

GERIATRIC MEDICINE

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Message from the Chief

I am pleased to share our latest issue of *Update in Geriatric Medicine*, especially our excitement for a major augmentation of our research through the creation of a new, focused geroscience initiative led by **Toren Finkel, MD, PhD**, one of the most distinguished scientists in the field of aging research.

Recruited from the National Institutes of Health in 2017, Dr. Finkel has assembled an impressive team of new investigators to join him. Based on the observation that age itself is the most important risk factor in many diseases affecting our geriatric patients — and data revealing dramatic extension of both lifespan and healthspan in experimental models — the goal is to determine which of these experimental strategies might hold the most promise for application in humans. Several of our Division faculty already are collaborating in this enormous effort.

Also in this issue of *Update in Geriatric Medicine*, we showcase new research findings from **Susan Greenspan, MD**, in preventing recurrent hip fractures; an important new initiative in chronic low back pain by **Debra Weiner, MD**; and new findings from **Neelesh Nadkarni, MD, PhD**, on the role of brain amyloid in gait abnormalities.

We also are proud to share news of several recent awards bestowed on faculty members, recent published research from the Division, and the arrival of three talented, new faculty members.

Finally, we celebrate the accomplishments of **Joe Hanlon, PharmD, MS**, whose internationally-recognized contributions have added immeasurably to our understanding of the role and risks of medications in the care of geriatric patients.

With kind regards,



Neil M. Resnick

Neil M. Resnick, MD
Division Chief and Thomas Detre Professor of Medicine
Associate Director, Aging Institute of UPMC Senior Services
and the University of Pittsburgh
Director, Hartford Center of Excellence in Geriatrics



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Geroscience: Frontiers in the Biology of Aging

Can we discover and understand the basic biological mechanisms and pathways that regulate the aging process? Moreover, by fundamentally understanding how and why processes of aging occur, can we devise the tools and technologies that will allow us to intervene, modulate, or perhaps reverse the full range of age-related diseases and disabilities that occur as consequence of the biology of aging?

This is the field of geroscience, and UPMC and the University of Pittsburgh are investing heavily in the pursuit of answers that will unlock the mysteries and complex processes of how and why human beings age, and ultimately how we can intervene to more effectively improve and extend one's quality of life for as long as possible.

Helping to lead these emerging efforts in geroscience is **Toren Finkel, MD, PhD**, director of the Aging Institute, professor of medicine in the Division of Cardiology, and the G. Nicholas Beckwith III and Dorothy B. Beckwith chair in translational medicine. Dr. Finkel arrived at the University of Pittsburgh and UPMC in June 2017 after a distinguished 25-year career with the National Institutes of Health, where he was the chief of the Center for Molecular Medicine in the National Heart, Lung, and Blood Institute (NHLBI) immediately preceding his arrival in Pittsburgh.

"The support and commitment from both the University of Pittsburgh and UPMC to grow into one of the premier basic biology of aging and translational research centers in the world was what really attracted me to come to Pittsburgh — to pursue my own research in the biology of aging front but also to help lead this effort with so many dedicated faculty across many disciplines," says Dr. Finkel.

Understanding and Modifying the Basic Biology and Pathways of Aging

We know much about the basic biology of aging and its pathways, but significant gaps remain to be explored and understood. At the molecular level, it is known that accumulated nuclear DNA damage, shortening of the telomeres, problems with mitochondria, protein aggregation

issues, and a host of quality control mechanisms can go awry as individuals age. Yes, there are multiple aspects or hallmarks of aging, and it's certainly complex. "But that is not to say these processes are not regulated or cannot in some sense be malleable to interventions on the cellular or molecular level. We know, for example, in simple organisms that modifications to certain genes or proteins can have profound effects on both lifespan and health span. Similar modifications are what we hope to accomplish with human aging and age-related conditions such as Alzheimer's disease," says Dr. Frankel.

Fundamentally, Dr. Finkel and the groups working on these problems believe that once we more fully understand the basic mechanisms that drive aging, we will be



"We are not necessarily looking for or hoping to develop disease-specific therapies per se. We are interested in the molecules and processes that underlie the biology of aging, which, if we can intervene in, we think will prevent these sorts of illnesses from happening in the first place."

