

SHINING A LIGHT ON AGING

Dear friends and colleagues,

Aging is an experience that all people share, whether we dread or embrace it. And the desire to unravel its scientific mysteries is a human imperative.

At the UF Institute on Aging, researchers work tirelessly to improve the health, independence and quality of life of older adults, from the bench science that examines the cell at a molecular level to the physician examining a patient bedside. Our commitment to research, health care and education is as strong as ever.

The institute's mission is more important than ever. Florida and the nation are growing older. Forecasts indicate nearly a third of the state's population will be over age 60 by 2030, an increase of about 34% since 2012. Florida's population growth is propelled by older adults more than any other age group.

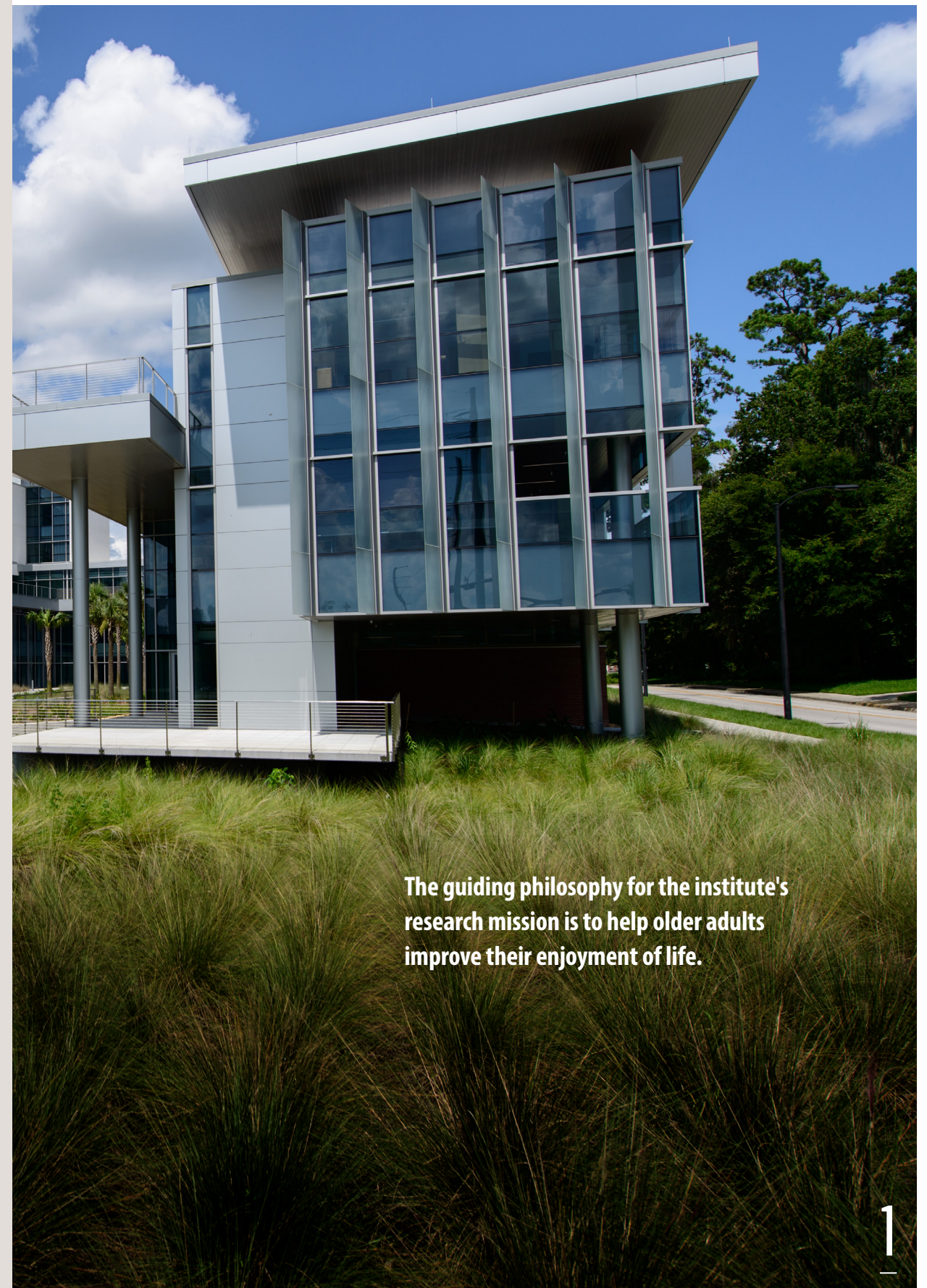
Aging remains an important risk factor for a range of diseases, including dementia, Alzheimer's, heart disease, diabetes and most forms of cancer. The cost to older adults, and the health care system generally, is enormous.

