risk stratification of intermediate risk PE might allow for better identification of those patients at higher risk of decompensation who might benefit from early intervention with CDT.

Catheter embolectomy is feasible with devices currently on the market in the United States. All have a similar mechanism of action, and work by introducing a catheter to the site of clot for retrieval by aspiration. In the FLARE study, 104 acute PE patients with elevated RV/LV ratio on CT were treated with catheter embolectomy using the FlowTriever System [Inari Medical, Irvine, California] in addition to systemic anticoagulation. This resulted in a significant reduction of RV/LV ratio, but only a modest decrease in PA pressure. Adverse event rate was 3.8% with no reported cases of intracerebral hemorrhage and only one case of adverse bleeding. This is currently the only embolectomy device that is FDA-approved for treatment of acute PE, although trials remain ongoing for several other catheter embolectomy systems. While catheter embolectomy offers the possibility of clot removal without exposure to thrombolytics, there are no trials comparing this to anticoagulation alone or to CDT. Similar to CDT, it remains to be seen if catheter embolectomy results in outcomes that are more clinically meaningful than an acute reduction in RV/LV ratio. The utility of CDT and catheter embolectomy systems as an effective treatment modality for acute PE depends largely on equipment availability at centers as well as requisite expertise of providers and staff. Its use remains an option in patients with contraindications to systemic thrombolysis or failure of thrombolysis, when surgical embolectomy is unavailable or infeasible, if the institution has the requisite capabilities. In our opinion, catheter-based interventions...
can be considered on a patient case-by-case basis so long as local technical capabilities allow and the decision should be made after a multi-disciplinary or PERT discussion.

**SURGICAL EMBOLECTOMY**

Current indications for surgical embolectomy include high-risk and intermediate-risk PE with an absolute contraindication to thrombolysis, failed thrombolysis, or hemodynamic collapse that may result in death prior to full effect of systemic thrombolysis. Pre-surgical systemic thrombolysis is not an absolute contraindication to surgical embolectomy. Presently, no randomized trials exist comparing systemic thrombolytics to surgical embolectomy, although both are associated with improvement in RV function and PA systolic pressure. Compared to systemic thrombolytics, surgical embolectomy is associated with a decreased risk of major bleeding; however, mortality from surgical embolectomy is estimated to be 4–11%. This modality should be used as reperfusion therapy in higher-risk patients who warrant reperfusion therapy but have an absolute contraindication to systemic thrombolysis. Surgical embolectomy is frequently considered in acute PE patients with presence of right heart thrombi, although optimal treatment for acute PE with “clot in transit” remains uncertain.

**CONCLUSION**

The management of high- and intermediate-risk PE is an evolving area that requires appropriate risk stratification, monitoring, and supportive care after acute PE diagnosis is made. Hemodynamically unstable patients should receive systemic thrombolysis unless there is a clear contraindication. The use of catheter-based interventions and surgical embolectomy should be reserved for patients with an absolute contraindication to systemic thrombolysis. There are currently insufficient data to recommend the use of CDT for acute intermediate-risk PE. As such, prospective, comparative randomized, clinical trials for CDT in acute PE are necessary in order to elucidate the possible role of this treatment modality in this subpopulation.

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Impact of a Novel Sex- and Gender-Based Medicine Preclinical Elective
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ABSTRACT
BACKGROUND: As sex and gender differences in health become clearer, physicians must adapt their practices. There are few interventions promoting knowledge of sex- and gender-based medicine (SGBM). Our medical school preclinical elective was designed to fill this gap.
METHODS: Pre- and post-course surveys were administered to evaluate the course’s impact on learners’ knowledge and attitudes. Quantitative data were analyzed using unpaired t-tests and Fisher’s exact test. Qualitative data were analyzed using grounded theory approach.
RESULTS: 30 pre- and 15 post-surveys were completed. Learners felt more familiar with SGBM (p=0.01) and more strongly agreed that they receive SGBM education in their medical school (p=0.02) after the course as compared to before it. There was also a trend towards increased knowledge of, familiarity with, perceived importance of, and interest in SGBM after the course. Qualitative data yielded various compelling themes.
CONCLUSION: The SGBM preclinical elective increased learner familiarity with SGBM.
KEYWORDS: Sex- and Gender-Based Medicine, undergraduate medical education, course evaluation

INTRODUCTION
Sex- and Gender-Based Medicine (SGBM) has emerged as a medical subspecialty that addresses the roles sex and gender have as determinants of health. The term “sex” refers to biological differences between men and women, while the term “gender” refers to one’s sociocultural roles, traits, and values.1 Both play important functions in the pathophysiology, presentation, diagnosis, and management of disease. As a result, the Office of Women’s Health was established by the Food and Drug Administration in 1994 to support research examining sex-based differences. More recently, the National Institutes of Health’s Office of Research on Women’s Health have begun requiring grant applications to address sex as a biological variable. Consequently, the body of literature in this area has increased.

While learners are interested in SGBM’s inclusion in their curricula, medical education has lagged behind. A 2015 national student survey found that 94% of students felt that SGBM should be included in curricula; most students were unclear, however, about whether this was already included.2 In Emergency Medicine, the majority of recent residency graduates felt that SGBM was relevant to their practice, but only 16% of program directors believed SGBM to be a priority.3 A similar study found that residents of all specialties were lacking knowledge in SGBM.4 This mismatch of priorities prompted the development of national gatherings to address curricular reform.5-7

While many curricular innovations have emphasized integration of SGBM into core curricula, few dedicated SGBM courses exist. The authors established an elective course, “Sex- and Gender-Based Medicine: an Overview,” at the Alpert Medical School of Brown University to introduce students to SGBM. This course, while designed for medical students in their preclinical years, is open to all medical students as well as undergraduate students enrolled in the Program in Liberal Medical Education. We hypothesized that learners would report greater knowledge pertaining to SGBM and attitudes reflecting increased familiarity, perceived relevance of, and interest in SGBM after course completion as compared to before.

MATERIALS AND METHODS

Course
The course includes multiple classroom-based sessions, which are presented through a combination of readings, lecture, case-based learning, and small group discussion. The sessions cover a range of topics and are frequently led by faculty who are experts in their field. These sessions are complemented by the Sex and Gender Specific Health Multimedia Case-Based Learning Modules developed by the Laura W. Bush Institute for Women’s Health at the Texas Tech University Health Sciences Center.8,9 The course’s final project entails a case study on a clinical topic of the student’s choice and is designed to focus a sex and gender lens on a routine patient encounter.

Assessment
Pre- and post-course, anonymous, paper surveys were administered to learners in order to evaluate the effectiveness of
the SGBM course with regard to cognitive and affective objectives. To accomplish this quantitatively, learners were asked Likert scale questions about their perceptions of and attitudes towards SGBM. Learners were also asked yes/no questions about the existence of sex and gender differences in various specialties. Additionally, learners were asked open-ended questions about the domains in which they envisioned SGBM having the greatest clinical impact, perceived barriers to teaching and learning about SGBM, strategies for incorporating SGBM into curricula, and sessions’ impact.

Statistical analysis of quantitative data was carried out via unpaired t-tests for the Likert scale questions and Fisher’s exact test for the yes/no questions. Study authors used grounded theory to analyze qualitative data. Comments were collated by topic area and iterative responses were coded. Our sample size was not large enough to reach saturation; however, multiple learners mentioned several themes repeatedly.

RESULTS
Quantitative Data
30 pre- and 15 post-surveys were completed. 26 women and 4 men participated in the pre-survey; 14 women and 1 man participated in the post-survey. Learners’ median age was 24 for the pre-survey and 25 for the post-survey. The majority of learners were first-year medical students; most were enrolled in the traditional MD program. Learners felt more familiar with SGBM (p=0.01) after course completion as compared to before. Learners also more strongly agreed that they receive SGBM education in their medical school after course completion as compared to before (p=0.02) [Table 1]. A larger proportion of learners acknowledged the existence of sex and gender differences in certain areas (musculoskeletal system, sports medicine, and neurology) (70% v. 100%, p=0.018; 73% v. 100%, p=0.027; 60% v. 100%, p=0.004) after course completion as compared to before [Table 2]. While analysis of other data did not demonstrate statistical significance, it did demonstrate a trend towards increased SGBM knowledge and a heightened familiarity with, perceived importance of, and interest in SGBM after course completion as compared to before [Table 1].

Table 1: Degree of learner agreement with various statements regarding SGBM ranked on a Likert scale from 1 (strongly disagree) to 5 (strongly agree).

<table>
<thead>
<tr>
<th>Question</th>
<th>Pre-Course Mean Score</th>
<th>Post-Course Mean Score</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am familiar with the topic of SGBM</td>
<td>3.57</td>
<td>4.13</td>
<td>0.01</td>
</tr>
<tr>
<td>I receive SGBM education at my medical school</td>
<td>2.64</td>
<td>3.14</td>
<td>0.02</td>
</tr>
<tr>
<td>SGBM is the same as women’s health</td>
<td>1.57</td>
<td>1.73</td>
<td>0.30</td>
</tr>
<tr>
<td>Except for inherent differences between their reproductive systems, there are no clinically relevant differences between men and women</td>
<td>1.47</td>
<td>1.33</td>
<td>0.51</td>
</tr>
<tr>
<td>The majority of medical knowledge is based on data obtained from males</td>
<td>4.52</td>
<td>4.47</td>
<td>0.79</td>
</tr>
<tr>
<td>SGBM knowledge improves one’s ability to care for patients</td>
<td>4.77</td>
<td>4.80</td>
<td>0.80</td>
</tr>
<tr>
<td>Medical education should include SGBM</td>
<td>4.80</td>
<td>4.80</td>
<td>1.00</td>
</tr>
<tr>
<td>I routinely incorporate SGBM knowledge into patient case discussions</td>
<td>2.80</td>
<td>3.14</td>
<td>0.16</td>
</tr>
<tr>
<td>SGBM knowledge will affect my clinical practice</td>
<td>4.50</td>
<td>4.47</td>
<td>0.85</td>
</tr>
<tr>
<td>I am interested in additional SGBM educational resources/opportunities</td>
<td>4.57</td>
<td>4.60</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Table 2: Percentage of learners who thought that there were sex and gender differences with regard to the topics listed.

