# 2016 Beeson Annual Meeting Program Book

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- BMJ Article: *Data sharing through an NIH central database repository: a cross-sectional survey of BioLINCC users*
- Janet Bickel’s Presentation Slides
- STAT Article: *'ICU delirium’ is terrifying — and incredibly common*
2016 ANNUAL MEETING

EAGLEWOOD RESORT AND SPA
ITASCA, ILLINOIS

NOVEMBER 9 – 12, 2016
AGENDA

WEDNESDAY, NOVEMBER 9, 2016

3:00 p.m.  
Hotel Check-in Time

4:30 – 5:00 p.m.  
Registration  
Red Oak Foyer

5:00 – 5:45 p.m.  
RECEPTION  
Red Oak Foyer

5:45 – 7:00 p.m.  
WELCOME AND KEYNOTE ADDRESS  
Red Oak B/C

Thomas Gill, M.D.  
Professor of Medicine and Professor of Epidemiology  
Yale School of Medicine and  
Chair, Beeson Program Advisory Committee; 1997 Beeson Scholar

Marie Bernard, M.D.  
Deputy Director, National Institute on Aging

Mark Lachs, M.D., M.P.H.  
Board member and president-elect, AFAR  
Psaty Distinguished Professor of Medicine  
Weill Cornell Medical College; 1995 Beeson Scholar

INTRODUCTION OF NEW SCHOLARS  
Chyren Hunter, Ph.D.  
Deputy Director and Training Officer,  
Division of Extramural Activities National Institute on Aging

KEYNOTE ADDRESS:  
The Next Era of Clinical Research: Digital Data, Participant Partnership, and Data Sharing  
Harlan M Krumholz, M.D., S.M.  
Harold H. Hines, Jr. Professor of Medicine and Epidemiology and Public Health,  
Yale School of Medicine; 1996 Beeson Scholar

7:00 – 9:00 p.m.  
DINNER  
Red Oak B/C
THURSDAY, NOVEMBER 10, 2016

7:00 – 8:00 a.m.
Breakfast
Burnham Dining Room

8:00 – 9:15 a.m.
Open Science and Data Transparency
Red Oak A

Funding agencies and biomedical research organizations are increasingly embracing the need for open science and data transparency, creating new opportunities to help address important public health and biomedical research challenges. This session will discuss the need for open science in clinical research, including reviewing prior studies on selective publication and selective outcome reporting, implications for clinical medicine and research, and the potential value of data transparency. The session will also discuss the National Institutes of Health’s efforts in this area, beginning with a brief history of open science policies and resource sharing to potential future directions in this rapidly evolving environment.

Introduction: Constance Fung, M.D., M.S.H.S.
David Geffen School of Medicine at University of California, Los Angeles

Joseph Ross, M.D., M.S.H.
Associate Professor of Medicine (General Medicine) and of Public Health (Health Policy)
Yale University School of Medicine; 2008 Beeson Scholar
Co-PI, the YODA project, http://yoda.yale.edu/welcome-yoda-project

Robin Barr, D. Phil.
Director, Division of Extramural Activities
National Institute on Aging

9:15 – 9:30 a.m.
Break

9:30 – 11:30 a.m.
Maximizing Return on Your Investment in Your Career:
Critical Skills for Thriving in Academic Medicine
Red Oak A

Negotiation does not come naturally to many physicians and scientists. This skills-based session will offer many insights on how to meet your goals while simultaneously building key relationships. The session, led by Janet Bickel, will empower you to better handle all phases of a typical career-related negotiation including articulating the value of what you bring to table, identifying the needs of the other party and what is negotiable, and implementing what is agreed upon. The main presentation will be followed by three breakout sessions that will further explore this topic. Attendees should choose the session that most closely aligns with their own interests.

Introduction: Kasia Lipska, M.D.
Yale University School of Medicine

Janet Bickel, M.A.
Leadership and Career Development Coach and Consultant

Breakouts Sessions:

- Group 1: Hollyhock
Moving from Assistant to Associate Professor
Moderator: Louise Walter, M.D.
University of California, San Francisco
• Group 2: Wildrye
Moving from Associate to Full Professor
Moderator: Ray Yung, M.D.
University of Michigan Medical School

• Group 3: Arrowhead
Gender and Racial Disparities in Academic Medicine
Moderator: Janet Bickel, M.A., Consultant

11:30 – 12:30 p.m.
LUNCH
Burnham Dining Room

12:30 – 2:30 p.m.
FREE TIME/MENTORING ACTIVITIES

2:30 – 3:00 p.m.
THE JOHN A. HARTFORD FOUNDATION – update
Rani E. Snyder, M.P.A., Program Director
Red Oak A

An update on The John A. Hartford Foundation funding initiatives.

3:15 – 5:15 p.m.
DATA BLITZ!
The academic equivalent of speed dating – a fast-track vehicle to understand research and possible synergies with others. Each session involves a research theme, with current scholars each presenting their research in seven minutes or less – the time limit will be strictly enforced. Groups will be arranged by content area. Other meeting participants are encouraged to attend these sessions to interact and provide feedback to the presenters.

Group 1: Hollyhock, Moderator: Cynthia Carlsson, M.D.
University of Wisconsin School of Medicine

Group 2: Wildrye, Moderator: Manish Shah, M.D., M.P.H.
University of Wisconsin School of Medicine

Group 3: Arrowhead, Moderator: George Kuchel, M.D., F.R.C.P., A.G.S.F.
University of Connecticut Health Center

5:15 – 7:00 p.m.
POSTER SESSION AND RECEPTION
Red Oak BC
Poster numbers can be found in the program booklet and will also be available. Please remove your poster at the conclusion of the session.

7:00 – 9:00 p.m.
DINNER
Burnham Dining Room

8:30 – 10:30 p.m.
BOWLING!
We have reserved three lanes at Kegler’s Bowling Alley! Kegler’s is just across the parking lot from the hotel in the same building as the Spa, Fitness Center and Pool.
FRIDAY, NOVEMBER 11, 2016

7:00 – 9:00 a.m.
Burnham Dining Room

**BREAKFAST**

Note: A private breakfast meeting for the Program Advisory Committee and other invited participants will be held in Burnham’s Private Dining Room from 7:30 – 8:45 a.m.

9:00 – 10:45 a.m.
Red Oak A

**SPOTLIGHT ON BEESON ALUMNI**

This session showcases three highly accomplished Beeson Alumni Scholars who will provide updates on their latest research. They will also reflect on some pivotal moments that have helped shape their careers as physician-scientists.

**Introduction:** William R. Hazzard, M.D.
Wake Forest University School of Medicine

*Enhancing Care for People with Serious Advanced Illness and Their Families*

Jean S. Kutner, M.D., M.S.P.H. - 2000 Beeson Scholar
Professor of Medicine, Chief Medical Officer
University of Colorado Hospital and
Associate Dean for Clinical Affairs,
University of Colorado School of Medicine

*Regional Vulnerability as a key to Alzheimer’s research*

Scott A. Small, M.D. - 2000 Beeson Scholar
Boris and Rose Katz Professor of Neurology
Taub Institute for Research on Alzheimer’s Disease and the Aging Brain
Columbia University College of Physicians and Surgeons

*Using your DIME towards a RETURN on Investment: how to make your BEESON experience matter*

Wesley Ely, M.D., M.P.H., F.C.C.P. - 2001 Beeson Scholar
Professor of Medicine and Associate Director of Aging Research
Vanderbilt University

10:45 – 11:00 a.m.

**BREAK**

11:00 a.m. – 12:30 p.m.
Red Oak A

**CAN BASIC AGING RESEARCH FINDINGS BE TRANSLATED INTO CLINICALLY-RELEVANT STRATEGIES?**

Until now, the focus of clinical studies/trials has been to treat or prevent individual age-related diseases, independent of other diseases or conditions. We will discuss whether a drug or drugs that target basic aging mechanisms can delay a composite outcome of age-related diseases.

**Steven Austad, Ph.D. – moderator/speaker**
Scientific Director, AFAR
Distinguished Professor, Department Chair
University of Alabama Birmingham

S. Jay Olshansky, Ph.D.
Professor,
University of Illinois at Chicago

**John Newman, M.D., Ph.D. - 2014 Beeson Scholar**
Assistant Professor,
University of California, San Francisco
Stephen Kritchevsky, Ph.D.
Professor of Internal Medicine and Translational Science;
Director, Stitch Center on Aging
Wake Forest University

12:30 – 2:00 p.m.
LUNCH
Burnham Dining Room

Lunch is served in the main dining room except for those who signed up for a Consultancy Session or the Aims Page Workshop (assignments can be found in the program booklet.)

Consultancy Session 1: Cottonwood
Consultancy Session 2: Burnham’s Private Dining Room
Aims Page Workshop: Dogwood

2:00 – 3:30 p.m.
GRADUATING SCHOLARS PRESENTATIONS
Red Oak A

Introduction: Chris Callahan, M.D.
Indiana University Center for Aging Research

Alison Huang, M.D. – 2011 Beeson Scholar
Associate Professor of Medicine
University of California, San Francisco

Jeff Caterino, M.D. – 2010 Beeson Scholar
Associate Professor and Vice Chair of Research
The Ohio State University

Keith Vossel, M.D. – 2011 Beeson Scholar
Assistant Professor of Neurology
University of California, San Francisco

3:30 – 6:30 p.m.
FREE TIME/ MENTORING ACTIVITIES

6:30 – 9:00 p.m.
DINNER... MADE BY YOU!
Meet in Lobby at 6:15 p.m.

Join us for a fun evening at Cooking Skills Academy (www.cookingskillsacademy.com) and learn how to make pasta and potato gnocchi—and then eat it! (Dinner in Burnham Dining Room is available at 6:30 pm for those not participating in the cooking class.)

SATURDAY, NOVEMBER 12, 2016

7:00 – 8:30 a.m.
BREAKFAST
Burnham Dining Room

8:30 a.m.
ADJOURN

12:00 p.m.
HOTEL CHECK-OUT TIME
### Program Advisory Committee Mentor Assignments

<table>
<thead>
<tr>
<th>Committee</th>
<th>Thursday, Nov 10 12:30 - 1:30 pm</th>
<th>Thursday, Nov 10 1:30 - 2:30 pm</th>
<th>Friday, Nov 11 12:30 - 2:00 pm (Lunch)</th>
<th>Friday, Nov 11 3:30 - 4:30 pm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Where to meet</td>
<td>Hotel Lobby</td>
<td>Hotel Lobby</td>
<td>Burnham Dining Room</td>
<td>Hotel Lobby</td>
</tr>
<tr>
<td>Liana Apostolova</td>
<td>Okonkwo</td>
<td>Pereira</td>
<td>Lucey</td>
<td>Hu</td>
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<tr>
<td>Ken Covinsky</td>
<td>Dharmarajan</td>
<td>Lipska</td>
<td>Cooper</td>
<td>Fung</td>
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<tr>
<td>Wes Ely</td>
<td>Hua</td>
<td>Deiner</td>
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<td>Prabharakan (meet Thu Nov 10, 7-8 am breakfast)</td>
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<tr>
<td>Tom Gill</td>
<td>Trevino</td>
<td>Rosen</td>
<td>Unroe</td>
<td>Kim</td>
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<td>Jean Kutner</td>
<td>Linos</td>
<td>Betz</td>
<td>Peterson</td>
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<td>Mark Lachs</td>
<td>Lum</td>
<td>Lai</td>
<td>Gifford</td>
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<td>Alison Moore</td>
<td>Brummel</td>
<td>Gardner</td>
<td>Maust</td>
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<tr>
<td>Raymond Yung</td>
<td>Teich</td>
<td>Hiniker</td>
<td>Smith, P.</td>
<td>Newman</td>
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**Assignments**

One of features of the Beeson Program is that we match current scholars with members of the program committee. One of the roles of the members of the Program Committee is to serve as external mentors to the Beeson Scholars. This is an informal mentorship and will give active Scholars the opportunity to discuss career and research issues with another senior investigator in aging research outside his/her own institution. Most of the interactions will be at this meeting, but Scholars may also call on this external mentor during the Beeson Award. Assignments are listed above (note this sheet has two tabs, assignments per mentor, and assignments per scholar.)

Please meet during the time and day that are listed above. We have tried to make sure there is no conflict with travel itineraries. If for some reason you cannot attend the scheduled session, or if you have any questions, please contact your assigned scholar or mentor.

We were not able to assign everyone a time, so if you wish, you can contact your assigned mentor/scholar directly.

2012 Scholars have not been assigned to mentors. Contact mentors directly to arrange to meet at other times during the meeting.
### 2012 Scholars

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Research Topic</th>
<th>Mentor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Han, S. Duke</td>
<td>Rush University Medical Center</td>
<td>Neural Correlates of Impaired Financial &amp; Health Care Decision-Making in Old Age</td>
<td>Mark Lachs</td>
</tr>
<tr>
<td>Kelley, Amy</td>
<td>Mount Sinai School of Medicine</td>
<td>Improving Care for Older Adults with Serious Illness</td>
<td>Raymond Yung</td>
</tr>
<tr>
<td>Smith, Alexander</td>
<td>University of California San Francisco</td>
<td>Late Life Disability: Epidemiology, Symptoms, Quality of Life</td>
<td>Jean Kutner</td>
</tr>
<tr>
<td>Moreno, Gerardo</td>
<td>University of California, Los Angeles</td>
<td>Health IT decision to support to improve medication management safety and quality</td>
<td>Ken Covinsky</td>
</tr>
<tr>
<td>Prior, Steven</td>
<td>University of Maryland Baltimore</td>
<td>Effects of Aerobic Exercise on EPCs and Vascular Dysfunction in Aging and T2DM</td>
<td>Mark Lachs</td>
</tr>
<tr>
<td>Panda, Alexander</td>
<td>Tufts University School of Medicine</td>
<td>Age associated defects in localization and trafficking of Toll-like receptor 1</td>
<td>Raymond Yung</td>
</tr>
</tbody>
</table>

### 2013 Scholars

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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Research Topic</th>
<th>Mentor</th>
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</thead>
<tbody>
<tr>
<td>Betz, Marian</td>
<td>University of Colorado Denver</td>
<td>Physician Screening of Older Drivers: Decision Rules for Geriatric Injury Prevention</td>
<td>Jean Kutner</td>
</tr>
<tr>
<td>Fung, Constance</td>
<td>UCLA David Geffen School of Medicine</td>
<td>Improving Older Adults’ Decision Making for Obstructive Sleep Apnea Treatment</td>
<td>Ken Covinsky</td>
</tr>
<tr>
<td>Hu, William</td>
<td>Emory University</td>
<td>Early CSF detection of FTLD</td>
<td>Liana Apostolova</td>
</tr>
<tr>
<td>Kramer, Daniel</td>
<td>Hebrew Rehabilitation Center</td>
<td>Patient-Centered Outcomes of Implantable Defibrillator Therapy in Older Patients</td>
<td>Tom Gill/SCHOLAR NOT ATTENDING</td>
</tr>
<tr>
<td>Okonkwo, Ozioma</td>
<td>The University of Wisconsin</td>
<td>Early detection of asymptomatic middle-age adults at risk for AD</td>
<td>Liana Apostolova</td>
</tr>
<tr>
<td>Peterson, Janey</td>
<td>Weill Cornell Medical College</td>
<td>INSPIRE: Intervention to Support Participation in Regular Exercise in the Elderly</td>
<td>Jean Kutner</td>
</tr>
<tr>
<td>Prabhakaran, Vivek</td>
<td>University of Wisconsin - Madison</td>
<td>Stroke Plasticity</td>
<td>Wes Ely</td>
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</tbody>
</table>

### 2014 Scholars

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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Research Topic</th>
<th>Mentor</th>
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</thead>
<tbody>
<tr>
<td>Dharmarajan, Kumar</td>
<td>Yale University School of Medicine</td>
<td>Geriatric Conditions and Readmission after Acute Myocardial Infarction</td>
<td>Ken Covinsky</td>
</tr>
<tr>
<td>Hiniker, Anne</td>
<td>University of California, San Francisco</td>
<td>Chemical-Genetic Approaches to Define Lrrk2 Kinase Function in Parkinson Disease</td>
<td>Raymond Yung</td>
</tr>
<tr>
<td>Lai, Jennifer</td>
<td>University of California, San Francisco</td>
<td>Frailty and Functional Status in Older Liver Transplant Patients</td>
<td>Mark Lachs</td>
</tr>
<tr>
<td>Lipska, Kasia</td>
<td>Yale University</td>
<td>Predicting Severe Hypoglycemia among Older Adults with Diabetes</td>
<td>Ken Covinsky</td>
</tr>
<tr>
<td>Maust, Donovan</td>
<td>University of Michigan</td>
<td>Preventable Hospitalization in Dementia: The Impact of Neuropsychiatric Symptoms</td>
<td>Alison Moore</td>
</tr>
<tr>
<td>Newman, John</td>
<td>University of California San Francisco</td>
<td>Epigenetic regulation of healthspan and longevity by ketone bodies</td>
<td>Raymond Yung</td>
</tr>
<tr>
<td>Trevino, Kelly</td>
<td>Weill Cornell Medical College</td>
<td>Anxiety With Cancer in the Elderly (ACE): A Cognitive-Behavioral Intervention</td>
<td>Tom Gill</td>
</tr>
<tr>
<td>Unroe, Kathleen</td>
<td>Indiana University</td>
<td>Delivering Hospice and Palliative Care Services to Nursing Home Patients</td>
<td>Tom Gill</td>
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### 2015 Scholars
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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Title</th>
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<tbody>
<tr>
<td>Kim, Dae Hun</td>
<td>Brigham and Women’s Hospital</td>
<td>Development and Validation of a Frailty Index Using Claims Data for Pharmacoepidemiologic Studies in Older Adults</td>
</tr>
<tr>
<td>Gifford, Katherine</td>
<td>Vanderbilt University</td>
<td>Cognitive Complaints in Aging Adults</td>
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<tr>
<td>Deiner, Stacie</td>
<td>Icahn School of Medicine at Mount Sinai</td>
<td>Optimizing postoperative cognition in the elderly</td>
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<tr>
<td>Bell, Susan</td>
<td>Vanderbilt University</td>
<td>Longitudinal Hemodynamic and Vascular Changes associated with Frailty</td>
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<tr>
<td>Ishii, Makoto</td>
<td>Weill Cornell Medical College</td>
<td>Pathobiology of Hypothalamic and Metabolic Dysfunction in Normal Aging and Alzheimer's Disease</td>
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<tr>
<td>Gardner, Raquel</td>
<td>University of California, San Francisco</td>
<td>Traumatic Brain Injury and The Aging Brain: Predictors of Clinical Trajectories</td>
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<tr>
<td>Hua, May</td>
<td>Columbia University Health Sciences</td>
<td>Determinants of Critical Care Intensity for Hospitalized Older Adults: the effect of hospital-based palliative care services</td>
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<tr>
<td>Milman, Sofya</td>
<td>Albert Einstein College of Medicine</td>
<td>Effect of longevity genomes on the GH/IGF-1 phenotype and disease-free survival</td>
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<tr>
<td>Brummel, Nathan</td>
<td>Vanderbilt University</td>
<td>LONG TERM OUTCOMES OF PHYSICAL ACTIVITY IN OLDER ADULTS WITH CRITICAL ILLNESS</td>
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<tr>
<td>Cooper, Zara</td>
<td>Harvard Medical School</td>
<td>BEYOND 30-DAYS: PATIENT-ORIENTED OUTCOMES AMONG OLDER ADULTS AFTER EMERGENCY GENERAL SURGERY</td>
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<tr>
<td>Linos, Eleni</td>
<td>University of California San Francisco</td>
<td>INVOLVING OLDER ADULTS IN DECISION MAKING FOR SKIN CANCER</td>
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<tr>
<td>Lucey, Brendan</td>
<td>Washington University School of Med</td>
<td>SLEEP QUALITY AND HUMAN AMYLOID-BETA KINETICS</td>
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<tr>
<td>Lum, Hillary</td>
<td>University of Colorado Denver</td>
<td>REFINING AN ADVANCE CARE PLANNING GROUP VISIT INTERVENTION ? A NOVEL INTERVENTION TO ENGAGE</td>
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<td>Pereira, Ana</td>
<td>Rockefeller University</td>
<td>ENHANCING GLUTAMATE TRANSPORT IN AGE-RELATED COGNITIVE DECLINE AND ALZHEIMER'S DISEASE</td>
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<td>Rosen, Anthony</td>
<td>Weill Cornell Medical College</td>
<td>IDENTIFYING INJURY PATTERNS AND FORENSIC BIOMARKERS DIAGNOSTIC OF PHYSICAL ELDER ABUSE</td>
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<tr>
<td>Smith, Phillip</td>
<td>University of Connecticut</td>
<td>REGULATORY MECHANISMS IN A HOMEOSTATIC MODEL OF GERIATRIC VOIDING PROBLEMS AND INCONTINENCE</td>
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<tr>
<td>Teich, Andrew</td>
<td>Columbia University Health Sciences</td>
<td>AN INTEGRATIVE ANALYSIS OF DNA METHYLATION, TRANSCRIPTOMIC CHANGES; AND COGNITIVE</td>
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<td>First</td>
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<td>Institution</td>
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<tr>
<td>Anne</td>
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<td>Raquel</td>
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<td>S. Duke</td>
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<td>Stacie</td>
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<td>Vivek</td>
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<td>Alexander</td>
<td>Panda</td>
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<td>Anthony</td>
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<td>Brendan</td>
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<td>Washington University School of Med</td>
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<td>Constance</td>
<td>Fung</td>
<td>UCLA David Geffen School of Medicine</td>
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<tr>
<td>Janey</td>
<td>Peterson</td>
<td>Joan &amp; Sanford I Weill Medical College of Cornell University</td>
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<td>Kumar</td>
<td>Dharmarajan</td>
<td>Yale University School of Medicine</td>
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<td>Harvard Medical School</td>
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<td>Kelly</td>
<td>Trevino</td>
<td>Weill Medical College of Cornell University</td>
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How a Consultancy Session works: This is a popular and effective group problem-solving activity known as a “consultancy.” This is structured to enable a set of people with a variety of knowledge and expertise to provide support, new perspectives, and ideas to one another, particularly around an important or difficult challenge.

Each Scholar will get approximately 10 minutes. Each Scholar will have 2-3 minutes or so to present what he/she views as the major career challenge he/she is facing (or will soon face).

Following each Scholar’s presentation, the group will ask clarifying questions for the next one-two minutes. For the bulk of the remainder of the time, the Scholar will receive feedback and advice from the group. In the last minute or so, the Scholar will then have a chance to respond to the ideas presented. We will follow a strict timetable, so that each person will have the same opportunity for constructive feedback.
Aims Page Workshop
Room: Dogwood
Friday, November 11, 12:30-2:00 pm

Moderators: Julie Bynum, Albert Shaw, Marcel Salive

Stacy Fischer x2
Connie Fung
Alex Smith
Dae Kim
Vivek Prabhakaran
Annie Hiniker
2016 Beeson Scholars

Nathan Brummel, MD, MSCI, Assistant Professor of Medicine, Vanderbilt University: “Long Term Outcomes of Physical Activity in Older Adults with Critical Illness”

Zara Cooper, MD, MSc, FACS, Assistant Professor of Surgery, Harvard Medical School: “Beyond 30-Days: Patient-Oriented Outcomes among Older Adults After Emergency General Surgery”

Eleni Linos, MD, DrPH, Assistant Professor, University of California, San Francisco: “Involving Older Adults In Decision Making For Skin Cancer”

Brendan Lucey, MD, Assistant Professor of Neurology, Washington University School of Medicine: “Sleep Quality and Human Amyloid-Beta Kinetics”

Hillary Lum, MD, PhD, Assistant Professor, University of Colorado, Denver and VA Eastern Colorado GRECC: “Refining An Advance Care Planning Group Visit Intervention? A Novel Intervention to Engage Older Adults In Advance Care Planning”

Ana Pereira, MD, Assistant Professor of Clinical Investigation, Rockefeller University: “Enhancing Glutamate Transport in Age-Related Cognitive Decline and Alzheimer's Disease”

Anthony Rosen, MD, MPH, Instructor in Medicine, Weill Cornell Medical College: “Identifying Injury Patterns and Forensic Biomarkers Diagnostic of Physical Elder Abuse”

Phillip Smith, MD, Assistant Professor, University of Connecticut: “Regulatory Mechanisms in a Homeostatic Model of Geriatric Voiding Problems and Incontinence”

Andrew Teich, MD, PhD, Assistant Professor, Columbia University: “An Integrative Analysis of DNA Methylation; Transcriptomic Changes; and Cognitive Dysfunction in Alzheimer's Disease”

2015 Beeson CARDI Fellow (did not attend last year)

Claire McEvoy, MPhil, PhD, Fellow, Queen's University Belfast: “Mediterranean diet and cognitive decline - strengthening the evidence base and encouraging behaviour change”
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Brummel, Nathan E., M.D., M.S.C.I.

eRA COMMONS USER NAME (credential, e.g., agency login): BRUMMELN

POSITION TITLE: Assistant Professor of Medicine

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

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<td>Resident</td>
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<td>07/08-06/09</td>
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<td>Fellow</td>
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A. Personal Statement
I am an aging-focused critical care clinical investigator. My NIH-funded research program seeks to understand better the processes that result in disabilities in basic self-care activities and mobility for the growing number of patients who survive a critical illness each year, with a focus on older adults. Because a majority of those admitted to ICUs are age 65 years and older, the aging US population is likely to result in a large, aging-related, public health problem in the form of large numbers of patients who suffer from newly acquired or exacerbated disabilities in basic self-care activities. My long-term career goal is to become a national (and eventually international) leader in advancing our understanding of disabling processes through the development of better tools by which to understand underlying mechanisms and then to design and conduct randomized controlled trials of novel interventional strategies to improve clinical outcomes.

B. Positions and Honors

Employment (all positions full-time)

2013-2016 Instructor in Medicine, Department of Medicine, Division of Allergy, Pulmonary Disease and Critical Care Medicine, Vanderbilt University School of Medicine, Nashville, TN (Division Director, Timothy Blackwell, MD) Mentor: E. Wesley Ely, MD MPH

2016-Pres. Assistant Professor of Medicine, Department of Medicine, Division of Allergy, Pulmonary Disease and Critical Care Medicine, Vanderbilt University School of Medicine, Nashville, TN (Division Director, Timothy Blackwell, MD) Mentor: E. Wesley Ely, MD MPH

Honors

2012 Travel Award, American Thoracic Society International Conference

2013 Best Paper Award (All Categories) American Geriatrics Society Annual Meeting

2014 Burroughs Wellcome Travel Award, Association for Clinical and Translational Science

2015 Travel Award, Society for Critical Care Medicine, Internal Medicine Section

Professional Societies and Public Advisory Committees

08/09-Pres. Member, Society of Critical Care Medicine (SCCM)

10/10-Pres. Member, American Thoracic Society (ATS)

03/12-Pres. Member, American Geriatrics Society (AGS)

08/15-Pres. Chair, ATS Assembly on Critical Care Aging and Geriatrics Working Group

C. Contribution to Science

My innovative program of clinical research is focused on understanding better the processes that result in disabilities in basic self-care activities and developing rehabilitation strategies that target the physical and cognitive impairments that are hypothesized to underlie the disabling processes in the setting of critical illness.

1. Understanding risk factors for the development of disabilities associated with critical illness.

Historical Background: Hospitalization, particularly for a critical illness, is a dramatic risk factor for disability.
A better understanding of risk factors during a hospitalization for critical illness is needed.  

**Central Findings:** Despite the high prevalence of disability after hospitalization, only 19 studies in older adults over the last 30 years have evaluated disability after a critical illness. These prior studies have significant limitations. Our work in observational cohorts found new or worsened disabilities ADLs were most prevalent among those age 65 years or older, but even younger patients were affected. We identified duration of delirium in the ICU to be an independent risk factor for disabilities in ADLs.  

**Influence of the findings:** By framing our work in the context of existing models of disabling processes, we are advancing the understanding of disabilities associated with critical illness.  

**Role:** Principal Investigator  

**Relevant peer-reviewed publications:**  


2. **Novel prevention and rehabilitation strategies for physical and cognitive impairment after critical illness.**  

**Historical Background:** Landmark studies in the last decade describe poor physical and cognitive function among survivors of critical illness perhaps linked to the harms of deep sedation and low activity.  

**Central Findings:** We demonstrated the feasibility of a novel, combined physical and cognitive rehabilitation intervention beginning in the ICU.  

**Influence of the findings:** This proof of concept study supports the hypothesis that critically ill patients can engage in combined physical and cognitive rehabilitation across the continuum of critical illness.  

