Focus on Research

Assessing life expectancy leads to better care for older adults

For doctors who care for older people with serious illnesses, broaching the subject of life expectancy can be a sensitive topic. Yet, if the goal is to ideally manage a patient’s symptoms and enhance her or his quality of life, conversations about “how much longer might I live” are crucial.

These discussions apply to older adults with medically complex conditions, who for example, undergo sometimes uncomfortable and invasive cancer screening, such as a colonoscopy, to flag slow-growing malignancies that might not be life-threatening for more than 10 years down the road.

Also common, are older patients with Type 2 diabetes who take insulin for glycemic control. While controlling blood sugar for younger patients may reduce their risk of kidney failure and vision loss many years down the road, the benefits for older patients may never be realized. At the same time, the risk of low blood sugar from too much insulin can be very serious.

Add to that the possibility of category treatments for high blood pressure, heart disease, osteoporosis, and more. It’s a long list of well-meaning treatments based on outdated guidelines and quality indicators that are primarily based on age.

“Many of these indicators may harm the elderly by promoting unnecessary screenings and treatments among patients who are not likely to live long enough to benefit from them,” said Sei Lee, MD, MAS, a geriatrician and palliative medicine Staff Physician and Senior Scholar for the San Francisco VA Quality Scholars fellowship at the San Francisco Veterans Affairs Health Care System (SFVAHCS).

“A more frank discussion of prognosis in the elderly is badly needed,” said Lee, an NCIRE-supported researcher who this year was appointed to the U.S.
Preventive Services Task Force to make evidence-based recommendations about clinical preventive services such as screenings, counseling, and preventive medications. “Without these discussions with patients, decisions are made that are more likely to hurt patients than to help them.”

The conversations among doctors, patients and their family members may also go beyond clinical treatment options. Often, they pave the way for important talks about nursing or at-home care options, getting their affairs in order, and goals for their remaining years of life.

“We want to challenge clinicians to think about not just incorporating prognosis in a clinical setting, but offering to discuss prognosis with their older patients,” said Alexander Smith MD, MPH, MS, who like clinical and NCIRE research colleague, Sei Lee, MD, MAS, is a geriatrician and palliative medicine Staff Physician at SFVAHCS and Professor of Medicine with the Division of Geriatrics at UCSF.

Studies by Smith and others have shown that most elderly patients do want to discuss prognosis and life expectancy with their doctors. “In our experience, many older adults are aware they are in life’s final chapter, so such a conversation would not come as a shock to them,” he said. “As physicians, we have an obligation to give them honest information.”

Smith acknowledges that there is a substantial minority of elderly patients who do not want to discuss prognosis. “A doctor might want to explore the reasons, but should never force the discussion,” he said.

Tools for estimating life expectancy

Lee and Smith do not just sit on the clinical sidelines advocating for discussions about life expectancy with patients. Over the past 15 years, they have researched and developed tools that doctors can easily use to estimate life expectancy in older adults.

In 2011, they, along with Eric Widera, MD, Director of the Hospice & Palliative Care Service at the SFVAHCS and a UCSF Professor of Medicine, and other geriatricians, launched ePrognosis (eprognosis.org). It’s an online compendium of prognostic calculators where clinicians can go to obtain evidence-based information on patients’ prognoses.

Since its launch 13 years ago, ePrognosis has grown to include 27 validated geriatric scales, which can be used for patients living in the community, in a nursing home, or those hospitalized. The calculators consider answers to questions about health history and current physical abilities to estimate morbidity and mortality.

One section of the online tool calculates whether breast or lung cancer screening would be helpful, and another feature is a “time to benefit” instrument that illustrates which interventions and screenings may be of value on the life expectancy scale.

While the ePrognosis tools are designed for health professionals, they are often used by the general public. Some 15,000 people a month use these tools. Users of the site are reminded that “the information provided by the website is designed to complement, not replace, the relationship between a patient and his/her own medical providers.”

And since these tools and estimates are designed to stimulate discussion between doctors and patients, the website offers videos on how to incorporate prognosis into discussions with patients.

