VISION
At the forefront of discovery and innovation, improving lives of people affected by critical illness.

MISSION
We advance knowledge, education, and models of care for people affected by critical illness.
In 1997, Dr. E. Wesley Ely came to Vanderbilt and began working with Drs. Robert Dittus and Gordon Bernard to advance strategies to reduce time ICU patients spent on mechanical ventilation. They suggested that a type of brain dysfunction called delirium was interfering with ventilator liberation and ICU survival. This notion was not initially well-received by the critical care community as there were no methods to measure delirium in the ICU, making their case difficult to prove. Dr. Ely recruited an advanced practice nurse, Brenda Pun, and together they developed an instrument, the Confusion Assessment Method for the ICU (CAM-ICU), and determined it had high validity and reliability. They used the CAM-ICU to prove that ICU delirium had a substantial effect on patient outcomes, including mortality, length of stay, and cost of care.

AN EXPANDED TEAM

In order to better understand the phenomenon of delirium in the critically ill, and develop methods for its prevention and management, the research team expanded to include Drs. Jim Jackson, Pratik Pandharipande, and Tim Girard. Over the years, the team grew to include collaborators in nursing, neuropsychology, general internal medicine, critical care medicine, anesthesiology, pulmonary, neurology, transplant immunology, surgery, psychiatry, epidemiology, and engineering. Also leveraged, was the leadership of two PhD Biostatisticians, Drs. Ayumi Shintani and Rameela (Chandrasekhar) Raman.

THE GOLDEN AGE

The team conducted many studies to uncover risk factors and determine opportunities for delirium prevention. They developed the hypothesis that reducing exposure time and the dose of certain medications like benzodiazepines, which were nearly universally used for patients on ventilators for decades, would reduce time on life support, incidence of ICU delirium, and improve patient outcomes. They tested this hypothesis in a randomized, controlled clinical trial that showed one of the largest improvements in survival of any ICU study to-date.

This protocol has evolved into the ABCDEF Bundle, which has reduced the incidence of delirium, mortality, length of stay in the ICU and hospital, nursing home transfers, and cost of care. The ABCDEF Bundle is being adopted by ICUs world-wide as the current best practice of care.
A LANDMARK DISCOVERY

During follow-up visits with ICU survivors, Dr. Ely found they were complaining of nightmares, not being able to perform work duties, and were unable to find their car in a parking lot or balance their checkbook. Our team surmised there must be something happening to the brain during ICU stays that leaves people suffering from dementia and executive dysfunction. In a landmark study, the team demonstrated that this was indeed the case. One year after their ICU stay, nearly a quarter of the ICU survivors studied had a newly acquired dementia similar to people with mild to moderate Alzheimer's dementia.

WHERE ARE WE NOW?

In 2019, the Vanderbilt Institute for Medicine and Public Health, led by Dr. Dittus, formally established the Critical Illness, Brain Dysfunction, and Survivorship (CIBS) Center, led by Drs. Ely and Pandharipande. Over the last 20+ years, research scientists and clinician investigators from CIBS, formerly the ICU Delirium and Cognitive Impairment Study Group, have received approximately $50 million in federal funding, have led studies and quality improvement investigations enrolling tens of thousands of patients, published nearly 500 peer-reviewed papers, trained hundreds of students, residents, fellows, and visiting scholars, and had their work translated into over 30. The CIBS Center is widely recognized as an epicenter for the discovery, evaluation, and dissemination of knowledge related to acute and long-term brain dysfunction during and after critical illness.

WHERE ARE WE GOING?

The global culture of medicine must change to accommodate all that we are learning, and the CIBS Center is leading the way in this challenging yet steady path. The team is currently embarking on new studies to determine the exact type of dementia these ICU survivors are suffering, with the ultimate goal of developing prevention programs. Our reach includes academic medical centers in the world's greatest cities, as well as resource-limited hospitals and clinics in sub-Saharan Africa, Latin America, and Asia. Inside the pages of this report, we offer you a glimpse of this journey...
Dear ICU Survivors, Families, Research Colleagues, and CIBS Center Benefactors,

We recently completed our inaugural year as the CIBS Center! Our team had tons of fun generating this “first ever” annual report for you. Starting in 1997 with just one physician and one nurse, it is humbling to consider the path of discovery, publications, and tens of millions of dollars in funding that have led to our burgeoning inter-professional program encompassing over 90 researchers from a dozen departments across Vanderbilt and the VA campuses in Nashville. Consider further the network of our research colleagues at multiple other institutions across the U.S. and internationally, and it is quickly apparent that the CIBS Center has a bright future.