Institute faculty from diverse disciplines are examining aging from a variety of perspectives, including basic and clinical sciences, interventions, as well as studying how public health policies impact older adults. Institute researchers find that collaborations across disciplines with colleagues throughout UF Health accelerate research discoveries for new treatments and approaches to medical care. This work helps improve the quality of life of aging adults.

The overarching mission for all of us is to identify ways to help older adults age successfully. This isn't simply to live a long life. It means lowering the burden of disease and disability so people can engage in life and remain active mentally and physically.

The guiding philosophy for the institute's research mission is to help older adults improve their enjoyment of life.

The UF Institute on Aging is dedicated to that mission.



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NEWLY INTEGRATED DEPARTMENT

The UF College of Medicine in 2022 created a newly integrated academic unit that combines the expertise of aging research and the study of how the body functions on the cellular level.

The new department of physiology and aging will consolidate educational programs and research endeavors under one umbrella, combining the former department of aging and geriatric research and the department of physiology and functional genomics.

The merger was completed with input from faculty of both departments.

The newly formed department of physiology and aging, home to 26 faculty members, is poised to enhance collaboration, with experts working side by side to conduct bench-to-bedside research examining all life phases of the human body.

"The new department will do everything from bench research to applied human research, and we will cover the lifespan of the human body," said Charles E. Wood, Ph.D., who served as chair of both former departments, said when the news was announced. "For example, as a fetal physiologist, I work with OB-GYN on placental biology and healthy pregnancies and outcomes. On the other end, we have great strength in terms of work that keeps older people healthy.

"I'm proud that we will now have everything from basic cell molecular biology to outcomes and applications that will cover the very beginning of life to the end of life under one department. The synergy with the faculty will be fantastic because now we're not just simply talking about aging; we're talking about the whole lifespan."

Plans for the integrated department include enhancing research efforts in each discipline and building a new master's program in medical physiology and gerontology.

"This study is a huge step forward," said Christiaan Leeuwenburgh, Ph.D., a professor at the institute. "Physicians sometimes say, 'Hey, don't go over the threshold of pain. Slow down.' But no pain, no gain."

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— Charles E. Wood, Ph.D.

IDENTIFYING WAYS TO COLLABORATE

Karyn Esser, Ph.D., a leading circadian rhythm researcher, has been named chair of the newly integrated UF College of Medicine's department of physiology and aging.

"My goal is to help the faculty succeed and hopefully help identify exciting areas for collaboration and program building — where the sum is greater than the parts," Esser said. "I have been with the physiology department for seven years, and they are a wonderful group of people. There will be great opportunities now that we are joining aging. There is a contagious sense of excitement that together, we can absolutely make a difference."

Esser is a faculty member of the UF Institute on Aging and serves as co-director of the Claude D. Pepper Older Americans Independence Center.

Esser is among the first generation of researchers to recognize the importance of circadian rhythms to cell and muscle health. She looks forward to increasing partnerships across divisions and specialties to build on preexisting strengths and advance the college's core missions.

"The new department of physiology and aging presents incredible opportunities to enhance collaboration and innovate how we think about lifespan research," said Dr. Colleen Koch, M.D., M.S., M.B.A., dean of the UF College of Medicine.