**Role:** Principal Investigator  

**Relevant peer-reviewed publications:**  


**Complete List of Published Work in MyBibliography:**  


**D. Research Support**  

**Ongoing Research Support**  

K76AG054864 (PI: Brummel)  

NIH/NIA  

Nearly two-thirds of all patients hospitalized for a critical illness are age 65 years or older. While these patients are more likely than ever to survive their illness, up to 75% will suffer with newly acquired or worsened disabilities. Thus, there is a looming and under-addressed public health problem that is emerging in the form of large and growing numbers of survivors of a critical illness with life-altering disabilities. A better understanding of the underlying risk factors for disability following critical illness is greatly needed. The Specific Aims of the proposed research are: a) To test the hypothesis that greater activity during critical illness will be independently associated with a lower prevalence, less severity and shorter duration of disability in activities of daily living and mobility at 3- and 12-month follow-up, b) To test the hypothesis that greater activity during critical illness will be independently associated with better physical function and cognitive function at 3- and 12-month follow-up, and c) To test the hypothesis that greater physical activity during critical illness will reduce biomarkers of systemic inflammation and coagulation at hospital discharge.  

**Completed Research Support**  

KL2TR000446 (PI: Bernard)  

R03AG045095 (PI: Brummel)  

T32HL087738 (PI: Bernard)
BIOGRAPHICAL SKETCH

NAME: Cooper, Zara

eRA COMMONS USER NAME (credential, e.g., agency login): zaracooper

POSITION TITLE: Associate Surgeon, Division of Trauma, Burn and Surgical Critical Care, Brigham and Women’s Hospital; Assistant Professor of Surgery, Harvard Medical School

EDUCATION/TRAINING:

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<td>Brigham and Women's Hospital/Dana Farber Cancer Institute, Boston, MA</td>
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<td>2008</td>
<td>Acting Fellow in Palliative Medicine</td>
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<tr>
<td>University of Washington, Seattle, WA</td>
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A. Personal Statement

I am a clinical innovator working at the intersection of acute-care surgery (trauma, emergency general surgery, surgical critical care), geriatrics, and palliative care to integrate palliative care into the routine care of seriously ill and injured surgical patients. This work is directly informed by my unique skill set, as one of only a few surgeons board certified in hospice and palliative medicine. My approach to advancing my agenda includes health services research, clinical innovation, and education. I have published over 50 manuscripts and over a dozen book chapters, most of which are focused on palliative care or geriatrics in surgery. I founded and now lead the SHARPP Research Program at the BWH Center for Surgery and Public Health, a multidisciplinary group of health services researchers focused on patient-centered outcomes for high-risk surgical patients.

I am a trauma and acute care surgeon and surgical intensivist who is a nationally recognized leader in outcomes research and improving clinical care for older injured patients. I was a co-investigator and the site-PI for the NIA-funded project on successful aging after surgery (SAGES), which was a prospective cohort study of over 500 older adults undergoing elective surgery. I was also the Principal Investigator on a GEMSSTAR (R03) Award from the NIA and a Jahnigen Career Development Award from the American Geriatrics Society (AGS) to examine one-year mortality and healthcare utilization among older patients who sustain cervical spine fractures after falls. This work showed that older patients who sustained cervical spine fractures after falls had higher rates of mortality and readmissions than patients with hip fracture, and that trauma center care did not improve outcomes for patients with cervical fracture. Subsequent work showed that older patients with other spinal fractures also did not benefit from treatment at higher level trauma centers, and that the proportion of older patients treated at a trauma center, rather than the volume, is associated with lower rates of mortality, failure-to-rescue and hospital readmissions. A concurrent study at our level-one trauma center showed that triggered geriatric consultation for older patients admitted to a trauma service is associated with better outcomes. I am also the Principal Investigator on a recently funded Geriatrics for Specialist Initiative Grant from the AGS to develop national best practice guidelines for care of older injured hospitalized patients.


B. Positions and Honors

**Positions and Employment**

2007-2008 Acting Instructor In Surgery, University of Washington, Seattle, WA

2008 Board Certification: General Surgery

2008 Board Certification: Surgical Critical Care

2008- Associate Surgeon, Brigham and Women’s Hospital, Boston, MA

2008-2010 Instructor of Surgery, Harvard Medical School

2008-2012 Associate Director, Surgical Critical Care, Brigham and Women’s Hospital, Boston, MA

2009 Massachusetts Medical License

2009- Faculty, Center for Surgery and Public Health, Brigham and Women’s Hospital, Harvard School of Public Health, Harvard Medical School, Boston, MA

2010- Assistant Professor of Surgery, Harvard Medical School, Boston, MA

2010-2012 Associate Director, Surgical Critical Care Fellowship, Brigham and Women’s Hospital, Boston, MA

2012 Board Certification: Hospice and Palliative Medicine

2012- Associate Faculty, Ariadne Labs, Brigham and Women’s Hospital, Harvard Medical School, Harvard School of Public Health, Boston, MA

2013-2014 Interim Associate Director, Center for Surgery and Public Health, Brigham and Women’s Hospital, Harvard School of Public Health, Harvard Medical School, Boston, MA

2016- Adjunct Scientist in Palliative Care Research, Hebrew SeniorLife Institute for Aging Research

**Honors**

2003 Resident’s Award for Excellence, Tufts University School of Medicine

2004 Claude Organ Resident Award, Society of Black Academic Surgeons

2005 BWH Minority Faculty Career Development Grant, Brigham and Women's Hospital

2006 Resident’s Award for Excellence, Tufts University School of Medicine

2007 Minority Faculty Development Grant, Brigham and Women's Hospital

2009 BWH President's Young Investigators Award, Brigham and Women's Hospital

2011 BWH Faculty Development Award, Brigham and Women’s Hospital

2014 American Academy of Hospice and Palliative Care Research Scholar

2016 Radcliffe Institute for Advanced Study Innovation at Harvard Exploratory Seminar Award

C. Contribution to Science

1. Outcomes in older adults after injury and emergency general surgery

I led a retrospective cohort study using data from the trauma registry at Brigham and Women’s Hospital, a level-one trauma center, and found that older patients who sustain a severe traumatic brain injury suffer a 71% 12-month mortality and experience poor end-of-life care. I also participated in two retrospective cohort studies of long-term mortality among older emergency surgery patients, using data from a single center and national cohort respectively, which both showed that mortality continues to rise more than 30 days after emergency surgery and that predictors of 30 day and 6-month mortality differed. These results illustrate the importance of understanding postoperative outcomes beyond 30-days to inform clinical decisions and set expectations for recovery in older acutely ill surgical patients.


2. Preoperative communication between patients, surrogates and surgeons before high-risk surgery

I have conducted two studies examining preoperative communication between patients and clinicians before high-risk surgery. One was a randomized controlled pilot study to facilitate structured conversations with patients and surrogates related to goals and preferences for medical treatment in the pre-operative testing center. The other study used structured interviews and qualitative analysis to examine conversations between surgeons and patients before high-risk elective surgery. I have also conducted a qualitative study to understand surgeons’ perspectives on avoiding nonbeneficial treatments in older surgical patients. All of this work has provided valuable insight into gaps in communication and clinicians’ ability to adequately describe postoperative treatment and recovery for patients.


3. Participation in national advisory committees to improve care for geriatric trauma and emergency surgery patients

I participated in the American Association for Surgery of Trauma (AAST) Ad Hoc Geriatric Trauma Committee that published a paper that outlined the current understanding of conditions under which geriatric trauma patients are receiving care, identified major problems associated with providing care, and suggested potential solutions. This information was disseminated as a publication through the Journal of Trauma and Acute Care Surgery in June 2015. I have also led a multidisciplinary advisory panel of 23 national experts to develop a framework for best communication practices for surgeons to facilitate goal-concordant care for seriously ill older patients with acute surgical emergencies. The resulting manuscript was published as a lead article in a high-impact surgical journal, demonstrating its importance to the field.


Complete List of Published Work
D. Research Support

**Current Research Support**

**K76AG054859** Cooper (PI) 09/15/2016-05/31/2021
NIH/National Institute of Aging
To describe one-year mortality, health utilization, palliative care needs and end-of-life outcomes among older adults who experience emergency abdominal surgery.
Role: PI

**5R01AG044518-02** Inouye (PI) 03/01/2015-02/28/2019
National Institutes of Health-NIA
Development and Validation of a Delirium Severity Toolkit
The goal of this study was to develop a toolkit that can be used to determine the severity of delirium in patients and then validate the toolkit in the available study population.
Role: Co-Investigator

**Sojourns Scholar Leadership Program** Cooper (PI) 10/01/2015-10/01/2017
Cambia Health Foundation
Identifying Palliative Care Needs of Older Adults Undergoing Emergency Abdominal Surgery
The goal of this project is to fully characterize the clinical trajectories, health-care needs, illness experience and palliative care needs of older adult patients during the first 6 months after non-elective major abdominal surgeries.
Role: PI

**1R35CA197730-01** Prigerson (PI) 11/01/2015-07/31/2017
National Institutes of Health-NCI
Psychosocial Approaches to Better Understanding & End-Stage Cancer Care (PROTECT)
The aim of this project is to develop and refine a tool to assess the extent of decedent’s quality of life in the last week of life in the Intensive Care Unit (ICU).
Role: Co-Investigator

**CDR-1502-27462** Schwarze(PI) 01/01/2016-12/31/2016
Patient-Centered Outcomes Research Institute
Navigating High Risk Surgery: Empowering Older Adults to Ask Questions that Inform Decisions about Surgical Treatment
The goal of this project is to develop a question prompt list to improve communication between surgeons and patients considering surgery, so patients can make treatment decisions that are right for them.

**Completed Research Support**

The John A. Hartford Foundation (Change AGEnts Action Award) 08/01/2014-07/31/2015
Implementing routine cognitive assessment for older elective surgery patients in a busy preoperative testing center
The goal of the project is to implement routine cognitive screening in the preoperative testing center for geriatric patients before elective surgery. Components of this project include training over 50 clinicians to administer the Mini-Cog using an educational video we created, didactics and coaching. We are collecting data regarding the accuracy of the screens, the number of screens completed and how screening impacts the workflow of the preoperative testing center. The goal is to screen over 2000 patients in a six month period.
Role: PI/Project Leader

**5P01AG031720** Inouye (PI) 04/01/2012-03/31/2015
NIH/National Institute of Aging
Delirium PPG-EPI Core
Interdisciplinary study of delirium and its long-term outcomes, project 2
The major goal of this project was to examine the interface of delirium and dementia, whether postoperative delirium alters the course of dementia, and whether delirium leads to longstanding cognitive impairment and pathologic changes in the brain.
Role: Co-Investigator
The serious illness communication program—surgery
The goal of this project is to use a mixed methods approach to develop a short communications tool to facilitate goal-concordant surgical treatment for seriously ill older patients with acute surgical emergencies.
Role: PI

Faculty Development Award, Brigham and Women’s Hospital  Cooper (PI)  07/01/2011-06/30/2014
Cervical spine fracture mortality in the elderly: incidence, treatment, and one year outcomes
The goal of this award was provide transitional funding during the early critical years of an academic career.
The project used National Medicare data to determine impact of site of care on the one-year trajectory of healthcare utilization in elderly patients who sustain cervical spine fracture.
Role: PI

American Geriatric Society/Jahnigen Career Development Award  Cooper (PI)  08/01/2012-07/31/2014
The one year trajectory of elderly patients after cervical spine fracture
This is a mentored grant to train subspecialists to conduct geriatric research. This grant provides training support for the GEMSSTRAR/R03 funded project below.
Role: PI

R03AG042361 GEMSSTAR/R03  Cooper (PI)  08/01/2012-07/31/2014
The one-year trajectory of elderly patients after cervical spine fracture
The major goal of this project was to conduct the first national examination the impact of site of care on the one-year health trajectory for elderly patients sustaining cervical spine fracture.
Role: PI

National Institutes of Health/NIMHD  Cooper (PI)  2011-2013
Health Disparities Research Loan Repayment Program
Disparities in the use of life sustaining therapy after surgical procedures
The focus of this research is to use the Nationwide Inpatient Sample to examine racial/ethnic disparities in the use of life-sustaining therapy after high-risk general surgical procedures.
Role: PI
NAME: Linos, Eleni

eRA COMMONS USER NAME (credential, e.g., agency login): ELENILINOS

POSITION TITLE: Assistant Professor of Dermatology

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training)

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A. Personal Statement

I am dually trained in epidemiology and dermatology, and I am passionate about improving the quality of life of older adults with skin disease. Skin cancer is more common than all other cancers combined; the goal of the proposed research is to develop decision tools for shared decision-making about skin cancer in late life. I am seeking a Beeson Emerging Leaders Career Development Award in Aging in order to develop into an independent clinical researcher, and to begin to establish myself as an international leader of research at the interface of aging and dermatology.

After medical school at Cambridge and Oxford Universities in the UK, I completed a master’s and a doctorate degree in Epidemiology at Harvard, where I gained substantial quantitative skills analyzing large cohort study data. In addition to my research interests, I have always been committed to caring for patients; so, I completed residency training in dermatology. As a resident, I realized that dermatology is focused on diagnostic expertise, with little emphasis on evidence-based treatments. Specifically, I recognized that we do not routinely tailor our care to the special needs of older adults. This gap motivated me to transition from pure epidemiology to patient-oriented research, focusing on the needs of older adults.

I am fortunate to work in the UCSF Dermatology Department, one of the strongest clinical dermatology departments in the country. As a KL2 fellow in the Department of Epidemiology and Biostatistics, I had regular contact with some of the best clinical researchers at UCSF, including several geriatricians and Beeson Scholars (Ken Covinsky, Alex Smith, Sei Lee, Louise Walter) who have helped me integrate a geriatric perspective in my research. However, as a clinician whose expertise is “skin-deep,” I need additional dedicated training on the broader needs of the aging patient and a deeper understanding of geriatric research methods in order to become a leader in geriatric dermatology. I have extensive training in quantitative methods; experience working with large clinical studies as well as patient engagement and recruitment; and have assembled an outstanding team of qualitative and quantitative researchers in geriatrics, dermatology, and decision science that guarantee successful completion of this proposal.

I want to become a leader in geriatric dermatology because I am frustrated by the lack of attention that has been traditionally paid to the needs of older adults with skin disease, and inspired by the challenge to improve care for this population. Examples of my leadership activities include the following: I established the first UCSF Geriatric Dermatology clinic, dedicated to patients aged 80 or older with general dermatologic concerns, including skin cancer. I am the Deputy Director of the Program for Clinical Research in the UCSF Department of Dermatology, which supports a total of 12 faculty, trainees and students. I also direct our center’s monthly patient-oriented research team (PORT) seminar. In 2015 UCSF made a significant effort to increase diversity,
and I was selected as the Department of Dermatology’s Diversity leader, heading our Diversity Committee, and representing our department in university-wide meetings focused on increasing diversity.

B. Positions and Honors

Positions and Employment

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<td>2011</td>
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Other Experience and Professional Memberships

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<td>2015</td>
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<td>2015</td>
<td>present Diversity Leader, UCSF Dermatology</td>
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<td>2016</td>
<td>present JAMA Dermatology, Section Editor</td>
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Honors

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<td>2001</td>
<td>Paton Fund Award, Moore-Beale Sargant, Mitchel Awards, Trinity Cambridge</td>
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<td>2007</td>
<td>Best Poster Award, Dana-Farber Cancer Breast Cancer Meeting</td>
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<td>2008</td>
<td>Internal Medicine Resident research award, Stanford University</td>
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<td>2009</td>
<td>Arnold P. Gold Foundation's Humanism and Excellence in Teaching Award</td>
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<td>2009</td>
<td>Albert M. Kligman Travel Fellowship, Society for Investigative Dermatology</td>
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<tr>
<td>2010</td>
<td>Women's Dermatologic Society Academic Research Award</td>
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<tr>
<td>2012</td>
<td>Dermatology Foundation Career Development Award</td>
</tr>
<tr>
<td>2014</td>
<td>UCSF Pepper Center Career Development Award</td>
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</tbody>
</table>

C. Contribution to Science

1. Introduced the concept of overtreatment at the end of life to the field of Dermatology

My work on optimal skin cancer treatment at the end of life introduced the concept of overtreatment and over-diagnosis of skin cancer in the field of dermatology. I found patients’ personal characteristics and preferences matter beyond the traditional factors used to choose skin cancer treatments (histology, size, location). My research suggested that there was potential over-use of surgery at the end of life and questioned the status quo. The experience has shaped my understanding of the role and potential impact of thought leadership in our profession.


2. Influenced public awareness and helped shape tanning bed policy

My research on the harms of tanning beds published in the BMJ and JAMA Dermatology received widespread media attention and was cited in state and federal legislative hearings on tanning bed bans for minors. In 2013 and 2014, several states banned indoor tanning for minors, and two landmark reports by the FDA and Surgeon
General called for better labeling on harms of tanning booths and for bans on tanning for minors. Most recently in December 2015, the FDA proposed a ban on tanning bed use for minors, citing this work. Because young adults using tanning beds use social media often, we have worked on two research papers focused on Twitter and Google online advertising for skin cancer prevention.


c. Wehner MR1, Shive ML, Chren MM, Han J, Qureshi AA, Linos E. Indoor tanning and non-melanoma skin cancer: systematic review and meta-analysis. BMJ. 2012 Oct 2;345:e5909. PMCID: PMC3462818


3. Analyzed nonmelanoma skin cancer treatment patterns to improve for patient care:
Nonmelanoma skin cancer (NMSC) is the most common malignancy. The many available therapies for NMSC vary greatly in cost, but data are lacking about their comparative effectiveness in preventing recurrence and improving quality of life. I have worked on several longitudinal datasets including a large prospective NMSC cohort study, a Veteran Affairs and Medicare datasets to examine differences in treatments for primary and recurrent NMSC. We have shown that two common treatments that vary in cost, excisional surgery and Mohs surgery, have similar tumor recurrence long-term after treatment. In addition we found that a large proportion of incompletely excised low-risk NMSCs do not recur even without any treatment. Finally we showed that the use of new expensive treatments for NMSC without long-term efficacy or safety data (electronic brachytherapy), rose dramatically in 2014. We have also studied the natural history of the development of subsequent new skin cancers in patients who present with NMSC. Together these studies speak to the urgent need for evidence-based guidelines for NMSC treatment.


4. Investigated melanoma epidemiology and primary prevention strategies
The incidence of malignant melanoma, the most lethal of skin cancers, has been increasing in the setting of stable mortality trends. This has led some to question whether this is due to over-diagnosis and detection of biologically indolent tumors. To better understand how melanoma incidence trends varied by severity at diagnosis and factors relevant to screening access, we assessed recent United States incidence and mortality trends by histologic type, tumor thickness, and area-level socioeconomic status (SES). We found that melanoma incidence increased for all tumors including ones >4mm in thickness (most advanced cancers) and melanoma incidence rates doubled in all SES groups. We concluded that screening-associated diagnosis of thinner melanomas cannot explain the increasing rates of thicker melanomas among low SES populations with poorer access to screening. We then analyzed national survey (NHANES) data to better understand current prevention strategies and how these relate to sunburn and vitamin D levels.


b. Linos E, Keiser E, Kanzler M, Sainani KL, Lee W, Vittinghoff E, Chren MM, Tang JY. Sun protective


5. **Discovered links between diet and breast cancer**

My doctoral work focused on the links between early life exposures, including dietary risk factors, and subsequent breast cancer risk. We found that red meat consumption - especially processed meat - is a strong risk factor for breast cancer when consumed during early life or adolescence. This work contributed to the World Health Organization’s classification of processed meat as a class 1 carcinogen in 2015.


D. **Research Support**

**On-going Research Support**

UCSF RAP Research Allocation Program – Independent Support Award  Linos (PI)  07/01/2015 – 06/30/2016

Involving older adults in decision making for Skin Cancer

The goal of this grant is to transition from career-mentored phase to being an independent researcher.

Role: PI

**Completed Research Support**

- 8KL2TR000143 Linos (Scholar)  07/01/2011 – 6/30/2015
  National Clinical and Translational Science Institute
  Skin cancer treatment in elderly patients

The goal of the CTSI KL2 career development award is to increase the number and quality of clinical and translational investigators skilled at leading multidisciplinary research teams.

Role:KL2 Fellow

- Dermatology Foundation Career Development Award  Linos (PI)  07/01/2012 - 6/30/2015
  Non melanoma skin cancer care in patients with limited life expectancy

The purpose of this career development award is to support preliminary studies needed to be competitive for NIH grants.

Role:PI

- Pepper Center Research Career Development Award  Linos (PI)  07/01/2014 – 6/30/2015
  The purpose of this grant is to support career development in Aging research.

Role: PI

- American Skin Association  Linos (PI)  01/01/11 - 12/31/12
  Non-melanoma skin cancer treatment and outcomes in patients with limited life expectancy

Role: PI
Name: Brendan P. Lucey, MD

Position: Assistant Professor of Neurology

Specialty(ies): Sleep Medicine, Neurology, EEG

Affiliation: Washington University School of Medicine

Research Interests: Sleep and Alzheimer’s disease

Year of Beeson Award: 2016
Other Funding: BrightFocus Foundation

Professional Website: https://hopecenter.wustl.edu/?faculty=brendan-lucey-md
Social Media Feed: None

Contact Info: Email: luceyb@wustl.edu

Brendan is board-certified in Neurology with added qualifications in clinical neurophysiology and sleep medicine. He is an Assistant Professor in the Sleep Medicine Division of the Department of Neurology at Washington University in St Louis. He has been a GEMSSTAR scholar and was also supported by a KL2 career development award through the Washington University CTSA prior to receiving a Beeson award.

Brendan’s research interests include sleep, aging, and neurodegeneration with a specific focus on Alzheimer’s disease. His Beeson award project will investigate if improving sleep efficiency (total sleep time/total bed time) has the potential to alter Aβ concentrations in the human central nervous system.
NAME: Lum, Hillary Day

eRA COMMONS USER NAME (credential, e.g., agency login): Hillary.Lum

POSITION TITLE: Assistant Professor of Medicine

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<td>Northwestern University</td>
<td>BA</td>
<td>06/2000</td>
<td>Biology</td>
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<tr>
<td>University of Wisconsin School of Medicine</td>
<td>MD,PhD</td>
<td>05/2008</td>
<td>Cellular and Molecular Biology</td>
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<tr>
<td>University of Pittsburgh Medical Center</td>
<td>Resident</td>
<td>06/2011</td>
<td>Internal Medicine</td>
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<tr>
<td>University of Colorado School of Medicine</td>
<td>Fellow</td>
<td>06/2012</td>
<td>Geriatric Medicine</td>
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<tr>
<td>University of Colorado School of Medicine</td>
<td>Fellow</td>
<td>06/2013</td>
<td>Hospice and Palliative Medicine</td>
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</table>

A. Personal Statement

My goal is to be a geriatric palliative care researcher and leader in advance care planning to improve the care of older adults with multiple chronic conditions. As a Board-certified geriatrician, palliative medicine physician, and clinician scientist, I am dedicated to improving ACP initiatives, especially in primary care and community-based settings. With a transdisciplinary research team, including my primary mentors Dr. Cari Levy and Dr. Jean Kutner, I developed a novel intervention to improve ACP in primary care settings – an Advance Care Planning Group Visit intervention. Building on data from three pilot grants and a National Palliative Care Research Center Career Development Award, I am refining my Advance Care Planning Group Visit intervention to meet the needs of patients from diverse cultural backgrounds, primary care providers, and practice managers. I will develop an Intervention Manual and fidelity tools, refine the intervention using in-depth key stakeholder input, and conduct a pilot randomized controlled trial (RCT) of the intervention among older adults. My educational objectives are to gain advanced skills in mixed methods analysis, implementation science, and clinical trials in older adults. I will pilot test a refined Advance Care Planning Group Visit intervention in a RCT to evaluate feasibility, acceptability, and preliminary efficacy of the intervention on increasing ACP action steps. This study will lead to a full-scale effectiveness-implementation study using appropriate fidelity assessments and implementation measures. To maximize the impact of my research related to ACP, I also invest in strategic relationships with aging policy leaders. I was selected as a 2015-2016 Health and Aging Policy Fellow, which provides a unique opportunity to engage in leadership, training and networking in aging policy, especially related to stakeholder engagement, policy development and implementation, and regional and national ACP initiatives.


b. Lum HD, Sudore RL. Advance Care Planning and Goals of Care Communication in Older Adults with Cardiovascular Disease and Multimorbidity. Clin Geriatr Med. 2016 May;32(2):247-60. PMID: 27113144


B. Positions and Honors

Positions and Employment

2013 - present Assistant Professor of Medicine, University of Colorado School of Medicine; and VA Eastern Colorado Geriatric Research Education and Clinical Center (GRECC)

Board Certifications

2011 - present Colorado Medical License
2011 - present Diplomat, American Board of Internal Medicine
2012 - present Geriatric Medicine Certification
2014 - present Hospice and Palliative Medicine Certification
Other Experience and Professional Memberships (selected)
2009 - Member, American Geriatrics Society
2009 - Member, American Academy of Hospice and Palliative Medicine
2014 - Member, Palliative Care Research Cooperative Group
2014 - 2015 Scholar, American Academy of Hospice and Palliative Medicine Research Scholar
2014 - 2016 Scholar, Clinical Faculty Scholars Program, Colorado Clinical and Translational Institute
2015 - Member, Public Policy Committee, American Academy of Hospice and Palliative Medicine
2015 - 2016 Fellow, Health and Aging Policy Fellows Program

Honors (selected)
2011 Department of Medicine Frank M Mateer Senior Resident Award, UPMC Internal Medicine
2012 - 2013 Hearst Foundation Fellow, University of Colorado Hospice and Palliative Medicine
2015 Poster Award, American Academy of Hospice and Palliative Medicine Annual Assembly
2015 – 2016 American Academy of Hospice and Palliative Medicine Year-Long Mentoring Scholarship

C. Contribution to Science
1. Understanding needs of community-dwelling older adults: I have conducted multiple secondary data analyses related to understanding the needs of older adults. Using the Medicare Current Beneficiary Survey, a longitudinal survey that comprehensively assesses patient-reported measures that are relevant to older adults, we demonstrated the strong association between hospital readmission and increased 1-year mortality among Medicare beneficiaries. With the National Survey of Residential Care Facilities, we conducted studies to understand pandemic influenza preparedness and older drivers who live in residential care facilities. I collaborated in survey-based studies of community-dwelling older adults to understand perspectives on physician input in life transition planning, including advance care planning, driving cessation, financial and housing planning, as well as a study on gun safety practices in older adults. Each of these studies involved Beeson Scholars (Dr. Susan Hardy, Dr. Adit Ginde, Dr. Marian Betz).


Complete List of Published Work in MyBibliography: (25 peer-reviewed, incl. 17 first-authored publications)

D. Research Support
Ongoing Research Support
K76 AG054782 Lum (PI) 09/15/2016-05/31/2020
NIH/NIA
Refining An Advance Care Planning Group Visit Intervention – A Novel Intervention To Engage Older Adults In Advance Care Planning

TCHF Lum (PI) 10/01/2016-09/30/2018
The Colorado Health Foundation
Leveraging Patient Portal Use to Increase Patient Engagement in Advance Care Planning

Completed Research Support
Junior Faculty Career Development Award Lum (PI) 7/1/2015-6/30/2017
National Palliative Care Research Center - Refinement of an Advance Care Planning Group Medical Visit
My research focuses on furthering our knowledge of the neurobiology of aging and Alzheimer's disease taking into account the selective vulnerability of glutamatergic neural circuits to synaptic changes in aging and neuronal loss in Alzheimer's disease, and seeks to explore mechanisms underlying these susceptibilities along with effective interventions. I have studied glutamatergic neuronal susceptibility with modern quantitative cell biology methods (at the synaptic and spine resolution with electron and confocal microscopy) in conjunction with novel molecular tools (next generation RNA sequencing and open arrays) and functional assays.

Importantly, glutamatergic dysregulation is also intimately related to the release and toxicities of amyloid-beta and phosphorylated tau, the hallmarks of the neuropathology of Alzheimer's disease. I have been studying the pathophysiological mechanisms of cognitive decline in the setting of glutamatergic dysfunction, and in particular with downregulation of the dominant glutamate transporter in the brain, EAAT2, which plays the key role of regulating synaptic transmission, and thereby learning and memory and of preventing glutamate spillover to the extrasynaptic space that make neurons exquisitely sensitive to excitotoxicity. I have utilized transgenic animal models, including a novel conditional EAAT2 knock-out mouse with differential astrocytic and neuronal lines and a diversity of methodological approaches to relate anatomical and molecular findings to functional changes.

With training in basic and translational neuroscience at the laboratories of Scott Small, MD, John Morrison, PhD, Bruce McEwen, PhD and at the Rockefeller University Center for Clinical and Translation Research, led by Barry Coller, MD in combination with previous training in clinical neurology, with Neurology Residency at Harvard University and sub-specialty in Cognitive Neurology at Columbia University, another of my important career goals is to design and conduct clinical studies driven by strong mechanistic neurobiological hypothesis that can advance prevention, diagnosis and effective treatments for cognitive disorders. I have utilized neuroimaging as an important translational approach. Notably, the loss of synaptic activity and neuronal function in Alzheimer's disease is closely associated with reduction in glucose metabolism, a primary energy source in the brain. There is a tight coupling between cerebral glucose metabolism and glutamatergic neuronal activity with stoichiometry close to 1:1. Thus, as a marker of both cerebral metabolism and glutamatergic activity, I have utilized $^{18}$F-fluorodeoxyglucose positron emission tomography (FDG-PET) in my clinical studies.
Additionally, I have been using in vivo proton magnetic resonance spectroscopy (1H MRS) which allows measurements of glutamatergic compounds - i.e., glutamate (Glu) or glutamate + glutamine (Glx) and neuronal viability markers. With these technologies, I have been testing the effect of glutamate modulators of mechanistic therapeutic relevance on the cerebral metabolism and cognition of patients with mild Alzheimer’s disease. In parallel, I have also been evaluating risk factors that can potentially dysregulate excitatory-inhibitory neural homeostasis in cognitively normal elderly individuals that could contribute to cognitive decline and/or increase the risk to Alzheimer’s disease. A potential risk factor is intermittent hypoxia, a potential inducer of hyperexcitability, which occurs in sleep apnea, an under-diagnosed and consequently under-treated disorder in the elderly population.