Here we will highlight three important new developments that happened in 2019:

• First, we received the largest grant we’ve ever obtained, over $17,000,000, for our upcoming BRAIN-ICU-2 study (we call it “BRAIN-2”), which we are conducting with Rush University’s Alzheimer’s Disease Research Center Primary Investigator (PI), David Bennett, MD, and Vanderbilt’s Memory and Alzheimer’s Center PI, Angela Jefferson, PhD. Building on our BRAIN-ICU-1 study, published in the New England Journal of Medicine (NEJM) in 2013, BRAIN-2 will allow us to better understand the type of dementia that ICU survivors develop.

• Second, we have added palliative care research as a major component of our Center’s portfolio. Our palliative care approach focuses on providing relief from symptoms, including pain, and physical and mental stress at any stage of illness, including toward the end of life. The priority of care is quality of life, for both the person and their family, which is the underpinning of “Survivorship” in CIBS. Ricky Shinall, MD, PhD is the PI for our ongoing SCOPE investigation, which is a randomized trial to determine better ways of reducing suffering for surgical oncology patients, even when a surgical cure may be possible for some.

• Third, we completed our MIND-USA study (published in NEJM), conducted at over 20 centers around the country. This study uproots over 40 years of practice of prescribing antipsychotics as the main medical treatment for delirium. That, along with our ABCDEF Bundle data on over 25,000 patients, helped us to determine that non-pharmacological care choices are much safer and more successful for management of ICU Delirium. The Center is also pleased to announce the completion of the MENDS2 study, a randomized controlled trial to determine best sedative regimens in patients with severe sepsis. Findings of these studies are likely to shape sedation practices for years to come.

Thank you for being such an important part of our mission to make lives better for people who suffer from critical illness. Our goal is nothing short of improving the arc of medical history. As co-directors, we want to “invite you in” to visit all the different components of the CIBS Center. As you review this 2019 Annual Report, please do so with an open mind to see how we can get better and grow stronger moving forward. Send us your thoughts, as we want and need your input and direction.
As we have grown as a Center, we have developed six research cores structured around our expanded executive team.

1. Clinical Core
   A team of experienced research nurses and research assistants responsible for coordinating day-to-day conduct of our inpatient studies. Responsibilities include optimizing study protocols for implementation, maximizing patient recruitment, delivering interventions, collecting study-related data, maintaining patient safety, ensuring data quality through active monitoring, and educating hospital personnel.

2. Long-Term Outcomes Core
   Comprised of six full-time neuropsychological coordinators and a variety of students and trainees. Our long-term outcomes core is a key resource for the CIBS Center in that it develops, implements, and oversees aspects of research at the CIBS Center pertaining to cognitive, physical, and psychological functioning after discharge.

3. Biostatistics Core
   Comprised of masters and PhD level biostatisticians who closely collaborate with CIBS Center PIs to ensure optimal study design and analysis, interpretation of results, and detailed study reporting.

4. Biomarkers Core
   Provides the expertise to appropriately collect, store, catalog, and analyze biospecimens integral to our understanding of the mechanisms of acute brain dysfunction, dementia, and functional decline after critical illness.

5. Imaging Core
   Comprised of world-renowned investigators with expertise in longitudinal neuroimaging studies of blood-brain barrier injury, cerebral blood flow, cerebral atrophy, and white matter functional connectivity. This team has developed robust, yet practical, imaging protocols to evaluate critically ill patients.

6. Animal Model Core
   A team focused on using animal models to study delirium and acute brain injury as well as long-term cognitive function using outcome measures that have face validity to allow pre-clinical testing of therapeutic interventions for delirium.

2019 ACCOMPLISHMENTS IN PATIENT ENGAGEMENT

The clinical core and long-term outcomes core are essential to our day-to-day study enrollment and complete participant experience.

Clinical Core
- Enrolled 182 patients in 2019 across all active studies. This is equal to approximately one patient enrolled every two days!
- Partnered with the Center for Emergency Care Research and Innovation (CERI) to assist with study enrollment and specimen processing to accommodate the growing needs of the Center.
- Completed inpatient enrollment of the MENDS2 study on December 28, 2018.
- Coordinated the co-enrollment of patients into seven ancillary studies that are embedded in the large cohort trials.
- Expanded one of those studies (MOSAIC) to a second site: The Ohio State University Wexner Medical Center.