Toren Finkel, MD, PhD

in a position to develop new drugs that can regulate those mechanistic processes, leading to effective treatments for a wide range of age-related diseases. These studies will "lead to new approaches and new classes of medicines that we think will improve the quality of people's lives," says Dr. Finkel.

A Translational Approach to Modifying Aging Processes Driving Disease

Cardiovascular disease, cancer, neurodegenerative diseases — these all have a powerful age-related component. Until now, most of the strategies for treating these broad categories of illness have been very disease-specific with some successes and equivalent number of failures. The approach that Dr. Finkel and colleagues are taking — the geroscience approach — means that, "We are not necessarily looking for or hoping to develop disease-specific therapies per se. We are interested in the molecules and processes that underlie the biology of aging, which, if we can intervene in, we think will prevent these sorts of illnesses from happening in the first place," says Dr. Finkel.

The Aging Institute, which Dr. Finkel now leads, has begun to expand its research focus and capabilities to pursue many avenues of basic and translational research with respect to the goals of geroscience writ large.

"In the end, we will have approximately 15 different laboratories all working on various aspects of aging biology, so the work here will be incredibly diverse. Coupled with the basic science labs will be a high throughput screening facility that will help significantly in our mission to develop entirely new classes of anti-aging drugs. We also hope

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New Model of Care Is Making a Difference in Osteoporosis Treatment

The risk of osteoporotic fractures in adults over the age of 50 remains significantly high. For women, 50 percent will sustain an osteoporotic fracture sometime during their life. Twenty-five percent of men will experience a fracture. These individuals also are at significant risk (more than two-fold) for a second fracture and concomitant morbidity and mortality.

"Generally speaking, we're grossly under-treating individuals hospitalized with osteoporotic fractures. Only about 20 percent of people are treated, and that is simply far too few. The reasons are many, but probably the largest problem we are facing is a breakdown in communication between providers coupled with the fact that the majority of these individuals have other serious health conditions that may take priority in their primary care," says **Susan L. Greenspan, MD**.

Dr. Greenspan is dually trained in geriatrics and endocrinology, and currently serves as director of the UPMC Osteoporosis Prevention and Treatment Center, director of the Bone Health Program at UPMC Magee-Womens Hospital, and as principal investigator of both the Pittsburgh Claude D. Pepper Older Americans Independence Center and the Division's NIH-funded T32 Program in Research Training in geriatrics. Dr. Greenspan's research focus encompasses the pathophysiology, evaluation, and treatment of osteoporosis.

In 2014, Dr. Greenspan and the Division of Geriatric Medicine piloted a Fracture Liaison Service (FLS) as part of a combined quality improvement (QI) study with two other open health care systems to evaluate its efficacy in preventing secondary osteoporotic fractures by identifying patients early in the process of recovery from a fracture and intervening accordingly to better manage their underlying osteoporosis. Based upon the success of that initial QI study, the present day FLS was started in 2015 and has been delivering quality post-fracture care to patients in UPMC Presbyterian hospital since that time. The interventions provided for patients enrolled in the QI study, as well as the current patients in the FLS includes a number of components. Most patients receive a DXA

scan and appropriate lab testing. The results of these tests and their implications are carefully reviewed with the patients to ensure they adequately comprehend the information. Treatment options are recommended and discussed, medications prescribed if necessary, and direct follow-ups with patients occur several months after the initial visit. "We discuss fall prevention and strategies at home to decrease that risk. If they smoke, we talk about its impact on bone density and the various cessation programs available. I explain the vital importance of calcium and vitamin D. Patients have my contact information, along with an education packet so they can call me directly with any questions or concerns once they leave," says Karen Vujovich, MSN, CRNP, who is the fracture liaison coordinator at UPMC working alongside Dr. Greenspan. Importantly, all of this is communicated to the patient's primary care provider for continuity of care and follow-up.

FLS Program Shows Positive Results in Newly Published Findings

In February 2018, Dr. Greenspan and her study colleagues at the other two participating FLS pilot sites published their initial findings in the journal *Osteoporosis International*. The paper, titled *Implementing a Fracture Liaison Service Open Model of Care Utilizing a Cloud-Based Tool* provides a full accounting of the study methods and findings for the initial cohort of patients (93 meeting all eligibility requirements) enrolled into the program between April and December 2014. Data on these patients was gathered through June 2015 in order to provide measurements for six months post-enrollment.