These training activities have put me in the unique position to perform multimodal translational research in cognitive neuroscience, generating knowledge of neural mechanisms that contribute to the development and progression of cognitive decline in aging and Alzheimer’s disease, development of novel targets and more effective treatments for cognitive syndromes.

Employment
2007-2008: Intern, Internal Medicine, Albert Einstein College of Medicine, Montefiore Hospital, NYC.
2008-2011: Residency in Neurology at Beth Israel Deaconess Medical Center, Harvard University, Boston.
Clifford Saper, MD, PhD, Chair.
2012-2015: Cognitive Neurology Subspecialty Training at Columbia University, NYC. Lawrence Honig, MD, PhD, Teaching attending neurologist and Karen Marder MD, Director.
2011-2014: Clinical Scholar at the Rockefeller University Center for Clinical and Translational Science (Master’s degree in Translational and Clinical Investigation). Barry Coller, MD, Director.
2013-2014: Chief Clinical Scholar at the Rockefeller University, NYC.
2011-2016: Instructor in Clinical Investigation, The Rockefeller University, NYC. Barry Coller, MD, Director and Bruce McEwen, PhD, Advisor.
2016-present: Assistant Professor in Clinical Investigation, The Rockefeller University, NYC.

Honors
2004 Top 1% of class, MD degree
2011 CTSA Pilot Project Award Recipient
2012 Diplomate of the American Board of Psychiatry and Neurology
2012 Rockefeller University Pilot Award Recipient
2012 Dana Foundation Award Recipient
2013 Alzheimer’s Drug Discovery Foundation Awarded Grant
2013 Appointed Chief Clinical Scholar at the Rockefeller University
2013 CTSA Pilot Project Award Recipient
2015 Young Investigator Award by the Alzheimer’s Drug Discovery Foundation
2015 Rockefeller University Pilot Project Award Recipient
2016 Dana Foundation Award Recipient
2016 BrightFocus Award Recipient
2016 Bernard L. Schwartz Award for Physician Scientists

Languages: Fluent in English, Portuguese, French, and Spanish

Licensure & Certification
New York Board of Registration in Medicine: (license # 262985)
American Board of Psychiatry and Neurology Certification (57754)
NAME: Rosen, Tony

eRA COMMONS USER NAME (credential, e.g., agency login): anrosen

POSITION TITLE: Instructor in Medicine, Attending Physician

EDUCATION/TRAINING

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<td>Yale University</td>
<td>BA</td>
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<td>History of Science, History of Medicine</td>
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<td>and Film Studies</td>
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<td>University of California, Los Angeles</td>
<td>MPH</td>
<td>06/06</td>
<td>Epidemiology</td>
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<td>Weill Cornell Medical College</td>
<td>MD</td>
<td>06/10</td>
<td>Medicine</td>
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<tr>
<td>NewYork-Presbyterian Hospital</td>
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<td>06/14</td>
<td>Emergency Medicine</td>
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A. Personal Statement

My research focuses on improving identification of and intervention for victims of elder abuse, neglect, and exploitation in health care settings, particularly the Emergency Department (ED). My research goal is to identify injury patterns and forensic biomarkers diagnostic of physical elder abuse. Colleagues and I have leveraged unique partnerships with prosecutors' offices to compare injury patterns in legally adjudicated cases of physical elder abuse to those sustained by older adults after an accidental fall. We have developed a novel comprehensive classification system for acute geriatric injuries and a protocol to photograph acute injuries for research and clinical practice. Through the Beeson award, I plan to expand this research to prospectively enroll prospectively and evaluate comprehensively victims of physical elder abuse in the ED. I have also recently developed a first-of-its-kind, ED-based, multi-disciplinary Vulnerable Elder Protection Team to respond in cases of suspected elder abuse or neglect.

B. Positions and Honors

Employment / Academic Positions / Public Advisory Committees

1995-2000 General Manager, Troma Studios / Troma Team Video / Tromaville.com
2000-2004 Partner, IX Solutions, Inc.
2003-2004 Chief Information Officer, 3 Arch Financial Services, Inc.
2004-2005 Senior Vice President, Strategic Business Planning, LandAmerica Default Services
2014-6 Fellow, Geriatric Emergency Medicine, Weill Cornell Medical College
2014- Instructor of Medicine, Attending Physician, Weill Cornell Medical College
2014- Physician Member, Brooklyn and Manhattan Elder Abuse Multi-Disciplinary Teams
2014- Physician Member, New York City Elder Fatality Review Team
2015- Member, Steering Committee, New York City Elder Abuse Center
2016- Executive Committee Member, Academy of Geriatric Emergency Medicine

Honors

2006 Delta Omega, Iota Chapter, University of California, Los Angeles
2007 Henry C. and Anne Hayworth First Honor Prize, Weill Cornell Medical College
2008 Viola Borkon Memorial Prize, Weill Cornell Medical College
2008 Medical Student Research Day Prize, Weill Cornell Medical College
2009 Hayworth-Gold Award for Medical Professionalism, Weill Cornell Medical College
2009 Alpha Omega Alpha, Weill Cornell Medical College
2010 Good Physician Award, Weill Cornell Medical College
2010 Harold G. Wolff Research Prize, Weill Cornell Medical College
2010 Henry Adelman Memorial Award for Excellence in Geriatrics, Weill Cornell Medical College
2010 George G. Reader Prize in Public Health, Weill Cornell Medical College
2012 First Prize, Resident Research Poster Presentation, AGS Annual Meeting
2013 NewYork-Presbyterian / Weill Cornell Alumni Council Distinguished House Staff Award
2013 NewYork-Presbyterian / Columbia Resident / Employee of the Month, September 2013
2014 Best Geriatric Emergency Medicine Resident Abstract at SAEM Annual Meeting
2015 Best Geriatric Emergency Medicine Trainee Abstract at Annual Meeting
C. Contributions to Science

1. Exploring resident-to-resident elder mistreatment (RREM) in nursing homes
   a. Rosen T, Pillemer K, Lachs M. Resident-to-resident aggression in long-term care facilities: An
      aggression in long-term care facilities: insights from focus groups of nursing home residents and staff. J
   c. Rosen T, Lachs MS, Pillemer K. Sexual aggression between residents in nursing homes: literature
   d. Rosen T, Lachs MS, Teresi J, Eimicke J, Van Haitsma K, Pillemer K. Staff-reported strategies for
      prevention and management of resident-to-resident elder mistreatment in long-term care facilities. J

2. Preliminary work identifying injury patterns, physical findings, and forensic biomarkers associated with
   physical elder abuse
   a. Rosen T, Bloemen EM, LoFaso VM, Clark S, Flomenbaum NE, Lachs MS. Emergency Department
      presentations for injuries in older adults independently known to be victims of elder abuse. J Emerg
   c. Rosen T, Bloemen EM, Harpe J, Sanchez AM, Mennitt KW, MCarthy TJ, Nicola R, Murphy K, LoFaso
      VM, Flomenbaum N, Lachs MS. Radiologists’ training, experience, and attitudes about elder abuse
   d. Rosen T, Hargarten S, Floemenbaum N, Platts-Mills TF. Identifying elder abuse in the emergency

3. Development of a novel injury classification system and a photography protocol, methodologic advances
   that may be useful for future injury research
   b. Bloemen EM, Rosen T, Schiroo JC, Clark S, Mulcare MR, Stern ME, Mysliwie R, Flomenbaum NE,
      Lachs MS, Hargarten S. Photographing Injuries in the Acute Care Setting: Development and Evaluation

Complete List of Published Work in MyBibliography:

D. Research Support

Ongoing Research Support
K76 AG054866-01, NIH / NIA, Rosen (PI) 9/2016-5/2021
Identifying Injury Patterns Diagnostic of Physical Elder Abuse

Change AGEnts Grant, John A. Hartford Foundation, Rosen (PI) 1/2016-12/2016
Developing the Vulnerable Elder Protection Team: An Emergency Department-Based Multi-Disciplinary
Intervention to Improve Care for Potential Victims of Elder Abuse and Neglect

Department of Justice, Mosqueda (PI) (Rosen PI of sub-award) 4/2016-3/2017
Practical Tool for Medical Practitioners when Examining an Elder who Might have been Abused

R03 AG048109-01 GEMSSTAR, NIH / NIA, Rosen (PI) 9/2014-5/2017
Improving Recognition of Elder Abuse through Analysis of Highly Adjudicated Cases

Dennis W. Jahnigen Career Development Award

Completed Research Support
Resident-to-Resident Aggression in Long-Term Care Facilities
NAME: Smith, Phillip

eRA COMMONS USER NAME (agency login): ppsmith

POSITION TITLE: Associate Professor of Surgery

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

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<td>Kenyon College, Gambier, Ohio</td>
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<td>Chemistry</td>
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<tr>
<td>University of Cincinnati College of Medicine, Cincinnati, Ohio</td>
<td>MD</td>
<td>06/1984</td>
<td>medicine</td>
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<tr>
<td>University of Cincinnati Hospital, Cincinnati, Ohio</td>
<td>Resident</td>
<td>06/1988</td>
<td>Obstetrics and Gynecology</td>
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<td>Baylor College of Medicine, Houston, TX</td>
<td>Fellow</td>
<td>06/2005</td>
<td>Urogynecology</td>
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<tr>
<td>Baylor College of Medicine, Houston, TX</td>
<td>Fellow</td>
<td>06/2007</td>
<td>Female Urology and Voiding Dysfunction</td>
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<tr>
<td>NIA, Bethesda, MD</td>
<td>Other training</td>
<td>08/2014</td>
<td>Butler-Williams Summer Scholar</td>
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A. Personal Statement

Our work, in the context of emerging evidence about brain control over lower urinary tract function, has led me to postulate that urinary symptoms and dysfunctions should not be viewed as bladder organ failures, rather as systemic homeostatic control failures. This is of particular importance as resilience diminishes concurrent with increasing physiologic challenges in later life. Developing this idea and the health consequences requires definition of specific mechanisms by which the brain, the viscera, and the soma interact in response to environmental challenges. My career trajectory is to now dedicate my subsequent efforts to closure of the lab-clinical intellectual gap, as a key target in improving health and therapeutic models applicable to aging. With my background and specific interests, I am focused on mechanisms of central nervous system / lower urinary tract interactions as they provide integrative control over perceptions and function in response to the biologic challenges of an aging system.

B. Selected Positions and Honors

2009 - Assistant Professor of Surgery, University of Connecticut College of Medicine, Farmington, CT
2014 - Research Associate, Center on Aging, UConn Health, Farmington, CT
2011 - Associate Professor of Surgery, University of Connecticut College of Medicine, Farmington, CT
2012 - Member, International Consultation on Incontinence Research Society (ICIRS)
2012 - 2013 Member, Pad Weight Testing Working Group, International Continence Society
2014 - Member, External Experts Panel, NIDDK Lower Urinary Tract Dysfunction Research Network
2015 - Member, Underactive Bladder Working Group, International Continence Society

C. Contribution to Science / Selected Bibliography


Complete List of Published Work in My Bibliography:

D. Research Support

Current

HCN - Interstitial Cell Interactions in the Autonomic Control of Bladder Muscle
The Connecticut Institute for the Brain and Cognitive Sciences, Seed Grant ($24100)
Phillip P. Smith PI, Dan Mulkey co-PI, 3/16-2/17

Regulatory Mechanisms in a Homeostatic Model of Geriatric Voiding Problems and Incontinence
Paul B. Beeson Emerging Leaders Career Development Award in Aging (K76) (NIA/NIH) ($600000)
RFA AG-16-023

Pending

Regulatory Mechanisms in the Aging Bladder: Model Development
PA-15-051 R21, NIA, Underactive Bladder in Aging ($275000)
Phillip P. Smith PI

Completed Research Support

Mechanotransduction and Bladder Sensations: A Pilot Methodology Study
American Urogynecologic Society / Astellas Research Award ($30000)
Phillip P. Smith MD, PI

Urethral sensory contributions to lower urinary tract function in old age
Dennis W. Jahnigen Career Development Award, John Hartford Foundation, American Geriatrics Society
Phillip P. Smith MD, PI; George Kuchel MD primary mentor
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

A. Personal Statement

I did my MD-PhD at Columbia University, where my PhD thesis concerned computational modeling of neural networks in primary visual cortex. I then completed my clinical training at Columbia, where I have obtained dual board certification in Anatomic and Neuropathology. I have subsequently performed post-doctoral work in the laboratory of Dr. Ottavio Arancio where I have investigated mechanisms of synaptic dysfunction in Alzheimer’s disease. My current research focus is on the intersection of systems biology and neurodegenerative disease. Specifically, ongoing work in my laboratory is focusing on computational analysis of DNA methylation and RNA expression data from Alzheimer’s disease brain tissue, with the goal of identifying master regulators of gene dysfunction in AD that contribute to synaptic dysfunction. We have identified several putative master regulators of synaptic dysfunction, and we are currently characterizing associated gene regulatory networks.

B. Positions and Honors

Positions and Employment

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<tr>
<td>2010-2011</td>
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<td>and Cell Biology, New York – Presbyterian Hospital, Columbia University</td>
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<tr>
<td>2011-</td>
<td>Assistant Professor and Attending in the Division of Neuropathology, Department of Pathology</td>
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<td>and Cell Biology, New York – Presbyterian Hospital, Columbia University</td>
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Honors and Awards

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<td>2011-2014</td>
<td>Gerstner Scholar, Columbia University, NY NY</td>
</tr>
<tr>
<td>2014</td>
<td>Margaret M. Cahn Research Award (Alzheimer’s Association)</td>
</tr>
<tr>
<td>2015</td>
<td>NYC Alzheimer’s Association Junior Committee Outstanding Achievement Award</td>
</tr>
</tbody>
</table>

C. Selected Peer-reviewed Publications (out of 21)


Jia Luo, Sue H. Lee, Lawren VandeVrede, Zhihui Qin, Manel Ben Aissa, John Larson, Andrew F. Teich, Ottavio Arancio, Yohan D’Souza, Ahmed Elharram, Kevin Koster, Leon M. Tai, Mary Jo LaDu, Brian M. Bennett and Gregory R. J. Thatcher. A multifunctional therapeutic approach to disease
modification in multiple familial mouse models and a novel sporadic model of Alzheimer’s disease. 

**Molecular Neurodegeneration**, 2016 Apr 29;11:35.


**Teich AF** and Qian N. V1 orientation plasticity is explained by broadly tuned feedforward inputs and intracortical sharpening. *Visual Neuroscience*. 27: 57-73, 2010.


**D. Research Support**

**Ongoing Research Support**

1K76AG054868-01 Teich (PI) 09/30/2016 – 09/29/2019

NIH-NIA

Title: An integrative analysis of DNA methylation, transcriptomic changes, and cognitive dysfunction in Alzheimer’s disease

This grant funds my training as a clinician-scientist, and will support protected time for my professional development. My scientific proposal for this award involves investigating the relationship between gene expression and DNA methylation in several different collections of Alzheimer’s disease brain tissue that I have carefully archived.

NIRG-16-396417 Teich (PI) 06/01/2016 – 05/30/2018

Alzheimer’s Association

Title: A Cross-Species Study of DNA Methylation in Alzheimer's Disease Dementia

This grant funds a study of DNA methylation in a mouse model of Alzheimer’s disease. The grant seeks to address three questions: 1) Do genes normally methylated during a learning event have abnormal methylation in APP-PS1 mice?, 2) Which genes are differentially methylated during a learning event in APP-PS1 mice?, and 3) Which of the candidate genes in Aims 1 and 2 are relevant for cognition in human Alzheimer's Disease patients? This last aim involves a comparison of the data from Aims 1 and 2 with an ongoing study of DNA methylation in human autopsy tissue.
BIOGRAPHICAL SKETCH

NAME
Caterino, Jeffrey M., MD, MPH

POSITION TITLE
Associate Professor of Emergency Medicine and Internal Medicine
Vice Chair for Research, Emergency Medicine

eRA COMMONS USER NAME
jcaterino

INSTITUTION AND LOCATION
DEGREE
FIELD OF STUDY
(year(s))

Dartmouth College, Hanover, NH
B.A.
History
1995

The Pennsylvania State University College of Medicine, Hershey, PA
M.D.
Medicine
1999

Allegheny General Hospital, Pittsburgh, PA
Residency
Combined Emergency/Internal Medicine
1999-2004

The Ohio State University College of Public Health, Columbus, OH
MPH
Clinical Translational Sciences
2011

B. POSITIONS AND HONORS

Positions and Employment
1999-2004 Resident & Chief Resident, Departments of Emergency Medicine and Internal Medicine, Allegheny General Hospital, Pittsburgh, PA

2004-2012 Assistant Professor, Departments of Emergency Medicine and Internal Medicine, The Ohio State University, Columbus, OH.

2012-
Associate Professor with Tenure, Departments of Emergency Medicine and Internal Medicine, The Ohio State University, Columbus, OH.

2015-
Vice Chair of Research, OSU Department of Emergency Medicine

Other Experience and Professional Memberships
2006-2008 Ohio Department of Public Safety, Trauma Committee, Geriatric Trauma Triage Workgroup

2012-2013 Chair, Academy of Geriatric Emergency Medicine, Society for Academic Emergency Medicine

2012-2013 Member, Council of Academy Chairs, Society for Academic Emergency Medicine

2012-2016 Chair, Ohio State University Wexner Medical Center Evidence Based Practice Committee

2012-
Member, Emergency Medicine Network (EMNet) Steering Committee

2014 Institute for Healthcare Improvement (IHI), Patient Safety Executive Development Course,

2015-
Co-chair, NCI-sponsored, Comprehensive Oncologic Emergencies Research Network

2016-
Associate Editor, Academic Emergency Medicine

Honors
2007,-11,16 Faculty Researcher of the Year. Ohio State University Department of Emergency Medicine

2009 Fellow, American College of Emergency Physicians

2011, -12,-14 Academic Emergency Medicine, Outstanding Peer Reviewer Award

C. SELECTED PEER-REVIEWED PUBLICATIONS - Sample


D. RESEARCH SUPPORT - sample

R01 AG050801 Caterino(PI)  4/01/16-3/30/21
NIH/NIA: Urine antimicrobial proteins in older adults: aging, infection, & innate immunity
The major goal is to identify the role of urinary antimicrobial peptides in diagnosing UTI in older adults and to develop a clinical decision rule for UTI in this population.
Role: PI

R01 MH107452 Marcus&Olfson (co-PIs)  4/01/16-3/30/20
NIH/NIMH: Improving the Emergency Department Management of Deliberate Self Harm
The major goal is to identify ED characteristics which predict improved outcomes in ED patients with deliberate self-harm through use of claims data.
Role: Role: Site Principal Investigator

R01 MH106726-01 Boudreaux(PI)  6/01/15-2/28/17
NIH/NIMH: ED-SAFE 2: Translating Safety Planning into Practice
The major goals are to identify sustainability of universal suicide screening in the ED, the impact of personalized safety planning for suicidal ED patients, and the sustainability of the safety planning intervention.
Role: Site Principal Investigator

U10NS080368 Torbey (PI)  09/01/12-08/30/17
NIH/NINDS “Neurological Emergencies Treatment Trials (NETT)” The goal of this network is to conduct large simple trials to reduce the burden of very acute injuries and illnesses affecting the brain, spinal cord, and peripheral nervous system.
Role: Co-investigator

R01 HL111033 Sun (PI)  4/1/14-3/30/18
Improving Syncope Risk Stratification in Older Adults
The major goal is to develop and validate a syncope risk stratification decision support instrument.
Role: Site Principal Investigator

1U01CE002175 Shah(PI)  9/30/12-9/29/15
CDC: Field Triage of Older Adults Who Experience Traumatic Brain Injury
The goal of this study is to develop specific triage mechanisms for older adults with traumatic brain injury.
Role: Consultant

1K23AG038351-01 Caterino (PI)  10/01/10-5/30/15
NIA/NIH “Expanding antimicrobial stewardship for long term care facility patients: implementation in novel clinical settings using information technology.”
The goals of this study are to validate definitions of acute infection in elder ED patients from long term care facilities and to develop an information technology decision support tool to improve empiric antibiotic prescribing for these patients.
Role: PI

Dennis W. Jahnigen Career Development Scholars Award Caterino (PI)  7/01/07-6/30/09
American Geriatrics Society/John A. Hartford Foundation.
“Predictors of Clinical Course in Infected ED Elders”
Project goals: To identify geriatric-specific predictors, including functional status, of adverse outcome in Emergency Department patients admitted with severe infections.
Role: PI
NAME: Huang, Alison Ju-tsu

eRA COMMONS USER NAME: HuangA

POSITION TITLE: Associate Professor of Medicine

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>Completion Date</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvard University</td>
<td>BA</td>
<td>06/1996</td>
<td>History &amp; Literature</td>
</tr>
<tr>
<td>Cambridge University</td>
<td>MPhil</td>
<td>06/1997</td>
<td>English Literature</td>
</tr>
<tr>
<td>University of California San Francisco</td>
<td>MD</td>
<td>06/2002</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of California San Francisco</td>
<td>MS</td>
<td>06/2008</td>
<td>Clinical Research</td>
</tr>
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</table>

A. PERSONAL STATEMENT

I am a general internist, clinical epidemiologist, and clinical trialist at the University of California San Francisco, where I lead a multidisciplinary research team in advancing scientific understanding and improving clinical management of aging-related genitourinary dysfunction in women. My research emphasizes the common physiologic mechanisms that underlie genitourinary symptoms and other clinical and geriatric conditions in middle-aged and older women, including sleep disorders, anxiety and depression, and cognitive and physical function decline. I have conducted multiple epidemiologic studies to identify predictors of the development, progression, and impact of urinary incontinence and other common urinary tract syndromes in middle-aged and older women of diverse backgrounds. I have also designed and/or led multiple randomized trials of behavioral and pharmacologic treatment strategies for lower urinary tract syndromes in middle-aged and older women, including an NIA-funded trial of a paced respiration intervention for overactive bladder syndrome in women, an NCCIH-funded trial of a group-based yoga therapy intervention for urinary incontinence in women, and the BRIDGES multicenter trial of a simplified diagnostic algorithm for initiating pharmacologic treatment for urgency-predominant incontinence in women. I have also developed and validated new patient-reported outcome measures of sexual function and menopausal genitourinary symptoms in older women. I am also active in teaching clinical research methods and skills to trainees at UCSF and other institutions, with a focus on clinical trial design and data and safety monitoring in research as well as publishing and presenting research.

B. POSITIONS AND HONORS

Employment and Positions

2007-2009  Assistant Adjunct Professor, UCSF Department of Medicine (Chair: Talmadge King, MD)
2009-2014  Assistant Professor in Residence, UCSF Department of Medicine (Chair: Talmadge King, MD)
2009-present  Director, Clinical Research Unit, UCSF Women’s Health Clinical Research Center
2014-present  Associate Professor in Residence, UCSF Department of Medicine (Chair: Robert Wachter, MD)
2014-present  Co-Director, Resident Research Training Program, UCSF Clinical & Translational Science Institute
2015-present  Mt. Zion Site Director, UCSF Primary Care Research Fellowship Program

Honors and Awards

2009  T. Franklin Williams Scholars Award in Aging Research from the Society of General Internal Medicine, Association of Chiefs of General Internal Medicine, & Atlantic Philanthropies
2010  American Geriatric Society/Merck New Investigator Award for research program on the impact of aging on women’s health
2011 Paul Beeson Patient-Oriented Career Development Award in Aging Research from the National Institute on Aging and American Federation of Aging Research
2014 American Geriatrics Society—Clinical Trials award

Professional Societies
2004-present Society of General Internal Medicine—Geriatric Task Force (2011-present); scientific abstract reviewer (2009-present); chair of women’s health scientific abstract committee (2014, 2016)
2013-present American Geriatrics Society—Steering Committee of Junior Research Faculty Group (2013-2014); scientific abstract and workshop reviewer (2014-present)

Government Service
2009 Office of Research on Women’s Health, NIH- Working group member for bladder and pelvic floor disorders for the “New Dimensions and Strategies for Women’s Health Research” conference
2011-present Longitudinal Assessment of Bariatric Surgery Workgroup - Women’s health advisory group member for NIH-sponsored cohort study of the long-term impact of bariatric surgery
2012, 2016 National Institute on Aging, NIH- Member of special emphasis review panels for clinical trials applications focused on treatment of menopausal symptoms
2016 National Institute on Diabetes, Digestive and Kidney Disorders, NIH- Member of special review panel for pilot and feasibility studies for urologic outcomes

C. CONTRIBUTIONS TO SCIENCE
1. As a clinical epidemiologist, I have advanced scientific understanding of the development, progression, and impact of urinary incontinence and other bladder syndromes that disproportionately affect older women. My research has examined the contribution of cognitive and physical function decline to the development of urinary incontinence in older community-dwelling women (reference a), critically evaluated the clinical significance of postvoid residual volume measurements in evaluation of lower urinary tract symptoms in postmenopausal women (reference b), identified demographic and clinical predictors of other urinary tract syndromes such as nocturia in middle-aged and older women (reference c), and evaluated the contribution of changes in body mass and contribution to risk of urinary incontinence in older women (reference d).


2. As a clinical trialist, I have designed, implemented, and interpreted data from multiple interventional studies addressing lower urinary tract syndromes in women. As co-principal investigator of the BRIDGES multicenter trial, I provided new evidence of the efficacy and safety of a simplified algorithm for initiating pharmaco logic treatment for urinary incontinence in ambulatory women (reference a). As principal investigator of the LILY randomized trial, I evaluated the feasibility, efficacy, and safety of a therapeutic yoga program for older women with urinary incontinence (reference b), leading to my current NCCIH-funded follow-up trial. Using data from the multicenter PRIDE and LABS-2 studies, I also provided new evidence to support the beneficial effects of a behavioral weight loss intervention (reference c) and bariatric surgery (reference d) in overweight and obese women suffering from urinary incontinence.


3. I have developed and validated several new patient-reported outcome measures to assess genitourinary health and functioning in middle-aged and older women. Drawing upon qualitative research on the impact of urogenital atrophy symptoms (reference a), I created a new structured-item questionnaire measure of the impact of postmenopausal urogenital symptoms on functioning and wellbeing, and validated its psychometric properties in women of diverse backgrounds (references b and c). This measure has since been translated into multiple other languages (Spanish, German, Italian, Persian) by outside investigators seeking to administer it in other cohorts. I have also contributed to the development and validation of a new structured-item questionnaire measure of sexual function in women with pelvic problems (reference d). This measure has been administered in observational and interventional studies both domestically and internationally.


4. Within the field of menopausal health, I have contributed to scientific understanding of risk factors for menopausal vasomotor symptoms and designed, conducted, and analyzed data from multiple clinical trials of behavioral and pharmacologic interventions for menopausal symptoms. My work has also demonstrated that hot flashes, which were once dismissed as a transient, benign phenomenon of the early menopausal transition, persist for decades after menopause in over 10% of women (reference a) and are a marker of menopausal bone loss in midlife women (reference b). As co-investigator and then principal investigator of the NIH-funded MaTURE randomized trial, I demonstrated that a behavioral slow-paced respiration intervention was associated with modest reductions in the frequency of hot flashes, but was less effective than a music-listening intervention in alleviating these symptoms in menopausal women (reference c). Using data from the PRIDE randomized trial of a behavioral weight loss intervention, I demonstrated that weight loss was associated with an over two-fold decrease in the severity and bothersomeness of hot flashes among overweight and obese menopausal women (reference d).


c) **Huang AJ**, Phillips S, Schembri M, Vittinghoff E, Grady D. Device-Guided Slow-Paced Respiration for Menopausal Hot Flushes: A Randomized Controlled Trial. *Obstetrics & Gynecology.* 2015
5. I have also evaluated the role of both endogenous and exogenous estrogens in the development, progression, and treatment of other estrogen-sensitive conditions in postmenopausal women, including osteoporosis, sexual dysfunction, breast cancer, and vaginal atrophy. I have demonstrated that the protective effects of low-dose estrogen therapy on postmenopausal skeletal health may be strongly influenced by women’s endogenous estrogen levels prior to treatment (ref a), that low-dose estrogen therapy is associated with improvements in vaginal dryness but not necessarily other aspects of sexual function in older postmenopausal women (ref b), and that women with lower pre-treatment endogenous estrogen levels are at greater risk of breast cancer during estrogen plus progestin therapy (ref c).