Long-Term Outcomes Core
- Expanded the team to six full-time research partners and four student interns to cover 12 different studies involving more than 50 different institutions.
- Partnered with other departments and institutions to investigate long-term effects of conditions such as cancer, lupus, chronic fatigue, surgery, and sepsis.
- Continued our strong partnership with Vanderbilt University’s Peabody College and started a new internship program with Lipscomb University’s graduate school.
- Implemented video conferencing to facilitate assessments of patients at institutions without trained neuropsychologists.
- Hosted a weekly support group for ICU survivors, family members, and loved ones, and introduced video conferencing technology to expand accessibility to patients across the U.S.
The Delirium Boot Camp was founded in 2013 through a career development award to Sharon Inouye to establish the Center for Excellence for Delirium in Aging: Research, Training and Educational Enhancement (CEDARTREE). The Delirium Boot Camp has evolved to be a major activity of the NIDUS Mentorship and Career Development Task Force, under the leadership of Donna Fick, PhD, MSN, and Wes Ely, MD, MPH. There are now over 70 alumni of the Delirium Boot Camp program, which has expanded to include international participants as well as participants from across the United States and Canada. The Boot Camp includes didactic sessions on a variety of delirium-specific research topics ranging from biomarkers to qualitative research, as well as a mock grant review, CAM and CAM-ICU training and more.
GLOBAL IMPACT

In 2019, the CIBS Center was represented at meetings across 43 cities and countries.

ACADEMIC TEACHING AND NATIONAL AND INTERNATIONAL MEETINGS

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TRANSLATIONS OF CAM-ICU MATERIALS

CAM-ICU materials have been translated into 31 languages.

- Arabic
- Chinese
- Czech
- Danish
- Dutch
- Egyptian
- English
- French
- German
- Greek
- Hebrew
- Hindi India
- Italian
- Japanese
- Korean
- Marathi India
- Norwegian
- Persian
- Polish
- Portuguese
- Portuguese Brazil
- Romanian
- Serbian
- Spanish
- Swedish
- Thai
- Tibetan
- Turkish
- Zambian
- (Bemba dialect and Nyanja dialect)
- Zulu

CIBS MULTI-CENTER RESEARCH NETWORK

CIBS Center has 37 sites in their research network.

- University of California
- San Francisco, CA
- Denver Health Medical Center
- Denver, CO
- Yale University School of Medicine
- New Haven, CT
- University of Miami
- Miami, FL
- Emory University
- Atlanta, GA
- University of Iowa Carver College of Medicine
- Iowa City, IA
- Rush University
- Chicago, IL
- Northwestern University
- Evanston, IL
- Indiana University and Methodist Hospital
- Indianapolis, IN
- Baton Rouge General Medical Center
- Baton Rouge, LA
- Our Lady of the Lake Regional Medical Center
- Baton Rouge, LA
- Brigham and Women’s Hospitals
- Boston, MA
- Massachusetts General Hospital
- Boston, MA
- Tufts Medical Center
- Boston, MA
- Baystate Medical Center
- Springfield, MA
- University of Maryland Medical Center
- Baltimore, MD
- University of Michigan Health Systems
- Ann Arbor, MI
- Jack D. Weiler Hospital
- Bronx, NY
- Montefiore Medical Center
- Bronx, NY
- Mission Hospital
- Asheville, NC
- University of North Carolina at Chapel Hill
- Chapel Hill, NC
- Moses Cone Memorial Hospital
- Greensboro, NC
- Wesley Long Hospital
- Greensboro, NC
- Wake Forest University Baptist Medical Center
- Winston-Salem, NC
- The Ohio State University Wexner Medical Center
- Columbus, OH
- University of Pennsylvania Medical Center
- Philadelphia, PA
- University of Pittsburgh
- Pittsburgh, PA
- Vanderbilt University Medical Center
- Nashville, TN
- Baylor Healthcare System
- Houston, TX
- Harris Fort Worth
- Fort Worth, TX
- Ben Taub Hospital
- Houston, TX
- Houston Methodist Hospital
- Houston, TX
- South Texas Veterans Health Care System
- San Antonio, TX
- University of Texas Health Science Center
- San Antonio, TX
- Harborview Medical Center
- Seattle, WA
- University of Wisconsin Madison, WI
- University of Wisconsin Madison, WI
- University of Gothenburg
- Gothenburg, Sweden
THE “S” IN CIBS: SURVIVORSHIP

THE ICU RECOVERY CENTER AT VANDERBILT

The ICU Recovery Center at Vanderbilt is a unique clinical resource and a “living laboratory" through which clinicians utilize insights generated by CIBS Center research. Led by CIBS Center members Drs. Carla Sevin and Jim Jackson, seeing an average of 100 patients per year, the ICU Recovery Center provides evaluation and treatment to ICU survivors from all over North America. The ICU Recovery Center was the recipient of the Society of Critical Care Medicine’s (SCCM) first “Innovation Award.”