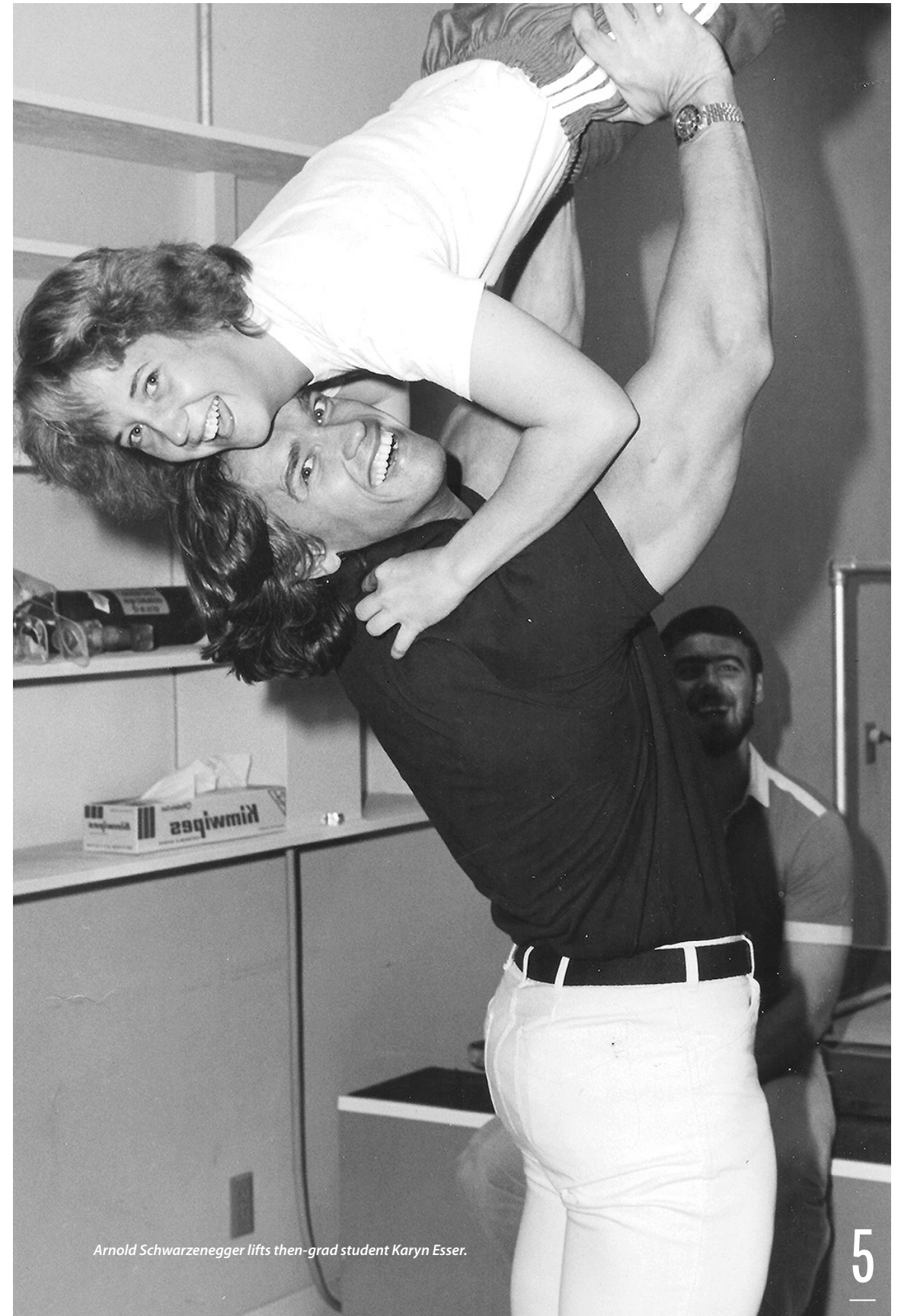
A future celebrity provided an odd highlight to Esser's graduate education.

"This very big man named Arnold Schwarzenegger had recently come to America, and he was visiting our lab," she says. "As part of his new movie career, he said: I have to practice picking up American women.' Before I had a chance to respond, he picked me up and held me over his head and fortunately a photographer was there to capture that moment. I had no idea he was going to be a future movie star and governor of California."



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— Karyn Esser, Ph.D.



Arnold Schwarzenegger lifts then-grad student Karyn Esser.

SLEEP MEDICATION USE DECLINES

Americans aren't turning to pharmaceutical options as often in the never-ending battle for a good night's sleep.

The use of medication to treat sleep disturbances has fallen dramatically in the United States in recent years after several decades of climbing steeply, according to a study by a team of researchers led by a UF Institute on Aging scientist.

The drop-off is particularly noteworthy for Americans over age 80, who are most susceptible to falls leading to injury when using sleep medications. The study showed an 86% decrease in this group.