<table>
<thead>
<tr>
<th>Topic</th>
<th>Pre-Course %</th>
<th>Post-Course %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease presentation</td>
<td>90</td>
<td>100</td>
<td>0.20</td>
</tr>
<tr>
<td>Patient communication style</td>
<td>83</td>
<td>100</td>
<td>0.09</td>
</tr>
<tr>
<td>Occupational and environmental health</td>
<td>83</td>
<td>100</td>
<td>0.09</td>
</tr>
<tr>
<td>Access to health care</td>
<td>90</td>
<td>93</td>
<td>0.71</td>
</tr>
<tr>
<td>Anatomy and physiology (excluding reproductive system)</td>
<td>80</td>
<td>100</td>
<td>0.06</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>90</td>
<td>93</td>
<td>0.71</td>
</tr>
<tr>
<td>Musculoskeletal system</td>
<td>70</td>
<td>100</td>
<td>0.02</td>
</tr>
<tr>
<td>Sports medicine</td>
<td>73</td>
<td>100</td>
<td>0.03</td>
</tr>
<tr>
<td>Neurology</td>
<td>60</td>
<td>100</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pharmacology</td>
<td>83</td>
<td>100</td>
<td>0.09</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td>47</td>
<td>73</td>
<td>0.09</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td>73</td>
<td>93</td>
<td>0.11</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>40</td>
<td>67</td>
<td>0.09</td>
</tr>
<tr>
<td>Dermatology</td>
<td>50</td>
<td>40</td>
<td>0.53</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
<td>47</td>
<td>60</td>
<td>0.40</td>
</tr>
<tr>
<td>Mental health</td>
<td>80</td>
<td>100</td>
<td>0.06</td>
</tr>
<tr>
<td>Sexual health</td>
<td>93</td>
<td>100</td>
<td>0.13</td>
</tr>
<tr>
<td>Leadership in medicine</td>
<td>90</td>
<td>100</td>
<td>0.20</td>
</tr>
<tr>
<td>Pain medicine</td>
<td>80</td>
<td>100</td>
<td>0.06</td>
</tr>
<tr>
<td>Interpersonal violence</td>
<td>90</td>
<td>100</td>
<td>0.20</td>
</tr>
</tbody>
</table>
Qualitative Data

Impact

Both pre- and post-course learners identified various realms in which SGBM might have maximal impact and why. Some thought SGBM would influence conditions that are experienced by women and gender minorities at higher rates. Others pointed out that SGBM could have an impact on areas where sex and gender differences exist but are not widely recognized. Learners expected that SGBM would lead to understanding patients better and holistically as well as providing “tailored” care. They suggested that SGBM would be relevant to fields in which gender differences in communication and gender bias play a role. Learners also viewed SGBM as having potential impact on public health by improving healthcare access. Finally, they noted that SGBM's greatest effect could be to enable learners to think more critically about the biases inherent in research and educational material.

Barriers

Pre- and post-course, learners recognized multiple barriers to SGBM education. Some identified the absence of SGBM from the current medical school curriculum as an obstacle to learning about it. Others mentioned unfamiliarity with and disinterest in SGBM among both instructors and learners – as well as their view that it is unimportant or “not real” – as barriers. Still others noted the field's novelty and complexity as well as confusion as to what SGBM means as impediments. Logistically, learners identified lack of resources such as time, money, and faculty expertise as barriers to integrating SGBM into the curriculum. They pointed out that it represented “one more thing to learn” and teach and would need to replace competing curricular material as well as noted the absence of “buy-in” from current medical education leaders. Many underscored sociocultural factors, such as the predominance of male leadership in medical education as well as bias against women and gender minorities. Others recognized hesitancy to teach politically incorrect topics and the compartmentalization of “women's health” as additional barriers. Finally, one learner felt that “simplification of...issues to...biological sex” posed a threat.

Strategies for Incorporation

Learners suggested numerous strategies to incorporate SGBM into the medical school curriculum. Some thought it would be best to present SGBM data through the existing curriculum whenever possible and to acknowledge when it is not. Others felt that having a dedicated session on SGBM within each “block” would make more sense. Some also suggested arranging optional lectures on SGBM, though one learner underscored the need to make learning about SGBM mandatory. Lastly, learners pointed to faculty education as well as increasing women's and gender minorities' representation on the faculty and in medical education leadership as strategies.

Impact of Lectures

Learners varied in their assessment of which sessions were most impactful. Some mentioned that the highest-yield lectures distinguished between biological and social influences on health and disease while addressing both. One learner mentioned the utility of learning inclusive language. Another found sessions that raised controversial issues to be fruitful. Yet another thought a most impactful session had relevance to their own career. Many mentioned that being at sessions attended by other “strong” women physicians was inspiring. Finally, learners felt that sessions which neglected the nuances of the interface between sex and gender as well as those that did not incorporate case-based learning were lacking.

DISCUSSION

The SGBM preclinical elective represents a novel means of incorporating SGBM into undergraduate medical curricula. Despite our small sample size, our educational intervention increased learners' familiarity with the topic of SGBM and their perception that they receive SGBM education in their medical school. Additionally, the qualitative data yielded various compelling themes.

Both prior to and after the course, learners felt that an effect of SGBM could be on increasing the provision of inclusive, holistic care and improving access to healthcare. Prior to the course, learners mentioned the role SGBM could play in elucidating gender differences in disease presentation. Interestingly, afterwards, learners focused more on the role SGBM could play in uncovering gender bias inherent in research and medical education, suggesting they gained a sense of the pervasiveness of this issue.

Both prior to and after the course, learners highlighted many similar barriers to SGBM education: the fact that SGBM is not integrated into the existing curriculum, lack of awareness of and interest in SGBM, limited resources, the nascent and complex nature of the field, as well as sociocultural factors. However, only after course completion did learners raise the issue of how difficult it can be to prioritize the competing lenses through which they are expected to view material, underscoring the benefit of an intersectional approach. Another theme unique to post-survey responses was the problem of biological reductionism. Finally, learners highlighted the dichotomy between approaches for curricular integration of SGBM in terms of incorporation of SGBM material into the existing curriculum versus time exclusively dedicated to SGBM, suggesting that there may not be a “right” way. Learners also emphasized the necessity of having non-male faculty, particularly in medical education leadership, in order to ensure the presence of appropriate stakeholders and promotion of SGBM.

Our study of a novel SGBM preclinical elective had a number of limitations. First, our sample size was small and...
the study therefore inadequately powered, which may have led to our finding largely statistically insignificant results. Furthermore, because course credit was awarded retroactively, and many learners did not attend all sessions, it was not always possible to track learners’ responses over time. Also, the course was and continues to be delivered to a self-selected group that is often already interested in and knowledgeable about SGBM, making it more difficult to detect the course’s true impact. The pre- and post-surveys assessed self-reported knowledge and attitudes; examining these domains through more objective means might provide a better sense of the course’s effect. Finally, the self-selected nature of the course’s participants may have limited the breadth and depth of the qualitative data gathered. Nevertheless, the SGBM preclinical elective is an example of an educational intervention that can increase learner familiarity with SGBM and enable learners to request the integration of SGBM into their medical education in order to improve their future patients’ health outcomes.

CONCLUSIONS
Knowledge of sex and gender differences in health and disease has burgeoned in recent years. The increase in knowledge has created a gap, however, between existing curricula and evidence based medicine. The SGBM preclinical elective was designed to address this gap by surveying SGBM across multiple specialties. This novel curriculum was found to increase learner familiarity with SGBM and their perception that they receive SGBM education in their medical school. The course was additionally associated with a non-significant increase in SGBM knowledge and a heightened familiarity with, perceived importance of, and interest in SGBM. Learners’ qualitative responses also yielded important insights. Similar courses at other institutions may be useful in positively affecting knowledge of and attitudes towards SGBM among learners.

References

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Evaluating the Impact of a Student-Run Women’s Clinic on Access to Gynecologic Care for Uninsured Women in Rhode Island

NATASHA R. KUMAR, MD; GABRIELE DUVERNOIS, MD, MPH; VALERIE ALMEIDA-MONROE, RN; NICOLE SIEGERT, MD; ANNE S. DE GROOT, MD

ABSTRACT
Clinica Esperanza/Hope Clinic (CEHC) is a free clinic providing primary care to a predominantly Spanish-speaking, uninsured patient population in Rhode Island with limited access to gynecologic care. In 2015, medical students at the Alpert Medical School of Brown University started the Women’s Clinic of Clinica Esperanza (WCCE), a “clinic within the clinic,” recruiting physician preceptors and obtaining funding to support WCCE operations. For complex issues, clinic services were supplemented by a subspecialty referral system at a local hospital. Interim results over a two-year period ending in May 2017 are reported here. Medical students organized 48 women’s clinics and provided 83 Pap smears, 138 breast exams, 42 mammogram referrals, 35 STI tests, and 19 vaginitis screens, among other activities. As the example of WCCE shows, student-run clinics can utilize medical students’ relationships with providers and unique funding sources to expand access to specialty care for uninsured patients.

KEYWORDS: free clinics, health disparities, gynecology, primary care

INTRODUCTION
While the Affordable Care Act (ACA) has improved access to gynecologic care, women who are unable to obtain insurance1 and women who are eligible but remain uninsured fare no better, and may be faring worse, since ACA passage. Medicaid expansion may be reducing access to care for uninsured patients at federally qualified health centers, where increasing proportions of patients who seek healthcare appointments are now insured.2 In this context, national attention has been drawn to the importance of free clinics that provide primary care to uninsured populations in the United States.

Significant disparities persist in access to gynecologic services for uninsured women. Uninsured women are far less likely to obtain screenings to detect breast or cervical cancer.3,4 While many gaps in primary care can be addressed by community health clinics (CHCs) and free clinics5, gaps in specialty services persist, particularly for gynecologic care. Only 43% of uninsured women report having either a gynecologic or obstetric visit in the past year, compared to 58% of women with Medicaid and 70% of women who are privately insured.1 A survey of 179 free clinics in New York City showed that only 53.1% of these clinics offered either obstetric or gynecologic services.6 Nationally, only 54.4% of eligible patients obtained Pap smears at CHCs in 2016.7

Student-run clinics, or clinics coordinated and staffed by medical students who are supervised by licensed physicians, can serve as an ancillary route for healthcare delivery to uninsured patients. Nationally, there are more than 100 student-run free clinics, which average 36,000 patient visits annually, affiliated with allopathic medical schools. Published reports on student clinics have focused primarily on their contribution to medical student education rather than their impact on access to patient care.8 However, student-run clinics provide preventive services at similar frequencies to other safety net institutions such as CHCs.9 Typically, patients of student-run clinics are highly satisfied with their care, although there are frequently long wait times to be seen by a provider once patients are checked in at student-run clinics.10

Here, we report the impact of a student-run clinic on access to gynecologic care for uninsured patients at a free clinic in Providence, Rhode Island. We describe (a) the range of gynecologic needs of this population, (b) the types and prevalence of services provided by WCCE, and (c) the challenges and strengths of specialized care delivery for this population. Our data indicate that uninsured patients have varied gynecologic needs and student-run clinics can play an important role in expanding access to gynecologic care for uninsured patients.

METHODS
CEHC is a free, volunteer-run clinic that provides primary healthcare to more than 3,000 patients residing in Providence, Rhode Island.11 In May 2015, medical students founded the Women’s Clinic of Clinica Esperanza (WCCE) to address the unmet needs of patients seeking gynecologic care, including but not limited to, routine screening (Pap smears and mammograms), contraception, preconception counseling, and management of gynecologic issues such as abnormal uterine bleeding, vaginitis, and infertility. This student-run clinic was established as a “clinic within a
CONTRIBUTION

Clinic operating quasi-independently within the preexisting infrastructure of CEHC. Patients were referred from Clinica Esperanza’s primary care clinic if they reported any specific gynecologic issues or were eligible for routine gynecologic screening. Depending on preceptor availability, between one to three women’s clinics were held each month, with six to ten patients scheduled per clinic.