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Susan L. Greenspan, MD

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UPMC Physician Resources

UPMCPhysicianResources.com is home to free CME courses, news, and events for physicians. Below is a selection of the current CME courses in geriatrics. For more information, please visit **UPMCPhysicianResources.com/Geriatrics**.

Calcium and the Elderly

Presented by James R. Johnston, MD

Dr. Johnston's presentation discusses normal calcium metabolism and an approach to calcium management in the older adult with an emphasis on identifying altered calcium metabolism.

A Systematic Approach to Improve the Outcomes of Pharmacotherapy of Late-Life Depression

Presented by Jordan F. Karp, MD

Dr. Karp discusses a protocol for late-life depression, including first line intervention and switch versus augmentation. Dr. Karp explains contingency rules for when to augment versus switch antidepressant pharmacotherapy, and the use of aripiprazole in older adults with treatment-resistant depression.

The Biology of Aging

Presented by Toren Finkel, MD, PhD

In this presentation, Dr. Finkel provides an overview of age-related incidence of major diseases, as well as the modifiable nature of aging and the role of mitophagy in aging and disease processes.

Geriatrics in the ED

Presented by Jason S. Chang, MD

Dr. Chang's presentation is focused on the goals of emergency care in the older adult and covers various topics that include triage, early intervention, and transitions of care, and it also discusses aspects of recognition and management of acute delirium.

Evaluation of Neuropathy

Presented by Neil A. Busis, MD

Dr. Busis reviews the spectrum of neuropathy disorders, their most common causes, proper diagnostic testing procedures, and recommendations for treatment approaches.

Treatment of Hyperlipidemia in Older Adults

Presented by Daniel E. Forman, MD

Dr. Forman's presentation on the treatment of hyperlipidemia covers such topics as statin therapy in the older adult and universal health outcomes. He explores the risks associated with statin therapy in older adults, and current perspectives on secondary prevention.

Even More Tips on How to Live Long and Prosper

Presented by Rollin M. Wright, MD, MPH, MS

Dr. Wright discusses how to effectively prescreen patients that are undergoing elective surgeries in order to anticipate and intervene in surgical complications. Dr. Wright's talk elaborates on the use of cognitive function screening in preoperative evaluations, assessment of volume and duration of bouts of sedentary time to prolong function and delay mortality, and the use of underlying functional and comorbidity status to guide therapeutic blood pressure targets.

Understanding the Role of Inflammation in Rheumatic Diseases

Presented by Terence Starz, MD

Dr. Starz gives a presentation on the mechanisms of inflammation on rheumatic diseases, including the initiation, stopping, and persistence.

TAVR 2018: Eligibility and Outcomes

Presented by John Schindler, MD

Dr. Schindler provides an update on transcatheter aortic valve implantation eligibility in patients, identifying which patients have been studied and shown to derive benefit from the procedure, as well as the risks associated with TAVR.

Pulmonary Hypertension: Diagnosis and Treatment

Presented by Jennifer Gonzalez McComb, MD, MPH, FACP

Dr. McComb gives a lecture on the diagnosis and treatment of pulmonary hypertension using a current case as an example for diagnostic testing and evaluation. .

Video Rounds

Video Rounds is a series of short, informative, and educational videos created for physicians and covering a variety of medical and surgical disciplines.

Care for Dementia Patients

Rollin M. Wright, MD, MPH, MS

Adverse Events in Skilled Nursing Facilities

Steven Handler, MD, PhD, CMD

Addressing Delirium With the Hospital Elder Life Program (HELP)

Fred Rubin, MD

New Meta-Analysis Shows Effects of Interventions on Adverse Drug Reactions

Adverse drug reactions (ADRs) in older adults are common, costly, and account for significant numbers of hospital admissions every year in the United States. Errors in prescribing or poor prescribing methods account for far more ADRs than do such things as nonadherence, allergies, or the usual and expected pharmacological effect.

Joseph T. Hanlon, PharmD, MS, BCGP, is a tenured professor of medicine in geriatrics with secondary appointments in pharmacy and therapeutics and epidemiology at the University of Pittsburgh School of Medicine. Dr. Hanlon also is a health scientist at the VA Pittsburgh Healthcare System Geriatric Research Education and Clinical Center

(GRECC). For more than 30 years, Dr. Hanlon has explored a diverse variety of topics through his research in geriatric pharmacotherapy and pharmacoepidemiology, having won numerous awards for his contributions to science.