The study documented a 31% decline in the use of common sleep medications between 2013 and 2018, a trend thought to be linked to a greater awareness of the potential pitfalls posed by these prescriptions.

"I was surprised and encouraged by the results because there's been a great deal of effort to

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minimize the long-term use of these pharmaceutical agents," said public health researcher Christopher Kaufmann, Ph.D., M.H.S., an assistant professor in the UF College of Medicine's department of health outcomes and biomedical informatics and lead author.

"A number of medical organizations, advocacy groups and policymakers have also strongly discouraged the use of these drugs to treat insomnia due to potential adverse outcomes associated with their use," he added. "There are highly effective behavioral treatments available that are growing in popularity."

The study's observed trend stands in marked contrast to the rapid rise of sleep medication use and prescribing in previous decades. An earlier study by some of the same researchers found that prescriptions for benzodiazepines, or BZDs, a class of drugs to treat anxiety and insomnia that includes diazepam (Valium) and alprazolam (Xanax), and non-BZDs, a similar class of medications including zolpidem (Ambien), climbed 69% and 140%, respectively, between 1993 and 2010.

OLDER ADULTS AND FAKE NEWS

Not being able to distinguish fake news from real news can have serious consequences for physical, emotional and financial well-being — especially for older adults, who generally have more financial assets and must make more high-stakes health decisions.

So, how good are older adults at detecting fake news?

A new study has found that older adults are no more likely to fall for fake news than younger adults, with age-related susceptibility to deceptive news evident only among those categorized as the "oldest old."

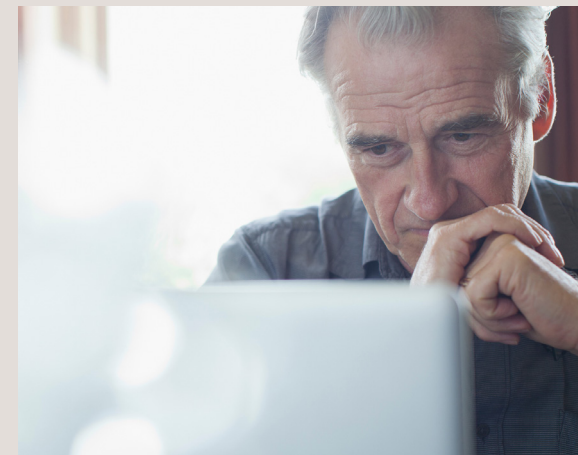
The study was conducted by researchers at UF and the University of Central Florida during the early phase of the COVID-19 pandemic.

"We wanted to see if there was an age difference in determining whether news is true versus false," said Didem Pehlivanoglu, Ph.D., lead author and a postdoctoral researcher in the lab of Natalie Ebner, a professor in psychology who is affiliated with the UF Institute on Aging.

"It is a particularly high-risk population with high stakes for wrong decision making, not just for themselves but also for society at large," said Ebner, a study co-author.

Research is scant regarding older adults' susceptibility to fake news and what factors might aid or impair a person's ability to judge the veracity of information. Raising concern, some previous work suggested that older adults shared false information over social media more often than did young adults during the 2016 presidential election. And the dramatic increase in misinformation during the COVID-19 pandemic heightened concern, given that the virus has been particularly deadly for older adults.

While many people show cognitive decline as they age, it is also true that with age comes a broader knowledge base, more life experience and, often, more positive affect. As a group, older adults also tend to consume more news than younger adults. These factors may filter and contextualize information processing in older adults.





THE AGING BRAIN

When physicians treat the body's aches and pains, are they also treating the brain?

UF Institute on Aging researcher Yenisel Cruz-Almeida, Ph.D., is studying the possible connection between chronic pain and premature biological brain aging and whether pain interventions can reverse or slow that process.

The idea, Cruz-Almeida said, is that doctors can intervene to stop or reverse that aging, perhaps taking someone off the path of or delaying eventual cognitive decline.

"Some of the processes involved in this accumulate gradually over time," she said. "That gives us a chance to intercept and change the trajectory. If we don't know that the brain aging is happening, then there is nothing we can do."

In a 2019 study, Cruz-Almeida and collaborators showed those who received treatments for their pain, from medication to even home remedies like a cold compress on an aching knee, had younger-appearing brains.