WCCE operations required close collaboration between medical students, CEHC staff and the physician volunteers at CEHC. Two senior medical students served in both clinical and administrative roles, staffing each clinic, acquiring grant support for clinic operations, and monitoring follow-up needs for patients. These medical students utilized their existing relationships with faculty to recruit preceptors and to build a subspecialty referral system for WCCE, spending between five to fifteen hours per week on WCCE operations. Six preclinical medical students also volunteered in WCCE for five hours per month. Obstetrician-gynecologists, family medicine physicians, and internists served as preceptors, supervising medical students staffing the clinics. Administrative staff at Clinica Esperanza provided operational support, such as reserving space for clinics, reviewing laboratory results, and following up on pending referrals. Community health workers, known as Navegantes at CEHC, assisted with appointment reminders, linked patients to charity care programs at local hospitals (if needed), and provided culturally sensitive education on contraceptives and family planning.

Funding for WCCE operations was obtained primarily through state-run public health programs and private grant support. The Rhode Island Department of Health’s Women’s Cancer Screening program provided access to reimbursement for imaging and laboratory services related to performance of Pap smears and mammograms. Grant funding for CEHC supported the work of the CHWs (Navegantes), the nurse manager, the medical assistant, and infrastructure costs (rent, heat, electricity and telephone costs). Medical students were able to obtain additional grants from the medical school to purchase supplies such as specula, lubricant for exams and glass slides for wet mounts. A microscope was donated to the WCCE by the medical school. Oral contraceptives were provided by Direct Relief and other agencies. A grant from Bayer provided free IUDs on a monthly, lottery-based system. March of Dimes funding provided support for small-group education about contraceptives and family planning, which were run by the Navegantes.

We performed a retrospective chart review to summarize the experience from the first two years of clinic operations. Namely, we describe patient demographics and number of encounters, types of medical problems, service provision and referrals made by the WCCE.

RESULTS

From May 2015 to May 2017, the Women’s Clinic at Clinica Esperanza (WCCE) served 138 patients. Patients ages 19–73 years old were primarily Spanish speaking (85.2%, Table 1) and of Hispanic ethnicity (89.6%), mostly Guatemalan (51.1%). CEHC patients are uninsured, however, 25% of patients at WCCE were able to obtain charity care for laboratory work and specialty referrals at a local hospital (Table 1). Only eight patients (5.8%) became insured and were able to transfer their gynecologic care to other institutions during this two-year period (Table 1).

Table 1. Patient Demographics (n=138)

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>African American</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>African</td>
<td>8 (5.9)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>121 (89.6)</td>
</tr>
<tr>
<td>Guatemalan</td>
<td>69 (51.1)</td>
</tr>
<tr>
<td>Mexican</td>
<td>13 (9.6)</td>
</tr>
<tr>
<td>Salvadoran</td>
<td>9 (6.6)</td>
</tr>
<tr>
<td>Dominican</td>
<td>7 (5.1)</td>
</tr>
<tr>
<td>Columbian</td>
<td>5 (3.7)</td>
</tr>
<tr>
<td>Bolivian</td>
<td>5 (3.7)</td>
</tr>
<tr>
<td>Other</td>
<td>13 (9.6)</td>
</tr>
<tr>
<td>Primary Language</td>
<td></td>
</tr>
<tr>
<td>Spanish</td>
<td>115 (85.2)</td>
</tr>
<tr>
<td>English</td>
<td>15 (11.1)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (3.7)</td>
</tr>
<tr>
<td>Insurance Status</td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>100 (72.5)</td>
</tr>
<tr>
<td>Lifespan FreeCare</td>
<td>30 (21.7)</td>
</tr>
<tr>
<td>Insured (with subsequent transfer of care)</td>
<td>8 (5.8)</td>
</tr>
</tbody>
</table>

*Due to missing values, n=135 for these variables.

Table 2. Visit Composition, May 2015–May 2017

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of clinics</td>
<td>48</td>
</tr>
<tr>
<td>Average number of scheduled encounters per clinic</td>
<td>7.3</td>
</tr>
<tr>
<td>Number of completed encounters</td>
<td>171</td>
</tr>
<tr>
<td>Number of new patient encounters</td>
<td>138</td>
</tr>
<tr>
<td>Missed encounter rate (%)</td>
<td>50.7</td>
</tr>
<tr>
<td>Types of missed encounters</td>
<td></td>
</tr>
<tr>
<td>No show (n)</td>
<td>137</td>
</tr>
<tr>
<td>Cancelled (n)</td>
<td>17</td>
</tr>
<tr>
<td>Rescheduled (n)</td>
<td>24</td>
</tr>
</tbody>
</table>

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Forty-eight WCCE clinics were held during a two-year period, with an average of 7 scheduled appointments per clinic [Table 2]. Over the 48 clinics, 171 appointments were completed and 80.7% of appointments were with new patients [Table 2]. The rate of missed encounters was 50.7%. Missed visits were more common than cancellations or rescheduled visits [Table 2].

Patients had a variety of gynecologic needs. Routine gynecologic screening in the form of Pap smears or mammograms was the most prevalent need (88.4% of patients, Table 3).

### Table 3. Healthcare Needs and Service Provision at Women’s Clinic, May 2015–May 2017

<table>
<thead>
<tr>
<th>Gynecologic Needs&lt;sup&gt;a&lt;/sup&gt; (n=138)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine gynecologic screening (Pap/mammogram)</td>
<td>122 (88.4)</td>
</tr>
<tr>
<td>No other issues</td>
<td>53</td>
</tr>
<tr>
<td>Cervical dysplasia among patients with Paps&lt;sup&gt;b&lt;/sup&gt; (n=80)</td>
<td></td>
</tr>
<tr>
<td>Atypical squamous cells of unspecified origin</td>
<td>9/80 (11.3)</td>
</tr>
<tr>
<td>Cervical intraepithelial neoplasia-1&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3/80 (3.8)</td>
</tr>
<tr>
<td>Atypical squamous cells-high grade</td>
<td>1/80 (1.3)</td>
</tr>
<tr>
<td>Cervical intraepithelial neoplasia-2,3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3/80 (3.8)</td>
</tr>
<tr>
<td>Invasive carcinoma&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1/80 (1.3)</td>
</tr>
<tr>
<td>Abnormal uterine bleeding</td>
<td>33 (23.9)</td>
</tr>
<tr>
<td>Preconception counseling</td>
<td>20 (14.5)</td>
</tr>
<tr>
<td>Contraception management</td>
<td>18 (13.0)</td>
</tr>
<tr>
<td>Abnormal vaginal discharge</td>
<td>17 (12.3)</td>
</tr>
<tr>
<td>Infertility</td>
<td>16 (11.6)</td>
</tr>
<tr>
<td>Breast issues</td>
<td></td>
</tr>
<tr>
<td>Mastodynia</td>
<td>9 (6.5)</td>
</tr>
<tr>
<td>Breast mass</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Nipple discharge</td>
<td>2 (1.4)</td>
</tr>
<tr>
<td>Stress urinary incontinence</td>
<td>5 (3.6)</td>
</tr>
<tr>
<td>Pelvic organ prolapse</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Vulvodynia</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td>Secondary amenorrhea</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Vulvar lesions (papillomas, warts)</td>
<td>3 (2.2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Service Provision</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap Smears</td>
<td></td>
</tr>
<tr>
<td>Initial screen after &gt;3 years</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>80/83 (96.4)</td>
</tr>
<tr>
<td>Mammograms (referrals)</td>
<td>42</td>
</tr>
<tr>
<td>Gonorrhea/chlamydia testing</td>
<td>35</td>
</tr>
<tr>
<td>Vaginitis testing</td>
<td>19</td>
</tr>
<tr>
<td>Wet mount</td>
<td>3</td>
</tr>
<tr>
<td>Urine pregnancy testing</td>
<td>6</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>3</td>
</tr>
<tr>
<td>Gardasil vaccination</td>
<td>3</td>
</tr>
</tbody>
</table>

<sup>a</sup> Some patients had multiple gynecologic needs, so n>138 for this section of the table.

<sup>b</sup> For patients with >1 pap smear (n=3), only the result from the initial Pap smear is included here.

<sup>c</sup> These results are from colposcopy or excisional testing after Pap smear.

A majority of patients who required routine gynecologic screening also presented with additional needs. Common issues included abnormal uterine bleeding [23.9%), preconception counseling [14.5%], contraception management [13.0%], abnormal vaginal discharge [12.3%], and infertility [11.6%].

Over two years, student providers and their mentors at WCCE provided 83 Pap smears, 42 referrals for mammograms, 35 STI testing panels, and 19 vaginitis screens [Table 3]. Of patients who got Pap smears, four of 83 patients (5.1%) had high-grade squamous intraepithelial lesions (HSIL) or invasive carcinoma. In addition, patients needed referrals to outside providers for infertility (n=8), colposcopy (n=7), urogynecology (n=5), and oncology (n=1) services. Eight patients requested long-acting reversible contraceptives.

Ongoing challenges to be addressed include the high no-show rates. In addition, patients continued to face significant barriers to seeking care (for mammograms, for example) at referral hospitals primarily due to lack of transportation and language barriers. To address these barriers, we created an instructional sheet on mammogram completion to guide peer-to-peer education by Navegantes during clinic visits. Patients also had brief appointments at WCCE before and after referrals to review their expectations for the visit and address any remaining questions. Referrals to reproductive endocrinology and infertility, the most common referral for WCCE patients, posed a particular challenge for patients because of significant out-of-pocket costs. Finally, WCCE patients faced significant barriers to access to long-acting reversible contraception. WCCE was unable to find consistent sources of funding to support provision of either IUDs or implants. There was insufficient demand for Depo Provera to purchase and store the injections at Clinica Esperanza; interested patients had to purchase the medication at an outside pharmacy.

**DISCUSSION**

The WCCE supports the principle that student-run clinics are an effective-source for specialty care for uninsured patients. Service utilization by clinic patients during the initial two years of WCCE operations demonstrated a high level of unmet needs for gynecologic care. Because of their unique role within the healthcare system, medical students developed relationships with individual providers, practical clinical experience and access to funding sources that supported expansion of clinical services. Altogether, our initiative creating WCCE indicates that student-run clinics have the potential to expand access to necessary specialty care at institutions that otherwise would not be able to provide these services.

Existing literature on student clinics focuses on these clinics’ contribution to medical student education, improving medical students’ cultural competency, professionalism,
and clinical skills. The limited data available on quality of care provided by student-run clinics supports the conclusion that it is equivalent to the services provided in other safety net settings.

Most literature on unmet needs for gynecologic services in safety net populations focuses primarily on screenings for cervical and breast cancer. Routine gynecologic screening was the most prevalent need for WCCE patients. Five percent of Pap smears completed on an initial visit showed high-grade dysplasia or invasive cervical carcinoma. However, more than half of WCCE patients who presented initially for routine screening had other gynecologic complaints, most commonly abnormal uterine bleeding (AUB). These results highlight the need for comprehensive gynecologic care at safety net institutions. Ideally, gynecologic services would include an established referral system to subspecialists in oncology, urogynecology and reproductive endocrinology.

The success of this intervention depended on several factors, some of which are unique to Rhode Island and others which can be replicated elsewhere. WCCE’s unique structure as a clinic within a preexisting primary care clinic provided a steady stream of patient referrals and administrative support from clinic staff to assist with WCCE operations [Figure 1]. WCCE served patients in close proximity to a large academic teaching hospital, which employed subspecialists with whom medical students interact during their clinical years; this proximity facilitated the creation of a subspecialty referral system for complex needs. The peer education groups held by Navegantes during each session of the women’s clinic provided a culturally-sensitive space for patients to discuss expectations and fears about the pelvic exam and questions about contraception. WCCE also provided routine preventive screenings with the financial support of the Women’s Cancer Screening Program.