Prognostic tools for hospitalized older adults

Drs. Lee and Smith continue to study and develop tools that will aid doctors and older adults in making better decisions about their care. A current NIH-funded research project, administered by NCIRE, aims to develop prognostic indices for hospitalized older adults.
with and without Alzheimer’s disease and related dementias.

The indices will predict a six-month mortality to guide hospice referral decisions and two-year mortality to guide outpatient palliative care and inform medication deprescribing in these patients.

“Function is critically important to prediction in older adults, particularly those with Alzheimer’s disease and related dementias; and we have shown that the prognostic power of function increases with age,” notes the research abstract. “A major limitation that has hindered the effectiveness of predictive indices for hospitalized older adults has been the lack of functional data in the EHR (electronic health records).”

Now, however, hospitals have started to routinely assess, and document functional data, which Lee and Smith’s research team will comb, analyze, and incorporate into prognostic indices.

The research team has established collaborations with UCSF, the Cleveland Clinic, Beth Israel Deaconess Medical Center, and Johns Hopkins to routinely collect physical function data, clinical diagnoses, standardized delirium assessments, laboratory values, and physiologic measures to validate and develop prediction tools for estimating short-term mortality risk for hospitalized older adults with and without Alzheimer’s disease.

Q: How does your clinical work inform and motivate your laboratory work, and vice versa?

A: Taking care of Veterans and patients with conditions ranging from stroke to Alzheimer’s disease, I am struck by how debilitating neurological diseases can be and how far we must go to improve treatments. The knowledge gap is huge, but the advancements I’ve seen in genetics, drug treatments, and rehabilitation therapies are very motivating.

Q: Explain your laboratory research and the neurological conditions/pathways that you are targeting?

A: I am using CRISPR gene editing to learn about the details of how Arctic ground squirrel brain cells survive conditions during hibernation with very little blood

Q and A: An Interview with Dr. Neel Singhal

Q: How did you become interested in neurosciences and, eventually, neurocritical care, and basic laboratory research?

A: As a second grader, my interest in the brain was piqued by textbooks my mother would bring home as part of her coursework to complete a degree in histotechnology. I later participated in summer research internships at the University of Texas in high school and college and came across passionate and gifted mentors that imparted a love for research and the brain.

Following college, I worked at the National Institute of Mental Health, where a fast-paced environment with dedicated researchers solidified this track. As a medical student and later resident in Neurology at the University of California, San Francisco (UCSF), I was fortunate to receive close mentoring from leaders in the field of brain injury research, such as Dr. Raymond Swanson, Staff Physician with the Neurology Service with the San Francisco VA Health Care System (SFVAHCS) and a Professor with the Department of Neurology at the UCSF Medical School.

Q: How does your clinical work inform and motivate your laboratory work, and vice versa?

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Q: Explain your laboratory research and the neurological conditions/pathways that you are targeting?

A: I am using CRISPR gene editing to learn about the details of how Arctic ground squirrel brain cells survive conditions during hibernation with very little blood
flow. I am applying these insights to mouse models of stroke with the hope of coming up with new treatments for patients with brain injuries.

**Q:** Your animal model—Arctic ground squirrel—is interesting. Why is this a good model?

**A:** The Arctic ground squirrel survives incredibly harsh conditions by hibernating. During hibernation, its heart rate slows to just a few beats a minute; and its blood flow is just a trickle—yet the animal awakens without any brain injury to speak of. We’ve shown that in part this is due to amazingly resilient brain cell metabolism. Learning the tricks evolution has given the Arctic ground squirrel could give us a new angle to protect brain cells that aren’t receiving blood flow during a stroke.

**Q:** What are some technologies you apply in the laboratory? What does your team look for?

**A:** We use gene editing technology to dissect pathways that have never been researched. We also use advances in nanoparticle technology to deliver compounds to the brain. We take advantage of state-of-the-art equipment available at UCSF to assess fine changes in our cells and mice as a result of manipulating the new pathways we’re studying.

**Q:** How is your research potentially promising?

**A:** We hope that by doing something outside of the box, we will find a critical combination of new pathways to target that have not been tried before. The advent of new genetic technologies makes this type of research more possible now than in the past.