Interestingly, Cruz-Almeida's studies suggest chronic pain might be associated with more rapid brain aging, with greater pain increasing the rapidity of brain aging. But this study showed that participants with more pain at baseline, who consistently used non-pharmacologic pain management, had decreased brain aging.

It could be, Cruz-Almeida said, that these people are simply able to do more activities because of pain management and that those activities play an important role in protecting the brain from accelerated aging.

"The problem is that chronic pain has always been viewed as a very peripheral problem," Cruz-Almeida said. "We have been advocating that it changes the brain."

Like a colonoscopy is beneficial in diagnosing colon cancer at an early stage, Cruz-Almeida sees the day when an MRI, even one performed because of an incidental car accident or fall, could also be used as a predictor of cognitive decline.



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— Yenisel Cruz-Almeida, PhD

AI HELPS PHYSICIANS QUICKLY ID SEPSIS

Quickly identifying patients most at risk of sepsis can be a matter of life and death.

Sepsis, the body's dysregulated response to infection, can cause widespread inflammation and organ failure. Identifying patients most at risk has relied on a clinician's own discretion and experience treating sepsis.

UF researchers have created and are using a diagnostic tool that leverages artificial intelligence to identify a patient's likelihood of developing sepsis, as well as its severity, as soon as 12 hours after hospital admission.

Sepsis is far more common in adults over age 65. The research, published in JAMA Network Open, received support from UF's Claude D. Pepper Older Americans Independence Center.

"There is no consistent way of recognizing and triaging critically ill patients when they're admitted to the ICU other than clinical judgment," said Lyle L. Moldawer, Ph.D., director of the Sepsis and Critical Illness Research Center. "While this may not pose a problem at large academic institutions with dedicated specialists, it can be harder for places where tertiary care is less developed."

In the event that sepsis is not recognized early and managed promptly, septic shock ensues, resulting in irreversible multiple organ failure and death.

"The worst thing you can do is have a patient sit in the ICU for 24 hours or even 72 hours without an intervention," Moldawer said.

This tool also lends a precision medicine perspective, allowing clinicians to tailor their care to the individual and the drugs they will respond best to before it's too late.

The algorithm has more than halved the time it takes doctors to get information they need to make decisions before it's too late.

EXCELLENCE IN GERIATRICS

UF Health geriatrics continues to shine nationally. U.S. News & World Report's 2023-24 Best Hospitals survey ranked the health system's geriatric program 42nd nationally. It is among four other UF Health specialties receiving national recognition for their excellence. Ratings are based on patient survival rates, care-related factors such as nurse staffing and the breadth of patient services, and a reputational score from specialty physicians at other hospitals.



SLEEP APNEA AND COGNITION

Can a common treatment for sleep apnea and snoring help reduce the risk of developing Alzheimer's disease and other forms of dementia in later life?

UF College of Medicine researchers hope to find out. With a 5-year, \$2 million grant from the National Institute on Aging, a team led by Christopher Kaufmann, Ph.D., M.H.S., will evaluate whether Continuous Positive Airway Pressure, or CPAP, machines used to treat obstructive sleep apnea can improve cognitive function and reduce the risk of Alzheimer's disease and dementia over time.

Sleep apnea, a potentially serious sleep disorder, causes a person to repeatedly stop and starting breathing while asleep. People with sleep apnea face an elevated risk of heart disease, high blood pressure and other complications.

"Studies have already shown that obstructive sleep apnea is highly prevalent and is associated with a risk of cognitive decline and dementia, particularly among older adults," said Kaufmann, an assistant professor in the college's department of health outcomes and biomedical informatics and a faculty member of the UF Institute on Aging.

"We also know that when used properly and regularly, CPAP machines are highly effective in treating sleep apnea," he said.

In this study, the researchers will analyze 14 years of data collected from two national studies of older adults in the U.S.: the Health and Retirement Study, and National Health and Aging Trends Study.

The team will use the data to evaluate whether consistent, regular use of CPAP treatments can help reduce the risk of Alzheimer's disease and other forms of dementia in people diagnosed with obstructive sleep apnea.

The researchers will also determine whether, in those with obstructive sleep apnea, the effects of CPAP treatment on cognition differ among groups of people that past research has shown face a higher risk for Alzheimer's disease.



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— Christopher Kaufmann, Ph.D., M.H.S.