Medical students can play a significant role in expanding the specialty services available to uninsured patients. Further attention should be given to promoting and facilitating the creation of student-run specialty clinics to supplement the existing network of student-run primary care clinics in the United States.

Acknowledgments
The authors would like to thank the staff of Clinica Esperanza, the Warren S. Alpert Medical School administration, and the medical students and preceptors who supported WCCE operations between May 2015 and May 2017.

References

The small size and predominantly Latina demographic of WCCE patients may limit the generalizability of findings to other populations. The infrastructure and resources available to the WCCE thanks to the CEHC as well as local and state resources in Providence, Rhode Island may also not be generalizable. The limited two-year follow-up period of this study makes it difficult to assess long-term effects of improved access to gynecologic care on patient outcomes.

Despite these caveats, student-run subspecialty clinics are an underutilized solution to address gaps in health equity.


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Submissions should include:

**Brief title**: 8 words or less

**Content**: Relevant clinical information, findings, clinical course, and response to treatment if initiated. Limit: 400 to 600 words

**Legends**: All labeled structures in the image should be described and explained in the legend. Any identifying information should be removed from the image.

**Author information**: Names, professional degree, academic/hospital affiliations, address, email and telephone number.

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How Many Parents are Reading with their Young Infants in Rhode Island?

KARINE MONTEIRO, MPH; HYUN (HANNA) KIM, PhD; WILLIAM ARIAS, MPH; PAMELA HIGH, MS, MD

Children who begin school with a love of books and with the requisite literacy-related knowledge and skill, including verbal abilities, familiarity with the basic purposes and mechanisms of reading, and the ability and desire to attend to the sounds of language, are less likely to have difficulty learning to read. Research indicates that there is a relationship between early book sharing and children’s development of language skills and acquisition of vocabulary.1-3 In Rhode Island, toddlers whose families received new children’s books and guidance about the importance of shared reading at their well-child visits starting when they were 6 months old understood and used more words by the time they were 18–24 months old, compared to those not receiving this guidance.1

In 2014, the American Academy of Pediatrics (AAP) released its first literacy policy statement formally recommending that pediatric providers promote early literacy experiences including shared reading for families with young children starting at birth and continuing at least until the age of kindergarten entry.4 This aligns with current Bright Futures Guidelines formulated by Health Resources and Services Administration (HRSA) and leaders in child health and development as well as with recommendations from Reach Out and Read (ROR), a national pediatric literacy program, that encourages pediatricians to be advocates for reading aloud to infants and toddlers.5-6 Despite the expanded endorsement and the well-documented benefits of shared reading on early brain and child development, nationally, only 37.0% of children from birth to age 5 are being read to every day. In Rhode Island 49.3% of the children under the age of 5 are being read to every day.7

The purpose of this study is to describe the prevalence of and disparities in shared-reading experiences of parents and infants 2 to 6 months old in Rhode Island. In addition, it describes the prevalence of risk behaviors and outcomes by early onset of shared reading in infants. Investigating this indicator will help us understand the implications of presence or absence of this parenting behavior and be able to formulate public health approaches to encourage literacy and language skills in the critical first few months of life.

METHODS

PRAMS is an ongoing state-based surveillance system of maternal behaviors, attitudes, and experiences before, during, and shortly after pregnancy and is conducted by the Centers for Disease Control and Prevention’s (CDC) Division of Reproductive Health in collaboration with state health departments.8 We also looked at prevalence data from RI PRAMS from 2009–2018, when the question about early reading was first added to RI’s PRAMS survey. The survey is sent in English and Spanish to a sample of mothers 2 to 6 months after the birth of a live infant. Mothers’ survey responses are linked to extracted birth certificate data items and are weighted to represent all women delivering live infants in Rhode Island.

Aggregate data from the 2016–2018 Rhode Island Pregnancy Risk Assessment Monitoring System [RI PRAMS] was analyzed. In the 2016–2018 RI PRAMS, 5,761 mothers were sampled from a total of 29,905 mothers who had a live infant during the period. Of those who were sampled, 3,350 mothers responded to the survey (3-year combined weighted response rate was 59.0%), which was analyzed for this study.

The prevalence of shared reading with infants was assessed via responses “yes” and “no” to the question, “Are you or any other family member currently reading or looking at books with your baby?” Among those who read to their infants, reading frequency in the past week was assessed via the following responses “Did not read to the baby this week”, “1–3 days this week”, “4–7 days this week” to the question: “During the past week, how many days did you or other family members read or look at books with your baby?”

To identify disparities, the prevalence of shared reading of parents and infants 2 to 6 months old was examined by maternal demographic characteristics, age, race/ethnicity, education, marital status, annual household income, insurance coverage postpartum, participation in the Women, Infants, & Children [WIC] Nutrition Program, maternal disability, infant gender, infant age, birth weight, birth parity, survey language and core city residence (Central Falls, Pawtucket, Providence and Woonsocket). Maternal health indicators and risk behaviors [pregnancy intention, prenatal care in the first trimester, infant safe sleep, postpartum depression, breastfeeding, postpartum checkup, cigarette use during pregnancy, social support postpartum, baby crying/fussiness and number of children’s book in the home] and

Dec 19, 2019
birth outcomes (low birth weight <2,500 grams and preterm birth <37 weeks gestation) were analyzed to determine the association with shared reading.

All data analyses were performed using SAS© software 9.4 (Copyright © [2019] SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA), where chi-square and Student’s t-tests were performed for descriptive analyses to report demographics and to compare the outcomes.

RESULTS
Prevalence and trends of families having begun to read with their infants, 2009–2018
Figure 1 shows the prevalence of and trend in reading with infants by mothers or any other family member. Although the prevalence of reading fluctuated year by year, the linear trend analysis indicated that the overall prevalence increased from 2009 to 2018 (p-value < 0.0001). A noticeable increase in reading prevalence was found in the year following the AAP policy statement implementation, from 78.7% in 2014 to 84.7% in 2015 (p-value < 0.01). We also observed that the reading prevalence was higher for all years after the AAP policy statement implementation, compared with the previous period. The average proportion before and after the AAP recommendation was respectively 76.2% and 81.1% (p-value <0.01), a percent increase of 6.5%.

Prevalence of families having begun to read with their infants by demographics, 2016–2018
Overall, the prevalence of having started to read with young infants in Rhode Island was 80.7% (95% CI: 79.2%–82.3%) between 2016 and 2018. Disparities in this book-sharing experience were seen among socio-demographic characteristics (Table 1). Women who were younger than 20 (69.7%), Hispanic (74.6%), had less than 12 years of education (69.5%), had an annual household income less or equal to $24,000 (75.6%), were uninsured (66.3%), participated in the WIC program (75.5%), had an infant 2–3 months of age (76.8%), had their second or later birth (78.0%), completed the survey in Spanish (70.0%) and resided in a core city (76.2%) were less likely to read to their infant. Among those asked how many days they read to their infants in the past week, 8.7% did not read, 53.8% read 1–3 times, and 37.4% read 4–7 days. Among those who were not currently reading to their infants, 73.4% planned to initiate reading by infant’s 11 months of age, 24.5% between 1–2 years, 0.8% between 3–4 years and 1.6% did not plan to read to their infants.

Behaviors and birth outcomes by families reading with infants, 2016–2018
Figure 2 shows the prevalence of risk behaviors and birth outcomes in families already reading verses those not yet reading with their 2–6 month olds in Rhode Island. Compared to women who read to their infants, women who did not read to their infants were more likely to have an unintended pregnancy (42.5%, p-value <0.01), not to place her infant to sleep on their back (21.7%, p-value <0.01), diagnosed with postpartum depression (15.9%, p-value <0.05),...
This study found a high rate of shared-reading initiation among mothers of 2–6 month old infants in Rhode Island, with about 4 in 5 mothers reporting that they are participating in this experience. The lower rate of shared reading we found in more vulnerable populations is consistent with other reports and supports the need to bring this important message with culturally responsive approaches and supports to families with young children in less advantaged circumstances.

Each year more than a third of children in the US enter kindergarten with their language and literacy skills 1 to 3 years behind their peers. Reach Out and Read has taken this on by supporting pediatric providers in offering new children’s books and guidance about the importance of reading with young children during their 6-month to 5-year-old health maintenance visits and by focusing first on those families in greatest need. Reach Out and Read RI has recently obtained philanthropic support to begin this intervention in Rhode Island as soon as young families come in pediatric primary care offices. One means of assessing the impact of this work will be by using RI PRAMS data starting in 2020.

This work also found an increase in initiation of shared-reading activities in Rhode Island families with young infants following the 2014 AAP Literacy Policy Statement release. It is reassuring to know that this message is being heard, the needle is moving in the right direction, and yet, there is a great deal of work to be done to assure that all families with young children have the knowledge and the tools (high-quality children’s books), resources, and supports to promote healthy early development in their infants.

### LIMITATIONS

PRAMS data are based on self-report by the survey respondent, so they may be subject to recall bias or bias towards the socially-desirable answer. In addition, women are sampled 2–6 months after giving birth; however, 9.0% of the surveys included in this analysis were received 7 to 9 months postpartum. Despite these limitations, the PRAMS survey is the best source of data to assess population based shared reading activities in Rhode Island families with young infants.

---

**Table 1. Prevalence of families having begun to read with their infants 2–6 month olds by socio-demographic characteristics, Rhode Island women who delivered a live birth, RI PRAMS, 2016–2018 combined**