Focused interventions and strategies can be effective in reducing and preventing

ADRs. Dr. Hanlon and collaborators conducted what was likely the first randomized controlled trial of an intervention protocol in 1996. This study along with a dozen others were recently analyzed by Dr. Hanlon and colleagues as part of a broad systematic review and

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Joseph T. Hanlon, PharmD, MS, BCGP: A Distinguished Career in Geriatrics



In September 2018, Dr. Hanlon will retire from his appointment as professor of medicine in the Division of Geriatric Medicine. Since joining the Division in April 2004, and spanning his entire career, Dr. Hanlon has authored more than 90 peer-reviewed articles and dozens of book chapters related to various important issues of drug management and drug prescribing in vulnerable older adult populations.

His work in developing the Medication Appropriateness Index (MAI) has become widely used internationally in randomized controlled trials. His recent and ongoing work uncovering the long-term effects of anticholinergic medications and their relationship to dementia is helping to reshape how these medications are used to prevent long-term harm from their use.

Preventing unintentional harm from prescribed medications has been a central theme of Dr. Hanlon's career with much work devoted to developing systems and studies to mitigate the risk of adverse drug reactions and their consequences in the older adult.

Dr. Hanlon's research, while broad and collaborative, has had a focus on three main areas. Drug-related problems related to adherence, prescribing, monitoring, adverse drug reactions, and others is the first of which he has spent much time investigating. The second area of focus has explored various drug-induced geriatric syndromes related to falls and fractures, delirium, and, notably, with several recent papers on the long-term effects of anticholinergic medications in older adults and the relationship with dementia. Dr. Hanlon also has led and authored numerous studies on racial differences and disparities in the use and prescription of medications.

Dr. Hanlon's past studies have led to new ways to account for and classify central nervous system medication burden across classes of medications, and he also has explored the prescription of statins before and after the development of the Medicare Part B system.

Dr. Hanlon is also part of the committee currently working on the next update of the Beers Criteria, a draft of which was released in August for public comment prior to the final version release sometime in the fall of 2018. The new Beers Criteria will have updated guidelines for clinicians on potentially inappropriate medication use in older adults. Dr. Hanlon has been a part of the Beers Criteria expert panel since 2011.

These are not small accomplishments. Dr. Hanlon's work has contributed greatly to the field of geriatric pharmacology and will be measured for many years to come.

Dr. Hanlon will remain associated with the Division of Geriatric Medicine as professor emeritus, and he will be continuing on at the VA Pittsburgh Healthcare System where he will be working on completing a number of active research projects that are currently in progress.

Testing New Models of Care for Chronic Low Back Pain

The origins and mechanisms of the experience of pain is a complex field of study. An individual's experience of pain is quite subjective in nature. Mitigating pain, be it acute or chronic, through various interventions of surgery, pharmacotherapy, physical therapy, and other methods is big business to the tune of tens of billions of dollars a year in the United States alone.



"Educating individuals about what contributes to their back pain is crucially important. I believe a big part of what drives excessive use of health care resources for this patient population is a lack of information, or inaccurately provided information."

Debra K. Weiner, MD

Chronic low back pain (CLBP) in older adults is all too common. Roughly a third of older adults (65+) experience low back pain, and an estimated three-quarters of those individuals suffer from CLBP. The effects of poorly controlled CLBP are well documented. However, many therapies and systems fail to deal with complex chronic low back pain effectively, leaving individuals in distress with reduced quality of life and susceptible to other conditions, such as anxiety and depression.

Debra K. Weiner, MD, has spent decades researching the causes and complexities of pain and chronic pain in the older adult, with significant recent efforts to address the need for a more rigorous and complete understanding of CLBP. Much of this research has manifested in a 12-part series of papers in the journal *Pain Medicine*, published under the heading *Deconstructing Chronic Low Back Pain in the Older Adult: Shifting the Paradigm From the Spine to the Person*.

"Chronic low back pain is a complex syndrome, one that usually presents or is expressed through many contributing factors, some of which lie not in the spine itself but outside the lumbar region. We may not be able to cure chronic low back pain, but we can do a much better job in treating chronic low back pain if we thoroughly evaluate and manage its multiple contributors," says Dr. Weiner.