**Q:** What have you learned about Veterans during your clinical work and research at the SFVAHCS?

**A:** There's no greater privilege and reward than to participate in the care of Veterans who have sacrificed so much for their country. I love hearing the stories Vets often share about their service. I appreciate the grit and resilience that is often a common theme of Veterans' experience.

**Q:** What would most people be surprised to know about you?

**A:** I sometimes take DIY to the extreme. Don’t be surprised to see me tackling any and all projects.

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**Research Community News**

**Improving Clinical Research Generalization with Digital Marketing and Online Recruitment: Insights from the Brain Health Registry and the Alzheimer’s Disease Neuroimaging Initiative**

It is widely recognized that clinical research in the United States, as well as in other countries, tends to overrepresent well-educated White individuals while under-representing people of color, individuals with lower education levels and those with lower socio-economic status compared to the census-defined population.

Several factors contribute to the lack of diversity in clinical research populations. Unfortunately, this absence of diversity undermines the generalizability of clinical research results. This could imply that the outcomes are limited to the participants involved in the study and may not hold true for individuals not represented in the research cohort. This issue is particularly relevant to neuroscience research and clinical trials of treatments aimed at Alzheimer’s disease.

To address this challenge, investigators from NCIRE and UCSF, collaborating with the Brain Health Registry, have launched several efforts. These initiatives utilize culturally tailored digital marketing to recruit under-represented populations and online assessments to evaluate their eligibility for various clinical studies. Specifically, these efforts include:

- The California Latino Brain Health Registry (CAL-BHR), sponsored by the California Department of Health, aims to improve the inclusion and engagement of older Latino adults using a community-engaged research approach. As a result of these efforts, within a span of 12.5 months, the proportion of Latino participants increased from 6% to 12% of the overall cohort, with a total of 5,662 Latino individuals enrolled into the project.
For more information, visit [https://es.brainhealthregistry.org](https://es.brainhealthregistry.org).

- The Community Engaged Digital Alzheimer's Research Study (CEDAR), sponsored by Genentech, Inc., aims to improve the retention and engagement of older adult individuals from Black/African American communities in the Brain Health Registry. For more information, visit [https://www.brainhealthregistry.org/cedarstudy/](https://www.brainhealthregistry.org/cedarstudy/).

- Both the CAL-BHR and CEDAR studies recently received funding to expand efforts for increasing participation from additional underrepresented groups.

The Alzheimer’s Disease Neuroimaging Initiative (ADNI), sponsored by the National Institute of Aging (NIA), aims to increase the enrollment of underrepresented people in its study. For this, the ADNI team is using multiple strategies, including a ‘boots on the ground’ approach to improving recruitment and retention of underrepresented participants, utilizing community engagement ambassadors to foster partnerships, encourage enrollment and connect participants directly with clinical site staff.

The team of scientists at ADNI is using culturally tailored digital marketing, including the creation of locally branded websites that incorporate themes specifically designed to resonate with older Black and Latino adults. These efforts help recruit participants for ADNI clinics across the United States. Presently, 49% of enrollments in the digital study are from underrepresented groups. Additional ADNI activities that focus on improving diversity are: 1) loosened criteria for study enrollment, 2) updated study design to make participation accessible to more people, 3) expanded capacity for assessment of individuals in the Spanish language, and 4) collection of detailed social determinant of health data.

It’s important to emphasize that our digital marketing/website registry approach complements the local ‘boots on the ground’ recruitment efforts. Our findings strongly indicate that digital marketing and web-based recruitment, assessment, and prescreening can help address the lack of generalizability observed in many clinical studies.