<table>
<thead>
<tr>
<th></th>
<th>n²</th>
<th>Percent b</th>
<th>95% CI</th>
<th>P-Value</th>
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<td><strong>Statewide</strong></td>
<td>2,592</td>
<td>80.7</td>
<td>79.2–82.3</td>
<td>0.0069</td>
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<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20 yrs</td>
<td>91</td>
<td>69.7</td>
<td>60.6–78.8</td>
<td>&lt; 0.0001</td>
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<tr>
<td>20 - 29 yrs</td>
<td>1,037</td>
<td>79.7</td>
<td>77.3–82.2</td>
<td>&lt; 0.0001</td>
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<tr>
<td>≥ 30 yrs</td>
<td>1,464</td>
<td>82.4</td>
<td>80.5–84.4</td>
<td>&lt; 0.0001</td>
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<td><strong>Race/Ethnicity</strong></td>
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<tr>
<td>White, Non-Hispanic</td>
<td>1,470</td>
<td>84.3</td>
<td>82.4–86.2</td>
<td>&lt; 0.0001</td>
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<tr>
<td>Black, Non-Hispanic</td>
<td>168</td>
<td>81.0</td>
<td>74.7–87.3</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>657</td>
<td>74.6</td>
<td>71.4–77.9</td>
<td>&lt; 0.0001</td>
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<tr>
<td>Other, Non-Hispanic</td>
<td>276</td>
<td>77.5</td>
<td>72.5–82.4</td>
<td>&lt; 0.0001</td>
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<tr>
<td><strong>Education, years</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt; 12</td>
<td>218</td>
<td>69.5</td>
<td>63.6–75.5</td>
<td>&lt; 0.0001</td>
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<tr>
<td>12</td>
<td>456</td>
<td>73.3</td>
<td>69.3–77.2</td>
<td>&lt; 0.0001</td>
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<tr>
<td>&gt; 12</td>
<td>1,736</td>
<td>84.6</td>
<td>82.9–86.3</td>
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<td><strong>Marital status</strong></td>
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<td>Married</td>
<td>1,572</td>
<td>82.1</td>
<td>80.3–84.0</td>
<td>0.0677</td>
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<td>Unmarried</td>
<td>1,007</td>
<td>79.1</td>
<td>76.5–81.6</td>
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<tr>
<td><strong>Annual household income</strong></td>
<td></td>
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<tr>
<td>≤ $24,000</td>
<td>753</td>
<td>75.6</td>
<td>72.6–78.7</td>
<td>&lt; 0.0001</td>
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<tr>
<td>$24,001 - $32,000</td>
<td>203</td>
<td>76.7</td>
<td>71.0–82.5</td>
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<td>$32,001 - $57,000</td>
<td>341</td>
<td>79.9</td>
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<td>$57,001+</td>
<td>1,142</td>
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<td>Uninsured</td>
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<td>57.8–74.9</td>
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<td><strong>WIC program participation</strong></td>
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<tr>
<td>No</td>
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<td>84.6</td>
<td>82.8–86.5</td>
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<tr>
<td>Yes</td>
<td>1,003</td>
<td>75.5</td>
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<td>&lt; 0.0001</td>
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<td>81.1</td>
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<td>Female</td>
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<td>76.8</td>
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<td>4-6 months</td>
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<td>80.6</td>
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<td>&gt; 6 months</td>
<td>229</td>
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<td>80.6</td>
<td>78.8–82.3</td>
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<td>Normal Birth Weight (≥ 2500 g)</td>
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<td>80.8</td>
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<td>1st birth</td>
<td>1,105</td>
<td>85.6</td>
<td>83.4–87.7</td>
<td>&lt; 0.0001</td>
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<td>2nd or later</td>
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<td>78.0</td>
<td>75.8–80.0</td>
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<td><strong>Survey language</strong></td>
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<tr>
<td>English</td>
<td>2,270</td>
<td>82.5</td>
<td>80.8–84.1</td>
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<td>Spanish</td>
<td>322</td>
<td>70.0</td>
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<td>1,031</td>
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<td>Rest of state</td>
<td>1,473</td>
<td>84.2</td>
<td>82.2–86.1</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Notes: a - Unweighted number of respondents who reported having begun to read with their infants; b - Weighted percentage; c - 95% Confidence Interval
References


6. https://www.reachoutandread.org


Acknowledgment

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Rhode Island Monthly Vital Statistics Report
Provisional Occurrence Data from the Division of Vital Records

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<td>Number</td>
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<td>9.9*</td>
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<td>5.6#</td>
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<td>50</td>
<td>4.5#</td>
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<td>Marriages</td>
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<td>6,634</td>
<td>6.3*</td>
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<tr>
<td>Divorces</td>
<td>197</td>
<td>2,945</td>
<td>2.8*</td>
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* Rates per 1,000 estimated population  
# Rates per 1,000 live births

<table>
<thead>
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<th>Underlying Cause of Death Category</th>
<th>REPORTING PERIOD</th>
<th>DECEMBER 2018</th>
<th>12 MONTHS ENDING WITH DECEMBER 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (a)</td>
<td>Number (a)</td>
<td>Rates (b)</td>
</tr>
<tr>
<td>Diseases of the Heart</td>
<td>218</td>
<td>2,442</td>
<td>231.0</td>
</tr>
<tr>
<td>Malignant Neoplasms</td>
<td>204</td>
<td>2,246</td>
<td>212.4</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>38</td>
<td>469</td>
<td>44.4</td>
</tr>
<tr>
<td>Injuries (Accident/Suicide/Homicide)</td>
<td>84</td>
<td>830</td>
<td>78.5</td>
</tr>
<tr>
<td>COPD</td>
<td>24</td>
<td>481</td>
<td>45.5</td>
</tr>
</tbody>
</table>

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.  
(b) Rates per 100,000 estimated population of 1,056,298 (www.census.gov)  
(c) Years of Potential Life Lost (YPLL).

NOTE: Totals represent vital events, which occurred in Rhode Island for the reporting periods listed above.  
Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.
It’s a new day.

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RIMS NOTES: News You Can Use

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RIMS NOTES is published electronically on alternate Fridays.

Contact Sarah if you’ve missed an issue, sstevens@rimed.org.
Working for You: RIMS advocacy activities

November 1, Friday
*RIMS Notes* issue production
*RIMJ* Medical Journal release

November 4, Monday
RIMS Board of Directors: Christine Brousseau, MD, MPH, President

November 5, Tuesday
RIMS Physician Health Committee: Herbert Rakatansky, MD, Chair

November 13, Wednesday
Governor’s Overdose Prevention and Intervention Task Force: Sarah Fessler, MD, Past President
Meeting of the New England Charter Medicine Academy Board: Bradley Collins, MD, Chair

November 14–15, Thursday–Friday
American Association of Medical Society Executives – meeting of state CEOs: Newell E. Warde, PhD

November 15–19, Friday–Tuesday
AMA 2019 Interim Meeting: Peter Hollmann, MD, Delegate; Alyn Adrain, MD, Delegate; Sarah Fessler, MD, Alternate Delegate; RIMS Past Presidents Yul Ejnes, MD, Nitin Damle, MD, and Barry Wall, MD, representing their respective national organizations.
Dr. Nitin Damle gave a major presentation on “Health Impact of Climate Change – Preparing Your Communities and Practices.”
Dr. Peter Hollmann, RI Delegation Chair, gave a major presentation on “Changes to Reporting Evaluation and Management Office Visits: How to Prepare for 2021.”
RIMS Executive Director Newell E. Warde, PhD, received the AMA Medical Executive Lifetime Achievement Award. (see page 76)

November 20, Wednesday
Brown School of Public Health *VILLAGE Project Workshop*, improving prevention efforts and health outcomes for people who use drugs.
Special Legislative Commission to Study the Impact of Insurer Payments on Access to Health Care: David Kroessler, MD

November 21, Thursday
Physician Health Program Governance Committee: Jerry Fingerut, MD, Chair
RI Quality Institute 2019 Health Information Technology (HIT) Survey/Data Sharing
Department of Health Continuity of Care Documentation Workgroup: Mark Braun, MD
Meeting with Warren Alpert medical students regarding advocacy: Michael Migliori, MD, Chair, RIMS Public Laws Committee

November 22, Friday
Meeting with RIMS Opioid Harm Reduction Initiative Workgroup

November 25 Monday
Meeting with RI Action Coalition Community Health Centers Association Annual Meeting

November 26, Tuesday
Conference call with Department of Health regarding Diabetes Prevention Program (DPP) presentation to RI Health Centers Association

Alyn Adrain, MD, Rhode Island Delegate, testified at the AMA Interim meeting in San Diego, California, on November 20.

Nitin S. Damle, MD, former president of the American College of Physicians and a former president of RIMS, spoke on climate change during a session on the topic at the Interim meeting of the American Medical Association held in November in San Diego.
The Rhode Island Medical Society continues to drive forward into the future with the implementation of various new programs. As such, RIMS is expanded its Affinity Program to allow for more of our colleagues in healthcare and related business to work with our membership. RIMS thanks these participants for their support of our membership.

Contact Marc Bialek for more information: 401-331-3207 or mbialek@rimed.org

Neighborhood Health Plan of Rhode Island is a non-profit HMO founded in 1993 in partnership with Rhode Island’s Community Health Centers. Serving over 185,000 members, Neighborhood has doubled in membership, revenue and staff since November 2013. In January 2014, Neighborhood extended its service, benefits and value through the HealthSource RI health insurance exchange, serving 49% the RI exchange market. Neighborhood has been rated by National Committee for Quality Assurance (NCQA) as one of the Top 10 Medicaid health plans in America, every year since ratings began twelve years ago.

RIPCPC is an independent practice association (IPA) of primary care physicians located throughout the state of Rhode Island. The IPA, originally formed in 1994, represent 150 physicians from Family Practice, Internal Medicine and Pediatrics. RIPCPC also has an affiliation with over 200 specialty-care member physicians. Our PCP’s act as primary care providers for over 340,000 patients throughout the state of Rhode Island. The IPA was formed to provide a venue for the smaller independent practices to work together with the ultimate goal of improving quality of care for our patients.
RIMS gratefully acknowledges the practices who participate in our discounted Group Membership Program

Ob-Gyn Associates
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Women’s Medicine Collaborative
A program of The Miriam Hospital
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Researchers identify potential nanotechnology therapy for chondrosarcoma

At Rhode Island Hospital, cancer physician collaborates with molecular researcher to study use of nanotechnology to deliver medicine inside cancer cells

PROVIDENCE – Researchers at Rhode Island Hospital have employed nanotechnology to identify a potentially groundbreaking treatment for chondrosarcoma, an aggressive bone cancer that is disappointingly unresponsive to existing cancer therapies.

In a paper published in the November Molecular Cancer Therapeutics, a journal of the American Association for Cancer Research, the researchers describe a new approach to treating the cancer, which typically afflicts adults and has poor survival rates. Their research, using a mouse model, suggests that deploying nanoparticles might prove to be an innovative and effective way to penetrate tumor cells. These “nanopieces,” as the research team call them, could then deliver nucleic acid therapeutics directly inside the cancer cells and slow tumor growth.

RICHARD TEREK, MD, chief of musculoskeletal oncology at Rhode Island Hospital, an orthopedic oncology surgeon with the Lifespan Cancer Institute, and a professor of orthopedic surgery at the Warren Alpert Medical School of Brown University, has long researched ways to fight chondrosarcoma. For this study, funded by the National Institutes of Health, he teamed up with molecular and nano-medicine researcher QIAN CHEN, PhD, director of the NIH-funded Center of Biomedical Research Excellence in Skeletal Health and Repair at Rhode Island Hospital and a professor of orthopedic research and medical science at Brown’s medical school.

“What is most novel about the work is that we have used a special type of nanoparticle which we call a ‘nanopiece delivery platform,’ developed by my collaborator Dr. Chen, for systemic delivery of anti-microRNA sequences [antagomirs],” said Dr. Terek. “The work has been performed in cell culture and in a mouse model. We have been able to inhibit metastatic pathways and slow down the spread of cancer. This approach is in keeping with current strategies to turn cancer into a chronic disease. An advantage of the nanopiece platform is its safety and ability to penetrate into the tumor matrix and deliver the cargo to the tumor cells.”

Said Dr. Chen, “This has very strong translational value in developing treatment for chondrosarcoma, a lethal disease that currently does not have any effective treatment. Dr. Terek devoted his whole career in developing treatment for this disease, and this may be the most promising potential treatment so far. The nanopieces delivery platform, which we developed at Rhode Island Hospital and Brown University, is able to penetrate the tumor, reduce tumor growth and prolong survival period in the mice model.”

He added, “Based on these promising pre-clinical data, the next step is to develop biologic therapeutics specifically targeting human chondrosarcoma.”