Dr. Weiner and colleagues' research sets down an interrelated set of 12 algorithms for the assessment, diagnosis, and treatment of chronic low back pain. The scope of the research touches many common conditions that older adults experience, and that either individually, or in some aggregate, along with degenerative changes of the lumbar spine, can contribute to or otherwise manifest as an individual's experience of chronic low back pain. Dr. Weiner and colleagues have identified and developed recommendations for evaluating and treating as contributors to CLBP and pain-associated disability the following conditions:

- Hip Osteoarthritis
- Myofascial Pain
- Lumbar Spinal Stenosis
- Sacroiliac Joint Syndrome

- Lateral Hip/Thigh Pain Syndrome
- Leg Length Discrepancy
- Insomnia
- Fibromyalgia
- Depression
- Anxiety
- Maladaptive Coping
- Dementia

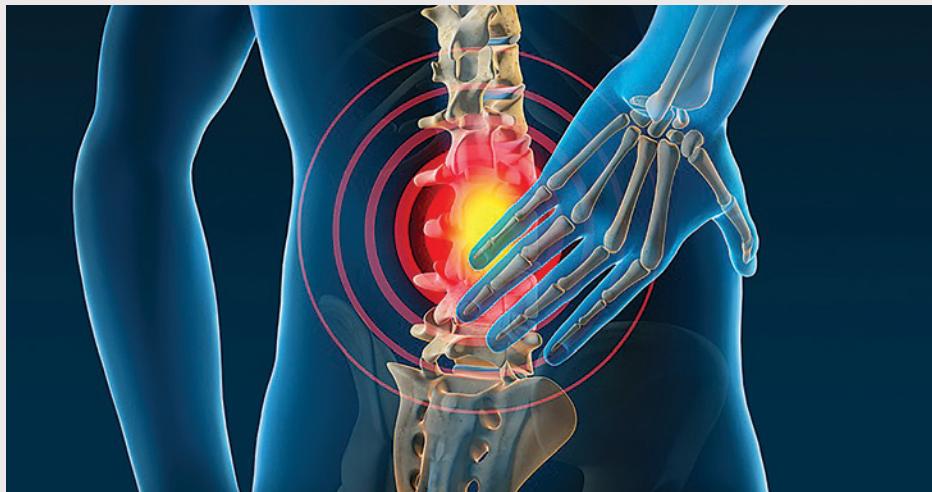
While there may be other contributing factors, the commonality of these 12 conditions should be evaluated routinely as potential contributors to pain and disability. While each of the 12 contributing factors is discussed in detail in separate papers, Dr. Weiner indicates that the body of work is meant to be used in tandem, as a single assessment tool, with each aspect coming into play, or not, as the case may be, during patient evaluation and subsequent ongoing management.

Clinical Trials Testing the New Treatment Paradigm

With funding from the VA Office of Research and Development, Dr. Weiner is leading a new multicenter clinical trial to test the efficacy of this new paradigm in the care of chronic low back pain with a cohort of older veterans who will be enrolled from three VA sites across the United States (Pittsburgh, Dallas, Richmond).

"We completed a small, 50-person pilot trial with six-months follow-up, and we are in the process of writing up the results. The bottom line is that the results showed promise when comparing pain and function measures between our whole-person centered care approach versus the standard imaging-directed usual care," says Dr. Weiner.

The new trial will randomize 330 older veterans into either the Aging Back Clinics model or usual care. Participants, regardless of the study arm, will all undergo the same comprehensive assessment that collects data based on the NIH minimum data set for CLBP. "The main outcomes we are interested in are pain and function, but we are collecting baseline measures on an extensive array of constructs, such as pain medications, gait speed, and many more."



A large part of the intervention in the comprehensive care model deals with patient education.

"Educating individuals about what contributes to their back pain is crucially important. I believe a big part of what drives excessive use of health care resources for this patient population is a lack of information, or inaccurately provided information. Part of the comprehensive assessment model we have designed is focused on educating patients about the contributing causes to their pain and how and why those issues need to be treated. For example, insomnia can lower a person's pain threshold and tolerance. Someone who is having difficulty sleeping likely is not able to make the correlation on their own that their insomnia can affect their back pain, so this education aspect is very important," says Dr. Weiner.

Dr. Weiner's team has developed the necessary educational materials, and this information is reinforced as part of the overall management process during every follow-up visit.