Complete List of Published Work in My Bibliography:

D. RESEARCH SUPPORT

Ongoing

1. Award: 1R01AT007921 (PI: Huang) 04/15/14-03/31/18
   Agency: NIH/National Institute on Aging
   Title: A Behavioral Slow-Breathing Exercise Program for Female Overactive Bladder Syndrome
   Goals: To conduct a randomized controlled trial of a 12-week behavioral slow-paced respiration intervention on the severity, bothersomeness, and impact of overactive bladder syndrome in women, and to explore changes in anxiety and stress and autonomic nervous system control as mediators of treatment effects.
   Role: Principal investigator

2. 1R34AT008028 (PI: Huang) 09/01/2014-06/30/2017
   Agency: NIH/National Center on Complementary and Integrative Health
   Title: Yoga to Enhance Behavioral Management of Urinary Incontinence in Women
   Goals: To conduct a pilot randomized trial of a 12-week yoga therapy intervention designed to improving the frequency and quality-of-life outcomes of urinary incontinence in women.
   Role: Principal investigator

3. 1R01AG050588-01 (PI: Huang) 04/15/16-03/31/2020
   Agency: NIH/National Institute on Aging
   Title: Transdermal Nitroglycerin Therapy for Menopausal Hot Flashes
   Goals: To provide rigorous evidence of the efficacy and safety of continuous transdermal nitroglycerin therapy for hot flashes in peri- and postmenopausal women.
   Role: Principal investigator

4. Award: VVA Grant #10280727 01/01/14-06/30/17 (NCE)
   Agency: Northern American Menopause Society & Pfizer Independent Grants for Learning and Change
   Title: Promoting Evidence-Based Diagnosis and Management of Symptomatic Vulvovaginal Atrophy in
Primary Care Using an Electronic Patient Portal
Goals: To develop and refine an electronic portal-based intervention to promote systematic identification and evidence-based management of postmenopausal genitourinary symptoms in the primary care setting.
Role: Principal investigator

5. Award: No grant number on file (PI: Amy Hsu) 08/01/15-12/31/16
Agency: Tideswell Foundation
Title: Video-based urinary incontinence care guidance for caregivers of older adults with dementia
Goal: To develop and evaluate a series of brief educational videos on management of urinary incontinence, designed for informal caregivers of older adults with dementia, using input from focus groups of caregivers.
Role: Co-investigator

**Completed (selected)**

1. Award: Beeson 1K23AG038335 (PI: Huang) 09/01/11 - 08/31/15 (NCE)
Agency: NIH/National Institute on Aging
Title: A Multidimensional Approach to Urogenital Aging in Older Women
Goals: To develop a multidimensional model of urogenital aging in women that incorporates both tissue-based markers of estrogenicity and aging factors such as comorbidity, functional decline, and frailty.
Role: Principal investigator

2. Award: Investigator Initiated Research Grant GA0221IX (PI: Brown) 03/01/08 - 06/30/13
Agency: Pfizer, Inc.
Title: Bringing Simple Urge Incontinence Diagnosis and Treatment (BRIDGES)
Goals: To determine the efficacy and safety of a simplified algorithm for evaluation and treatment of women with urgency-type urinary incontinence using the 3 Incontinence Questions (3IQ)
Role: Co-principal investigator of the coordinating center

3. Award: 1R03AG035207 (PI: Huang) 09/30/10 - 9/29/14 (NCE)
Agency: National Institute on Aging
Title: The Impact of Vaginal Atrophy Symptoms on Quality of Life in Postmenopausal Women
Goals: To validate the psychometric properties of a new, structured-item questionnaire measure of the impact of vaginal atrophy symptoms on quality of life in postmenopausal women.
Role: Principal investigator

4. Award: R01 AT005491 (PI: Huang) 07/15/11 - 3/31/15
Agency: NIH/ National Center for Complementary and Alternative Medicine
Title: Slow-Paced Respiration for Treatment of Menopausal Symptoms
Goals: To conduct a randomized trial to determine the efficacy of device-guided slow-paced respiration to decrease the frequency of menopausal symptoms in women.
Role: 2011-2013 Co-investigator; 2013-present: Principal investigator

5. Award: T. Franklin Williams Scholars Award in Aging Research (PI: Huang)07/01/09 - 06/30/12
Agency: Society of General Internal Medicine, Association of Chiefs of General Internal Medicine, Atlantic Philanthropies
Title: The Impact of Urogenital Aging on Functioning and Wellbeing in Women
Goals: To develop a self-administered, structured-item questionnaire measure of the impact of urogenital atrophy symptoms on functioning and wellbeing in older women
Role: Principal investigator

5. Award: GA9001U6 Overactive Bladder-LUTS Grant (PI: Huang) 07/01/08 - 12/31/10
Agency: Investigator Initiated Research Grant: Pfizer, Inc.
Title: The Role of Vaginal Microbial Flora Alterations in the Development and Natural History of Overactive Bladder Symptoms in Postmenopausal Women
Goals: To examine the role of postmenopausal vaginal microbial flora alterations in the development and progression of overactive bladder symptoms in women
Role: Principal investigator
NAME: Keith A. Vossel, M.D., M.Sc.

eRA COMMONS USER NAME (credential, e.g., agency login): KVOSSEL

POSITION TITLE: Assistant Professor of Neurology, Staff Scientist

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

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<td>University of Tennessee</td>
<td>B.S.</td>
<td>12/1995</td>
<td>Engineering Sci. &amp; Mechanics</td>
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<tr>
<td>Univ. of Tennessee &amp; Univ of Memphis</td>
<td>M.Sc., thesis</td>
<td>12/1998</td>
<td>Biomedical Engineering</td>
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<td>University of Tennessee</td>
<td>M.D.</td>
<td>05/2003</td>
<td>Medicine</td>
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<td>Harvard–Brigham and Women’s Hospital</td>
<td>Internship</td>
<td>06/2004</td>
<td>Internal Medicine</td>
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<tr>
<td>Harvard–Massachusetts General Hospital &amp; Brigham and Women’s Hospital</td>
<td>Residency</td>
<td>06/2007</td>
<td>Neurology</td>
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<tr>
<td>University of California, San Francisco</td>
<td>Fellowship</td>
<td>06/2009</td>
<td>Behavioral Neurology</td>
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<tr>
<td>Gladstone Institute of Neurological Disease</td>
<td>Fellowship</td>
<td>06/2010</td>
<td>Neurodegeneration</td>
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A. Personal Statement
My research focuses on mechanisms, biomarkers, and novel treatment approaches for neural network hyperexcitability in Alzheimer’s disease (AD). I have demonstrated that seizures and silent epileptiform activity are more common in AD than previously recognized and are strongly associated with accelerated cognitive decline. I lead a phase 2a clinical trial of the antiepileptic drug (AED) levetiracetam to treat AD-associated network hyperexcitability. As part of this investigation, we are developing neurophysiological biomarkers to assess pharmacodynamics of AEDs and related strategies. My laboratory investigation concentrates on mechanisms of convergence between tau and amyloid-β (Aβ), which are linked to aberrant neuronal activity in AD. Using axonal transport and excitotoxicity models, I have discovered that tau protein-protein interactions, involving regions outside of tau’s microtubule-binding domain, are critical for Aβ-dependent neurotoxicity and excitotoxicity. These regions on tau and their influence on cell signaling are the focus of current studies using tau-mutant knock-in models that I have created. The goal is to discover therapies that target novel aspects of tau in AD pathobiology and counter its impact on network hyperexcitability in AD and related disorders.

B. Positions and Honors

Positions and Employment
2003–2004 Intern, Brigham and Women’s Hospital Internal Medicine Residency, Boston, MA
2004–2007 Resident and Chief Resident in Neurology, Massachusetts General Hospital and Brigham and Women’s Hospital, Harvard Neurology Residency Program, Boston, MA
2007–2009 Clinical Fellow in Behavioral Neurology, Memory and Aging Center, UCSF
2008–2010 Postdoctoral Fellow, Gladstone Institute of Neurological Disease, San Francisco, CA
2009–2011 Clinical Instructor, UCSF, Department of Neurology
2010–2011 Research Scientist, Gladstone Institute of Neurological Disease
2011– Assistant Professor of Neurology, UCSF
2011– Staff Scientist, Gladstone Institute of Neurological Disease

Honors
1998 J. William Fielding Award, Cervical Spine Research Society
C. Contribution to Science

1. **Treatment approaches for network hyperexcitability in AD and related disorders.** In an observational study, we found that epileptic activity is more prevalent in the early stages of AD than previously recognized, and it often escapes detection because it is nonconvulsive or subclinical in nature (Vossel et al. JAMA Neurology 2013). In a prospective study using the combination of overnight long-term monitoring with video-EEG (LTM-EEG) and magnetoencephalography with simultaneous EEG (M/EEG), we detected subclinical epileptiform activity in 42% of AD patients (p = 0.02 vs. controls), compared to previous reports of 2% based on routine awake EEGs. While the impact of this activity on cognitive functions in AD was previously unknown, we found that it associates with accelerated cognitive decline (Vossel et al. Annals of Neurology 2016). Our results highlight similarities between AD and transgenic animal models of the disease, in which chronic epileptiform activity mediates synaptic and cognitive impairments. The therapeutic implications of our findings are far reaching given the large proportion of AD patients who could potentially benefit from antiepileptic treatments. Guided by these discoveries, I initiated a phase 2a clinical trial of levetiracetam to treat AD-associated network hyperexcitability.

2. **Neurophysiological biomarkers in neurodegenerative disease.** I have developed EEG and MEG biomarkers of network dysfunction in early stages of AD and related dementias. My group collaborated with Dr. Srikantan Nagarajan to conduct the first study of MEG-based functional connectivity, directly in brain, in AD. Using an unbiased, whole-brain approach, we identified regions in the brain where reduced alpha-band functional connectivity (i.e., regions where alpha rhythms were not well synchronized with the rest of the brain) predicted specific cognitive deficits (Ranasinghe et al. NeuroImage Clinical 2014).

3. **Mechanisms of tau in pathobiology of AD.** In initial studies, I showed that tau critically impairs axonal transport of mitochondria and TrkA receptors in the presence of Aβ, a co-pathogen in AD derived from the human amyloid precursor protein (Vossel et al. Science 2010). In a follow up investigation, I discovered that tau enables Aβ-induced activation of glycogen synthase kinase 3β (GSK3β), a central kinase in AD pathogenesis and excitotoxicity (Vossel et al. JCB 2015). While the major focus on GSK3β has been on pathogenic cascades in which it phosphorylates tau, my study reversed this notion by showing that tau, in turn, can regulate GSK3β in an upstream manner. This cell signaling function of tau is completely distinct from its traditional role as a microtubule-binding protein, and it represents an important new area of investigation.

4. **Influence of apolipoprotein E isoforms on AD and non-AD neuropathology.** During my clinical fellowship, I showed that the apolipoprotein E4 isoform (apoE4), a major genetic risk factor for AD, enhances brain atrophy in disease-specific regions in both FTD and AD (Agosta and Vossel et al. PNAS 2009). This work supported Aβ-independent influences of apoE on neuropathology. In follow up investigation, I found that apoE4 enhances the production of toxic apoE fragments within diseased brain regions in FTD and forms protein complexes with the FTD-associated disease protein TDP-43 (Vossel et al. Neurocase 2013).

Complete List of Published Work in My Bibliography:
A native of Scotland, Dr. Barr's undergraduate and doctoral degrees on psychology were obtained from the University of Oxford, England. He completed postdoctoral work at the University of Pennsylvania before joining the faculty of Ball State University in Indiana in the Department of Psychological Sciences. He is married with one son.

After some funding from the National Institute on Aging to support research on attention and aging, Dr. Barr joined the Institute in 1987 and became a program administrator in the Behavioral and Social Research Program (now Division of Behavioral and Social Research). He was responsible for a program on cognitive functioning and aging. During that time he helped to develop the Institute's initiative on human factors, worked as the founding secretary of the Committee on Safety and Mobility of Older Drivers of the Transportation Research Board (part of the National Academy of Sciences) to develop research on older drivers; and helped both to establish the NIA Roybal Centers of Research on Applied Gerontology and to develop the Institute's initiative examining cognitive interventions to improve functioning in older adults (ACTIVE). During an interval as Acting Assistant Director for Special Populations (1995-1996) Dr. Barr developed the Resource Centers for Minority Aging Research initiative.

From 1994 to 2006 he was Deputy Head of the Division of Extramural Activities - contributing to policy development and coordination at the NIA - and the NIA Training Officer. In this latter capacity he had particular responsibility for overseeing training initiatives, for anticipating the need for new kinds of training and for working with the National Institutes of Health in shaping overall research training policy. During this time he developed the research dissertation (R36) program aimed at increasing the number of students from underrepresented backgrounds who obtain research doctoral degrees. He has also overseen and helped to shape substantial growth in the career development awards program at NIA and has played a key role in establishing public-private partnerships to pursue career development and training initiatives. He helped to develop the joint Beeson career development initiative (a collaboration between NIA and a number of foundations) to continue this important program and was more recently involved in developing the GEMMSTAR (R03) program for early career specialty-trained physicians.

In April 2006, Dr. Barr became Acting Director of the Division of Extramural Activities, NIA and was appointed Director of the Division in June 2007. Since that time he has worked at the NIH level to help shape NIH’s policies towards new and early stage investigators. He was centrally involved in managing NIA’s response to the American Recovery and Reinvestment Act of 2009. His leadership role at NIA includes managing the National Advisory Council on Aging and advising the Director, NIA on all extramural activities of the Institute.

More recently he was founding co-editor of the NIA blog and continues in that capacity. He reports enjoying both editing and writing these blogs.
Janet Bickel is a nationally recognized expert in faculty, career and leadership development with over 40 years of experience in academic medicine and science. Over 125 academic health centers and 35 professional societies have invited her presentations and consultations. In addition to a wide-range of individual coaching clients, organizational clients have included United American Nurses, US Department of Commerce, and American Association for Cancer Research. She is an Adjunct Assistant Professor of Medical Education at George Washington University School of Health Sciences.

During the 25 years prior to creating her own business, Janet held positions of increasing national leadership at the Association of American Medical Colleges, including Associate Vice President for Medical School Affairs. She established an influential Office of Women in Medicine, including a series of leadership development programs that have stimulated the careers of thousands of women physicians and scientists. She also led AAMC’s first programs in faculty affairs and in student professionalism. Janet continues to publish broadly, with over 65 peer-reviewed articles and two books.

Between 1972-76, Janet served as founding admissions, financial aid and student affairs officer at the new Brown University Medical School. She holds a M.A. in sociology from Brown University and an A.B. in English from University of Missouri-Columbia.

Janet is certified to administer the Myers-Briggs Type Indicator, the Center for Creative Leadership’s multi-rater feedback instruments, and the Emotional Intelligence In Relationships profile. She has completed Relationship Centered Health Care’s fellowships (Courage to Lead and Leading Organizations to Health) and NTL’s Human Interaction Laboratory on Transforming Interpersonal Relationships. She has participated in Authentic Leadership in Action’s Shambhala Summer Institute and studied yoga and meditation at Kripalu.

Leadership and Career Development Coach
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Dr. E. Wesley Ely, MD, MPH is a professor of medicine at Vanderbilt University School of Medicine and Associate Director of Aging Research for the TN-Valley VA GRECC, with subspecialty training in Pulmonary and Critical Care Medicine and a particular passion for care of older critically ill patients. He is the Associate Director of Aging Research for the VA Tennessee Valley Geriatric Research and Education Clinical Center (GRECC). His research has focused on improving the care and outcomes of critically ill patients with sepsis and respiratory failure, with special emphasis on the problems facing older patients in the ICU (e.g., weaning from mechanical ventilation, delirium and cognitive impairment in the ICU, neuropsychological deficits post ICU care, and quality of death in the ICU). Dr. Ely has over 300 peer reviewed articles. As the founder of the Vanderbilt ICU Delirium and Cognitive Impairment Study Group, he currently serves as the principal investigator for the Coordinating Center's ongoing clinical trials in sedation and delirium and post-ICU cognitive impairment. Dr. Ely designs and leads a team of investigators in conducting both large cohort studies and randomized controlled clinical trials seeking both better understanding and management of critically ill patients in the ICU. He has recently had other reflective writing publications in the Wall Street Journal and in medical journals including JAMA and the Annals of Internal Medicine. He has been awarded membership into the Alpha Omega Alpha (AOA) medical honor society, the American Society of Clinical Investigation (ASCI), the Association of American Physicians (AAP).
Stephen B. Kritchevsky, PhD is a Professor of Medicine and Translational Science and Director of the Sticht Center for Healthy Aging and Alzheimer’s Prevention at Wake Forest School of Medicine. Dr. Kritchevsky received his BA in Geography from the University of Chicago, and his Master’s and Doctorate in Epidemiology from the University of North Carolina, Chapel Hill. He spent 14 years on the faculty of the University of Tennessee Health Sciences Center in Memphis, TN where he led the Memphis Field Center of the Health Aging and Body Composition (Health ABC) Study. He moved to Wake Forest School of Medicine in 2003 where he led the Wake Forest Claude D. Pepper Older Americans Independence Center (P30 AG 21332) since 2006. He is Associate Dean for Research Development and PI of the Clinical and Translational Science Institute’s early career mentored faculty development program.

Dr. Kritchevsky is an internationally known expert on nutritional influences that affect trajectories of health and disability in older adults including vitamins, protein, energy balance, exercise and obesity. He is the Editor-in-Chief of the Journal of Gerontology: Medical Sciences, and serves on a number of advisory and review panels nationally and internationally. He has authored or co-authored over 400 research publications and was named a Thomson-Reuters Highly Cited Researcher in 2014 and 2015. He is on the executive committee of the Targeting Aging with Metformin study group which seeks to determine whether targeting age-related pathways can slow the onset of age-related disease.
Harlan Krumholz is a cardiologist, health care scientist, and health care improvement expert at Yale University where he is the Harold H. Hines, Jr. Professor of Medicine. He is Director of the Yale-New Haven Hospital Center for Outcomes Research and Evaluation and Co-Director of the Robert Wood Johnson Foundation Clinical Scholars Program at Yale. He has led research and initiatives to improve the quality and outcomes of clinical decisions and health care delivery, reduce disparities, enable transparency in practice and research, and avoid wasteful practices. His team is guiding federal efforts to measure and promote health care value. He began the Yale Open Data Access Project to promote data sharing and open science. He is leading efforts in China to create a national learning health system. He founded Hugo, a mobile app to empower people with their health-related data, promoting the possibility of a consumer-mediated information platform. He is a founding member of the Board of Governors of the Patient-Centered Outcomes Research Institute. Dr. Krumholz received a BS from Yale, an MD from Harvard Medical School, and a Masters in Health Policy and Management from the Harvard University School of Public Health. He was in the 1999 class of Beeson Scholars.
Jean S. Kutner, MD, MSPH  
Professor of Medicine and Associate Dean for Clinical Affairs, University of Colorado School of Medicine  
Chief Medical Officer, University of Colorado Hospital  

Dr. Kutner is a tenured Professor of Medicine in the Divisions of General Internal Medicine (GIM), Geriatric Medicine, and Health Care Policy and Research in the Department of Medicine at the University of Colorado School of Medicine (UC SOM). Dr. Kutner received her MD from the University of California San Francisco (UCSF) in 1991 and completed residency training in internal medicine at UCSF in 1994. Subsequently, she completed a NRSA primary care research fellowship, earning an MSPH degree with honors, and a fellowship in geriatric medicine at UC SOM (1994-1997). She is Board Certified in internal medicine, geriatric medicine and hospice and palliative medicine and cares for patients on the palliative care service and in general internal medicine clinic. Her research focuses on improving symptoms and quality of life for patients with serious illness and their family caregivers. Dr. Kutner is Co-Chair of the NIH-funded Palliative Care Research Cooperative Group (PCRC). She was a member of the Institute of Medicine (IOM) Transforming End of Life Care Committee and is a past-president of the American Academy of Hospice and Palliative Medicine (AAHPM). Dr. Kutner served as the Head of the University of Colorado Division of General Internal Medicine from 2002 until 2014. Dr. Kutner became the inaugural Chief Medical Officer of University of Colorado Hospital and Associate Dean for Clinical Affairs, UC SOM in July 2014.
Dr. Newman is a Visiting Scientist at the Gladstone Institutes, and Assistant Professor in the Division of Geriatrics at UCSF. His research work is in the laboratory of Eric Verdin at Gladstone, studying the molecular details of how environmental cues like diet and fasting regulate the genes and pathways that in turn control aging. As a basic scientist and a practicing geriatrician, Dr. Newman hopes to translate what we are learning of these conserved pathways that control aging into therapies that will improve the lives and preserve the independence of older adults at risk for multiple chronic diseases and functional decline. Dr. Newman is also a staff physician at the San Francisco VA Medical Center, where his clinical work focuses on the care of hospitalized older veterans. Dr. Newman attends on the inpatient medicine service and the acute care of elders unit. He completed an MD/PhD at the University of Washington in Seattle, then residency training in Internal Medicine and a fellowship in Geriatrics at UCSF before joining the faculty in 2014. Dr. Newman is a 2014 Beeson Scholar from the National Institute on Aging and the American Federation of Aging Research.
S. Jay Olshansky, Ph.D.
Biographical Sketch

S. Jay Olshansky received his Ph.D. in Sociology at the University of Chicago in 1984. He is currently a Professor in the School of Public Health at the University of Illinois at Chicago and a Research Associate at the Center on Aging at the University of Chicago and at the London School of Hygiene and Tropical Medicine. The focus of his research to date has been on estimates of the upper limits to human longevity, exploring the health and public policy implications associated with individual and population aging, forecasts of the size, survival, and age structure of the population, pursuit of the scientific means to slow aging in people (The Longevity Dividend), and global implications of the re-emergence of infectious and parasitic diseases, and insurance linked securities. During the last twenty-five years, Dr. Olshansky has been working with colleagues in the biological sciences to develop the modern "biodemographic paradigm" of mortality – an effort to understand the biological nature of the survival and dying out processes of living organisms. Dr. Olshansky's work on biodemography has been funded by a Special Emphasis Research Career Award (SERCA) and Independent Scientist Award (ISA) from the National Institute on Aging – awards that were designed to permit him to obtain additional graduate-level training in the fields of evolutionary biology, molecular biology, genetics, epidemiology, population biology, anthropology and statistics. Dr. Olshansky is a member of the Board of Directors of the American Federation for Aging Research, he is an Associate Editor of the Journal of Gerontology: Biological Sciences and Biogerontology, he is on the editorial board of several other scientific journals, and is a member of the American Association for the Advancement of Science, the New York Academy of Sciences, and the Gerontological Society of America. Dr. Olshansky is also listed in Who's Who in Science and Engineering, Who's Who in American Education, Who's Who in Medicine and Healthcare, American Men & Women of Science, and Who's Who in America. He was an invited speaker at the December, 2002 President's Council on Bioethics, Fortune Magazine's 2004 Brainstorm meeting, the 2004 Nobel Conference devoted to the science of aging, the Institute of Medicine -- 2004, the 2005 UNESCO conference on Health and Longevity in Paris, the 2007 United Nations conference on Health and Aging, the 2007 World Ageing and Generations conference in Switzerland, the 2007 and 2011 Global Financial Services CEO Roundtables in Italy, the 2009 Horizon21 symposium on Insurance Linked Securities, the 2010 AO Foundation conference in Lisbon, the 2010 Techonomy conference, the 2011 Sci Foo camp, the Rethink Lecture at the World Ageing and Demographic Forum in St. Gallen Switzerland in 2012, and he has testified before the trustees of the Social Security Administration where his research has influenced forecasts of the nation's entitlement programs. Dr. Olshansky is the recipient of a 2005/2006 Senior Fulbright Award to lecture in France; he was an adviser to U.S. Preventive Medicine; he is a founding member of the HSBC Global Commission on Ageing and Retirement; he is a member of the MacArthur Foundation Research Network on an Aging Society; he was co-chair of the Council on an Ageing Society at the World Economic Forum; he is on the Program Advisory Group and Senior Associate at the International Longevity Center (US); he has been invited to lecture on aging throughout the world; and has participated in a number of international debates on the future of human health and longevity. Dr. Olshansky appears routinely in newspaper, magazine, and television stories about aging – a few notable examples include Barbara Walters, Charlie Rose, Dan Rather, Dr. Sanjay Gupta, 60 Minutes, Anderson Cooper, The O’Reilly Factor, Discovery Channel, New York Times, Washington Post, Scientific American, and National Public Radio. Dr. Olshansky is the first author of The Quest for Immortality: Science at the Frontiers of Aging (Norton, 2001).
Joseph S. Ross, MD, MHS, is an Associate Professor of Medicine (General Medicine) and of Public Health (Health Policy and Management), a member of the Center for Outcomes Research and Evaluation at the Yale-New Haven Hospital, and an Assistant Director of the Robert Wood Johnson Foundation’s Clinical Scholars program at Yale. He completed his undergraduate degrees in biological science: neuroscience and psychology at the University of Rochester and his medical degree at the Albert Einstein College of Medicine, Bronx, NY. After completing his post-graduate training in primary care internal medicine at Montefiore Medical Center in Bronx, NY, Dr. Ross was a fellow in the Robert Wood Johnson Foundation Clinical Scholars program at Yale University, earning a Master’s degree in health sciences research. Using health services research methods, Dr. Ross’s research focuses on examining factors which affect the use or delivery of recommended ambulatory care services for older adults and other vulnerable populations, evaluating the impact of state and federal policies on the delivery of appropriate and higher quality care, and issues related to pharmaceutical and medical device evidence development, postmarket surveillance, and clinical adoption. In addition, he collaborates with a multi-disciplinary team of investigators under contract for the Centers for Medicare and Medicaid Services to develop statistical models that are used to measure and publicly report hospital and ambulatory care clinical outcomes using administrative data. Dr. Ross has published more than 200 articles in peer-reviewed biomedical journals and is currently an Associate Editor at JAMA Internal Medicine.
Scott A. Small, MD

- Boris and Rose Katz Professor of Neurology (in the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, the Gertrude H. Sergievsky Center and in Radiology)
- Director, Alzheimer's Disease Research Center

Scott A. Small M.D. is the Director of the Alzheimer’s Disease Research Center at Columbia University, where he is the Boris and Rose Katz Professor of Neurology. He is appointed in the Departments of Neurology, Radiology, and Psychiatry.

With an expertise in Alzheimer’s disease and cognitive aging, Dr. Small’s research focuses on the hippocampus, a circuit in the brain targeted by these and other disorders, notably schizophrenia. He has pioneered the development and application of high-resolution functional MRI techniques that can pinpoint parts of the hippocampus most affected by aging and disease. His lab then uses this information to try to identify causes of these disorders. Over the years, his lab has used this ‘top-down’ approach to isolate pathogenic mechanisms related to Alzheimer’s disease, cognitive aging, and schizophrenia. More recently, his lab has used this insight for drug discovery and to develop novel therapeutic interventions, some of which are currently being tested in patients.

Dr. Small has co-authored over 120 articles and his neuroimaging and molecular work has led to 7 patents. Dr. Small is the recipient of numerous awards, including the Beeson Scholar Award in Aging Research from the American Federation on Aging, the McKnight Neuroscience of Brain Disorders Award, the Derek Denny-Brown Young Neurological Scholar Award from the American Neurological Association, and the Lamport Award for Excellence in Clinical Science Research from Columbia University.
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Suicide Prevention in Older Adults: Pilot Data for an Emergency Department Based Trial

Marian E. Betz, MD, MPH1; Tim Platts-Mills, MD, MSc2; Jeffrey Caterino, MD, MPH3; Christopher Carpenter, MD, MSc4; Ula Hwang, MD5; Maura Kennedy, MD, MPH6; Manish Shah7; Lauren Southerland3; Robert Schwartz, MD8

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8Division of Geriatric Medicine, Department of Medicine, University of Colorado School of Medicine

Background/Objectives: Depression and suicidal ideation and attempts (SI/SA) remain unfortunately common—and often difficult to identify—in older adults. A promising suicide prevention approach from primary care is to identify older adults with thwarted belongingness and perceived burdensomeness (upstream risk factors for suicide) and refer them to appropriate interventions. In preparation for a trial testing this program in an emergency department (ED) setting, we sought to describe the social and psychological state of older ED patients.

Design: Confidential cross-sectional survey.

Setting: Two urban EDs located at tertiary care centers.

Participants: Convenience sample of community-dwelling older (≥65 years) ED patients who understood English and were medically and cognitively able to participate.

Measurements: Confidential survey, self-completed or read aloud by research staff. Measurement domains included social connections, symptoms of depression, need for help with activities of daily living, chronic pain that interferes with life, interest in resources or referrals from the ED for various services, patient- and provider-ratings of frailty categories, and potential interest in participating in a future trial.

Results: To date, 96 older patients at 2 EDs have completed the survey; 47% were female, the median age was 71 years (interquartile range 68-76), and 66% wanted the survey read aloud by the research assistant. The majority (80%) reported going out of their homes on a regular basis, and 74% reported driving. However, 25% of respondents had responses suggesting depression (based on the Geriatric Depression Score); 40% screened positive for perceived burdensomeness and 22% for thwarted belongingness. When asked about which programs the ED should refer older patients to, the highest proportion identified transportation options (73%), followed by food assistance (69%), housing (61%), mental health resources (55%), volunteer opportunities (49%), and peer companionship programs (44%). Half of patients said they would be somewhat or very interested in participating in a related study.