Learn more: [https://adni.loni.usc.edu/](https://adni.loni.usc.edu/)

**IMPROVE Study Achieves Record High Patient Enrollment!**

Under the leadership of NCIRE-supported Principal Investigator Dr. Jeffrey Zimmet, 62 patients have enrolled thus far in the IMPact on Revascularization Outcomes of intravascular ultrasound-guidance treatment of complex lesions and Economic impact (IMPROVE) Trial. This is the highest number of participants enrolled in a single randomized control trial from the San Francisco VA Health Care System Cardiac Cath Lab. Enrollment is ongoing and continues to flourish under Dr. Zimmet’s leadership with the assistance of sub-investigator Dr. Joseph Yang and study coordinators, Cynthia Huynh, Kitty Stanley, Gina Saelee, and Samantha Norris. In addition, Dr. Zimmet’s team was also the first VA site in the U.S. to treat a patient using Boston Scientific’s AGENT Paclitaxel drug-coated balloon (DCB) to treat in-stent restenosis. The AGENT DCB is the first FDA-approved and commercially available device of its kind in the U.S. and was approved based on the AGENT-IDE clinical trial. The San Francisco VA, through its research collaboration with NCIRE, was the only VA site to participate in the AGENT-IDE trial and demonstrates the impact of clinical research in transforming patient care for not only our Veterans but also many patients throughout the world.
New Federal Funding Awards

Congratulations to the following Principal Investigators for your recently funded awards!

**Duygu Tosun-Turgut, PhD**
- **Project Title:** The Alzheimer's Disease Tau Platform Clinical Trial
- **Sponsor:** California Air Resources Board (CARB) via subaward from UCSF
- **Activation Date:** 2/1/2024

**Kristine Yaffe, MD**
- **Project Title:** TBI Rehabilitation and Activation in Veterans (TRAIN-Vets)
- **Sponsor:** Dept. of the Army - USAMRAA
- **Activation Date:** 9/1/2024

**Jorge Kizer, MD**
- **Project Title:** Epidemiology of Diet, Metabolism and Non-alcoholic Fatty Liver Disease in Hispanic/Latino Adults
- **Sponsor:** NIH via subaward from Albert Einstein College of Medicine
- **Activation Date:** TBD

NCIRE Board Member Dr. Kristine Yaffe receives Federal Grant Award!
Congratulations to Kristine Yaffe, MD for receiving a new multi-year grant award for her research project titled "TBI Rehabilitation and Activation in Veterans (TRAIN-Vets)"! The award is sponsored by the U.S. Department of Defense, with the activation date of September 1, 2024.

**Funding Opportunities**

**Industry Opportunities**
Please contact Newton Ong, newton.ong@ncire.org, or Adan Pinedo, adan.pinedo@ncire.org, for further information on the following Industry Opportunities.

**Daiichi Sankyo**
A Randomized, Open-label, Phase 3 Trial of Dato-DXd Plus Pembrolizumab vs Pembrolizumab Alone in Treatment-naive Subjects With Advanced or Metastatic PD-L1 High (TPS =50%) Non-Small Cell Lung Cancer Without Actionable Genomic Alterations.

**AbbVie**
A Phase 3 Open-Label Study to Evaluate the Safety and Efficacy of Epcoritamab in Combination with Rituximab + Lenalidomide Compared to Lenalidomide in Subjects with Relapsed or Refractory Follicular Lymphoma.

**AVM Biotechnology**
An Open Label, Phase 1/2 Study Evaluating Immunomodulatory AVM0703 in Patients With Lymphoid Malignancies.

Please visit the Office of Sponsored Research page on the NCIRE SharePoint at https://ncire.sharepoint.com/ or click here for the full list of Industry Opportunities.

**Federal Funding Opportunities**
Please contact Jessica Schmidt, jessica.schmidt@ncire.org, for further information on the following Federal Funding Opportunities.

**NIH:** Research Program Award (R35 Clinical Trial Optional) (RFA-NS-22-038)
- Application Deadline: July 15, 2024

**NIH:** Functional Target Validation for Alzheimer's Disease-Related Dementias (R61/R33 Clinical Trial Not Allowed) (RFA-NS-25-011)
National Institute of Neurological Disorders and Stroke
Funding Opportunities continued

National Institute on Aging

- Application Deadline: November 8, 2024

NIH: Safety and Efficacy of Amyloid-Beta Directed Antibody Therapy in Mild Cognitive Impairment and Dementia with Evidence of Lewy Body Dementia and Amyloid-Beta Pathology (U01 - Clinical Trial Required) (RFA-NS-25-010)
National Institute of Neurological Disorders and Stroke
National Institute on Aging

- Application Deadline: January 24, 2025

Please visit the Office of Sponsored Research page on the NCIRE SharePoint at https://ncire.sharepoint.com/ or click here for the full list of Federal Funding Opportunities.