"For part of the trial, we developed a tablet application that participants will be using with our screening processes, and we also will deliver educational information through it that we hope will provide relevant and timely knowledge about the patient's condition," says Dr. Weiner.

Concluding Remarks

As Dr. Weiner explains, it is unlikely that this new approach to assessment and treatment can completely eliminate the existence of chronic low back pain. The complexity and variety of experiences of the condition likely preclude such a broad outcome.

"However, I'm absolutely confident that we can lessen the degree to which CLBP affects people's lives and daily activities. This is, of course, an individualized approach given the complexities of CLBP. The ways that best optimize treatment outcomes, as we have seen through our preliminary research and through taking care of these patients, treat all of the individual potential contributors to pain. That is really what this trial is designed to investigate and what we believe will be shown in the results," says Dr. Weiner.

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Osteoporosis Treatment

(Continued from Page 3)

Results of the pilot intervention showed considerable improvements across all of the primary outcomes, which were percentages of individuals receiving bone mineral density tests (DXA), vitamin levels, calcium and vitamin D supplementation, and prescription of medication therapy for osteoporosis if warranted by standard guidelines.

In aggregate across the three pilot study sites, the percentages of individuals getting BMD testing increased from 21.2 percent to 92.9 percent. Serum vitamin D measurements went from 25.2 percent to 84 percent.

The percentage of patients recommended supplements for calcium and/or vitamin D increased to 92.6 percent from the baseline of 35.8 percent. Finally, medications prescribed for osteoporosis treatment jumped from 19.5 percent pre-FLS intervention to 54.1 percent after the FLS intervention.

"When you look at the pilot study as a whole, I think we can confidently say that this type of intervention can work in an open system, and we can use it to intervene positively with these at-risk patients. The intensive approach and intervention of the fracture liaison shows significant promise."

"We don't yet know if this kind of intervention will stave off subsequent fractures in this population, nor do we know yet if we can scale these systems up to the size needed for a large, open health care system, but our future studies will be examining these important aspects," says Dr. Greenspan.

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Brain Amyloid Deposition and the Cognition-Mobility Interface

Neelesh Nadkarni, MD, PhD, FRCPC, joined the Division of Geriatric Medicine in 2010. He is also a past scholar at the Pittsburgh Claude D. Pepper Older Americans Independence Center, and he is currently a co-investigator at the Pittsburgh Alzheimer's Disease Research Center, which is co-directed by Drs. Oscar Lopez and William Klunk.



"Interactions between cognition and mobility are very important for older adults. Those who have problems performing two tasks simultaneously have been found in past research to exhibit an increased risk of mobility decline and falls."

Neelesh Nadkarni, MD, PhD, FRCPC

Dr. Nadkarni's main research focus looks at the interaction between cognition and mobility in older adults, and how changes in the brain with aging affect this interaction. His current K23 grant from the NIA — The Aging Brain and the Cognition-Mobility Interface in Clinically Normal Older Adults — sees Dr. Nadkarni studying the application of brain imaging techniques with respect neurodegenerative disorders, small vessel disease, and amyloidosis to better understand changes in the brain as a result of aging, and their relationship to cognition and mobility.

Dr. Nadkarni also is a primary investigator or co-investigator on more than a dozen current studies, all largely related to Alzheimer's disease, cognition, and mobility. Past published works by Dr. Nadkarni include studies on gait characterization and cognition-mobility interactions in Alzheimer's disease, statins and brain integrity in older adults, cerebellar gray matter volumes and gait speed, interleukin-6 levels and slow gait, and others.

Dual-Tasking in Cognition and Mobility Studies

Dual-task studies, with respect to Dr. Nadkarni's work, involve both a mental task and a physical task, done independently of one another to establish baseline results, then done in tandem. For example, walking and dialing a phone, or walking and performing a memory recall task. "There is a whole body of literature looking at dual-tasking, how completing a mental task while walking can constrain one's performance with both tasks. However, not much is known about dual-tasking in patients with dementia, or with healthy older adults. Prior to arriving at the University of Pittsburgh, my doctoral work looked at how changes in walking affect patients with early Alzheimer's disease compared to healthy older adults. We found that older adults — healthy patients without early Alzheimer's disease but with amyloid deposition — have some subtle gait changes when you have them perform dual-task activities. Vascular

disease changes in the brain, which happen with aging, seem to affect this interaction between performing a mental task while walking," says Dr. Nadkarni.