Conclusion: In this convenience sample of older ED patients, many patients appeared to have risk factors for suicide and might benefit from interventions. Many expressed interest in referral to programs or future study participation.
Independent functioning is the most important factor in health-related quality of life and healthcare utilization. Hospitalization, particularly for critical illness, is a significant risk factor for new and long-lasting disabilities that are present in up to 75% of older Americans who survive critical illness. A better understanding of clinical risk factors and biological mechanisms of the disability process after critical illness is needed.

For decades, standard practice in intensive care units (ICUs) was to sedate and immobilize patients. Pilot randomized trials of early activity, beginning in the ICU, have garnered much enthusiasm despite the fact that their results are conflicting and inconclusive with regard to the effect of early activity on long-term disability and physical and cognitive functioning. Convincing data from larger, multi-center trials will be needed to resolve these conflicts and dictate appropriate clinical management.

In hospitalized older adults, low levels of activity are associated with short-term disability after discharge. The association between activity and longer-term disability has not been well studied. The pathways by which low activity may result in disability are also unclear. For example, delirium is common in ICU patients and its duration predicts both long-term disability and cognitive impairment. Activity and the disability process are potentially related via pathways that are in need of further study. A key step in building the next series of randomized trials, is to study the relationship of activity during critical illness (independent variable) with long-term disability (dependent variables) (Aim 1) and with long-term physical and cognitive function (dependent variables) (Aim 2).

Chronic inflammation and coagulopathy are associated with ADL disability, but whether these mechanisms—which are proven to cause acute organ dysfunction during critical illness—promote disability after critical illness is unknown. Acute inflammation and coagulopathy are implicated in the pathogenesis of delirium and ICU-acquired neuromuscular weakness, two important risk factors for disability in survivors of critical illness. Elevated markers of inflammation and coagulopathy persist even after clinical resolution of acute illness, a process that could be curtailed if early activity affects these pathways. This proposal will study the association between activity during critical illness (independent variable) and biomarkers of inflammation and coagulation (dependent variables) (Aim 3).

We therefore designed the MOSAIC observational study to evaluate the association between activity (measured more rigorously than in prior investigations) with disability, physical function, and cognitive function in survivors of critical illness and study underlying mechanisms of the disability process in those with critical illness, the majority of whom will be age 65 years old or older.

**Aim 1:** To test the hypothesis that greater activity during critical illness will be independently associated with lower prevalence, less severity and shorter duration of disability in activities of daily living and mobility at 3- and 12-month follow-up.

**Aim 2:** To test the hypothesis that greater activity during critical illness will be independently associated with better physical function and cognitive function at 3- and 12-month follow-up (Aim 2a) and determine whether these impairments mediate disability at 3- and 12-month follow-up (Aim 2b).

**Aim 3:** To test the hypothesis that greater activity during critical illness will be independently associated with lower levels of biomarkers of inflammation (Interleukin [IL]-6, IL-10, and C-reactive protein [CRP]) and coagulation (D-dimer) at hospital discharge (Aim 3a) and to determine the independent association between IL-6, IL-10, CRP and D-dimer and disability, physical and cognitive function at 3- and 12-month follow-up (Aim 3b).
Beyond 30 Days: Patient-Oriented Outcomes Among Older Adults After Emergency General Surgery

Authors: Cooper, Z1,2,3, Weissman, JS1,2,3, Lipsitz, SR2,3,5, Tulsky JA 3,6, Rosenthal, RA7, Mitchell SL3,4
1. Department of Surgery, Brigham and Women’s Hospital
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5. Department of Medicine, Brigham and Women’s Hospital
6. Department of Psychosocial Oncology and Palliative Care, Dana Farber Cancer Institute
7. Department of Surgery, Yale University School of Medicine

ABSTRACT:

**Background:** As an increasing number of patients require emergency general surgical (EGS) treatment for life-threatening conditions, such as small bowel obstruction and intestinal perforation, major reforms in practice and outcomes measurement have occurred to respond to this crisis in care. Compared to elective procedures, EGS procedures are associated with 5-fold greater 30-day mortality, 30% higher risk of complications, and longer lengths of stay. Approximately 40% of EGS patients are over 65 years old, and often have multiple comorbid illnesses, thus it is not surprising that their short-term outcomes are especially poor: in-hospital death rates range from 15-22%, 11-48% die within 30-days, complication rates approximate 37-50%, and over 50% are discharged to nursing homes (NHs). These poor outcomes, together with current demographic trends, underscore the importance of better understanding of the clinical course and care needs of older patients undergoing EGS. We hypothesize that older EGS patients experience high rates of poor health outcomes and have unmet palliative care needs in the year after surgery.

Prior nationwide studies of older EGS patients utilized data from the National Surgical Quality Improvement Project (NSQIP) or the Nationwide Inpatient Sample (NIS), which provide only in-hospital or 30-day outcomes. However, traditional surgical metrics focusing on 30-day complications and mortality rates do not address other key outcomes relevant to older patients such as functional and cognitive trajectories symptom burden, quality of life, health services utilization (e.g., re-hospitalization, nursing home admission, hospice) and end-of-life experiences. While prior research has demonstrated the benefits of palliative care among other patients with serious medical illnesses, very little work has been done to examine the palliative care needs of older surgical patients.

**Objectives:** The specific objective of this research is to identify opportunities to improve the care of older EGS patients by fully characterizing their clinical trajectories and care needs beyond 30-days after surgery.

**Methods:** This project will use multiple data sources and complementary methodologies including: 1) National Medicare Claims to obtain data about 12-month survival and healthcare utilization unavailable in NSQIP or NIS; 2) Primary prospective data from older EGS patients and their proxies to describe outcomes particularly relevant to older adults that are unavailable in Medicare Claims data; and 3) Qualitative analysis from semi-structured interviews with patients and proxies to obtain an in-depth understanding of their lived experience.
Processed EEG to Save Elderly Cognitive Reserve (PRESERVE) Save Elderly Cognitive Reserve (PRESERVE)

Stacie Deiner

Postoperative cognitive dysfunction has been described to occur in approximately 15% of elderly (>65 years old) surgical patients at 3 months after surgery and is associated with increased 5 year mortality. Intrinsic patient factors (preexisting cognitive impairment, cognitive reserve, burden of illness) have been demonstrated to be highly associated with cognitive decline after surgery. However, the issue of whether anesthetic technique can moderate the effects of surgery and illness remains unanswered. In this study we focus on whether depth of anesthesia as measured by processed electrical (EEG) activity (raw parameter of burst suppression, or processed number “depth”) will be associated with transient (several day) or longer term (3 months and ultimately 1 year) cognitive impairment. In specific we will take a detailed look at which domains of cognition (executive function vs. memory) are affected by anesthesia.

In this abstract we present an interim analysis of 45/175 major noncardiac surgery patients who have completed 3 month follow up. The median age is 72 years old, 50% are female, with 12 years of education. By 7 days postoperative 14/45 (31%) did not achieve cognitive recovery. At 3 months 8/45 (17.8%) patients worsened at Trails B and 5/45 (11%) Logical Memory Delayed. By 7 days 40% (18/45) patients were not recovered in ADLs, 17.8% (8/45) IADLs at 3 months. Patients in the top tertile of time in burst suppression appear to more often have had either an episode of delirium, short term cognitive impairment, and/or ADL disability. No trend can be seen with total time in deep states (by processed number) or mean/median Bispectral index value. At 3 months only one patient who did worse on Trails B was in the top tertile of BIS suppression. The rest were split between the middle and lowest tertiles. The patients who did worse on Logical Memory at 3 months were split between all 3 tertiles.

This data suggests that burst suppression is associated with poor short term recovery (7 days) in the elderly. By comparison, processed EEG values correlate poorly with cognitive or physical recovery, which is not surprising since the algorithms are not accurate for the elderly. Whether intraoperative burst suppression is truly associated with three month or one year outcomes (e.g. fewer patients with executive function decline) remains to be seen. Additional data and multivariable models are required to take into account patient baseline demographics and delineate whether burst suppression is a marker of anesthetic overdose or a marker of a vulnerable brain.
Mobility and Functional Impairments are Common One Week After Hospitalization for Acute Myocardial Infarction: Results from a Prospective Pilot Study

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\textbf{Key Words:} geriatrics, mobility, functional status, health status, myocardial infarction

\textbf{Background:} Hospitalization is associated with declines in mobility, function, and physical health among older persons. Little is known about the time course of recovery following hospital discharge.

\textbf{Objective:} To characterize recovery in mobility, functional status, and physical health between the pre-hospital period 1 month prior to hospitalization for acute myocardial infarction and the post-hospital period 1 week after hospital discharge.

\textbf{Methods:} In a prospective pilot study, we enrolled 26 patients \(\geq 75\) years-old hospitalized with acute myocardial infarction (AMI) participating in the SILVER-AMI study (R01HL115295) at Yale-New Haven Hospital. Information about patient demographic characteristics, chronic health conditions (Charlson comorbidity index), pre-hospital mobility (ability to walk ¼ mile or two to three blocks), pre-hospital functional status (ADLs/IADLs), and pre-hospital physical health (SF-12 Physical Health Component Summary Measure) was collected during the hospital stay. These assessments were repeated during a home visit targeted for one week after hospital discharge. Summary statistics were calculated using frequencies and percentages.

\textbf{Results:} We enrolled 26 patients, of whom 20 completed a home visit an average of nine days (range four to 20 days) after hospital discharge. Two patients died before completion of the home visit and four patients refused the visit. The average age of patients was 83.9 years, and the average Charlson comorbidity index score was 4.5. At one month prior to admission, 45\% of patients were unable to walk ¼ mile or two to three blocks. This proportion increased to 85\% one week after discharge. Similarly, at one month prior to admission, 5\% of patients needed help to bathe, dress, get in and out of a chair, and walk around the home. These proportions increased to 35\%, 35\%, 25\%, and 20\%, respectively, one week after discharge. The SF-12 Physical Health Component Summary Measure score was 35.9 one month prior to admission and 33.5 one week after discharge.

\textbf{Conclusions:} Pilot results suggest that one week after hospitalization for acute myocardial infarction, older persons continue to have significant deficits in mobility and functional status compared to pre-hospitalization levels. Further work is needed to characterize the timing and extent of recovery in mobility and functional status after hospitalization and identify hospital and outpatient factors that are most important to promoting timely return to baseline health.

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\textbf{Disclosures:} Dr. Dharmarajan works under contact with the Centers for Medicare & Medicaid Services to develop and maintain performance measures, is a member of the Standing Cardiovascular Committee of the National Quality Forum, and is a consultant and scientific advisory board member for Clover Health. All other authors declare no potential conflicts of interest.
The Impact of Older Age on Obstructive Sleep Apnea Treatment Preferences Weights Elicited from a Discrete Choice Experiment

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Introduction: Treatment options for obstructive sleep apnea (OSA) include positive airway pressure (PAP; first-line), oral appliance, and surgical therapies, as well as no treatment. Ideally, when patients make decisions about treatment, they examine and weigh treatment risks and benefits. The weights that patients assign to risks and benefits of treatment versus no treatment may also influence adherence to therapy. We examined the impact of age on the relative weights placed on various aspects (“attributes”) of treatment options for OSA.

Methods: In an unlabeled discrete choice experiment that used an orthogonal fractional factorial design, 30 individuals aged > 65 years were provided a scenario in which they were newly-diagnosed with a sleep condition resembling OSA and needed to decide which treatment to begin. They were informed that treatments had 4 attributes: minor and major side effects and long-term and short-term benefits (definitions for the attributes were provided). Participants completed a warm-up exercise in which they rated their preference for each treatment in isolation. Then, they viewed 9 sets of treatments and for each set, chose between two treatments that differed in attributes or chose “no treatment,” which had the same combination of attributes across the 9 sets. Participants also completed a brief demographic questionnaire. Multilevel mixed-effects logistic regression models were used to identify the relative importance of treatment attributes and to examine the effect of age on preference weights. Margins plots were generated to compare choices between the oldest age quartile versus other age quartiles.

Results: The mean age was 71 years (range: 65-91), and 27 (90%) participants had OSA. Odds ratios for the attributes were: 1.28 (1.10, 1.49, p=.001) for minor side effects, 1.33 (1.13, 1.56, p=.001) for major side effects, 2.64 (2.29, 3.06, p<.001) for long-term benefits, and 1.54 (1.34, 1.78, p<.001) for short-term benefits, suggesting that participants weighed long-term benefits most strongly. Age significantly impacted the weights for the 4 attributes (interaction terms for age*each attribute p values <.001). Compared to the younger three quartiles, participants in the oldest quartile (>71 years) were more likely to choose treatments with the most favorable minor (fig C) and major (fig D) side effect profiles than younger participants and were less likely to choose treatments with the most favorable long-term (fig A) and short-term (fig B) benefit profiles.

Discussion: In this discrete choice experiment, we found that participant age significantly impacts preference weights for long-term and short-term benefits and major and minor side effects when choosing an OSA treatment. Older participants are more likely to choose treatments with the most favorable major and minor side effects and less likely to choose OSA treatments with the most favorable long-term and short-term benefits. These results have potential implications for interventions designed to improve acceptance and adherence to OSA therapy among older adults.

Key Words: obstructive sleep apnea, treatment, discrete choice experiment

Additional funding: In addition to Beeson Award funding, this work received statistical support from CTSI grant UL1TR000124UCLA (Clinical and Translational Science Institute)
Subjective And Objective Cognitive Function Among Older Adults With Remote Traumatic Brain Injury: A Population Based Study

Raquel C. Gardner, Kenneth M. Langa, and Kristine Yaffe

**Background:** Traumatic brain injury (TBI) is extremely common across the lifespan and is an established risk factor for dementia. The cognitive profile of the large and growing population of older adults with prior TBI who do not have a diagnosis of dementia, however, has not been well described. Our aim was to describe the cognitive profile associated with prior TBI exposure among community-dwelling older adults without dementia – an understudied but potentially vulnerable population.

**Methods:** We studied 984 community-dwelling older adults without dementia who had been randomly selected from respondents to the 2014 wave of the Health and Retirement Study to participate in a comprehensive TBI survey and who either reported no prior TBI (n = 737) or prior symptomatic TBI resulting in treatment in a hospital (n=247). Mean time since first TBI was 38±19 years. Outcomes assessed included measures of global cognitive function, verbal episodic memory, semantic fluency, and calculations as well as a measure of subjective memory (“how would you rate your memory at the present time?”). We compared outcomes across TBI groups using regression models adjusting for demographics, medical comorbidities, and depression. Sensitivity analyses were performed stratified by TBI severity (TBI +/- loss of consciousness).

**Results:** Respondents with TBI were younger (mean age 64±10 vs. 68±11 years), less likely to be female, and had higher prevalence of medical comorbidities and depression compared to respondents without TBI. Respondents with TBI did not perform significantly differently from respondents without TBI on any measure of objective cognitive function. Sensitivity analyses stratified by TBI severity produced similar results. TBI was associated with significantly increased risk for subjective memory impairment in models adjusted for demographics and medical comorbidities (35% vs. 27%; risk ratio (RR) [95% confidence interval (CI)]: 1.26 [1.01-1.57]). After further adjustment for active depression, however, risk for subjective memory impairment was attenuated (RR [95% CI]: 1.18 [0.95-1.46]). Sensitivity analyses revealed that risk of subjective memory impairment was only increased among respondents with TBI with LOC but not among those with TBI without LOC. Furthermore, adjustment for depression reduced, but did not attenuate, the risk of subjective memory impairment among those with TBI with LOC (RR [95% CI]: partially adjusted 1.37 [1.09-1.74]; fully adjusted 1.28 [1.01-1.61]).

**Conclusions:** In this population-based study of community-dwelling older adults without dementia, those with prior TBI with LOC were more likely to report subjective memory impairment compared to those without TBI even after adjustment for demographics, medical comorbidities, and active depression. Lack of greater objective cognitive impairment among those with versus without TBI may be due to poor sensitivity of the cognitive battery, survival bias, or suggests that post-TBI cognitive impairment primarily affects the executive domain, which was not assessed in this study. Our findings show that among community-dwelling non-demented older adults, remote TBI is common but may not preferentially impact cognitive domains of episodic memory, attention, working memory, verbal semantic fluency, or calculations.
Title: Early identification of Alzheimer's disease using subjective cognitive decline

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Key Words: subjective cognitive decline, mild cognitive impairment, Alzheimer's disease, early diagnosis

Background: Evidence suggests that subjective cognitive decline (SCD) is associated with increased presence of AD pathology in non-demented individuals, CSF amyloid-beta42 and tau changes, increased amyloid-β burden, smaller medial temporal lobe gray matter volumes, increased white matter hyperintensities (WMH), and decreased regional blood flow in cognitively normal older adults. SCD is also related to cognitive performance and diagnostic outcome in dementia-free older individuals. Despite strong evidence for the clinical significance of SCD, there is inconsistency in the extant literature suggesting that SCD may not predict disease progression. One plausible explanation for the variable findings is the use of inconsistent methodology to assess SCD. My laboratory has identified a subset of 25 SCD items that reliably measure the construct. These questions will be validated in the same rigorous manner as other established markers of unhealthy brain aging (e.g., objective cognitive performance, brain morphology, amyloid and tau markers).

Methods: Participants included 335 older adults free of clinical dementia or stroke, including 175 cognitively normal (73±7, 41% female), 132 mild cognitive impairment (MCI; 73±6, 44% female), and 27 cognitively ambiguous (73±7, 26% female) individuals. All individuals complete a SCD protocol, comprehensive neuropsychological assessment, 3T brain MRI (including structural and functional imaging), and cardiovascular assessment (i.e., echocardiogram, cardiac MRI). A subset of the cohort also completes a lumbar puncture for cerebrospinal fluid collection. The work will cross-sectionally relate SCD items to markers of unhealthy brain aging.

Results: Linear regression models stratified by diagnosis and adjusting for age, sex, education, race/ethnicity, depressed mood, and APOE-ε4 status suggested increasing amyloid deposition (decreasing Aβ42 concentrations) related to increasing total SCD in cognitively normal (β=0.997, p=0.003) but not MCI participants (β=1.00, p=0.86).

Significance: A possible preferential association between SCD and one of the first pathological processes in the proposed cascade of AD was noted. Results provide continued support for the use of SCD as a marker of early AD pathology and indicate preliminary evidence of the validity of these 25 SCD items. With further validation, results will provide primary care providers and their staff a time- and cost-effective screening method for use in CMS Annual Wellness Visits for patients' age ≥65. Such a screener could also be used to enrich research cohorts and monitor disease progression.
**TITLE:** Financial Literacy is Associated with White Matter Integrity in Old Age

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**TOPIC AREA:** Neuroimaging

**KEYWORDS:** financial literacy, white matter, diffusion tensor imaging (DTI)

**ABSTRACT:**

Background: Literacy has been associated with maintenance of neurocognitive function in aging, and financial literacy is important for beneficial financial decision making in old age. We previously showed that higher financial literacy is associated with greater functional connectivity between anterior and posterior brain regions even after adjusting for cognitive function. Here we tested the hypothesis that higher financial literacy would be associated with indicators of white matter integrity in older persons without dementia.

Methods: Three hundred and forty-six participants without dementia (mean age=81.36, mean education=15.39, male/female=79/267, mean MMSE=28.52) from the Rush Memory and Aging Project, a clinical-pathological cohort study of aging, were scanned using diffusion tensor imaging (DTI). Financial literacy was assessed using a series of questions imbedded as part of an ongoing decision making study. Fractional anisotropy (FA) was calculated using TORTOISE. We tested the hypothesis that higher financial literacy is associated with higher FA in white matter according to voxel-wise analyses using Tract-Based Spatial Statistics (TBSS), adjusting for the effects of age, education, sex, and white matter hyperintensities. We then repeated the analysis also adjusting for cognitive function.

Results: Analyses revealed multiple significant voxels of positive associations between FA and financial literacy, and many of these remained significant even after accounting for cognitive function. Significant FA results implicated white matter tracts connecting anterior and posterior brain regions. No negative associations were observed for FA and financial literacy.

Conclusions: Greater financial literacy is associated with higher diffusion anisotropy in white matter of nondemented older adults, even after adjusting for cognitive function. These results suggest that greater white matter integrity may be a mechanism that supports functional connectivity associations observed with financial literacy in old age.

**DISCLOSURES:** None.
Global proteomic analysis of Lrrk2 interactions in cell culture and the human brain: A path to novel diagnostics and therapeutics for Parkinson’s Disease

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Point mutations in the multidomain kinase LRRK2 are the most common known genetic cause of Parkinson’s disease (PD), a progressive and fatal neurodegenerative disorder that strikes 1-2% of individuals over 65 years of age. Currently, little is known about LRRK2’s normal functions or how LRRK2 point mutations cause neuronal death. We used mass spectrometry to perform global interactome studies of wild type and PD-driving LRRK2 point mutations. This method allowed us to identify novel LRRK2 interacting partners and to identify binding partners with differential affinities for wild type versus PD-driving LRRK2. Now, we are beginning to adapt the approach to human brain tissue. This technique provides an unbiased starting point from which to delineate pathways of interest in PD. More broadly, the approach is generally applicable to neurodegenerative diseases and may represent a new path to the development of rational diagnostics and therapeutics.
Resolving Conflicting CSF Biomarker Information in Alzheimer's Disease

William Hu, MD, PhD

Background: Different CSF biomarker combinations can provide conflicting diagnostic information in Alzheimer's disease (AD). This is often attributed to differences in sensitivity and specificity, at the cohort level, between CSF markers (Aβ42, t-Tau, p-Tau181, t-Tau/Aβ42, and p-Tau181/Aβ42). When these biomarkers are analyzed against the same gold standard independently, conflicting biomarker information can also result from biomarker substructures not obvious to investigators. Previous studies have not examined conflicting biomarker information at the individual level (e.g., a profile showing normal Aβ42 levels but abnormal t-Tau/Aβ42 ratio may be interpreted as AD-like even though the normal Aβ42 level argues against amyloid pathology). The prevalence of these conflicts and ways to resolve them are unknown.

Methods: We measured CSF AD biomarker levels in one consecutive series (n=431) from Emory University using the multiplex AlzBio3 assay and surveyed the concordance rates between CSF biomarkers at the individual level. We also compared these results with those from clinical testing through a comparable ELISA. To resolve the issue of differential sensitivity and biomarker substructure, we then analyzed CSF AD biomarker levels through two-step clustering to identify naturally existing subgroups of biomarker profiles. Finally, to determine if the cluster membership or the combination of independent biomarker information confers greater information on prognosis, we analyzed if either predicted longitudinal cognitive changes in the Alzheimer's Disease Neuro-Imaging Initiative (ADNI, n=409).

Results: Conflicting CSF biomarker information was very common: 59% of the Emory subjects and 37% of ADNI subjects had at least one biomarker providing diagnostic information distinct from the other biomarkers. Clustering analysis revealed three groupings: one characterized by p-Tau181/Aβ42>0.131 and longitudinal cognitive decline in MCI, and two others (including one characterized by Aβ42>258.5pg/mL) associated with cognitive stability. Within each cluster, concordant or discordant biomarker findings did not further distinguish rates of longitudinal cognitive decline.

Conclusions: Conflicting information from different CSF AD biomarkers was common. A data-driven strategy accounting for all biomarker combinations identified naturally existing groupings each characterized by similar biochemical and prognostic profiles.
Validation of the V66.7 code for palliative care consultation in a single academic medical center

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**Background:** Use of administrative data to study the effectiveness of specialized palliative care is limited by the lack of a reliable method to identify patients receiving palliative care consultation. The International Classification of Diseases, Ninth Revision (ICD-9) code V66.7 has been used, but its validity for this purpose is unknown.

**Objective:** To examine the validity of the ICD-9 code V66.7 for identifying whether hospitalized patients received palliative care consultation.

**Design:** Retrospective cohort study.

**Setting/Subjects:** All patients age ≥ 18 years admitted to a single academic medical center between August 2013 and August 2015.

**Measurements:** Sensitivity and specificity of the V66.7 code for palliative care consultation for all patients and several a priori subgroups. The reference standard was the presence of a palliative care consultation note in the electronic medical record.

**Results:** Of 100,910 admissions, 1,999 received a palliative care consultation (2.0%) and 1,846 (1.8%) had usage of the V66.7 code. Sensitivity and specificity for the V66.7 code were 49.9% and 99.1% respectively. Sensitivity was considerably higher for certain subgroups, such as patients with dementia (76.3%) and metastatic cancer (66.3%); addition of age restrictions further improved sensitivity while maintaining high specificity. Specificity was substantially lower for patients who died during hospitalization (sensitivity 53.9%, specificity 75.1%).

**Conclusions:** In a single center, the ICD-9 code V66.7 had poor sensitivity and high specificity for identifying hospitalized patients who received a palliative care consultation. Appropriate use of this code for this purpose should take these characteristics into consideration.

Keywords: palliative care, validation studies, international classification of diseases.
Non-clinical Factors Predict Treatment Intensity in Setting of Poor Prognosis

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Background: Understanding factors associated with treatment intensity among the seriously ill may help to ensuring high-quality, patient-centered care.

Objective: This study investigates factors associated with treatment intensity among prospectively identified, seriously ill older adults, and examines if baseline prognosis influences the impact of these factors on treatment.

Methods: Using the nationally-representative, longitudinal Health and Retirement Study and linked Medicare claims, we prospectively identified people with incident serious illness (a serious medical condition, e.g. metastatic cancer, or functional impairment). We used baseline characteristics to calculate each subject’s 1-year mortality risk and then followed them for 1 year. We examined the relationships between subjects’ characteristics and total Medicare costs over 1 year, then performed stratified analyses by 1-year mortality risk: low (<10%), moderate (10-25%) and high (>=25%).

Results: From 2002-2012, 5208 subjects had incident serious illness: mean age 78 years, 60% women, 76% non-Hispanic white, and 39% hospitalized in the past year. During 1-year follow-up, 12% died. Total Medicare costs averaged $20,607. In multivariable analyses, several indicators of poor health (e.g. cancer, end stage renal disease, advanced heart and lung disease, multimorbidity, functional impairment and others) were significantly associated with higher costs (p values<0.05). In models limited to those with low and moderate risk of death the same relationships persisted. However, among those with high mortality risk, health-related variables were no longer significant. Instead, African American race (rate ratio 1.56) and moderate-to-high spending regions (RR 1.31 and 1.54, respectively) were significantly associated with higher costs.

Conclusions: Among seriously ill older adults, indicators of poor health are associated with higher costs. Yet, among those with poorest prognoses, non-medical characteristics - race and regional practice patterns- have greater influence on treatment. This suggests there may be novel opportunities to improve care quality and value by assuring patient-centered, goal-directed care.
Frailty Assessment and 6-Month Functional Status and Mortality After Aortic Valve Replacement

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**Objectives:** After attending this session, participants will be able to 1) describe the 6-month change in functional status after transcatheter and surgical aortic valve replacement; 2) select an appropriate frailty assessment in preoperative evaluation of older patients undergoing aortic valve replacement.

**Abstract:**
Preoperative frailty assessment may be useful to predict functional status and mortality in older adults undergoing aortic valve replacement (AVR). We conducted a single-center prospective cohort study to compare frailty phenotype versus comprehensive geriatric assessment-based frailty index (CGA-FI) in predicting 6-month functional status and mortality after transcatheter and surgical AVR. Between February 2014 and December 2015, we assessed frailty phenotype and CGA-FI in patients 70 years or older who underwent transcatheter AVR (N=124) or surgical AVR (N=88). Telephone interviews were performed at 1, 3, and 6 months to assess the ability to perform 22 functional activities. The composite poor clinical outcome, defined as death or functional decline with the New York Heart Association class 3 or 4, occurred in 31 (26%) of 120 transcatheter AVR patients (drop-out: 4) and 8 (11%) of 76 surgical AVR patients (drop-out: 12). The risk of poor clinical outcome did not differ between patients with and without frailty phenotype undergoing transcatheter AVR (24 of 96 [25%] versus 7 of 24 [29%]; p=0.68) and surgical AVR (5 of 27 [19%] versus 3 of 49 [6%]; p=0.11). However, the risk increased with CGA-FI (≤0.20, 0.21-0.40, >0.40) in transcatheter AVR (1 of 12 [8%], 12 of 64 [19%], 18 of 44 [41%]; p=0.01) and surgical AVR (1 of 29 [3%], 5 of 42 [12%], 2 of 5 [40%]; p=0.04). In conclusion, CGA-FI predicts 6-month functional status and mortality after transcatheter and surgical AVR, but frailty phenotype has a limited role in this population with high prevalence of frailty.

**Funding source:** Harvard Catalyst, National Institute of Health, Canadian Institutes of Health Research
A Novel Frailty Index for Patients with End-Stage Liver Disease

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Background: Cirrhosis is characterized by muscle wasting, malnutrition, and functional decline that confer excess mortality not well quantified by the MELD\textsuperscript{a} score. We aimed to develop a frailty index to capture these extrahepatic complications of cirrhosis and enhance mortality prediction in cirrhotics.