SLEEP AND COVID-19

Taking time to go places, to visit friends or take a walk in the park, to socialize and meet new people or to simply stroll outside the familiar walls of our home, is more than a social necessity.

It's good for our physical and mental health.

Unfortunately, older adults who aren't sleeping well don't stray far from their home turf.

A UF College of Medicine study by a team that included UF Institute on Aging researchers found that older adults who reported a worsening of their sleep patterns during the COVID-19 pandemic were apt to restrict their movement outside the bedroom and into the wider world.



Reporting that sleep got a little worse or a lot worse during the pandemic was associated with more limited movement in their environment."

— Emily Smail, Ph.D.

The association was seen even when controlled for the restrictions imposed by the coronavirus.

"Reporting that sleep got a little worse or a lot worse during the pandemic was associated with more limited movement in their environment," said lead author Emily Smail, Ph.D., a former postdoctoral fellow at UF who was an affiliate member of the institute.

"Life space mobility is linked to many adverse health outcomes," she added. "Preserving this mobility, especially during health threats like the COVID-19 pandemic, can help maintain the health of older adults and improve their well-being during a particularly stressful time."

It's important, Smail said, for people to continue to socialize and get out of the house in a manner that does not expose them to the virus. She said sleep disturbance is common during times of stress.

Smail said protecting sleep is an important intervention to help older adults maintain movement and avoid adverse outcomes such as depression, reduced cognitive function, obesity, frailty and even death.

Study co-authors include Institute on Aging faculty members Christopher Kaufmann, Ph.D.; Mamoun Mardini, Ph.D.; and senior author Todd Manini, Ph.D.





UF CLAUDE D. PEPPER OLDER AMERICANS INDEPENDENCE CENTER: 2022 KEY RESEARCH FINDINGS

Pain and the brain

Chronic pain remains a significant public health challenge, accounting for the majority of disability and disease burden globally. Chronic pain becomes more common as we age, along with greater pain sensitivity. Little research exists related to pain sensitivity and the structures of parts of the brain. Our study was a secondary analysis of data from the Neuromodulatory Examination of Pain and Mobility Across the Lifespan study. Our work involved 62 adults, ages 60 to 94. We examined pain sensitivity as it related to brain structure. We found initial evidence for the potential neurobiological mechanisms underlying pain sensitivity in older adults. Identification of mechanisms contributing to pain in older adults is clinically relevant and might inform treatment.

Wilson AT, Johnson AJ, Laffitte Nodarse C, Hoyos L, Lysne P, Peraza JA, Montesino-Goicolea S, Valdes-Hernandez PA, Somerville J, Bialosky JE, **Cruz-Almeida Y.**

Experimental pain phenotype profiles in community-dwelling older adults. *Clin J Pain.* 2022 Jul 1;38(7):451-458.

Sepsis and the elderly

Sepsis is the immune system's extreme response to an infection, triggering inflammation throughout the body. It can cause organ damage and death and has been called the "quintessential disease of the elderly." Hospital deaths after sepsis have decreased substantially and most young adults rapidly recover. However, many older survivors develop chronic critical illness, with poor long-term outcomes. Biomarkers reflecting a persistent inflammation, immunosuppression and destructive metabolism have been seen in elderly chronic critical illness patients after sepsis. The major findings of this study are that older and older chronic, critically ill patients demonstrate persistent aberrations in host response biomarkers over 14 days after the onset of sepsis.

Mankowski RT, Anton SD, Ghita GL, Brumback B, Darden DB, Bihorac A, **Leeuwenburgh C,** Moldawer LL, Efron PA, Brakenridge SC, Moore FA.

Older adults demonstrate biomarker evidence of the persistent inflammation, immunosuppression, and catabolism syndrome (PICS) after sepsis. *J Gerontol A Biol Sci Med Sci.* 2022 Jan

A cautionary tale

Our review highlights a clear need for research to evaluate the potential long-term cognitive effects of chronic pain. A review of multiple studies shows an association between accelerated cognitive decline for older adults with chronic pain. These studies, however, have limitations, notably the difficulty in measuring self-reported pain in cognitively impaired persons. Older adults also are often prescribed medications for pain, neurological disorders and depression which might confound results. We highlight a clear need for multidisciplinary, confirmatory studies using neuroimaging and pain biomarkers, such as cytokines, that can serve as independent verification of chronic pain levels. This activity is urgently needed as the population ages and chronic pain diagnoses increases.