They are seeking collaboration with industry and academia to advance development of the potential chondrosarcoma drug.

This study is supported by NIH funding (CA166089 and GM122732). It was previously published online.

$6.8M in NIH grants will enable Brown researchers, RI to evaluate, expand opioid interventions

PROVIDENCE [BROWN UNIVERSITY] – With opioid drug overdose deaths skyrocketing in recent decades, researchers at Brown University’s School of Public Health are confronting the epidemic in multiple ways. Two new five-year grants from the National Institutes of Health, totaling $6.8 million, will expand those efforts.

The first will launch a partnership with the State of Rhode Island that will result in neighborhood-based intervention strategies across the state’s cities and towns informed by a new predictive forecasting model. The second will enable researchers to evaluate the effectiveness of test strips used to detect fentanyl, a highly potent prescription opioid often used to lace other heroin or cocaine, but hard for drug users to detect.

“Both projects are trying to bring innovative technologies to help solve the overdose crisis,” said BRANDON MARSHALL, an associate professor of epidemiology at Brown and principal investigator for both projects. “That’s the long-term goal – to reduce the risk of overdose and to save lives.”

The first project – titled Preventing Overdose Using Information and Data from the Environment (PROVIDENT) – expands on several years of collaboration among Brown researchers and agencies across Rhode Island.

PROVIDENT will unite Brown scholars with colleagues from NYU School of Medicine [Magdalena Cerdá, associate professor of population health, is co-principal investigator] and the University of California, Berkeley, to develop a machine-learning forecasting model to predict which neighborhoods in Rhode Island are most at risk for outbreaks of opioid overdose.

Next, the Brown team will work with the Rhode Island Department of Health [RIDOH] to test whether the
model’s predictions can help deliver interventions — peer recovery coaching, opioid agonist therapy or naloxone distribution — specifically to neighborhoods that would benefit most. In a randomized trial, half of the state’s 39 cities and towns will be assigned PROVIDENT model predictions that will guide RIDOH’s distribution of resources, while the other half will receive interventions without the targeting of particular neighborhoods.

“We hope that in towns where we develop the predictions, we’ll see a 40% reduction in all overdoses, fatal and nonfatal,” Marshall said. “That’s an ambitious target. But we think we can get there by working collaboratively across the state and with organizations that deliver services.”

DR. NICOLE ALEXANDER-SCOTT, RIDOH director and an associate professor at Brown, said the state/university partnership is illustrative of the collaborative approach that often leads to the most innovative solutions to public health challenges.

“This research partnership between the talented public health professionals throughout RIDOH who are responding to the overdose epidemic and the Brown University School of Public Health, with support from the RIDOH Academic Institute, represents a cutting-edge intervention to get tools and resources related to substance-use disorder into the communities where they are needed most,” Alexander said. “By synchronizing existing statewide overdose surveillance systems with powerful predictive analytics and data forecast tools, we will be leveraging data in powerful new ways to prevent overdoses and safe lives. Saving lives remains our absolute priority in this crisis.”

Marshall, an expert adviser to Rhode Island Gov. Gina Raimondo’s Overdose Prevention and Intervention Task Force, said that if the trial proves successful, the research team’s long-term goal is to ultimately expand the use of the model beyond the Ocean State.

“Rhode Island is a perfect laboratory for this particular project, to see whether we can successfully predict overdoses at a neighborhood level,” Marshall said. “If we can, then the next steps would be disseminating the forecasting tool to other states and evaluating whether it’s useful in other contexts.”

The second NIH grant, which will fund a project titled Rhode Island Prescription and Illicit Drug Study (RAPIDS), will address a very different facet of the opioid crisis — fentanyl. The highly potent synthetic opioid can be deadly even in trace amounts and is a major factor in the rise in fatal overdoses.

“Fentanyl is about 50 to 100 times more powerful than heroin or morphine, and it has cut into the illicit drug supply,” Marshall said. “Essentially, people can’t find pure heroin on the East Coast — nowadays, it’s all adulterated with fentanyl. In the last couple of years, we’ve seen evidence that it may be appearing in other types of illicit drugs as well.”

About five years ago, fentanyl test strips became available. Originally developed for urine drug screens, the rapid-acting strips have increasingly been used to detect the presence of fentanyl in illicit drugs. They work essentially like over-the-counter pregnancy tests. Each single-use strip is dipped into water containing a bit of drug residue, and after a minute, either one or two red lines appear — one line means the liquid contains fentanyl, and two lines means the test did not detect the drug.

The RAPIDS project will consist of a randomized trial that includes individuals who use drugs and are at risk for fentanyl overdoses. The project will test whether informing people about the dangers of fentanyl and teaching them to use the strips reduces risk of overdose. Marshall said he expects the trial to launch in December 2019, and the research team hypothesizes that the test-strips will lower overdose rates.

“The hope is that people at risk for fentanyl overdose will use these strips, like them and take actions that meaningfully reduce their risk,” Marshall said. “I’m optimistic that we will see those reductions.”

The project will expand significantly on the results of a 2018 pilot study led by Marshall. The study provided test strips to 93 young adults who reported injecting opioids or using heroin, cocaine or prescription pills bought off the streets. The preliminary results were promising.

If the expanded trial indicates that strips can decrease overdose rates, Marshall and his colleagues will next evaluate the extent to which they’re disseminated, and how. Participant safety is a top concern, he added.

“There are other adulterants out there that increase the risk of overdose that the strips don’t detect, including some fentanyl analogs,” he said. “So the strips aren’t perfect, and we’re focusing on how to communicate that to participants – to let them know that they should take universal precautions whenever they use an illicit substance, like not using alone and having someone there who could call 911 in the event of an overdose.”

National Institutes of Health funding for PROVIDENT [No. R01DA046620] is expected to total $3.3 million over five years. NIH funding for RAPIDS [No. R01DA047975] is expected to total $3.5 million over five years.
RI MomsPRN, new statewide initiative, addresses maternal depression and related behavioral health needs

To help perinatal-care providers meet the behavioral healthcare needs of pregnant and postpartum women in Rhode Island, the Rhode Island Department of Health (RIDOH) and the Center for Women’s Behavioral Health (CWBH) at Women & Infants Hospital have partnered to create the Rhode Island Maternal Psychiatry Resource Network (RI MomsPRN).

This new statewide program provides real-time psychiatric teleconsultation services for healthcare providers, who can call 401-430-2800, Monday through Friday, 8am to 4pm. The telephone service is staffed by a team of perinatal behavioral health experts from CWBH, including a resource and referral specialist, perinatal psychiatrist, and perinatal psychologist. They are available to help with diagnosis, treatment planning, and medication management for pregnant and postpartum patients.

“We want to make sure that all babies, moms, and families in every ZIP code in Rhode Island have an equal opportunity to be healthy,” said Director of Health NICOLE ALEXANDER-SCOTT, MD, MPH. “The most common medical complication of childbirth is depression. It is crucial that we equip healthcare providers in Rhode Island with the tools and resources they need to support women during this critical phase. Connection is everything.”

An estimated 20% of Rhode Island women experience depression before, during, or after pregnancy. Depression symptoms in the perinatal period can range from a sad mood and loss of interest in activities to feelings of worthlessness, problems in concentrating or making decisions, and changes in eating or sleep. There is also growing evidence that perinatal substance use is increasing. Routine screening for maternal depression and related behavioral health needs throughout the perinatal period is a recommended best practice and results in better outcomes for mother and child.

“Perinatal mood and substance use disorders are highly treatable,” said Director of CWBH MARGARET HOWARD, PhD. “Rhode Island is fortunate to have a robust community of perinatal mental health experts, unique programming at CWBH, and services at the Day Hospital at Women & Infants. However, there is still a need for more specialized providers. RI MomsPRN is designed to build provider capacity in treating mild to moderate cases of perinatal mood complications and to prioritize specialty resources for high-risk women with more complex conditions.”

The RI MomsPRN team can also help identify community-based resources, such as mental health care, recovery services, support groups, and other case-dependent resources for pregnant and postpartum patients.

This program is funded by a five-year grant from the US Health Resources and Services Administration and draws on the successful outcomes of Rhode Island’s PediPRN Program at the Emma Pendleton Bradley Hospital that helps pediatricians manage children’s psychiatric needs.

To learn more about RI MomsPRN phone consultation service for healthcare providers, visit http://www.womenandinfants.org/services/behavioral-health/ri-momsprn.cfm

This project is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $650,000 with 1% financed with non-governmental sources. The contents included in this news release were prepared by RIDOH and the CWBH and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government.

Groundbreaking for Providence VAMC’s Research Service

From left to right, U.S. Sen. Sheldon Whitehouse; U.S. Sen. Jack Reed; Dr. Susan MacKenzie, director of the Providence VA Medical Center; Jessica Ramos-Tinney, project manager from Ironclad Services of Springfield, Mass.; and Erin Clare Sears, associate director for operations at the Providence VAMC, officially broke ground on Nov. 8th on the project to renovate the former Harwood U.S. Army Reserve Center in Providence for use by the Providence VAMC’s Research Service. The $12 million project is scheduled for completion next year.

[PROVIDENCE VA MEDICAL CENTER PHOTO BY WINFIELD DANIELSON]
Dr. Elizabeth Goldberg awarded $1.1M in NIH funding to study fall prevention

*Named recipient of the Paul B. Beeson Career Development Award*

**PROVIDENCE – ELIZABETH GOLDBERG, MD, ScM,** an emergency medicine doctor with Brown Physicians, Inc. and an attending physician at The Miriam and Rhode Island Hospitals, was named the recipient of the Paul B. Beeson Career Development Award. Dr. Goldberg will lead a five-year, $1.1 million research project funded by the National Institute of Health, titled “the Geriatric Acute and Post-Acute Fall Prevention Intervention II” project (GAPcare II).

The Beeson Award is given annually to a handful of physician-researchers across the country who have demonstrated leadership potential in the field of geriatrics research, and are at the early stage of their career.

The project, currently underway, is examining the effectiveness of multi-disciplinary approaches when caring for older adults who have been admitted to the ED after a fall.

The study of falls among older adults should be prioritized, Dr. Goldberg says, given the prevalence of this type of injury. One in three adults over the age of 65 fall each year and many falls are preventable. Statistics indicate that falls remain one of the most common causes of ED visits among older adults, and people who seek emergency care after falls are 30 percent more likely to experience another fall within six months.

One reason older adults return to the ED is because the cause of their fall was never determined, according to Dr. Goldberg. “We are doing a pretty good job at injury assessments, but doctors are at a standstill when it comes to removing obstacles that led to a fall in the first place,” Dr. Goldberg added.

Dr. Goldberg says falls often go unreported since older patients might have cognitive impairments such as dementia. Alternatively, she says some people avoid care due to the stigma associated with falls and old age.

As part of her effort to pinpoint causes of falls and help connect older individuals with specialists that can help them prevent future falls, Dr. Goldberg will be equipping patients with Apple Watches to help detect when a fall occurs. Participants who experienced a fall would be connected with physical therapists and pharmacists as part of an effort to reduce the likelihood of another fall.

A separate clinical study found that this coordination of care is effective in preventing falls. Dr. Goldberg is hopeful that the results of her research project could provide the sufficient evidence needed to roll out similar programs across the country.