RICKEY SHINALL, MD, PhD

I Am…
Grateful for my family
Grateful for my friends
Grateful to be alive
Grateful for this Group

I am alive because of this Group
Therefore, I am thankful for this Group

A POEM BY TOMMY RODEN
ICU SUPPORT GROUP MEMBER

2019 PALLIATIVE CARE RESEARCH HIGHLIGHTS

• The SCOPE Trial, studying the effect of palliative care for patients having surgery for cancer, reached the half-way point in its enrollment.
• Aimee Hoskins was recognized as a top site coordinator for the multi-site REACH-PC trial of palliative care in lung cancer patients.
• Drs. Shinall and Ely along with colleagues published the results of the COMPASS Trial that showed palliative care for patients with liver disease helped them stay out of the hospital longer.
• Dr. Shinall was selected for an NIH Rising Star Award for his innovative palliative care research.

PALLIATIVE CARE

At its heart, the CIBS Center has always been about finding ways to relieve suffering for ICU patients. As our team and expertise have grown, we have continuously looked for new ways to reduce suffering both in the ICU and out of it. As part of the CIBS Center’s focus on Survivorship, we have launched a research program in palliative care.

What is Palliative Care?

Palliative care is specialized medical care that focuses on relieving the suffering caused by serious illness. Palliative care doctors work to help relieve physical symptoms like pain, and also help patients navigate the psychological, emotional, and spiritual strain brought on by life-threatening illness.

Our Palliative Care Research

Traditionally, palliative care specialists have been called near the end-of-life, but we are finding that involving these specialists much earlier in the course of serious illness improves quality of life and survival. The CIBS Center is on the cutting edge of this research as we help discover who benefits from palliative care specialists and when. Our team of palliative care researchers, led by Ricky Shinall, MD, PhD, and Aimee Hoskins, RN, BSN, participates in multiple federally-funded studies to discover how palliative care can improve the lives of patients with a range of serious diseases.
**MOSAIC**  
*Measuring Outcomes of Activity in Intensive Care*

An observational study of the association between physical activity in the ICU vs. cognitive and functional outcomes in ICU survivors.

**INSIGHT**  
*The Illuminating Neuropsychological Dysfunction and Systemic Inflammatory Mechanisms Gleaned After Hospitalization in Trauma-ICU*

A comprehensive, long-term study of cognitive impairment study after traumatic injury and critical illness.

**INMO EEG**  
*INSIGHT, MOSAIC*

A nested pilot study investigating EEG (brain activity monitoring) as a marker of brain injury in critically ill patients on a ventilator.

**DECAT**  
*Delirium and Catatonia Cohort Investigation*

An investigational cohort study of delirium and catatonia in critically ill patients.

**SCOPE**  
*Surgery for Cancer with Option of Palliative Care Expert*

A randomized controlled trial to evaluate the effect of specialist palliative care on quality of life for patients undergoing major abdominal operations for cancer.

**MIND-USA**  
*Modifying the Impact of ICU-Associated Neuropsychological Dysfunction*

The only Phase III study in critically ill patients in which we determined that antipsychotic medications were ineffective for treating delirium. This leads us to focus attention on non-pharmacological treatments like the ABCDEF Bundle.

**BRAIN-ICU-2**  
*Bringing to Light the Risk Factors And Incidence of Neuropsychological Dysfunction (Dementia) in ICU Survivors, 2nd Study*

Designed to understand the link between delirium and dementia after critical illness, this study will explain this unfortunate and life-changing brain damage in ICU survivors, and will pave the way for preventive programs, strategic rehabilitation, and targeted future interventions.

**CADUCeuS**  
*Cholinesterase Activity and Delirium During Critical Illness Study*

The first of its kind, this study will determine the validity of circulating AChE and BuChE activities as biomarkers of delirium during critical illness and subsequent cognitive impairment after discharge.

**APICS**  
*Addressing Post Intensive Care Syndrome*

A study assessing the relationship between early unmet needs after hospital discharge and subsequent clinical outcomes among survivors of acute respiratory failure. The investigators hypothesize that early unmet needs are associated with poor outcomes at three months.