Banik RK, Peng S, Hussain N, Goel V, Hagedorn JM, Chai T, Anitescu M, **Fillingim RB.**

The relationship between chronic pain and cognitive decline in older population: a cautionary tale from current literature. *Pain Med.* 2023 Feb 1;24(2):110-112.

Disc degeneration of the spine

Intervertebral disc degeneration occurs, as the name implies, when one or more of the discs separating the vertebrae composing the spine break down. This often can lead to intense pain in the arms and legs. The mechanism of this degeneration remains unclear. An inflammatory cytokine called lymphotoxin- α , or LT α — cytokines are proteins that play a role in cell communication — is associated with various pathological conditions. Our study explored the relationship between LT α and disc degeneration. We found that LT α is closely associated with intervertebral disc degeneration and might induce cell death in the nucleus pulposus, which is the inner core of a disc. In a sense, the nucleus pulposus acts as a shock absorber for the spine.

Guo Z, Qiu C, Mecca C, Zhang Y, **Bian J,** Wang Y, Wu X, Wang T, Su W, Li X, Zhang W, Chen B, Xiang H.

Elevated lymphotoxin- α (TNF β) is associated with intervertebral disc degeneration. *BMC Musculoskelet Disord.* 2021 Jan 13;22(1):77. doi: 10.1186/s12891-020-03934-7.

THE CLAUDE D. PEPPER OLDER AMERICANS INDEPENDENCE CENTER

The overarching mission of the UF Pepper Center is to optimize older adults' physical performance and mobility through interdisciplinary approaches; and to train new investigators in aging and disability research while developing their leadership qualities.

Time-restricted eating

A popular diet regimen, time-restricted eating, or TRE, also called intermittent fasting, involves eating during specific times during the day, often between 12 p.m. to 8 p.m. Previous research shows TRE provides multiple health benefits. Emerging evidence suggests one benefit might involve a category of intercellular communicators, miRNA, that helps carry out instructions from DNA. miRNAs are found to be dysregulated in metabolic disorders, such as obesity. In this pilot study, we took blood samples from nine individuals age 65 and older and identified 14 circulatory miRNAs that changed after fasting. These changes could promote cell survival and healthy aging. Findings warrant further investigation on these miRNAs in more subjects over longer time periods.

Saini SK, Singh A, Saini M, Gonzalez-Freire M, **Leeuwenburgh C, Anton SD**

Time-restricted eating regimen differentially affects circulatory miRNA expression in older overweight adults. Nutrients. 2022 Apr 28;14(9):1843.

Frailty and risk of death

Frailty in older adults is a reflection of physical decline and vulnerability to disease. But the role frailty plays in survival of older adults with a prior cancer diagnosis is limited. We analyzed data from the National Health and Nutrition Examination Study involving 2,050 people surviving at least a year beyond a cancer diagnosis, in addition to 9,474 people without a cancer history. Frailty also was measured. We found that older cancer survivors are at higher risk of mortality if they are living with a substantial burden of frailty. Understanding an older adult's frailty status is

informative for developing long-term interventions for promoting the health of older cancer survivors.

Zhang D, Mobley EM, **Manini TM, Leeuwenburgh C, Anton SD**, Washington CJ, Zhou D, Parker AS, Okunieff PG, **Bian J, Guo Y**, Pahor M, Hiatt RA, **Braithwaite D**.

Frailty and risk of mortality in older cancer survivors and adults without a cancer history: Evidence from the National Health and Nutrition Examination Survey, 1999-2014. Cancer. 2022 Aug 1;128(15):2978-2987. doi: 10.1002/cncr.34258. Epub 2022 May 24. PMID: 35608563; PMCID: PMC9671088.

Inflammation and walking speed

Walking speed, also known as gait speed, is an objective measure of overall physical functioning, with slower performance associated with mobility disability and other adverse outcomes in older adults. Gait speed is improved with exercise in this population. However, not all older adults respond in the same way to a physical activity intervention. It is important to know the biological mechanisms impacting gait speed as measured over 400 meters. So, we examined whether yearly variations in a protein, interleukin-6, or IL-6, a biomarker of inflammation, had an impact on walking speed. We found that variations of IL-6 between -1 and +2 picograms (a picogram is one-millionth of a gram) per milliliter had a small but meaningful benefit to 400-meter gait speed. This benefit was confined to the physical activity group and was not seen in an education group that simply read topics of interest for older adults.