The first two years of the project will involve assessing participants’ ability to use an Apple Watch effectively and suggesting revisions to improve the usability of the wrist watch.
RI researchers, policymakers outline new framework for opioid use disorder treatment

PROVIDENCE [BROWN UNIVERSITY] – Every day, more than 100 Americans lose their lives to the opioid crisis, and researchers from across the nation are racing to find solutions. One of the latest strategies—a cascade of care model for the State of Rhode Island—was developed collaboratively by a diverse group of stakeholders, including experts from Brown University, state agency leaders and community advocates.

The research team detailed the model in a paper published in the journal PLOS Medicine in November.

“We hope we’ve created a tool that policymakers and state agencies can use to make data-driven decisions that improve care in our state,” said JESSE YEDINAK, the study’s lead author and a project director at the Centers for Epidemiology and Environmental Health at the Brown University School of Public Health.

To create the model, the team revised an existing framework to define five stages of care for people with opioid use disorder (OUD):

- Stage 0: at risk for OUD
- Stage 1: diagnosed with OUD
- Stage 2: initiated a medication-based treatment plan
- Stage 3: continuously engaged with this treatment plan
- Stage 4: recovery

Next, the team consulted national surveys and statewide insurance claims databases to estimate the number of Rhode Islanders in each stage. These estimates help to identify gaps in care, the researchers said.

For instance, 47,000 Rhode Islanders were estimated to be at risk for OUD in 2016, meaning that they reported using heroin or taking other opioids for non-medical purposes. However, only about 26,000 of those individuals—55 percent—had received an OUD diagnosis.

“This first gap suggests that we need a lot more screening to identify people who have active opioid use disorder or are significantly high risk of overdose,” said BRANDON MARSHALL, an associate professor of epidemiology at Brown and senior author of the paper.

The model also highlights a significant gap between diagnosis and linkage to treatment: Of those estimated 26,000 individuals who had been diagnosed, less than half had initiated medication-based treatment. As a follow-up to this finding, further research is being done to evaluate the factors that make people more likely to seek treatment after an OUD diagnosis.

Stage 3, which contained an estimated 8,300 Rhode Islanders, consisted of individuals who stayed in medication-based treatment for more than 180 days. Stage 4—recovery—contained about 4,200 and was a unique feature of this model.

“In many of the other opioid use disorder care continua, the final stage is remission, which is clinically defined as the absence of opioid-related problems,” Marshall said. “The committee did not feel this was very inspiring or patient-centered, so they strongly encouraged us to define the final stage as recovery—which is more positive and moves beyond the absence of OUD-related problems to look at the person as a whole.”

During the development process, the team was also conscious of the broader impact the model could have. To that end, they tried to make it adaptable for implementation in other states. The paper includes a specific glossary, for example, and the data sources that the model drew from should be available throughout the nation.

Marshall and Yedinak added that they hope to update the model at least once a year, and they have several long-term goals in mind.

One goal is to use the model’s data to aid in the prevention of OUD by reducing the number of people who are classified as at risk. As a longer-term implication, they also hope to start generating population health targets. For example, the United Nations AIDS organization, UNAIDS, set a 90-90-90 target for HIV. By 2020, they aim for 90 percent of all people living with HIV to have received a diagnosis. Of those, 90 percent will receive treatment. And of the 90 percent receiving treatment, 90 percent will have achieved viral suppression.

“We don’t have a target like that for opioid use disorder yet,” Marshall said. “But now that we have the estimates, we can start thinking: What should we reach toward, given our current resources—and given more resources, what would be realistic to achieve?”

In addition to Yedinak and Marshall, WILLIAM C. GOEDEL, MAXWELL S. KRIEGER and JOSIAH D. RICH were other Brown University authors on the study. Additional contributors include KIMBERLY PAULL, REBECCA LEBEAU and CHEYENNE THOMPSON from the RI Executive Office of Health and Human Services, ASHLEY L. BUCHANAN from the University of Rhode Island’s College of Pharmacy, TOM CODERRE from the State of Rhode Island’s Office of the Governor, and Rebecca Boss from the R.I. Department of Behavioral Healthcare, Developmental Disabilities and Hospitals.

The study was funded by the COBRE on Opioids and Overdose, supported by the National Institute of General Medical Sciences of the National Institutes of Health [P20GM125507].
PROVIDENCE – An old industrial site on Corliss Street has gained a new lease on life after its owner and Lifespan collaborated on transforming the underutilized property into a modern healthcare facility. The redevelopment enhances a growing medical hub for Lifespan and The Miriam Hospital in the Mount Hope section of Providence.

The new building at 180 Corliss St. is about to become the Lifespan Ambulatory Care Center. It will be home to The Men’s Health Center and The Infectious Diseases and Immunology Center – both relocated from The Miriam – as well as a Lifespan Pharmacy and a Lifespan Laboratory. Another key tenant is Lifespan-affiliated Anchor Medical Associates. The building will be leased to The Miriam Hospital.

During a November 18 ribbon-cutting ceremony, the medical center was dedicated to the late EVERETT A. AMARAL, who as president of Amaral Revite, oversaw the project until his death in 2018. His wife, SHERYL AMARAL, who assumed the presidency of the company and saw the project through to completion, participated in the ribbon-cutting and called attention to a plaque dedicating the building in her husband’s memory.

The three-story, 57,000-square-foot building was built on the former site of Clifford Metal and was most recently being used for vehicle storage. Virtually all the original structure had to be razed during the 13-month construction project, which employed close to 150. Several hundred will be employed at the facility when it opens.

Services at 180 Corliss Street will include:

- **The Men’s Health Center** Formerly located in the Fain Building on Summit Avenue, the center offers a variety of specialized services related to male sexual health and experts in family practice, internal medicine, urology, psychology and physical therapy.

- **The Infectious Diseases and Immunology Center** Formerly located on North Main Street, the center includes clinics for HIV/AIDS screening and treatment, viral hepatitis, Lyme and tick-borne diseases, and other communicable diseases.

- **Anchor Medical Associates** Formerly located 1 Hoppin St., Providence, this relocated Anchor practice offers primary care services provided by a staff of six physicians and three physician assistants, and a support staff of about 20.

- **Lifespan Laboratory** These conveniently located labs perform a variety of tests for patients and deliver faster results thanks to a centralized, automated system.

- **Lifespan Pharmacy** This will be the third Lifespan Pharmacy, adding to existing locations at the The Miriam and Rhode Island hospitals. It will offer a full range of services, including free home delivery, courtesy refills, and both scheduled and walk-in vaccinations.
Providence – University Surgical Associates has welcomed Peter C.W. Kim, MD, PhD, to its team of physicians in the Pediatric Surgery Division. Dr. Kim, a pediatric general and thoracic surgeon, will support the mission of University Surgical Associates to enhance patient care using the latest technological advancements.

“Dr. Kim has demonstrated an exceptional commitment to advancing research through his work with medical startups. His vision for intelligent surgical devices in procedures reflects his devotion to improving the quality of care for all patients,” said William Cioffi, MD, president of University Surgical Associates.

Dr. Kim has clinical interests in surgical airway reconstructions, minimally invasive surgery, and vascular reconstructive surgery for conditions related to the liver and gallbladder.

“Surgeons are increasingly turning to technology to deliver better patient outcomes. As the surgical field looks to implement new and innovative techniques, I am excited to impart key research findings that could help support the mission of University Surgical Associates,” said Dr. Kim.

The founding lead for two medical-based startups, Dr. Kim has focused his entrepreneurial efforts in digital health technology for monitoring and decision support, and an intelligent surgical device to democratize surgery. He is also the co-lead for the Centre for Image-Guided Innovation and Therapeutic Intervention (CIGITI) at SickKids Hospital in Toronto.

At Children’s National Hospital in Washington, D.C., Dr. Kim was also the founding lead for the Sheikh Zayed Institute for Pediatric Surgical Innovation, among his many other achievements.

Dr. Kim received his medical degree from McGill University with the distinction of Master of Surgery. He completed his surgical residency training, and pediatric surgery fellowship at the University of Toronto.

Lindsay Tse, DO, joins Center for Surgical Weight Loss at CNE

Kent Hospital recently announced the arrival of Lindsay Tse, DO, at The Center for Surgical Weight Loss at Care New England.

Dr. Tse completed her general surgery training at Hackensack University Medical Center in Hackensack, New Jersey, where she served as the chief academic and administrative resident during her final year. She then completed her fellowship training in minimally invasive surgery, bariatric surgery, and flexible endoscopy at Houston Methodist Hospital in Houston, Texas.

She has performed many complex laparoscopic intra-abdominal surgeries including advanced foregut procedures, fundoplications, hiatal hernia repairs, revisional bariatric surgery, roux en Y gastric bypass, sleeve gastrectomy, common bile duct explorations, and esophageal surgeries. She received extensive training in advanced flexible endoscopy including stent placement, dilations, endoscopic mucosal resections, and polypectomies. She also performs many minimally invasive general surgery procedures including cholecystectomy, appendectomy, hernia repair, and colon resections.
South County Health has been recognized with the 2019 Gold Level Health Impact Award by AHA

South County Health has been recognized with the 2019 Gold Level Health Impact Award by the American Heart Association for creating a culture of health in the workplace. South County Health will be recognized along with other national Gold and Silver Health Impact Award recipients in the November issue of Forbes Magazine.

The Workplace Health Achievement Index was created by the American Heart Association to evaluate the overall quality and comprehensiveness of workplace health programs.

Studies show that worksites with a culture of health with evidence-based policies and programs and senior leadership support are more likely to have engaged employees and a healthier, more productive workforce.

A unique feature of the Index is that it calculates an average heart health score for employees of participating companies that securely submit aggregate health data. Companies receive benchmarking reports, which allow them to identify potential areas of improvement so that they can advance their annual performance and recognition.

The American Heart Association’s Workplace Health Achievement Index measures the extent to which the company has implemented workplace health best practices. Companies recognized at the Gold level have achieved an Index score of 175–217 out of a maximum 217 points.

The Index is a web-based portal that fuses health content, personal health data and consumer engagement opportunities that evaluate the overall quality and comprehensiveness of workplace health programs.

“The American Heart Association has defined best practices for employers to use to build a culture of health for their employees in the workplace,” said AARON ROBINSON, President and CEO of South County Health. “South County Health has a long-standing commitment to employee health and wellness, which is reflected by this 2019 Gold Level Health Impact Award.”

The Index also integrates Life’s Simple 7®, the American Heart Association’s definition of ideal cardiovascular health based on seven risk factors, into the scoring process. Life’s Simple 7® includes smoking status, physical activity, weight, diet, blood glucose, cholesterol and blood pressure. South County Health has a number of programs and initiatives to improve employee health, many of which abide by Life’s Simple 7. Among those are a tobacco free policy on campus, the availability of healthier food and beverage choices, free use of the hospital gym, yoga and other group exercise classes, smoking cessation programs, and health counseling for blood pressure, cholesterol, and other important indicators.

Women & Infants raises more than $500,000 at community event; proceeds will support Birth Center

Women & Infants Hospital’s “Bright Night for Little Stars,” held on October 19, raised over $514,000 and was attended by more than 300 community leaders, grateful patients, friends, and colleagues. Proceeds of the event will support the hospital’s new Birth Center.