Methods: Consecutive outpatients listed for LT without MELD exceptions were assessed with candidate physical frailty measures. Best subset selection analyses with Cox regression identified subsets of candidate frailty measures that predicted waitlist mortality (=death or delisting due to sickness). We selected the Frailty Index by balancing statistical accuracy with assessments of clinical utility. The net reclassification index (NRI) evaluated the %patients correctly reclassified by adding the Frailty Index to MELD\textsuperscript{a}.

Results: Included were 536 cirrhotics with median MELD\textsuperscript{a} of 18. 107(20\%) died/were delisted. The final Frailty Index consisted of: grip strength, chair stands, and balance. The ability of MELD\textsuperscript{a} and the Frailty Index to correctly rank patients according to their 3-mo waitlist mortality risk (i.e., C-statistic) was 0.80 and 0.76, respectively, but 0.82 for MELD\textsuperscript{a} + Frailty Index together. Compared with MELD\textsuperscript{a} alone, MELD\textsuperscript{a} + Frailty Index correctly re-classified 16\% of deaths/delistings (p=0.005) and 3\% of non-deaths/delistings (p=0.17) with a total NRI of 19\% (p<0.001). Compared to those with robust Frailty Index scores (<20\%ile), cirrhotics with poor Frailty Index Scores (>80\%ile) were more impaired by gait speed, IADL difficulty, exhaustion, and low physical activity [p<0.001 for each].

Conclusions: Our Frailty Index for cirrhotics, comprised of 3 performance-based metrics, has construct validity for the concept of frailty and improves risk prediction of waitlist mortality over MELD\textsuperscript{a} alone.
**Title: Trajectories of impaired fasting glucose in older adults**

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**Objective:** Impaired fasting glucose (IFG) is common among older adults, but little is known about its natural history. We describe trajectories of fasting plasma glucose (FPG) among older adults with untreated IFG, identify their predictors, and examine their associations with progression to diabetes.

**Research Design and Methods:** We evaluated 511 older adults with IFG (FPG 100-125 mg/dL, no self-reported history of diabetes or current treatment with glucose-lowering medications) from the Health, Aging, and Body Composition Study, a longitudinal cohort of ambulatory older adults (ages 70-79) whose FPGs were measured repeatedly over 11 years. Participants had ≥2 total FPGs, which were censored at first reported use of a glucose-lowering medication or last follow-up. Glycemic trajectories were identified using trajectory modeling, and multivariable logistic regression was used to identify predictors of trajectory membership. Incident diabetes was defined as any HbA₁c ≥6.5%, FPG ≥126 mg/dL, or glucose-lowering medication use.

**Results:** Among the 511 participants with IFG, two distinct trajectories were identified: 83.4% had stable and 16.6% had rising FPGs. Independent predictors of a rising FPG trajectory included age <75 years (Odds ratio (OR) 2.19 [95% CI, 1.24-3.85]), Black race (OR 1.83 [1.06-3.14]), baseline FPG ≥110 mg/dL (OR 4.60 [2.76-7.67]), and baseline triglycerides ≥150 mg/dL (OR 2.48 [1.42-4.31]). Diabetes developed in 92.9% of adults in the rising trajectory compared with only 19.4% of those in the stable trajectory (p<0.001).

**Conclusions:** The majority of older adults with IFG had stable glycemia over time but those who did have rising FPGs developed diabetes at a high rate.
Title: Effect of sleep deprivation and sodium oxybate on CSF Aβ kinetics

Authors: Brendan P. Lucey, Terry J. Hicks, Jennifer S. McLeland, Cristina D. Toedebusch, Jill Boyd, Robert Swarm, Kwasi G. Mawuenyega, Vitaliy Ovod, Tom Kasten, John C. Morris, Randall J. Bateman

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Key words: Sleep, amyloid-beta, Alzheimer’s disease

Abstract

Objectives: In rodents and humans, amyloid-β (Aβ) concentration fluctuates with the sleep-wake cycle as a diurnal pattern. Animal studies suggest that Aβ concentration and deposition may be modifiable through manipulation of the sleep-wake cycle. The purpose of this study is to determine if Aβ concentrations in the human central nervous system are modifiable through manipulation of sleep.

Methods: We collected serial cerebrospinal fluid (CSF) samples via intrathecal lumbar catheter every 2 hours for 36 hours in adults 18-60 years old during behavioral sleep deprivation (N=12), pharmacologic sleep induction with sodium oxybate (N=11), and control (N=12). All participants were infused with $^{13}$C$_6$-leucine to measure Aβ kinetics. Aβ40 and Aβ42 isoforms were quantitated by mass spectrometry. Sleep-wake activity was monitored with polysomnography.

Results: We found that concentrations of Aβ38, Aβ40, Aβ42, and total Aβ increased 25-30% during sleep deprivation compared to control. This increase occurred during the sleep period, hours 18-24 or 01:00-07:00. Participants with increased sleep efficiency were found to have decreased area under the curve for Aβ40 and Aβ42.

Discussion: Sleep is hypothesized to be the primary driver of the Aβ diurnal pattern. Sleep deprivation increased Aβ40 and Aβ42 25-30% compared to controls. Since changes in Aβ concentration of 25-40% have been associated with causing or preventing Alzheimer’s disease, manipulation of sleep has potential as a preventive therapy. Future investigations will be needed to assess if Aβ concentrations are increased in individuals with poor sleep quality compared to controls and if this increase can be normalized with a sleep-inducing medication.

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A Group Visit Intervention Improves Advance Care Planning Readiness, Conversations, and Documentation

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Background: Primary care settings need new systems to improve advance care planning (ACP) and facilitate values-based ACP discussions. Group visits provide a safe environment that facilitates peer learning. This study aimed to assess the impact of an ACP Group Visit intervention on older adults’ ability to engage in ACP discussions, documentation of ACP preferences, and readiness to discuss ACP with their doctor.

Methods: We implemented an ACP Group Visit intervention in 3 University of Colorado Hospital primary care clinics consisting of two sessions, one month apart, for groups of 8-12 older adults (age ≥ 65). A geriatrician and social worker facilitated the visits. The intervention emphasizes collaborative learning to promote group dynamics, peer-based learning, and engagement in the ACP process. Patient outcome data (i.e. ACP discussions with loved ones; readiness to discuss ACP with their doctor) were assessed after the 2nd session. Electronic medical records were reviewed at baseline and 3-months for documentation of decision maker(s), advance directives, and resuscitation preferences.

Results: We enrolled 118 patients (mean age 76; 62% female, and 82% white) in 16 ACP Group Visit cohorts. After participating in the 2nd session, more patients reported having ACP conversations with loved ones (19% to 42%, p<0.001). From baseline to 3-month follow up, documentation rates at least doubled for decision maker(s) (39% to 80%), advance directives (20% to 57%), and resuscitation preferences (21% to 42%) (p<0.001 for all). Many patients reported being “fairly” or “extremely” ready to talk with their doctor about choosing a medical decision maker (78%), health situations that make life not worth living (81%), flexibility for decision makers (89%), and asking questions to make good medical decisions (85%).

Conclusions: The ACP Group Visit intervention significantly increased ACP discussions and ACP documentation in the medical record. The ACP Group Visit is a viable new system of completing ACP in primary care, may facilitate CMS reimbursement for ACP, and warrants further development to maximize its effectiveness and implementation.

Key words – advance care planning, primary care, patient-physician communication
IMPLEMENTATION OF DECISION AIDS FOR IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS: LESSONS LEARNED AND PATIENT PERSPECTIVES

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Purpose: Evaluate the implementation process and explore patient perspectives regarding the acceptability and usability of four decision aids (DAs) to support decision making for Implantable Cardioverter Defibrillators (ICDs).

Method: Heart failure patients eligible for an ICD for primary prevention at three sites in the Denver metropolitan area were randomly assigned to intervention or control in a 2:1 ratio. Intervention patients received four decision aids: a one-page option grid; a four-page in-depth decision aid; a 17-minute video; and an interactive website. Controls received usual decision making as provided by the clinic. We conducted semi-structured qualitative telephone interviews with patients one month after the electrophysiology (EP) visit and three months after enrollment. Interviews addressed acceptability and usability of the decision aids and data were analyzed for themes related to decision influence.

Result: Across the three sites, six patients were randomized to the control arm and 15 to the intervention arm. Most patients preferred the infographic and video decision aids over the option grid and website. At least half of the intervention patients reviewed the tools prior to meeting with their EP; many reviewed with a family member. “I've used that to explain what's going on and why I made that decision, to my family.” A minority brought the tools with them to the EP appointment yet patients found tools stimulated additional questions to pose to the EP, “[It] guided me in the right direction… I had enough information to ask intelligent questions.” Suggested improvements included providing just one or two tools to avoid repetition among information and to promote patients’ independent use of the DAs. The timing of delivery of the DAs was acceptable. Patients identified the volume of accompanying research-related paperwork as overwhelming and therefore sometimes ignored. Access to a nurse during the decision window encouraged patient questions and improved patient perceived confidence.

Conclusion: Patients determined for themselves how they used the decision aids to augment the decision context (e.g., to prompt more questions for the EP, to explain their decision to family, to confirm or re-confirm the decision already made, or to revisit post-decision.) Further exploration of this larger context of DA use as well as strategies to promote independent use related to EP visit are needed.
Predictors of Unmet Need among Caregivers of Persons with Dementia
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Introduction: Among caregiving provided to community-dwelling older adults, care for those with dementia accounts for one-third of the persons providing care and 41% of total caregiving hours.1 As of the need for informal caregiving increases with the aging of the population, healthcare providers and the public health system must identify those caregivers in greatest need of training and intervention. Two ongoing initiatives include public health surveillance of caregiving: Health People 2020, the federal government’s goals for improving the health of Americans2; and the Healthy Brain Initiative of the Centers for Disease Control and Prevention (CDC) and Alzheimer’s Association.3 The Caregiver Module of the CDC’s Behavioral Risk Factor Surveillance System was developed in order to estimate the national burden of unmet caregiver need, which we use to understand which caregivers are at greatest risk.

Methods: The BRFSS is a system of state health surveys that include >400,000 adult interviews each year; with weighting, the survey represents all unique adult households in each state. In the CM, each respondent is asked: “During the past 30 days, did you provide regular care or assistance to a friend or family member who has a health problem or disability?” If “yes,” respondents are asked additional questions, including the health condition of the person for whom they care (e.g., dementia) and need for additional support services. Among the 24 states that used the CM in 2015, 3,012 respondents (9.6%) reported being the caregiver of a person with dementia, representing over 1.7 million adults. We compared characteristics of dementia caregivers with and without unmet need for additional support services and then completed multivariate logistic regression to determine caregiver characteristics associated with unmet need.

Results: Among dementia caregivers, 25.8% reported unmet need, representing 446,557 caregivers. The most common need was “help in getting access to services”, reported by 50.8%. This was followed by: respite care (16.2%), individual counseling (12.9%), support groups (11.3%), and caregiving classes (8.8%). Female caregivers reported more unmet need than men (OR 1.45, p<0.001), while the 55-74 year-old age group was most likely to report unmet need (OR 1.36, p<0.001). Caregivers that were adult children were more likely to report unmet need than spouse caregivers (OR 1.33, p<0.001). The caregiver characteristic most strongly associated with unmet caregiver need was time spent in caregiving. Compared to respondents reporting ≤8h/wk of caregiving, those who reported ≥40h/wk had 2.43 odds of unmet need (p<0.001). In the multivariate model, time burden of caregiving was again most strongly associated with unmet need. Unexpectedly, compared to caregivers who rated their health as excellent or very good, those caregivers who rated their health more poorly were less likely to report unmet need.

Conclusions: A significant number of caregivers experience unmet need. The findings on age, employment, and caregiver relationship all suggest that younger, employed, child caregivers experience the greatest degree of unmet need. It was unexpected that the caregivers who rate their own health worse would report less unmet caregiver need. Our findings suggest that, rather than investing in expanding the services available, there may be significant benefit through increasing outreach to caregivers to help them access services that may already be available in many communities.

http://www.cdc.gov/aging/pdf/2013-healthy-brain-initiative.pdf%5BPDF-2.2M%5D.
Mediterranean diet and cognitive decline: strengthening the evidence base and encouraging dietary behaviour change

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Given the lack of pharmacological treatment for impaired cognition, and a projected increased prevalence of dementia, there is considerable interest in examining diet for prevention of age-related cognitive decline. The Mediterranean Diet (MedDiet), characterized by a high intake of fruits, vegetables, wholegrains, nuts, legumes and olive oil, may reduce cognitive decline, even in patients with mild cognitive impairment (MCI)1. However, findings are limited, firstly by the small number of studies conducted to date, and secondly by limitations and heterogeneity, both in the methods to determine MedDiet adherence and in respect to cognitive outcome(s) assessed. Evidence is required to comprehensively investigate relationships between the MedDiet and cognitive functions, from the earliest through to the latest stages of cognitive decline. Furthermore, there is a need to test the efficacy of MedDiet on cognition, which will require knowledge of how best to support dietary behaviour change. Therefore, this research seeks to address gaps in the evidence base by integrating epidemiologic and pilot intervention data in Non-Mediterranean populations. The first aim of this project is to investigate links between MedDiet adherence, cognitive decline and dementia risk in populations from both the UK (using data from the Prospective Epidemiological Study of Myocardial Infarction study) and the USA (using data from, Health, Ageing and body Composition study and the Coronary Risk in Young Adults Study). A second aim is to conduct a 12-month randomised controlled trial to test the feasibility of a tailored educational resource to encourage dietary behaviour change toward a MedDiet, in 60 patients with MCI. Data will be used to inform the design of a future larger trial to test the clinical effectiveness of a MedDiet as a therapeutic prevention strategy for age-related cognitive decline. Ultimately, this research will increase knowledge on how diet contributes to cognitive health to inform clinical practice and impact on the lives of older people.

Key Words: Mediterranean diet; cognitive decline; dementia

Longevity and healthspan effects of ketogenic and high-fat diets in mice

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The ketone body $\beta$-hydroxybutyrate (BHB) is produced during physiological states that are associated with improving health, including dietary restriction, fasting, and exercise. The emerging signaling functions of BHB, such as deacetylase inhibition and inflammasome inhibition, suggest that it may be a molecular effector mechanism of some of the health benefits from these states.

We sought to determine if long-term exposure to BHB through dietary manipulations would affect the longevity and healthspan of C57BL/6 male mice. As a proof of concept, we used a set of carefully-matched diets including AIN-93M control (10\% calories from protein), zero-carbohydrate ketogenic (KD, 90\% calories from fat), and very high-fat non-ketogenic (HF, 75\% calories from fat). Both KD and HF were markedly obesogenic, but cycling between KD and the control diet each week prevented obesity. Overall caloric intake was similar between cycling groups and groups fed only control diet. In a small pilot study (N=10/group) started at 17 mo, cyclic KD increased median lifespan by 10\% over the control diet.

Preliminary data from a larger study (N=36-71/group) started with mice aged 12 mo shows increased longevity from cyclic KD. In healthspan testing, cyclic KD results in enhanced cognition, maintenance of youthful exploratory behavior, and slowing of immune aging. In summary, non-obese exposure to ketogenic diets may enhance longevity and improve healthspan, including enhancing cognition in old age.
Impaired Orthostatic Blood Pressure Behaviour is associated with Unexplained and Injurious Falls

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Key words: Falls, Blood pressure, Orthostatic Hypotension, Epidemiology, Falls risk, Unexplained falls, Impaired blood pressure stabilization, Injurious falls

Background

Cardiovascular disorders are recognised as important modifiable risk factors for falls. However the association between falls and orthostatic hypotension (OH) remains equivocal, particularly because of poor measurement methods of previous studies. Our goal was to determine for the first time to what extent OH (and variants) are risk factors for incident falls, unexplained falls (UF), injurious falls (IF) and faints using dynamic blood pressure (BP) measurements in a population study.

Methods

4127 participants were included who completed wave 1 (2009-2011) and wave 2 (2012-2013) of The Irish Longitudinal Study on Ageing (TILDA), a nationally representative longitudinal cohort study of community dwelling adults aged ≥50 years resident in Ireland. Continuous beat-to-beat BP recordings measured during active stands were analysed. OH and variants (initial OH and impaired orthostatic BP stabilization OH(40)) were defined using dynamic BP measurements. Associations with the number of falls, UF, IF and faints reported two years later were assessed using negative binomial and modified Poisson regression, with adjustment for a broad range of demographic and health related covariates.

Results

Mean age of participants was 61.5(8.1) years, 52.9% female. 34% had IOH, 13% had OH40, and 5% had OH. 22% experienced ≥1 falls between wave 1 and 2, 4.2% had an unexplained fall, 8.9% had an injurious fall and 4.8% had ≥1 faints. After adjustment for all covariates, OH(40) was associated with increased relative risk of UF (RR:1.52 95%CI:1.03-2.26). OH was associated with all-cause falls (IRR:1.40 95%CI:1.01-1.96), UF(RR:1.81 95%CI:1.06-3.09), and IF(RR:1.58 95%CI:1.12-2.24). IOH was not associated with any outcome and none of the OH variants were clearly associated with faints.

Conclusion

Impaired orthostatic BP behaviour is an independent risk factor for future falls, unexplained falls, and injurious falls. Impaired BP stabilisation and OH should be considered in the future assessment of falls risk in older adults.
Longevity gene KLOTHO alters APOE4-related cortical thinning: Findings from the Wisconsin Registry for Alzheimer’s Prevention

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Background: APOE4 allele carriage is the most established genetic risk factor for late-onset Alzheimer’s disease (AD) and is associated with regional cortical thinning and atrophy. Recently, a longevity gene, KLOTHO, has been identified as a potential resilience factor against aging and AD. In humans, being heterozygous for the KL-VS haplotype of KLOTHO is associated with enhanced cognition and greater regional cortical volumes. Elucidating the protection conferred by KL-VS, especially in those who are at increased risk for AD, is of great interest. Accordingly, this study examined whether KL-VS heterozygosity modifies the association between APOE4 and cortical thickness in late-middle-aged adults.

Methods: 325 cognitively-healthy enrollees in the Wisconsin Registry for Alzheimer’s Prevention (mean age= 60.3±6.4 years) were genotyped for APOE and KLOTHO (n=139 KL-VS non-carrier & APOE4 non-carrier, n=100 KL-VS non-carrier & APOE4 carrier, n=55 KL-VS heterozygote & APOE4 non-carrier, and n=31 KL-VS heterozygote & APOE4 carrier). Because there were only four KL-VS homozygote cases, we excluded those individuals from our analyses. Participants also underwent a 3D T1 MRI scan on a 3.0T GE x750 scanner. Cortical thickness measurements were derived from 12 a priori regions of interest involved in AD using FreeSurfer software. Linear regression analyses, adjusted for age and sex, were used to test whether the association between APOE4 and cortical thickness was altered in KL-VS heterozygotes compared to non-carriers.

Results: We observed significant APOE4*KLOTHO interactions for several regions including the entorhinal cortex (p=.035), precuneus (p=.040), posterior cingulate (p=.048), supramarginal gyrus (p=.036), superior parietal cortex (p=.018), and caudal middle frontal (p=.037) cortex. Follow-up stratified analyses revealed that among KL-VS non-carriers, possessing an APOE4 allele was associated with thinner cortex in these AD-sensitive regions compared to APOE4 non-carriers. However, in KL-VS heterozygotes we observed no significant differences in cortical thickness between APOE4 carriers and non-carriers.

Conclusions: In a sample comprised of late-middle-aged individuals, KL-VS heterozygotes showed a diminution of APOE4-related alterations in cortical thickness in select regions associated with AD. These findings support the notion that carrying the longevity-promoting haplotype of KLOTHO may provide resilience to cortical thinning, specifically in those at increased risk for AD.
Title: Vitamin E boosts the ability of human PMNs to kill *Streptococcus pneumonia*

Authors: Elsa Bou Ghanem, Simin Meydani, John Leong and Alexander Panda

Despite the availability of vaccines, *Streptococcus pneumoniae* remains a leading cause of life-threatening invasive infections such as pneumonia, bacteremia and meningitis. Polymorphonuclear leukocytes (PMNs) are a key determinant of the course of disease, as optimal host defense requires an initial robust pulmonary PMN response to control bacterial numbers followed by modulation of this response later in infection. The elderly are at increased risk of developing pneumococcal pneumonia, and manifest a decline in immune function and higher basal levels of inflammation. Using an aged mouse infection model, we previously showed that oral supplementation with vitamin E decreases pulmonary inflammation, at least in part by modulating neutrophil migration across lung epithelium into alveolar spaces, and reverses the age-associated decline in resistance to pneumococcal pneumonia. The objective of this study was to test the effect of vitamin E on the ability of neutrophils isolated from young (22-35 years) and elderly (65-69 years) individuals to migrate across epithelial cell monolayers *in vitro* in response to *S. pneumoniae* and kill to complement-opsonized pneumococci. We found that basal levels of pneumococcal-induced transepithelial migration by PMNs from young or elderly donors were indistinguishable, suggesting that the age-associated exacerbation of pulmonary inflammation is not due to intrinsic properties of PMNs of elderly individuals but rather may reflect the inflammatory milieu of the aged lung. Unexpectedly, we found that PMNs isolated from elderly donors were more efficient at *ex vivo* killing of complement-opsonized bacteria than their younger counterparts, suggesting that PMNs of older donors, when purified, display a high complement receptor-mediated bacteriocidal activity. Notably, vitamin E treatment diminished migration of the PMNs regardless of the age of the donor, and boosted the ability of PMNs from young donors to kill complement-opsonized pneumococci. These findings demonstrate that VE is a potent modulator of human neutrophil responses and is a potential nutritional intervention to combat infection.
Ana C. Pereira

Title: Glutamatergic Dysregulation in Age-Related Cognitive Decline and Alzheimer’s disease

The neural circuits affected in aging and in Alzheimer’s disease (AD) are similar, involving the glutamatergic connections among cortical areas and with the hippocampal formation. In aging, synaptic changes occur with minimal neuronal death while in AD, there is frank loss of neurons. With the goal of further understanding the susceptibility of glutamatergic neural circuits to aging and AD that culminates in cognitive decline, the proposed project utilizes a multi-dimensional investigative approach focusing on the major glutamate transporter in the brain, EAAT2. EAAT2 plays a critical role in determining glutamate levels synaptically and extrasynaptically, and regulating physiological glutamatergic neurotransmission, that all are critical for learning, memory, and synaptic health. Importantly, EAAT2 activity is significantly decreased in both aging and AD, and associated with neurodegeneration in the latter. We have been investigating EAAT2’s pathophysiological role in aging and AD by, first, quantifying changes at the synaptic level, with correlative behavioral assays, and gene expression profiles in aging and AD mouse models, and second, with an intervention with an EAAT2-enhancer, the glutamate modulator riluzole. Moreover, we have been using a newly developed conditional EAAT2 knock-out (KO) mouse for further mechanistic studies on EAAT2’s impact on gene expression patterns and behavior in the aging brain. These studies will delineate the biology of EAAT2 in aging and AD brains at the structural, molecular and functional levels and will test EAAT2 enhancement as a therapeutic target for age-related cognitive decline and AD.
Motivating physical activity in older adults with high risk chronic disease: Intervention refinement & evaluation

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Background: Physical activity interventions have been developed for older adults who are frail or at risk for disability, but none have explicitly considered the needs of the growing number of older adults with multiple high-risk chronic diseases.

Objectives: Tailor and pilot test a novel behavioral intervention (induction of positive affect) vs. an educational control to motivate low levels of physical activity in older adults with multiple high risk chronic diseases.

Design: Focus groups with patients and providers to elucidate values, attitudes and beliefs about physical activity and gain feedback about potential new candidate intervention components, followed by a one year randomized controlled pilot study.

Results: Qualitative focus groups were completed among 40 participants (15 providers and 25 patients). In total, 28 women and 12 men were enrolled in the focus groups and participants were 35% Black, 53% Hispanic, and 5% Asian. Several new intervention components were suggested, including: weekly ‘check-in’ phone calls to participants, additional time points for feedback of physiological data from the Fitbit, and incorporating elderly peer counselors.

To date, 27 participants have enrolled in the randomized controlled pilot study and completed baseline questionnaires. Their mean age is 70.3 years (range 61.0-91.5), 55% are female and 18.5% are married. With regard to racial characteristics, 44% are Black, 33% Caucasian, 15% more than 1 race, 4% American Indian/Alaska Native and 4% Asian/Pacific Islander. 18.5% are Hispanic. Overall, 18.5% have a Charlson Index of ≤ 4, 59.3% have a score of 5-6 and 22.2% have a score of ≥ 7. Baseline Fitbit data collection is underway.

Conclusion: Recruitment and follow-up of participants is ongoing. Initial enrollment has enabled important refinements to the study protocol, such as adjustments to the questionnaire battery, planned expansion to additional recruitment sites and the addition of wristbands for Fitbits.
Brain-Computer Interface Therapy for Upper Extremity Stroke Rehabilitation Induces Corticospinal Tract Changes that Track with Individual Behavioral Gains

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Introduction: A better understanding of brain changes underlying functional gains with brain-computer interface (BCI) use in stroke rehabilitation is needed.

Hypothesis: BCI therapy will produce observable neuroplastic changes, and behavioral gains will relate to changes in diffusion tensor imaging (DTI) metrics of the corticospinal tracts (CSTs).

Methods: We obtained DTI and behavioral data from 16 stroke patients with upper extremity motor impairment before, during, and after BCI therapy. Additional DTI and behavior data were obtained from 9 control subjects at similar time intervals before receiving any BCI therapy. Behavioral measures included Stroke Impact Scale (SIS), Action Research Arm Test (ARAT), 9-Hole Peg Test (9HPT), and grip strength. We performed tractography of the ipsilesional CST (iCST) and contralesional CST (cCST) and extracted DTI metrics (fractional anisotropy, axial diffusivity, radial diffusivity, trace) from each. DTI and behavioral metrics were analyzed for changes from baseline between therapy and control groups. Individual changes in DTI metrics were analyzed for correlation with behavior changes.

Results: Group by time interactions were identified in DTI metrics of the iCST, with multiple metrics increasing with therapy. Changes in individual SIS Activities of Daily Living and 9HPT scores correlated with individual changes in both the iCST and cCST. Similarly, changes in SIS Hand Function correlated with cCST changes, and changes in grip strength correlated with iCST changes. Correlations between changes in ARAT scores and cCST changes trended to significance. Correlations significant at p<= 0.05; trending at 0.05<p<0.1 after fdr correction.

Conclusions: BCI therapy can induce structural neuroplastic changes during stroke recovery. These changes may be used to track both subjective and objective behavioral gains.
Circulating factors from older adults with T2DM impair endothelial network formation

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Type 2 diabetes mellitus (T2DM) is associated with microvascular rarefaction, impaired angiogenesis, and increased risk for cardiovascular disease (CVD). These vascular complications may, in part, be attributable to endothelial dysfunction that is mediated by circulating factors. We tested the hypothesis that circulating factors in serum from individuals with T2DM and impaired glucose tolerance (IGT) reduce \textit{ex vivo} capillary-like network formation of human retroviral telomerized endothelial cells (HRVT-ECs) and human primary coronary artery endothelial cells (CAECs), compared with normal glucose tolerant (NGT) controls.

Subjects were sedentary older (>55 yrs) adults and groups were matched for BMI. HRVT-ECs or CAECs were cultured in triplicate on Matrigel® using endothelial basal medium supplemented with 7.5% serum from individuals with NGT, IGT, or T2DM (n=10/group). Despite higher plasma glucose levels in the T2DM patients compared to the NGT and IGT groups (P<0.05 for both), the glucose levels that the cells were exposed to were similar across conditions (99.3±0.16, 99.7±0.38 and 103±0.55 mg/dL for NGT, IGT and T2DM, respectively). After incubation for 15 hours, the samples were imaged and network length was analyzed using ImageJ Angiogenesis Analyzer (NIH). Subsequently, serum concentrations of angiogenic factors [vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and placental growth factor (PlGF)] and inflammatory factors [interleukin-6 (IL-6), interleukin-8 (IL-8), and tumor necrosis factor-α (TNF-α)] were measured using multiplex ELISA.

In the HRVT-EC assay, serum from T2DM patients resulted in 32% and 35% lower endothelial network length than serum from the NGT and IGT groups, respectively (P<0.05 for both). In the CAEC assay, serum from T2DM subjects resulted in 11% and 8% lower network length than when using serum from NGT and IGT subjects, respectively (P<0.05). There were no statistically significant differences in serum concentrations of angiogenic growth factors among the groups; however, the T2DM group had ~100% higher concentrations of IL-6 compared with the NGT and IGT groups (P < 0.05 for both), and tended to have ~40% higher concentrations of IL-8 compared to the NGT group (P = 0.08).