Custodero C, **Pahor M**, Mazzocchi C, **Manini TM, Anton SD**, Mazzocca A, Lozupone M, Panza F, Sabbà C, Solfrizzi V.

Effect of change of interleukin-6 over time on gait speed response: Results from the Lifestyle Interventions and Independence for Elders study. Mech Ageing Dev. 2023 Mar;210:111763.

Peripheral artery disease and walking pace

The first therapy for those with peripheral artery disease, or PAD, is walking. But ischemic leg symptoms, including severe pain and extremity numbness, are major barriers to walking. Patients with PAD can often walk without pain if they keep to a slower pace. We analyzed data from 264 participants in the Low Intensity Exercise Intervention in Peripheral Artery Disease randomized clinical trial and found PAD patients who walked more slowly without ischemic symptoms did not improve walking speed after six months. The group that walked at a comfortable pace without symptoms also performed more poorly on tests designed to measure lower extremity functioning in older adults, which can predict lower quality of life, loss of mobility, disability and early death. A faster gait that did induce symptoms, however, improved speed after six months, indicative of mobility improvement. But this benefit persisted for 12 months.

Hammond MM, Spring B, Rejeski WJ, Sufit R, Criqui MH, Tian L, Zhao L, Xu S, Kibbe MR, **Leeuwenburgh C, Manini T**, Forman DE, Treat-Jacobson D, Polonsky TS, Bazzano L, Ferrucci L, Guralnik J, Lloyd-Jones DM, McDermott MM.

Effects of walking exercise at a pace with versus without ischemic leg symptoms on functional performance measures in people with lower extremity peripheral artery disease: the LITE randomized clinical trial. J Am Heart Assoc. 2022 Aug 2;11(15):e025063.

Musculoskeletal pain

Chronic musculoskeletal pain is among the most common reasons adults seek medical attention and is a leading causes of disability. Older adults with chronic musculoskeletal pain often cognitive impairments and diminished lower extremity physical function. Prior work suggests these impairments may be interrelated. Our study examined the

association between cognition and walking performance to determine if cognition affects the relationship between pain severity and walking performance in older adults with chronic musculoskeletal pain without cognitive impairment. We found that global cognition and pain severity were associated with walking performance in older adults with chronic pain. But pain severity, not cognition, primarily explained walking performance in our sample.

Lipat AL, Peterson JA, **Clark DJ, Cruz-Almeida Y**.

Decreased cognitive function is associated with impaired spatiotemporal gait performance in community dwelling older adults with chronic musculoskeletal pain. Brain Cogn. 2022 Jun;159:105862. doi: 10.1016/j.bandc.2022.105862. Epub 2022 Mar 28.

A wrinkle in time

Aging is associated with a decline in physiologic functions, leading to impaired resilience to stressors and development of cardiopulmonary diseases. An overlooked element of pulmonary vascular disease is time. Cellular responses to time, which are regulated by the core circadian clock, have only recently been deciphered. Even so, the roles of key aspects of the circadian clock in pulmonary hypertension remain understudied. We reviewed the current dialogue regarding common pathways in circadian biology. We highlight several outstanding challenges and propose potential experimental approaches. We found that a search for biomarkers indicating a disrupted circadian clock is necessary. Research is also needed to tease out whether a disrupted clock contributes to pulmonary vascular disease, or if the disease causes the disruption. Additionally, scientists need to study the role of environmental factors, such as smoking, on clock disruption and how the influence of sleep can impact pulmonary vascular disease.

Bryant AJ, Ebrahimi E, Nguyen A, Wolff CA, **Gumz ML, Liu AC, Esser KA**.

A wrinkle in time: circadian biology in pulmonary vascular health and disease. Am J Physiol Lung Cell Mol Physiol. 2022 Jan 1;322(1):L84-L101. doi: 10.1152/ajplung.00037.2021.



UF Claude D. Pepper Older American Independence Center colleagues attended a retreat in July 2022.



PROGRES

2020
2021
2022 ◀ Annual Report
2023

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