**MENDS2**  
*Maximizing the Efficacy of Sedation and Reducing Neurological Dysfunction and Mortality in Septic Patients with Acute Respiratory Failure 2nd Study*

A randomized controlled trial to determine the best sedative medication to reduce delirium and improve survival and long-term brain function in ventilated, septic patients.

**RETURN III**  
*Returning to Everyday Tasks Utilizing Rehabilitation Networks-III*

A pilot randomized clinical trial assessing whether post-ICU long-term cognitive impairment (ICU-LTCI) can be improved by computerized cognitive rehabilitation. 160 VA patients with ICU-LTCI will be evaluated. This research has high potential to influence rehabilitation strategies for veteran and civilian ICU survivors.
Mr. D AND THE ICU

Mr. D was an ICU patient who was on life support (a ventilator and dialysis) for many days. Every day he was there, we made sure to prioritize his pain control and his brain function. Working diligently with a safety bundle called the ABCDEFS, we were able to help him think more clearly. In this picture, you see him living out his final wishes. Dr. Ely asked him, “Mr. D, what matters most to you?” His answer was two things: “My wife Wanda, and I’d really like a beer.” His wife, whose name is tattooed on his hand, spent the entire day at his bedside. In addition, as you can see, we got him a beer. Mr. D died that night and thanks to the Bundle, he was lucid, not delirious, and able to tell us what mattered most to him.

Imagine if your commercial airline pilot didn’t run through a safety checklist before takeoff in the massive jet you are about to take across the ocean. Things could go poorly, to say the least. In a similar vein, going through an ICU with a big surgical procedure or infection requiring life support can be a “complicated flight across the ocean.” We need a safety checklist to make sure all the right things are done each day for every ICU patient. We, at the CIBS Center, have worked diligently over the past decade using the world’s best research findings to develop what is now known as the ABCDEF Bundle, which is used to help manage millions of patients in ICUs around the world every day.

The overall goals of the ABCDEF Bundle are to help you or your loved ones have a more complete recovery and live a better life. After publishing data from a study of over 25,000 patients, we now know that the more an ICU team complies with the bundle each day, the shorter the time patient’s spend in the hospital, the less delirium and coma they have, and the more often they survive.

The Society of Critical Care Medicine’s (SCCM) ICU Liberation initiative, an international plan to improve outcomes from critical illness, uses the ABCDEF Bundle as the cornerstone of how to “liberate” patients from the ICU. Importantly, the F in the bundle is FAMILY. The bundle engages family members in important and novel ways to make things better during and after the ICU.

In upcoming months, the two largest electronic medical records (EMR) companies, EPIC and CERNER, will be releasing their ABCDEF Bundle “builds” to all hospitals using their EMR platforms. The CIBS Center is working with both to make this process as seamless as possible, and to help individual medical centers successfully navigate implementation and culture change associated with this process, in order to improve the care of your loved ones when they get admitted to an ICU.

Dr. Wes Ely performs a delirium assessment as part of the ABCDEF Bundle

A Assess, Prevent, Manage Pain
B Both Spontaneous Awakening Trials & Spontaneous Breathing Trials
C Choice of Analgesia and Sedation
D Delirium: Assess, Prevent and Manage
E Early Mobility and Exercise
F Family Engagement and Empowerment

Learn More about the ABCDEF Bundle: ICUdelirium.org/ABCDEF
Through the generosity of those who support our work, we have been able to impact treatment and care for critically ill patients, and embark on new research initiatives and projects that never would have been possible without these funds.

Gifts of any size help to make our mission possible. Your generosity will directly help to support ICU patients, survivors and family members, and CIBS Center research and educational initiatives in efforts to improve clinical care for critically ill patients around the world.

Donate Now:
Give.VanderbiltHealth.org/CiBS

THANKS TO OUR DONORS

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Mr. and Mrs. Milton Smith  
Society of Critical Care Medicine
For more information, visit our website where you can find:

- Resources for medical professionals including resource downloads
- Resources for patients and family members
- Information about our ICU Recovery Center and Support Group
- Detailed study descriptions
- Patient videos and testimonials
- News articles, featured podcasts, and recent publications

ICUDelirium.org

Photo top:
Amy Kiehl, MA; and Mary Martinez-Schmidt

Photo bottom:
CIBS Center student interns, Lily Valiulis and Aidan Wells, and CIBS Center Co-Director, Pratik Pandharipande, MD, MSCI

Photo opposite page:
Ricky Shinall, MD, PhD; Allen Wolf, MD, PhD; and Joanna Stollings, PharmD.