These results suggest that factors present in the serum of older adults with T2DM impair \textit{ex vivo} endothelial cell function in both telomerized and primary endothelial cell lines leading to alterations in angiogenic potential. Thus, identification of the specific circulation factors that impair network formation may have implications for the microvascular complications associated with T2DM. We speculate that higher concentrations of IL-6 and IL-8 in older adults with T2DM may contribute to the impairment in endothelial network formation; however, empirical evidence of their role is still necessary.
Identifying Injury Patterns Associated with Physical Elder Abuse: Analysis of Highly Adjudicated Cases

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Background: Elder abuse is common and has serious health consequences but is under-recognized and under-reported. As assessment by health care providers may represent the only contact outside the family for many older adults, physicians have a unique opportunity to diagnose suspected elder abuse and initiate intervention. Despite this, physicians seldom identify or report elder abuse. Among the most important reasons for this is the difficulty in distinguishing between elder abuse and the sequelae of unintentional trauma. Little systematic research exists examining injury patterns consistent with elder abuse. Our goal was to identify injury patterns associated with physical elder abuse in comparison with patients presenting to the Emergency Department (ED) with unintentional falls.

Methods: We conducted a case-control study to identify differences in injury characteristics and patterns between physical elder abuse and unintentional fall injuries. We partnered with a large, urban district attorney’s office and examined 100 successfully prosecuted case files from 2003-2014 of physical abuse of a victim aged ≥60 where the perpetrator had been convicted or pled guilty. We evaluated police, legal, and medical records from these highly adjudicated cases, focusing on descriptions and photographs of injuries. To facilitate completely and accurately characterizing injuries, we developed a novel classification system / taxonomy. As a comparison group, we prospectively enrolled control subjects who presented to the ED after an unintentional fall from 9/2014 – 6/2016 in a large, urban, academic medical center. These controls were matched to cases by age, and photographs were taken of all injuries.

Results: Physical abuse victims were significantly more likely than unintentional fallers to have bruising (75% vs. 53%, p=0.01) and injuries on the maxillofacial/dental/neck region (61% vs. 38%, p=0.01). Abuse victims were less likely to have abrasions (33% vs. 54%, p=0.02), fractures (7% vs. 37%, p<0.001), or injuries on the lower extremities (9% vs. 43%, p<0.001). Examination of precise injury locations yielded additional differences. Physical elder abuse victims were more likely to have injuries in the left peri-orbital area (21% vs. 7%, p=0.03). Also, injuries to the ulnar forearm (10% vs. 2%, p=0.06), or neck (9% vs. 0%, p=0.01) occurred commonly among abuse victims but not among fallers.

Conclusion: Specific, clinically identifiable differences may exist between unintentional injuries and those from physical elder abuse. This includes potentially pathognomonic injury patterns that very infrequently occur after an accident. Future prospective research comparing abuse-related injury patterns to those sustained by older adults after an accident such as a fall and examining the findings described here is critically needed to assist health care providers in identifying suspicious injuries and protecting vulnerable older adults.
Implementing a Choosing Wisely™ Intervention to Reduce Low Value Preoperative Testing for Cataract Surgery

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BACKGROUND: Pre-operative testing for cataract surgery provides no discernible benefit to patients and substantially raises costs—representing the quintessential example of low value care. Despite multiple randomized controlled trials demonstrating no benefit, physicians continue to routinely order pre-operative testing for most patients undergoing cataract surgery.

METHODS: Supported by the American Board of Internal Medicine’s Choosing Wisely™ campaign to reduce low value care, we implemented and evaluated a quality improvement (QI) initiative to reduce pre-operative visits and testing for cataract surgery at LAC+USC Medical Center, the largest safety-net health system in the nation. We used electronic health records to identify patients with a CPT (procedure) code for cataract surgery from October 1, 2014—February 28, 2016. Using Institute for Healthcare Improvement PDSA (plan, do, study, act) cycle methodologies, our QI team implemented the following steps: (1) reviewed randomly sampled charts, (2) showed local data on over-testing to hospital leadership, (3) obtained buy-in from chairs of anesthesia and ophthalmology, (4) recruited an ophthalmology resident champion, and (5) empowered nurses to stop scheduling pre-operative visits. On October 13th, 2015, the resident champion and department chairs emailed clinical guidelines for pre-operative care to faculty, trainees, and staff. Primary outcomes included pre-operative medical visits, laboratory testing, and electrocardiograms within 80 days of surgery for patients undergoing cataract surgery. Secondary outcomes included 30-day post-operative complication rates and wait-times starting from diagnosis of cataracts until surgery. In this pre-post, quasi-experimental analysis, we constructed generalized linear models accounting for clustering by practice site and adjusting for patient characteristics, and assessed pre vs. post intervention time as our primary variable of interest.

RESULTS: We identified 959 patients who underwent 1,139 cataract surgeries during the study period; mean patient age 61.0 years, 52.1% female, and 79.5% Latino. Among patients undergoing cataract surgery, 76.2% of pre-intervention patients (n=734) vs. 12.0% of post-intervention patients (n=225) had unnecessary pre-operative medical visits (p<0.001); 90.2% of pre-intervention patients vs. 31.6% of post-intervention patients had unnecessary pre-operative laboratory testing (p<0.001); and 74.3% of pre-intervention patients vs. 18.2% of post-intervention patients had unnecessary pre-operative electrocardiograms (p<0.001). In addition, 3 pre-intervention patients vs. 1 post-intervention patient experienced a post-operative complication. Before the intervention, patients waited a median of 239 days until surgery; after the intervention, patients waited a median of 68 days (p<0.001).

CONCLUSIONS: This multidisciplinary quality improvement intervention led to substantial reductions in unnecessary pre-operative visits, laboratory testing, and electrocardiograms, and markedly shortened the wait from diagnosis to operation among patients undergoing cataract surgery. These findings have important implications for policymakers, practice leaders, and clinicians who have a stake in improving the efficiency of healthcare delivery.

Funders: American Board of Internal Medicine Foundation, National Institutes of Health/National Institute on Aging Midcareer Award in Patient-Oriented Translational Research in Aging (1K24AG047899).
Background/Objectives: For older adults with late-life disability, learning their long-term prognosis, or life expectancy, can inform clinical and personal decisions. Clinicians worry that telling patients their prognosis may harm them. We therefore conducted a study to explore the safety and reactions to prognosis communication in late-life disability.

Design/Measurements: Participants were asked to estimate their own life expectancy and were then presented their calculated life expectancy using the Lee index from ePrognosis.org. Their reactions were ascertained using a qualitative semi-structured interview guide. Interview transcripts were analyzed using constant comparison. Psychological and behavioral outcomes were assessed using metric measures and re-assessed by telephone 2-4 weeks later.

Setting: Community-dwelling older adults age 70+ with at least one disability in activities of daily living from the San Francisco Bay Area.

Participants: 35 older adults with a mean age of 84

Results: Self-estimates of life expectancy were similar to calculated life expectancy for the overwhelming majority of participants. One participant reported feeling extremely anxious about the results, though she later stated she was an anxious person in general. An overarching theme of fitting life expectancy into one’s narrative emerged from the qualitative data. Discussing life expectancy led participants to express how they saw their present health, their ability to alter their life expectancy, and their hopes and fears for the remaining years of their lives. They framed and estimated their own life expectancy in the context of their narrative, informing their reaction to the acceptability or usefulness of the calculated life expectancy.

Conclusion: Communicating long-term life expectancy does not appear harmful in this sample. Older adults’ reactions centered on the acceptability and usefulness of the information in the context of their life narrative. This study enhances our understanding of patients’ perspectives on life expectancy communication. Future research should be conducted in a clinical setting to examine how patients respond when physicians rather than research assistants discuss long-term prognosis.
REGULATORY MECHANISMS IN A HOMEOSTATIC MODEL OF GERIATRIC VOIDING PROBLEMS AND INCONTINENCE

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PROJECT ABSTRACT

Urinary symptoms become more prevalent with advancing age, and contribute to social isolation, institutionalization and morbidity. Current pharmacologic approaches are directed at correcting abnormalities of bladder pressure and frequently prove ineffective and/or poorly tolerated. Furthermore, many older adults are asymptomatic yet exhibit bladder functions often considered abnormal. Standard formulations relating symptoms, function and therapeutics are insufficient to address urinary control problems, especially within the complex multisystem nature of urinary dysfunction in the elderly.

The transduction of bladder volume to sensory afferent activity underpins control of the lower urinary tract. Recent evidence suggests that the transduction of bladder volume to bladder afferent activity is an adjustable gain system under continuous autonomic influence. Autonomic regulation of detrusor myocyte activity is a factor in determining sensitivity of the transduction process. A key target is the mechanism of autonomic control over detrusor myocyte activity and therefore the sensitivity of volume sensory transduction.

A network of Cx43 gap-junction linked interstitial cells (IC) is postulated to be a control network, mediating the autonomic regulation of detrusor myocyte activity. These cells have recently been found to express the molecular analog of the “funny current” involved in pacemaker functions, the Hyperpolarization activated, Cyclic Nucleotide gated (HCN) channel. HCN channels have a high propensity for modulation by transmitters of the autonomic nervous system and therefore, we hypothesize that HCN channels in IC cells contribute to autonomic regulation of bladder tension. Age-associated change in HCN isoform expression exists in other tissues, and could contribute to altered autonomic detrusor control responses in older bladders. We have recently developed a flow cytometry technique permitting isolation and electrophysiologic study of individual ICs. Using analytic tissue studies, cellular and molecular biology tools and electrophysiologic patch clamp techniques, we propose to determine the role of HCN in autonomic regulation of IC-based mechanisms controlling detrusor tension in an established mouse system. We will further test the impact of aging on these mechanisms via loss or isoform change in HCN expression, and provide tissue-level descriptive confirmation of mechanistic models.

This work integrates institutional expertise in physiology/cystometry, gerontology, geriatrics, immunology, and neurophysiology, making use of excellent core services in flow cytometry, histology, electrophysiology and ultimately single cell genomics. The focused training provided by this Award represents the final step in the career development of the PI and will provide important preliminary data for planned R01-level grant writing later in 2016 and beyond.
ZCCHC17 impairment contributes to synaptic dysfunction in Alzheimer’s Disease

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Our laboratory is using bioinformatic tools to investigate potential master regulators of gene expression in cortical neurons that are disrupted in Alzheimer’s disease (AD). This analysis has resulted in the identification of a protein (called ZCCHC17) which is ranked highly in our analysis in two important ways: 1) As a potential master regulator of gene expression generally, and 2) As a potential master regulator of synaptic genes specifically. Our analysis predicts that ZCCHC17 has impaired activity in AD, and that this impairment may partially explain dysregulation of synaptic gene expression in AD. ZCCHC17 was discovered in 2002, and there is limited literature on this protein. It has previously been localized to the nucleus as well as the nucleolus in a variety of tissues, and its structure implies possible roles in RNA processing as well as in ribosomal genesis/function. It has not been previously studied in the nervous system. We have now identified 38 synaptic genes that are predicted to be regulated by ZCCHC17 in human neurons and that are subsequently impaired when ZCCHC17 is knocked-down in rat cortical cultures. Of these 38 synaptic genes, 28 also have decreased mRNA in human AD brain tissue. Finally, patch-clamp recordings from rat cortical culture neurons after ZCCHC17 knock-down show an impairment in the potassium current, and calcium imaging after ZCCHC17 knock-down reveals aberrations in calcium-mediated activity. Taken together, these data indicate that ZCCHC17 supports normal neurophysiology in several different ways, and further supports the hypothesis that ZCCHC17 impairment contributes to synaptic dysfunction in AD.
Managing Anxiety from Cancer (MAC): A Psychological Intervention for Anxiety in Older Adults with Cancer
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Anxiety is common among older adults (OAs) with cancer and is associated with greater fatigue, nausea, pain, and dyspnea; poor quality of life, physical performance status, and emotional, social, and cognitive function; poor communication with the healthcare team, and a weaker patient-oncologist alliance. There is also evidence that anxiety negatively affects treatment adherence and response and decision-making. Yet, over half of cancer patients who meet diagnostic criteria for a psychiatric disorder do not receive mental health services. Cognitive Behavioral Therapy (CBT) is a validated and effective treatment for anxiety in OAs and cancer patients. However, CBT interventions have not been modified to address the unique needs of older adults (OAs) with cancer.

Informal caregivers of cancer patients are at increased risk for psychological, physical, and social decline due to their caregiving role and may have more severe anxiety than patients. Further, caregivers of advanced cancer patients who meet criteria for a psychiatric diagnosis are 7.9 times more likely to have a psychiatric diagnosis themselves; this mutuality is particularly prominent for anxiety disorders. Therefore, addressing caregiver anxiety is necessary in its own right and vital to effective treatment of patient distress.

The purpose of this study is to develop and evaluate Managing Anxiety from Cancer (MAC), a six-session telephone-delivered cognitive-behavioral therapy (CBT) intervention designed specifically for anxiety in OAs (≥65 years) with cancer and primary informal caregivers of OAs with cancer. Sessions occur weekly for 50-60 minutes and are delivered individually to patients and caregivers by separate therapists. Patient and caregiver workbooks and corresponding therapist manuals were developed (Phase 1). Feedback on these manuals was obtained from patients, caregivers, and oncology providers informed modifications to MAC (Phase 2).

Phase 3 is ongoing and is a trial proof-of-concept evaluation of MAC. The purpose of this open trial is to examine the feasibility and acceptability of MAC and study procedures, determine whether MAC has a clinically significant impact on anxiety, and prepare the manuals and study procedures for a pilot RCT. Inclusion criteria include patient age ≥65 years when diagnosed with cancer, patient and/or caregiver score ≥8 on the anxiety subscale for the Hospital Anxiety and Depression Scale, patient and caregiver are able to communicate over the telephone, and caregiver is ≥21 years old. Dyads are excluded if one member is not fluent in English, is too weak or cognitively impaired to participate in MAC and complete study measures, screens positive for a psychiatric condition, or endorses active suicidal ideation. Patients are being recruited from the lung, gynecologic, lymphoma, gastrointestinal, and myeloma cancer clinics at Weill Cornell Medicine. Study measures are administered over the telephone pre and post MAC. To date, six patient-caregiver dyads have been enrolled in MAC; three of these dyads have completed all study procedures. Recruitment is ongoing with a target sample size of n=10 dyads.

Phase 4 will be a pilot randomized controlled trial (RCT) of MAC to examine feasibility and acceptability, replicate the clinically significant signal obtained in Phase 3, test the adequacy of the control group, and prepare the operations manual for a future efficacy trial protocol. The long-term goal of this research program is to develop an efficacious, clinically feasible, scalable, and cost effective psychosocial intervention for anxiety that is acceptable to OAs with cancer and their primary informal caregivers.

Keywords: Anxiety, Cancer, Older adult, Caregiver
Utilization of Hospice Services in Nursing Homes: A comparison with other settings

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Key words: Hospice, Long Term Care, Financing Health Care, Health Reform

Objectives: To describe differences in hospice services for patients living at home, in nursing homes or in assisted living facilities, including the overall number and duration of visits by different hospice care providers across varying lengths of stay.

Design: Retrospective cohort study using hospice patient electronic medical record data.

Setting: Large, national hospice provider

Participants: Data from 32,605 hospice patients who received routine hospice care from 2009-2014 were analyzed.

Measurements: Descriptive statistics were calculated for utilization measures for each type of provider and by location of care. Frequency and duration of service contacts were standardized to a one week period and pairwise comparisons were used to detect differences in care provided between the three settings.

Results: Minimal differences were found in overall intensity of service contacts across settings, however, the mix of services were different for patients living at home vs. nursing home vs. assisted living facility. Overall, more nurse care was provided at the beginning and end of the hospice episode; intensity of aide care services was higher in the middle portion of the hospice episode. Nearly 43% of the sample had hospice stays less than two weeks and up to 20% had stays greater than six months.

Conclusion: There are significant differences between characteristics of hospice patients in different settings, as well as the mix of services they receive. Medicare hospice payment methodology was revised starting in 2016. While the new payment structure is in greater alignment with the U shape distribution of services, it will be important to evaluate the impact of the new payment methodology on length of stay and mix of services by different providers across settings of care.
Abstract for submission to the 2016 annual AFAR Beeson meeting

**IVIg for apparently autoimmune small-fiber polyneuropathy—first look at efficacy and safety**

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**OBJECTIVE:** To study the efficacy and safety of intravenous immunoglobulin (IVIg) for apparently autoimmune small-fiber polyneuropathy (aSFPN).

**BACKGROUND:** Emerging data suggest that systemic or organ-specific autoimmunity may contribute to some SFPN cases, and IVIg, a standard treatment for autoimmune large-fiber neuropathies, is sometimes empirically prescribed for severe treatment-refractory cases. Given IVIg’s scarcity, cost and risks, even preliminary information about efficacy and safety would be useful.

**METHODS:** With IRB approval, we analyzed our records of consecutive aSFPN patients treated with IVIg dosed at $\geq 1$ gram/kg/4 weeks for at least 3 months. Inclusion required a neurologist’s impression of SFPN plus confirmation by skin biopsy, nerve biopsy, or composite autonomic function testing (AFT). The outcomes were change in AFT interpretations, in pain severity, safety events, and impressions of change.

**RESULTS:** Among the 55 participants, 27% had systemic autoimmunity (8 with Sjögren’s, 4 with lupus, 2 with rheumatoid arthritis, 1 with Churg-Strauss). Another 15% had organ-specific autoimmunity (3 with Hashimoto’s thyroiditis, 3 with inflammatory bowel disease, and 1 each with diabetes-I, Grave’s disease, psoriasis). 80% had inflammatory serologies (35% ANA $\geq 1:160$, 33% ESR $\geq 15$ mm/h, 20% C4$<14$ mg/dl, 14% C3$<85$ mg/dl). Treatment duration averaged 28±25 months. The 89% pre-treatment prevalence of abnormal AFTs attributed to SFPN fell to 55% post-treatment ($p=0.001$) and quantitative sweat production improved. Among the 32 participates with baseline $\geq 3/10$, pain severity averaging 6.3±1.7 reduced to 5.2±2.1 ($p=0.007$). 74% of patients rated themselves as “improved” and neurologists labeled 77% as “responders”. 16% entered remissions sustained even after IVIg withdrawal. No adverse events were unusual. Four participants stopped IVIg because of infusion reactions and one because of hemolytic anemia. Two continued despite deep vein thromboses.

**CONCLUSIONS:** This very large case series provides Class IV evidence that IVIg may be safe and effective for selected patients with apparently autoimmune SFPN. Preliminary clinical guidelines should be formulated and clinical trials considered.

Supported in part by the National Institutes of Health (NINDS R01NS093653).
Validation and continuing development of a patient-reported survey of small-fiber polyneuropathy symptoms

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Objective: To improve our comprehensive symptom screen for diagnosing small-fiber polyneuropathy (SFPN).

Background: Because the small unmyelinated C-fibers and thinly myelinated A-delta peripheral axons have myriad functions, SFPN causes varying symptoms including widespread pain and itch, cardiovascular, gastrointestinal, and sweating concerns. While there are validated questionnaires for pain and dysautonomia as well as neuropathy from diabetes or chemotherapy, there are no pan-symptom screens, nor surveys for other causes. Thus we developed and are validating a comprehensive, patient-completed, Small-fiber Symptom Survey (SSS). Beginning with items from clinical experience and literature reports, we refined the SSS by soliciting input from patients and 21 medical/scientific experts.

Methods: With IRB consent, the SSS version 4 was administered using the REDCap web-based application for secure data capture, or surface mail. Internal consistency, test-retest reliability, and convergence with other instruments, including SF-MPQ-2, SF-236, and COMPASS-31 were evaluated in 179 adults spanning the range of symptom severity. They included normal controls and patients being tested for SFPN. 85 had diagnostic confirmation by skin biopsy and/or autonomic testing. Face-to-face debriefings verified participant comprehension and measured completion time.

Results: Participants’ mean age was 47 years, 73% were female, and 92% were Caucasian. The most common symptoms among confirmed cases were fatigue (100%), reduced endurance (98%), and tingling/paresthesias (91%). Five rounds of exploratory factor analysis yielded 22 items grouped into 5 medically appropriate clusters that explained 59% of the variance. This one-page questionnaire had good internal consistency (Cronbach’s alpha=0.893), excellent 2-week test-retest reliability (r=0.927; p<0.001) and convergent validities of 0.64-0.80. Symptoms were more severe in participants with confirmed SFPN (p=0.009) indicating potential diagnostic validity. Ongoing experiments include measurement of diagnostic sensitivity and specificity, optimizing the reporting period, and ROC analysis.

Conclusions: The SSS captures a wide range of SFPN symptoms, including new patient-identified symptoms. It has good psychometric properties and potential clinical and research utility.

Study supported by the National Institutes of Health [R01-NS093653 and UL1 TR001102]; Lundbeck Foundation Scholarship in Neurology; and the U.S. Department of Defense [GW140169].
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ABSTRACT

Objective: To characterise experiences using clinical research data shared through the National Institutes of Health (NIH)’s Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) clinical research data repository, along with data recipients’ perceptions of the value, importance and challenges with using BioLINCC data.

Design and setting: Cross-sectional web-based survey.

Participants: All investigators who requested and received access to clinical research data from BioLINCC between 2007 and 2014.

Main outcome measures: Reasons for BioLINCC data request, research project plans, interactions with original study investigators, BioLINCC experience and other project details.

Results: There were 536 investigators who requested and received access to clinical research data from BioLINCC between 2007 and 2014. Of 441 potential respondents, 195 completed the survey (response rate=44%); 89% (n=174) requested data for an independent study, 17% (n=33) for pilot/preliminary analysis. Commonly cited reasons for requesting data through BioLINCC were feasibility of collecting data of similar size and scope (n=122) and insufficient financial resources for primary data collection (n=76). For 95% of respondents (n=186), a primary research objective was to complete new research, as opposed to replicate prior analyses. Prior to requesting data from BioLINCC, 18% (n=36) of respondents had contacted the original study investigators to obtain data, whereas 24% (n=47) had done so to request collaboration. Nearly all (n=176; 90%) respondents found the data to be suitable for their proposed project; among those who found the data unsuitable (n=19; 10%), cited reasons were too complicated to use (n=5) and data poorly organised (n=5). Half (n=98) of respondents had completed their proposed projects, of which 67% (n=66) have been published.

Conclusions: Investigators were primarily using clinical research data from BioLINCC for independent research, making use of data that would otherwise have not been feasible to collect.

Strengths and limitations of this study

- Data sharing policies are increasingly promoted and being adopted by research funders to improve access to clinical trial data to inform evidence-based practice. The National Institutes of Health (NIH)’s Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC) has been actively sharing data from its clinical research data repository for >10 years.
- In the first survey of the experiences of investigators who have requested and been approved to use data from BioLINCC, we found that users were primarily focused on conducting independent research studies, making use of data that would otherwise have not been feasible to collect, because of insufficient time and resources.
- We also found that shared data from BioLINCC could be used to successfully pursue clinical research; 90% of BioLINCC users found the data to be suitable, half had completed their research projects thus far, and two-thirds had published their findings.
- Our study of user experiences with BioLINCC offers important insights for newly initiated and ongoing clinical trial data sharing efforts and illustrates the potential and value of data sharing for the broader scientific field, as well as the challenges that remain to be overcome.
- Our study is limited by a low response rate and may have been affected by recall bias and social desirability bias, perhaps suggesting that our findings overestimate the perceived value of BioLINCC data and their usability for the broader scientific community.

Over the past 5 years, several major research funders, including the US National Institutes of Health (NIH), the US Patient-Centered Outcomes Research Institute, the UK Medical Research Council and the Bill and Melinda Gates Foundation, as well as private industry, have adopted policies supporting or mandating clinical research data sharing. In January 2015, the Institute of Medicine of the US National Academies further supported these efforts with its report, ‘Sharing Clinical Trial Data: Maximizing Benefits,
Minimizing Risks’, recommending that stakeholders foster a culture in which data sharing is the expected norm and commit to responsible strategies aimed at maximising benefits, minimising risks and overcoming challenges of sharing clinical trial data. In January 2016, the International Committee of Medical Journal Editors issued a proposal to require authors to share with others the de-identified individual patient data underlying the results presented in the article no later than 6 months after publication as a condition of consideration for publication of a clinical trial report in its member journals.

In response to these new policies and proposals, funded investigators will increasingly be asked to prepare and make collected data available to other investigators with whom they are not collaborating so that the second can pursue independent research. To support these efforts and inform developing policies, a number of prior studies have examined the willingness of clinical trial investigators to share clinical research data, generally finding broad support, and characterised anticipated challenges to and concerns with data sharing. However, few studies have focused on the investigators who have actually received de-identified individual patient data from a centralised data sharing platform, in order to understand their perspectives regarding challenges encountered with requesting and using the data, and disseminating findings.

While most of these data sharing efforts have been relatively newly established, the US National Heart, Lung, and Blood Institute (NHLBI) of the NIH established a formal data repository in 2000, now managed by the Biologic Specimen and Data Repository Information Coordinating Center (BioLINCC), to facilitate access to, maximise the scientific value of, and promote the availability and use of the biorepository, data repository and other NHLBI-funded population-based biospecimen and data resources by investigators worldwide. The BioLINCC data repository includes individual-level data on >580,000 participants from over 110 institute supported clinical trials and observational studies, beginning as far back as the 1980s. Each data set is prepared independently by the NHLBI-funded investigator to comply with specific requirements and data standards, with oversight by BioLINCC, including provision of baseline, interim visit, ancillary study and outcome data for clinical trials and provision of all examination and ancillary study data, along with follow-up information, for epidemiology studies. As BioLINCC has been actively sharing data for more than a decade and currently receives over 100 requests for clinical trial and other prospective cohort clinical data per year (ref; personal communication, Sean Coady, NHLBI data repository manager), there is an opportunity to learn from data users’ experiences to inform clinical data sharing efforts. Accordingly, we surveyed all investigators who requested and received access to clinical research data from BioLINCC between 2007 and 2014. We specifically sought to understand their experiences with clinical research data sharing and status of their research project, as well as perceptions of the value, importance and challenges of accessing data through BioLINCC.

METHODS

Study sample and design

We conducted a cross-sectional survey from May to August 2015 of all investigators who requested and received access to clinical research data from BioLINCC between 2007 and 2014. This time period was chosen to ensure a contemporaneous sample of investigators whose contact information was less likely to have changed over ensuing years. In accordance with NIH policy, BioLINCC provided our study team with a list of investigators who had requested and received access using a public email address; contact information was available for the lead investigator who was responsible for the BioLINCC request, not each member of the study team. For investigators who had requested and received access using a private email address, BioLINCC first sent an opt-in/opt-out email in May 2015, asking if they would be willing to participate in the survey (see online supplementary appendix). Non-respondents were sent two follow-up requests by email; those that did not respond by the end of the third week were considered to have opted out. BioLINCC subsequently provided our study team with a list of those investigators who opted in.

In addition to contact information, BioLINCC provided our study team with information on the following for all investigators who had requested and received access to clinical research data: lead investigator location, affiliation with an academic institution or for-profit organisation and total number of requests ever submitted to BioLINCC, as well as the request year, the number of data sets requested and self-reported availability of external funding to support the research project using the requested data.

In May 2015, the Yale team sent all potential survey respondents an initial email to describe the purpose of the study, request their participation and provide a link to the survey; three follow-up requests were sent by email over the course of June 2015. Non-respondents were contacted by telephone to solicit their participation up to twice per week, but no more than once per day, until one contact was made. In July 2015, internet searches to update contact information for non-respondents were conducted. For all non-respondents whose updated contact information was identified, the initial survey email was sent, followed by three follow-up requests.

Invitations to participate did not reference a specific hypothesis of the study, but stated that investigator participation would further the understanding of investigators’ experience with BioLINCC and inform future clinical trial data sharing efforts (see online
supplementary appendix). Participation was voluntary and included an opportunity to win one of five $100 gift certificates for Amazon. All internet-based responses were collected using a web-based survey platform (Qualtrics Labs, Provo, Utah, USA).

Survey instrument development

The design of our 50-item survey instrument was informed by previously published surveys, a review of the literature on clinical trial data sharing, and discussion with multiple experts and stakeholders, including representatives from NHLBI and academic investigators. Experts recommended survey topics that they considered to be compelling for the field of data sharing and reuse of data. The survey was pretested with six medical students and staff at the Center for Outcomes Research and Evaluation, Yale New Haven Hospital (New Haven, Connecticut) and modified iteratively to improve clarity, face validity and content validity. Adaptive questioning was used to decrease response burden. Items were presented in multiple response, Likert scale and open-ended formats; many of the multiple response questions enabled respondents to select multiple answers. The complete instrument is provided within the online supplementary appendix.

Survey domains

Reasons for data request and planned research project

We used multiple response and yes/no questions to assess investigators’ primary research purpose and reasons for requesting data from BioLINCC. Multiple response questions were also used to determine the primary research objective, funding used to support the project and other details of the planned research project. Knowing what these clinical research data are being used for will help tailor future data sharing efforts to the needs of investigators.

Interactions with original study investigators

We used yes/no questions to determine whether original study investigators were contacted prior to or after requesting data through BioLINCC to obtain the data or to collaborate. These were followed by multiple response questions to determine why collaborations were sought, whether the requests for data or collaboration were approved and reasons for not approving. Answers to these questions could potentially demonstrate the value of a data resource such as BioLINCC.