In the Helix

Joan S. Wakefield
Research Assistant III, NCIRE

Q: If you could travel to any other planet (real or fictional), where would you go and why?
A: It’s not a planet, though it is a fictional land, called the Land of Mo, near the Land of Oz (created by Frank Baum in early 1900s)—all foods as well as clothing and other items grow (free) on trees or plants, the rivers are root beer or milk, the islands are cheese, and no one ages after a certain point—what’s not to love?!

Q: What type of music do you listen to?
A: Elton John, Bruce Springsteen, Madonna, Amy Winehouse, Dido, Sheryl Crow, as well as the music my kids grew up loving.

Q: What is your favorite thing to do by yourself?
A: I love to read, stand on my head, juggle, walk on stilts and get up from a cross-legged seated position without using my arms—but I don’t do all those things at the same time.

Lénie Torregrossa
Research Specialist, NCIRE

Q: If you could travel to any other planet (real or fictional), where would you go and why?
A: Venus. It’s our sister planet so I like to think that it would feel eerily familiar to visit. It’s also the brightest of all planets, which earned it its beautiful name.

Q: What type of music do you listen to?
A: My musical taste is eclectic. I love R&B, tropical house, indie, rap, and pop. I also listen to the Yoga Electronica Spotify playlist on repeat when I am working.

Q: What is your favorite thing to do by yourself?
A: Walking! It’s my time to think, listen to a podcast or audiobook, catch up with friends and family, people watch, and marvel at the incredible nature surrounding us here in San Francisco. I always seem to find myself in a new park, or on top of a hill with a breathtaking view.

If you or someone you know is an NCIRE employee and would like to be featured in In the Helix, contact us at dna@ncire.org.
Message from the Chief Executive Officer

The sunshine in June has been a welcome surprise. Summer is almost here. I am looking forward to the warm, long summer evenings.

Many thanks to the wonderful contributors of the Summer 2024 Newsletter: Alexander Smith, MD, MS, MPH; Sei Lee, MD, MAS; and Neel Singhal, MD. We are grateful to them for the synergy and dedication to research at SFVAHCS.

On May 13th I had the pleasure of attending the VA Research Week kick-off ceremonial event with VA Secretary Denis McDonough at the VA Headquarters in Washington, D.C. The 2024 theme was Building Community Through Research. The ceremony recognized 5 extraordinary VA Researchers.

Earlier this fiscal year we shared updates on the utilization rate or NCIRE Administrative Accounts. At the end of the seven months, 4/30/24, the utilization rate was 80%, which is a slight increase from (71%) previously reported. Ideally, the utilization rate should be closer to 100% for NCIRE to maintain its current indirect cost rate of 53.3%. The fiscal 2024 budget was based on 90% utilization of these accounts. Continually maintaining the delicate spending rate between direct and indirect costs is critical to NCIRE’s ability to maintain the provisional indirect cost rate. Please be mindful of these accounts.

In June, NCIRE implemented a system enhancement in our existing Acumatica system that will support the Office of Sponsored Research. For the last year staff in the Core Office (OSR and IT) have mapped out a new tool to support the various data points and compliance related sponsored research. We are excited to have leveraged these resources to streamline various aspects of grants management.

The annual NCIRE Principal Investigator and Research Community 2024 Survey was recently sent out. The goal this year is to achieve >50% participation. Every voice is important. This is an anonymous survey. Once the data is compiled, results will be shared.

NCIRE is proud to support Veterans Research at SFVAHCS. Thank you for reading our Summer 2024 Newsletter. Please let me know if you have any questions or comments.

Rebecca Rosales, MBA, CRA
Chief Executive Officer

About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support nearly 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

NCIRE is a 501(c)3 nonprofit. (Tax ID #94-3084159). Visit NCIRE at www.ncire.org

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