The event, held at the Rhode Island Convention Center, was emceed by NBC 10 News Sunrise anchor, Mario Hilario and co-chaired by Ann Marie and Steve Johnson and Virginia and Jim Roberts.

“I am truly humbled by the generosity and support shown by so many for Women & Infants Hospital and our new Birth Center. I am also grateful to the many volunteers and committee members who worked so hard to make this year’s event a great success,” said MATT QUIN, interim COO.

For more than 130 years, Women & Infants’ mission has been to provide exceptional health care to the families in our region. New technologies, personalized delivery options, and more patients with significant chronic illness have led to the need for an innovative model of care and a new Birth Center.

Additionally, CYNTHIA B. PATTERSON received the inaugural Cynthia B. Patterson Lifetime Service Award for her 50 years of service to Women & Infants Hospital.

CNE Board Chair CHARLIE REPUCCI recognized Patterson as an ardent champion of Women & Infants and women’s health. She started as a volunteer at Providence Lying-In Hospital and rose to be the first woman chair of the hospital’s board of trustees. She has served on the CNE Board since 1996. For her dedication, generosity, and wise counsel the hospital has established this new award bearing her name.
Recognition

Newell E. Warde, PhD, honored with AMA Medical Executive Lifetime Achievement Award

SAN DIEGO – The American Medical Association (AMA) honored NEWELL E. WARDE, PhD, executive director of the Rhode Island Medical Society (RIMS), with the Medical Executive Lifetime Achievement Award. The award honors a medical association executive who has contributed substantially to the goals and ideals of the medical profession.

“Over the past 34 years, Newell E. Warde has provided continuity, experience, and a steady hand during challenge, crossroads, and legislative battle waged by the Rhode Island Medical Society,” said AMA President Patrice A. Harris, MD, MA. “A talented writer, advocate, and jack-of-all-trades, Warde has led RIMS during a period of rapid change in health care – and done so with a clear and fair mind, as well as bold focus on the task at hand and the future.”

Beyond serving members of the RIMS, Warde ensured that the organization adopted community outreach strategies. He launched and oversaw the scholarship fund of the Providence Medical Association, which helps local high school students attend college. He used the society’s grant money to create a $1 million loan repayment program for primary care physicians and promoted public health awareness among local children through bicycle helmet campaigns and anti-smoking initiatives.

Warde is a senior member of a group of New England medical society executives and served two terms as chair of the AMA Litigation Center Board. An historian by training, Warde showed interest in the history of the Rhode Island Medical Society, one of the oldest state medical societies in the country, by maintaining the society’s original, historic building.

The AMA presented the award to Warde during the 2019 AMA Interim Meeting.

Arun K. Singh, MD, receives AHA Lifetime Achievement Award

The America Heart Association’s 2019 Lifetime Achievement Award was awarded to DR. ARUN K. SINGH, Clinical Professor Emeritus of Surgery at the Alpert Medical School of Brown University, “for his incredible contributions throughout his career towards cardiovascular care.”

The award was presented to Dr. Singh at the Southern New England Heart and Stroke Ball held in September.

He is the author of “Your Heart, My Hands,” which was awarded the Gold Medal in Inspirational Memoirs by Living Now Book Awards for 2019.

ROBERT M. DOWBEN, MD, passed away peacefully on November 11 at age 92 surrounded by his loving family.

Dr. Dowben had a distinguished career as a physician, scientist and academician. He earned degrees from AB, Haverford College, 1946; MS, (Biochemistry) in 1947, and MD, University of Chicago, 1949. As a professor, he had faculty appointments at the University of Pennsylvania, Northwestern University, a joint professorship between The Massachusetts Institute of Technology and Harvard Medical School, Brown University, University of Bergen Norway, University of Texas Southwestern Medical Center Dallas, and most recently again at Brown University as an emeritus Professor.

He was the author of more than 150 scientific publications and four books regarding cell and muscle physiology. He received many accolades for his contributions to medicine and science including the University of Chicago Alumni Award for Exceptional Service, the National Foundation for Neuromuscular Disease Award, and served as a representative on the Baylor Research Foundation. He was named on eight patents and was a prolific writer on many topics beyond science and medicine well into his 80s.

Dr. Dowben served as a Captain in the United States Air Force at the Air Force Medical College shortly after the Korean War. While serving, he conducted research at Los Alamos National Laboratory during the 1950s.

He is survived by wife, Carla Dowben, of Providence; children Peter Dowben, PhD, Jonathan Dowben, MD, and Susan Day, MS, and six grandchildren. A memorial service is being planned for January. In lieu of flowers, contributions in his memory may be directed to the Rhode Island Community Food Bank or Crossroads.

HAROLD MILTON HORWITZ, MD, 76, died at home on October 28.

He is survived by his wife, Eileen Shaw Horwitz, and his children, Joshua Mark Horwitz and his wife, Carmel, of Boulder, CO; Jill Horwitz Cohen and her husband, Andrew, of Berkeley, CA; two grandsons, Jasper and Eli, and a brother, Bruce and his wife, Lois, of Newton, MA. He was the son of Dr. Manuel and Minette Horwitz.

Dr. Horwitz was a graduate of Classical High School, Union College, and Tufts Medical School. He began his medical training as an intern and resident at Rhode Island Hospital and then continued his residency at University Hospital in Ann Arbor, Michigan.

He then spent two years in the United States Army Medical Corps at Fort Bragg, NC, after which he completed a fellowship at Duke University Medical Center.

Dr. Horwitz was one of the first rheumatologists in Rhode Island and went on to develop a highly respected private practice in his community. He was a Clinical Associate Professor of Medicine at the Alpert Medical School of Brown University, and was the Chief of Rheumatology and an attending physician at both the Miriam and Pawtucket Memorial Hospitals. Dr. Horwitz was also an attending physician at the Rhode Island Hospital and a member of the consulting staff at Kent County Hospital.

During his career, he was the President of the RI Chapter of the Arthritis Foundation and was the first recipient of its Hall of Fame Award; he was also the President of the RI Society of Internal Medicine. Dr. Horwitz was on the board of the Lupus Society and Temple Beth El.

Dr. Horwitz, an accomplished cyclist, skier and sailor, who loved to travel the world, will be remembered as a physician devoted to his wife, family and patients. He will be missed by all who knew him.
Dr. H.P. Lovewell: Traversing the woods, bogs and backwaters in search of *Materia Medica*

MARY KORR
RIMJ MANAGING EDITOR

**DR. HENRY P. LOVEWELL** (1866–1934) shared his studies of *Materia Medica* – the collected knowledge of the therapeutic properties of plants and other substances, in the May 1922 issue of the *Rhode Island Medical Journal* (RIMJ). At that time RIMJ was but a sprout, just five years into publication.

“We have found our State a very satisfactory hunting ground for the botanical collector,” wrote Dr. Lovewell, a graduate of Brown (AB, 1889) and Harvard (MD, 1894). “It has a varied topography and abounds in bogs, swamps and marshes, running streams and quiet ponds. It possesses a flora that is unique in many respects.”

Dr. Lovewell’s article is drawn from a lecture he gave several months prior at an exhibit of the Rhode Island Medical Society’s botanical specimens’ collection. He describes some of the more than 300 medicinal plants he collected in the Ocean State and neighboring Massachusetts, and refers to medical botanists such as **CHARLES F. MILLSPAUGH, MD**, who published a definitive guide on medicinal plants in 1887 and whose illustrations are reproduced on this page. In the Prospectus of his guide, “American Medicinal Plants,” Dr. Millspaugh described how he illustrated the plants. “The author has in every case drawn and colored the plants represented in this work by his own hand from the specimens as they stood in the soil; making mathematically accurate drawings, and avoiding the misrepresentations of wilted individuals, or too highly colored fancy pictures,” he wrote. (Figure 1)

The following are excerpts from Dr. Lovewell’s article with some accompanying illustrations by Dr. Millspaugh:

**Apocynum cannabinum** – Dogbane
It was in common use among the Sioux Indians and the Cheyennes as a cure for the bite of the rattlesnake. The dose of the powdered root given internally was two pinches for a child and three pinches for an adult.

**Podophyllum peltatum** – Mandrake or May-Apple (Figure 2)
When your walks lead in the direction of deserted farmhouses, if you explore the region of the old apple orchard, you may find a plant not native of the State, but set out years ago for its medical value; we allude to the Mandrake or *Podophyllum*. It has very large leaves and a single white flower about two inches in diameter upon a short, curved peduncle, blossoms in May and ripens its fruit in August and September. Parts used: the rhizome and rootlets. Over one hundred years ago the Shakers of Lebanon, NY, extracted an active principle which was very much sought by physicians. Mandrake was used by the Eclectics as a substitute for mercury in the treatment of syphilis and has even been dominated “Vegetable calomel.”

**Figure 1. Aesculus Hippocastanum** – Horse Chestnut
Illustration of medium-size leaf with flower, stamen, nut.
Sources: American Medicinal Plants, pub. 1887, Charles F. Millspaugh, MD

**Figure 2. Podophyllum peltatum** – Mandrake, May-Apple
Sources: American Medicinal Plants, pub. 1887, Charles F. Millspaugh, MD
Cornaceae – Flowering Dogwoods

In our tramps in early spring the Cornels or Flowering Dogwoods are of much interest, and the more so when we learn they possess an active principle cornine an alkaloid having properties similar to quinine and much used by the Southerners during the Civil War as a remedy in malaria.

Geranium maculatum – Cranesbill

...Schoepf recommended this as a remedy in the second stages of dysentery and cholera infantum. This has justly been considered as one of our best indigenous astringents. The rhizome has a considerable percentage of both tannic and gallic gases. Geranium root is official in the U.S.P. [United States Pharmacopoeia] in the form of the fluid extract.

Veratrum viride – American Hellebore

Found abundant in swamps and low grounds, associated with skunk-cabbage. Parts used: the rhizome and rootlets. Official US Pharmacopoeia, classed as a cardiac depressant; it is probably less likely to cause cardiac depression than is aconite, but is less efficient in the doses generally used.

Apocynum cannabinum – Dogbane

...It was in common use among the Sioux Indians of Dakota and Montana and the Cheyennes in Indian Territory. It was one of their favorite remedies as a cure for the bite of the rattlesnake. The root was used freshly grated or dried. The dose of the powdered root given internally was two pinches for a child and three pinches for an adult.

Advice to botanical sleuths

For those interested in taking up this pursuit of viewing and collecting medicinal plants of yore, Dr. Lovewell’s advice from the article is applicable today as it was in 1922:

“In pursuit of the medicinal plants of this State, it is first necessary to find if the species sought are native to this region. We have found Bennett’s Flora of Rhode Island of decided help. Provide yourself with topographical maps of the region you are to visit. A camera should add interest to these trips, but do not expect satisfactory pictures of plants taken when the wind is rated at sixty miles per hour.”

Today, the following resources at the University of Rhode Island’s College of Pharmacy medicinal gardens, and the Brown University Herbarium are a wealth of information which so intrigued Drs. Lovewell, Millspaugh and many others referred to in the RIMJ article:

https://web.uri.edu/youngken-garden/
https://www.brown.edu/research/projects/herbarium/links-and-resources