BioLINCC experience

Multiple response, yes/no and Likert-type questions were used to obtain information regarding investigators’ experience using BioLINCC, including whether the data were suitable and useful for their project. Knowledge gained from these questions can help to improve BioLINCC and other data sharing efforts.

Project details

We used multiple response and yes/no questions to characterise the completion stage of investigators’ projects. For those that did not complete their project, multiple response and yes/no questions were used to ascertain reasons why the project was incomplete. For those with completed projects, we used multiple response and yes/no questions to determine whether the final project differed from the prespecified project as well as to obtain publication information. Multiple choice and multiple response questions were used to identify any funding sources, and whether using the data from BioLINCC aided in any future grant applications. It is important to demonstrate that these data are being requested, and they are also being used to potentially generate new knowledge to advance science and public health.

Requestor demographics

Respondents were asked to characterise their primary employer and career status using multiple choice questions, including whether they had ever been closely involved (as principal or coinvestigator) in the conduct of a randomised controlled trial and/or ever deposited clinical trial data in the BioLINCC repository. Respondent sociodemographic characteristics, including age, gender and ethnicity, were also collected. While these characteristics were collected for descriptive purposes only, age, along with the professional characteristics collected, are of importance to demonstrate the value of the availability of BioLINCC data to investigators who are in certain stages of their career.

Patient involvement

Patients were not involved in the design or conduct of this study. Results will be directly disseminated via email to all individuals invited to participate in the survey on publication.

Statistical analysis

To compare characteristics of survey respondents and non-respondents, we used two-sided χ² tests and Fisher’s exact tests when appropriate with a type 1 error level of 0.05. Next, we conducted descriptive analyses of the reasons for requesting data from BioLINCC, prior interactions with original trial investigators, experience using BioLINCC and project details, as well as respondent demographic characteristics. Data were analysed using JMP Pro V.11.2.0 (SAS Institute, Cary, North Carolina, USA).

RESULTS

There were 536 investigators who requested and received access to clinical research data from BioLINCC between 2007 and 2014 (figure 1). Investigators for which a public email address was not available were sent an opt-in/opt-out letter (n=74); 23 opted in, 3 opted out, 7 could
not be reached and 41 were not responsive. Survey participation requests were thus sent to 485 eligible respondents, 44 of whom were subsequently excluded due to the following reasons: invalid contact information \((n=31)\), the investigator had no recollection of requesting the data \((n=5)\) or the data had been requested by someone other than the investigator \((n=8)\). Of the remaining 441 respondents, 195 completed the survey, yielding a survey response rate of 44.2%. However, of the 536 total investigators who requested and received access to clinical research data from BioLINCC, 195 completed the survey \((response\ rate\ of\ 36.3\%)\).

Survey respondents did not differ from non-respondents with respect to investigator location, affiliation with an academic institution or for-profit organisation and total number of requests ever submitted to BioLINCC, as well as the number of data sets requested \((p\geq0.10; table\ 1)\). However, respondents were more likely than non-respondents to have requested data more recently \((p=0.004)\ and to have self-reported external funding to support the research project \((p=0.009)\).

Half of survey respondents were between 35 and 49 years of age \((n=97; 50\%)\, while 59\%\ were male \((n=116)\, 68\%\ were white \((n=133)\ and 90\%\ identified as not Hispanic/Latino \((n=175; table\ 2)\). The vast majority of respondents were primarily employed by an academic institution \((n=165; 85\%)\ and 78\% \((n=152)\ have been engaged in clinical research for at least 3 years. While 42\% \((n=82)\ had been closely involved in the conduct of a randomised controlled trial, only 3\% \((n=5)\ had ever deposited data in the BioLINCC repository.

**Reasons for data request**

Overall, respondents’ motivations for requesting data from BioLINCC were largely focused on using the data to conduct and disseminate new research studies, as 89\% \((n=174)\ indicated that data were requested for an independent study, 17\% \((n=33)\ to use the data for pilot/preliminary analysis. For 63\% \((n=122)\ of respondents, the decision to request data through BioLINCC was influenced by the belief that collecting data of similar size and scope was not feasible, while insufficient financial resources for primary data collection \((n=76; 39\%)\, individual participant-level data being unavailable elsewhere \((n=71; 36\%)\, and insufficient time for primary data collection \((n=64; 33\%)\ were also commonly cited reasons for requesting data through BioLINCC (figure 2).
Respondents largely (n=149; 76%) planned research projects that used the requested BioLINCC data as a standalone data source for at least one project, while 43% (n=83) planned to combine the data with other data sources; of these, 27% (n=22) planned to conduct a meta-analysis. Nearly all respondents (n=186; 95%) indicated that at least one of their primary research objectives was to complete new research, whereas only 7 (4%) had a primary research objective solely to replicate prior analyses. Of those pursuing new research, 56% (n=104) planned to leverage the data for a research question unrelated to the original research design, while 40% (n=74) planned to examine subgroup populations and 32% (n=60) planned to examine secondary end points.

Only 13% (n=26) of respondents indicated that the focus of their research was a medical product or intervention; of these, 73% (n=19) planned analyses to examine product/intervention efficacy, 54% (n=14) safety. Finally, 52% (n=102) of respondents had funding to support the research project, most commonly from the NIH (n=44; 23%), whereas 43% (n=84) primarily self-funded the research project.

**Interactions with original study investigators**

Fewer than one in five (n=36; 18%) respondents indicated that they had contacted the original study investigators to obtain data prior to requesting the data from BioLINCC; among these, 44% (n=16) reported that the original study investigator approved their request and these investigators most commonly requested access to the data from BioLINCC anyway because the process to access data was more straightforward through BioLINCC (n=11). Among the 20 (56%) respondents who indicated that the original study investigator denied their request, the most common response given by the original investigator was to direct the respondent to BioLINCC (n=11; 55%).

Nearly one-quarter of respondents (n=47; 24%) indicated that they contacted the original study investigator to request collaboration, most commonly because of an interest in working with the original study investigators (n=23) and need for additional content expertise due to study design complexity (n=20). Of the respondents who requested collaboration, two-thirds (n=31; 66%) indicated that the request was accepted.

**Data repository experience**

Nearly all respondents indicated satisfaction with the data available through BioLINCC and that they were suitable for their originally proposed project (n=176; 90%). Among the 19 (10%) respondents who indicated that the data were not suitable, the two most commonly cited reasons were that the data were too complicated to use, preventing them from determining whether the data were suitable (n=5); and that the data were poorly organised, preventing adequate preparation for analysis (n=5).

**Research project details**

Half of all respondents (n=98; 50%) reported that their projects have been completed, of which 67% (n=66) have been published. Respondents who had requested data prior to 2012 were more likely to have completed their project when compared with those who had requested data in 2012 or afterwards (73% vs 44%; p=0.008). However, among those who completed their project, rates of publication did not differ among those who had requested data prior to 2012 and those who...
had requested data in 2012 or afterwards (63% vs 69%; p=0.57). Of those who have completed their research, 48% (n=47) indicated that no substantive concerns were raised about the use of data from BioLINCC during the peer-review process, while 8% indicated that concerns were raised about research methodology and analysis (n=8), 7% about the original study design that the investigator could not address (n=7), and 6% about their research project design that they could not address without additional data (n=6).

Of the 97 respondents (50% of total) who have not yet completed their proposed projects, 84% (n=81) explained that they planned to complete their project; 65% (n=63) indicated that their project is in analysis/manuscript draft phase, while 28% (n=27) explained that they have thus far been too busy with other activities.

Figure 2  Factors influencing decision to request clinical research data through BioLINCC between 2007 and 2014 (n=195).
Note: Respondents were able to select multiple answers in response to this question. BioLINCC, Biologic Specimen and Data Repository Information Coordinating Center; EMR, electronic medical record; IPD, individual participant data.

Figure 3  Flow chart showing completion rates of research projects using clinical research data requested from BioLINCC between 2007 and 2014. Note: Respondents were able to select multiple answers in response to this question.
responsibilities to complete the research project using the data from BioLINCC and 13% (n=13) reported that lack of funding to support the project was a problem (figure 3). A total of 16 investigators explained that they did not intend to complete their project, most often because the age of the data made the project now less relevant or because of data issues, such as missing values for the variable of interest.

Of the 179 respondents who already completed or planned to complete their proposed project, 54% (n=96) reported that there would be one research project resulting from their single request for data from BioLINCC, 23% (n=42) reported two and 25% (n=41) reported three or more. In addition, 15% (n=27) of respondents who have completed or planned to complete their project indicated that their completed/anticipated final project differed from their prespecified project; the most commonly modified aspects were the statistical analysis plan (n=18) and the selection of the main independent variables (n=12).

DISCUSSION
In this survey of investigators who had requested and received access to clinical research data from BioLINCC between 2007 and 2014, the vast majority had requested the data in order to conduct independent research projects, primarily because collecting data of similar size and scope was not feasible, due to insufficient time and resources. Half of the investigators had completed their research projects thus far, two-thirds of which published their findings, and among those investigators whose projects were incomplete, two-thirds were actively engaged in analysis or manuscript preparation. These findings offer important insights for newly initiated and ongoing clinical trial data sharing efforts and illustrate the potential and value of data sharing for the broader scientific field, as well as the challenges that remain to be overcome.

First, the BioLINCC experience suggests that when clinical research data are made available to investigators, there is likely to be interest in using the data for independent research projects. There are currently 654 publications associated with the data repository available through BioLINCC. This large number of publications suggests that these data are being used by investigators, better maximising the NHLBI investment in and scientific value of clinical research data. Many investigators responding to our survey noted that collecting data of similar size and scope was not feasible, or that they had insufficient financial resources or time for primary data collection, justifying the need to request data from BioLINCC for their research.

Second, the BioLINCC experience suggests that clinical data can be collected by one set of investigators and made available to another set of investigators who, for the most part, can use it to successfully pursue an independent research project. While some surveyed investigators noted challenges in using the data made available through BioLINCC, 90% found the data to be suitable for their originally proposed project, even without input from the original research team. Few reported that the data were too complicated to use, preventing them from determining whether the data were suitable, or that the data were poorly organised.

Finally, the research enterprise is not optimally efficient, and the BioLINCC experience reflects this shortcoming. In aggregate, >100 research projects were completed as a result of respondent investigators using data made available through BioLINCC. However, despite all investigators having received data from BioLINCC at no cost, only half of investigators who had received data had completed their research projects thus far. While many more continue to work on their projects and intend to complete their work, the investment by NHLBI to make these data available should be matched by the effort of investigators to ensure that the projects are completed. Moreover, even among completed projects, only two-thirds were published. While BioLINCC maintains an updated list of publications that have resulted from use of this shared data, mechanisms should be established to ensure that results from research made possible through data sharing are publicly disseminated, either through publication or through a results reporting initiative similar to ClinicalTrials.gov.

For the potential and value of data sharing to be fully realised, more needs to be accomplished. Part of the success of BioLINCC may be attributed to the NHLBI policy that supported studies with direct costs equal to or ≥$500K in any 1 year and identified as being of high programmatic interest, along with cooperative agreements with 500 or more participants, are required to submit data as part of the grant award. This policy establishes clear expectations for data sharing, so that data can be properly organised and de-identified and supportive documentation and materials prepared in anticipation of submitting data to BioLINCC. However, it is not clear whether this policy allows researchers to budget resources for this work. Currently, the NIH is seeking ways to broaden data sharing efforts across its institutes, to enhance the likelihood of success of data sharing efforts, it should be clarified whether NIH–granted independent research funds can be used to prepare collected data for sharing through initiatives such as BioLINCC.

Similarly, financial support for investigators to use clinical research data that are being shared and made available would enhance efforts. In total, 43% of investigators using data from BioLINCC had self-funded their research efforts, while 23% were relying on funding from the NIH. However, among surveyed investigators who had not yet completed their proposed projects, lack of funding to support the project was a commonly cited problem. Without financial support, efforts to share data are likely to fail to achieve their...
potential, even despite the strong policies and proposals in favour of data sharing from other research funders, the Institute of Medicine and the International Committee of Medical Journal Editors.

There are important limitations of our study to consider. First, only 44% of potentially eligible respondents completed our survey, perhaps suggesting that our findings overestimate the perceived value of BioLINCC data and its usability for the broader scientific community. Individuals who chose not to respond to our survey may have found the data to be more problematic and less useful than those who responded. Furthermore, even among respondents, our findings may have been biased by recall bias, including an inability to remember using the data made available by BioLINCC, and social desirability, as respondents may have been less likely to self-report experiences and project completion plans that may be negatively perceived by others. In addition, there were a few observed differences between survey respondents and non-respondents. As we would expect that investigators who made more recent requests and who had secured external funding to support the research project would be more likely to remain enthusiastic about the project and to complete it, our findings may be biased towards higher project completion rates. However, our response rate compares favourably with other surveys of physicians and investigators, perhaps reflecting that we used several mechanisms to prospectively improve response rates, including a web-based survey platform for ease of completion, we employed several reminder contacts, including three emails and at least one telephone contact and we offered financial incentives for participation.

Second, our study was limited to investigators who had received data from BioLINCC and our findings may not be applicable to the experience of investigators obtaining data from other repositories. There is currently great interest and scrutiny of existing clinical trial data sharing efforts, many of which require submission of a research proposal, as does BioLINCC, and some of which only make data available via a virtual, secure data sharing environment, as opposed to BioLINCC which provides de-identified data directly to approved researchers. One recent study evaluated how many clinical trials were publicly available to the research community through three open access data sharing platforms: ClinicalStudyDataRequest.com, the Yale University Open Data Access (YODA) Project and the Supporting Open Access for Researchers (SOAR) Initiative, finding that while >5000 trials were available, only 15.5% had been requested by a limited number of investigators. The authors concluded that data sharing efforts are being underused, implicitly questioning the value of continued resource investment. However, the results of our survey of BioLINCC users suggests this conclusion may be premature, as use of data from these open access platforms can be expected to grow with time, although more remains to ensure the use of these data, and the successful completion and publication of the resulting research, to justify the investments being made in data sharing.

A third limitation of our study is that some information of interest was not asked in order to reduce survey response burden, including questions asking about the time and effort invested to manage and analyse the data from BioLINCC and the impact of the publications resulting from the research project. Finally, our study made no attempt to judge the impact of the research that was able to be completed because of the clinical research data made available through BioLINCC. Other efforts should consider whether the investment being made by NIH and NHLBI in data sharing is justified by the information and knowledge being generated for medical science and society.

In conclusion, we found that the vast majority of investigators who had requested and received access to clinical research data from BioLINCC between 2007 and 2014 had either succeeded in completing their research project or reported being actively involved in data analysis or manuscript preparation. In aggregate, >100 research projects were completed as a result of respondent investigators using data made available through BioLINCC. Experience with BioLINCC illustrates the potential of data sharing for the broader scientific field and the importance of funding these efforts, particularly when collecting data of similar size and scope is not feasible for many investigators.

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Ethics approval  Ethics approval from the Yale University School of Medicine Human Research Protection Program was obtained prior to study conduct and consent was considered to be implied when participants completed the online survey.

Provenance and peer review  Not commissioned; externally peer reviewed.

Data sharing statement  Extra data can be accessed via the Dryad data repository at http://datadryad.org/ with the doi:10.5061/dryad.j38b7.

Transparency  The lead author (JSR) affirms that this manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Data sharing through an NIH central database repository: a cross-sectional survey of BioLINCC users

Joseph S Ross, Jessica D Ritchie, Emily Finn, Nihar R Desai, Richard L Lehman, Harlan M Krumholz and Cary P Gross

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Career Development Competency Areas

• know *what* (clinical expertise)
• know *why* you are doing what you’re doing (goals, values)
• know *whom* (build key relationships)
• know *how* (communication skills, political savvy)
• know *when* (adaptable, take smart risks)
Please Assess Yourself:

- Do I know what “success” means to me?

- Am I learning how to capitalize on my strengths and take my weaknesses into account?

- Is my understanding of my organization becoming more sophisticated?

- Am I expanding my circle of colleagues?

- Am I getting better at communicating with individuals very different from myself?

- Am I generally good at meeting my goals while also building relationships?
Negotiation is...

-- A way of life

-- Reveals how you take your seat at the table

-- An attitude about both self-efficacy and building relationships
Negotiation: a communication process aimed at achieving agreement when there are both divergent and convergent interests

Negotiation skills include:
* identifying shared interests
* asking good questions and listening generatively
* adapting quickly to new information
* realistic confidence
Relationships = Leverage

Approach negotiations with the goal of:

* creating value, identifying potentials for mutual gains and identifying alignments of interests

* sustaining critical relationships

* enhancing your credibility (have to be “likeable”)

* capturing an appropriate share of the value
Negotiation involves.....

--Preparation

--Information exchange

--Bargaining

--Commitment/ implementation
Preparation

--Gather information, eg “market value”
--Uncover shared interests, eg “role reversal”
--Generate a WIIFT (What’s In It For Them) (ie connect your issues to theirs)
--Identify all alternatives that could meet your needs

Practice and Role play

*Try out different levels of intensity and informality and varying your tone
*Practice responses to tough questions and challenges
*Act as if you were hired to represent you (or are negotiating for your best friend)
Common Put-offs

*You put me in a difficult position.

*I'd like to pay you X, but Y won't let me.

*Nobody makes above the AAMC mean here

*How much did you make in your last job?

*Doesn't your husband make a lot?
Identify what's negotiable

*what questions might you ask to get more information?

*find options for mutual gain and “yes-able propositions”

*framing techniques
  --link to mission/core values
  --heighten concerns about loss/risk
  --enlarge the pie
What do you need to negotiate or renegotiate?

How will you prepare?

What additional information do you need and how will you get it?
Speaking up about Your Goals and Accomplishments

**Problem or Purpose or Opportunity**
What needs/ed to be fixed?
What are the opportunities and challenges?

**Action:** What will/did you do?

**Result/Benefit:** What difference will you make?
Seeing our Assumptions

*We ignore evidence contradicting our assumptions and “cherry pick” data that confirms our opinions.

*We over-estimate what we know about others and the extent to which others agree with us.

Therefore:
--Analyze what surprises and disappoints you
--Seek feedback
--Create dialogue

See D Kahneman's Thinking Fast and Slow
Examples of clarifying, nonjudgmental questions to elicit others' assumptions, perspectives, feelings and goals

--Please give an example of what you mean and how you came to that decision.

--Can you walk me through how you came to that conclusion?

--What is your interpretation of.....?

--What are you concluding at this point?

--What needs of yours does this solution not address? What would represent a solution that works for you?

--What do you see that I don’t?
*how formal does the agreement need to be?

*if the agreement contains “fine print,” have a lawyer look at it (anything you sign is considered a contract)

*if a formal agreement is not indicated, write a brief memo, eg: “this is my understanding of our agreement.......; please let me know if you have a different understanding; if I don’t hear from you in X, I will assume that you agree.”
Best Alternative to a Negotiated Agreement (BATNA)

*If you cannot reach an agreement, what will it take for you to be able to walk away with dignity and relationship intact?

*Is the status quo an acceptable BATNA?

*Possible exit line: “This discussion does not seem to be leading to the outcome I'd hoped for but I hope the door stays open for future dialogue.”

NB: the inability to reach an agreement is not a personal failure
Anxiety is normal

Big sources of stress:

--most people don't like to talk about money

--lack of control

--unpredictability [eg unknowns with regard to how hard the other will bargain]

--absence of feedback [it's often hard to know how it's going or if you could've pushed harder]
Relational Communication Skills

* Self-monitoring
  -- Notice negative emotions and ask “what hooked me?”
  -- Pause and recenter

* Inquiry and Listening
  – Ask questions that encourage the other to go deeper
  – Listen with curiosity

* Advocacy
  – Explain your reasoning and intent [e.g. “This is why I’m raising this and how I arrived at this conclusion”]
  – Ask for help in understanding your own thinking
**Automatic Listening**

- Right/Wrong
- Win/Lose
- Agree/Disagree
- Good/Bad
- Either/Or

Listening to diagnose or fix the problem or the person

Listening to my own agenda

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**Generative Listening**

What could make that possible?

What could that allow us to do?

What goals could that idea advance?

What do you see that I don’t?

Say more...
Why is Negotiating often harder for Women and Minorities?

--Under-estimate their own abilities

--Allowed a narrower band of assertive behavior

--Need to please, make others comfortable

--Less likely to be effectively mentored

--Less “social capital”

--Fewer role models

–??
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<td>He follows through</td>
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<td>They’re debating</td>
<td>They’re catfighting</td>
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RECOMMENDED READING


'ICU delirium' is terrifying — and incredibly common

STAT

FROM

Usha Lee McFarling

When his fever spiked, he thought someone was setting him on fire. When orderlies slid him into an MRI, he thought he was being fed into an oven. Frequent catheter changes seemed like sexual abuse. Dialysis? He thought someone was taking blood out of a dead woman's body and injecting it into his veins.

The horrifying, violent hallucinations plagued David Jones, now 39, during a six-week stay in the intensive care unit at Chicago's Northwestern Memorial Hospital — and for months after he was discharged. He thought he was going crazy and felt very alone.

He wasn't.

Recognizing the prevalence of the problem, doctors and nurses across the country are now pushing an ambitious campaign to change practices in intensive care units to reduce cases of "ICU delirium" — a sudden and intense confusion that can include hallucinations, delusions, and paranoia.

Anywhere from a third to more than 80 percent of ICU patients suffer from delirium during their hospital stay. And one-quarter of all ICU patients suffer from post-traumatic stress disorder once they leave, a rate that's comparable to PTSD diagnoses among combat veterans and rape victims. Patients with
ICU delirium are less likely to survive and more likely to suffer long-term cognitive damage if they do.

"This is a massive, massive public health problem," said Dr. Wes Ely, a pulmonologist and professor of medicine and critical care at Vanderbilt University Medical Center in Nashville, Tenn., who was among the first to recognize the scope of the problem.

Ely is pushing his colleagues in ICUs across the country to reduce the use of sedatives and ventilators and push patients to get on their feet as soon as possible, in a bid to minimize delirium. The talks he gives to highlight the issue show patients talking and texting while on ventilators — a major break from the traditional practice of heavily sedating them. He also shows patients walking through hospital halls despite grievous injuries.

The "ICU Liberation Campaign," which Ely cochairs, is organized by the Society for Critical Care Medicine, a professional group for ICU clinicians. If it works, it'll both improve patient outcomes and lower hospital costs.

But it's been a hard sell.

Despite its heavy clinical toll, ICU delirium is often ignored. Intensive care units are so stressful, so noisy, and so fast-paced that delirium is often overlooked.

"You may have one patient going into shock while another needs to be reintubated, so people get busy," said Dr. Matt Aldrich, an anesthesiologist who has been implementing the ICU Liberation Campaign at the University of California, San Francisco, Medical Center, where he directs adult critical care. "Delirium has definitely taken a backseat."

It's not that clinicians don't believe in the protocols, Aldrich said. It's just hard to make time to implement them. "The challenge is to slow yourself down and do the things you need to be doing. It's daily work. It's maintenance," he said. "It's not letting little things slide and falling into old patterns."

Keeping patients alive — but at a cost
In a way, ICU delirium is a problem born of success: Today's intensive care units keep alive patients who would not have survived 20, 10, or even five years ago. ICUs have come so far in curbing problems like sepsis and acute respiratory distress syndrome that they've created a huge population of "ICU survivors" — those who make it out alive but end up severely impacted mentally and psychologically.

"We used to call it ICU psychosis," said Justin DiLibero, a clinical nurse specialist working to reduce ICU delirium in the neuro and surgical ICUs at Beth Israel Deaconess Medical Center in Boston. "We knew it was common but thought patients got better when they got home. Now we know they come into the hospital as one person and leave as someone else."

Family members are often the first to see that their loved ones "aren't themselves." Patients may act paranoid, lash out in anger, or simply seem quite silly, for example planning large galas while still intubated.

While the exact causes of ICU delirium are not fully understood, risk factors seem to include ventilation, which can reduce the flow of oxygen to the brain, and heavy sedation, especially with benzodiazepines, which can have neurotoxic effects. Immobility and physical restraints appear to contribute to psychological distress as well. The lack of sleep, noisy alarms, constant prodding by nurses and doctors, and patients' inability to keep their hearing aids and glasses on may contribute, too.

The effects can linger long after discharge.

"As soon as I got home there were cognitive issues, really bad panic issues, flashbacks, all very gruesome," said Jones. "I felt like I'd endured months of torture. I was scared to go to sleep. I'd wake up in a cold sweat."

Jones had entered the hospital in 2012 with stomach pains that turned out to be caused by acute necrotizing pancreatitis. His pancreas was literally digesting itself; then his other organs started to fail. He was put on life support: On a respirator and dialysis, fed through a tube, the stocky and athletic Jones lost 70 of his 260 pounds. Nine days into his hospital stay, doctors gathered his family to say goodbye.
Thanks to surgery, a flood of antibiotics, and dedicated hospital staff, Jones survived. He's incredibly thankful for the care he received.

But he's also angry, now that he knows how widespread ICU delirium is, that not a single person talked to him or his family about the mental and psychological issues that so many ICU patients face.

"I thought, 'Why in the world is this not included in post-discharge instructions?'" Jones said in a telephone interview from Chicago, where he has returned to work as a legal analyst. "They were so happy they had saved my life. But no one told me to expect any of this."

**A culture of 'protecting' patients with sedation**

Ely has always been proud of the work done at his ICU. But in the late '90s, he started to notice something deeply unsettling: Many of his patients weren't doing well after they left the hospital. Some were severely impaired. Many couldn't return to work.

"They couldn't find their cars or balance their checkbooks," he said. "We wondered, 'What happened to them in the ICU? What went wrong?'"

Ely was shaken by the encounters, but when he tried to bring up the issue with fellow intensive care physicians, or critical care specialists, or even with the National Institutes of Health, he got no traction.

His call to ease up on restraining and sedating patients butted up against what Ely says was a deeply entrenched — and deeply paternalistic — ICU culture. "The idea has long been: 'We want to keep you unconscious so you don't suffer.'" Ely said. "We thought we were 'protecting' patients."

There were practical issues too: Heavily sedated patients are far easier for nurses to work with than patients who are frightened, agitated, or in pain. And it can be very hard to detect delirium in patients who are lethargic and seem unaware — but may still be delusional and suffering. "They told me I was in a coma," Jones said. "But I was aware."

Ely has spent the past two decades studying the issue and amassing the kind of data that are starting to convince his colleagues. A 2013 study, for
example, showed nearly 75 percent of ICU patients developed delirium during their hospital stay. In roughly one-third of those cases, their cognitive problems were so severe that even one year after discharge, they mimicked mild traumatic brain injury.

To minimize such damage, Ely developed a protocol dubbed ABCDEF, with steps such as assess for delirium, choose sedation wisely, and push patients to early mobility.

When the procedures are implemented, they seem to work wonders.

At Beth Israel Deaconess Medical Center, care teams in the medical ICUs have reduced the number of delirious patients by 60 percent since 2012, at a cost savings of thousands per patient. They did this by carefully assessing patients for delirium, making sure multiple care team members agreed on those assessments, and then reducing sedation and particularly benzodiazepine use whenever possible.

"We discussed every patient every day, and delirium was part of the discussion," said DiLibero, the nurse specialist who ran the project, which was funded by the American Association of Critical-Care Nurses, which recently issued a practice alert about delirium to its members. When nurses weren't sure what to do, DiLibero said, they could call in "nurse champions," who act as mentors and leaders.

Looking for delirium is especially important in elderly patients. Without a careful assessment, elderly patients with delirium may be misdiagnosed with dementia and sent to nursing homes unnecessarily.

The project at Beth Israel worked so well, it's been adopted by other ICUs at other regional hospitals. But it wasn't easy to get there. DiLibero has been working on the issue since 2010, his commitment sparked by seeing so many ICU patients, including his own grandmother, succumb to delirium.

"It's taken years of concerted effort to get to this point," he said. "It's been about changing a culture." That change is now palpable in his unit.

"When I started in ICU, anyone who was going to be intubated, they'd all be sedated, pretty deeply sedated," DiLibero said. "Now some patients are
completely off sedatives while still on a ventilator. I never thought I'd see that."

While there is agreement that it's crucial to prevent delirium whenever possible, many questions still remain on how best to treat it after it occurs. Vanderbilt is one of the few hospitals that offers a post-ICU treatment center; opened in 2012, it draws patients from around the country. At the center, patients are treated by a team that includes an ICU physician, nurse, pharmacist, case manager, and neuropsychologist who work together to help patients understand and alleviate symptoms.

Jones said therapy in Chicago was a great help to him, and included revisiting his ICU room to better understand his hallucinations.

He's also committed to talking publicly about his experience in hopes others won't suffer as he did. And he always carries a carefully worded life directive in his briefcase that makes clear that any intensive treatment he might need is provided in a way that is less likely to cause delirium.

"As bad as my illness was," he said, "the post-ICU was more traumatic."

http://theweek.com/articles/657987/icu-delirium-terrifying--incredibly-common This story was produced by STAT, a national publication covering health, medicine, and life science. Read more and sign up for their free morning newsletter at statnews.com. You can also follow STAT on Twitter and like them on Facebook.