Dual-task studies are an integral part of Dr. Nadkarni's research and have led to several interesting findings in recent years. "Interactions between cognition and mobility are very important for older adults. Those who have problems performing two tasks simultaneously have been found in past research to exhibit an increased risk of mobility decline and falls. Performance on dual-task measures has been shown to predict cognitive decline and Alzheimer's disease," says Dr. Nadkarni.

Amyloid Deposition and Slow Gait in Cognitively Healthy Older Adults

Amyloid- β deposition in the brain is a key feature of Alzheimer's disease. The discovery of Pittsburgh compound B (PiB) by Drs. Klunk, Mathis, and colleagues at the University of Pittsburgh has allowed for the *in vivo* detection and mapping of beta-amyloid deposits in the brain via positron emission tomography (PET) imaging. While beta-amyloid deposition is definitively linked to Alzheimer's disease, less is known about the effects of the protein on other physiological functions or disease processes.

Dr. Nadkarni and colleagues are actively studying the role of beta-amyloid on cognition and mobility in healthy older adults who do not have cognitive impairments or Alzheimer's disease, but some of them have high levels of beta-amyloid deposits in the brain. This research seeks to determine the effects of amyloid accumulation on cognition and mobility, and also how changes in mobility and cognition in preclinical Alzheimer's disease, which in otherwise healthy adults may be predictive of future clinical progression.

In their study titled *Brain Amyloid- β and Slow Gait in Older Adults Without Dementia: Influence of Cognition and APOE-e4 Genotype*, published in *JAMA Neurology* in 2017,

Dr. Nadkarni and colleagues examined walking speeds in a cohort of 184 dementia-free older adults, 140 of whom were cognitively normal on neuropsychological testing. These individuals also received PET scans in order to quantify the amount of beta-amyloid deposits in the brain. They found that high levels of beta-amyloid in the brain was associated with slow walking speeds in the whole cohort, but in the cognitively normal population, cognition and APOE-e4 genetic carrier status influenced this association between beta-amyloid and slow walking.

In another study titled *Cerebral Amyloid Deposition and Dual-tasking in Cognitively Normal, Mobility Unimpaired Older Adults*, published in *Journal of Gerontology Medical Sciences* in 2017, Dr. Nadkarni and colleagues showed the relationship between beta-amyloid and cognition-mobility interaction measures. They used dual-tasks, which refers to performing cognitive tasks while walking, as a means to quantify the cognition-mobility interface.

"In this study, these healthy older adults were cognitively normal and had no mobility impairments, with normal gait speeds and no history of falls. We then ran them through our dual-task paradigms to see if we could detect subtle changes in either gait or cognition and correlate that to

the individuals who have high levels of brain amyloid," says Dr. Nadkarni.

At the conclusion of the study, they found that on these dual-task tests, cognitively normal older adults with higher beta-amyloid in the brain slowed down significantly more than those with low levels of brain beta-amyloid. In effect, they found that dual-task performance is not only affected in those with Alzheimer's disease, but also in those with preclinical Alzheimer's disease.

Practical Applications of Dual-Task Studies

PET scans are expensive. Having some kind of mechanistic test, such as dual-task mobility/cognition studies, may in the future prove useful front-line assessments to point to who may be at higher risk for developing dementia and mobility impairments, and who may benefit more from a PET scan to assess amyloid deposition. "Dual-task assessments should be able to help us target at-risk individuals for the expensive and confirmatory brain imaging tests that can detect abnormal aging related brain pathologies so that we can target these individuals early on for interventions to prevent cognitive and mobility decline," says Dr. Nadkarni.

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Effects of Interventions on Adverse Drug Reactions (Continued from Page 5)

meta-analysis of interventions designed to optimize medication use in older adults and their effect on mitigating adverse drug reactions.

Published in the *Journal of the American Geriatrics Society* in 2018, the meta-analysis is the first of its kind to look at ADR interventions broadly. The reviewed studies varied in size, type of intervention, setting, and geographic location. They also varied in terms of the interventions being pharmacist-led, clinician-led, or an education or technology intervention.

Overall, the intervention cohort was 21 percent less likely to experience an ADR versus the control. On subsequent analysis, looking specifically at the pharmacist-led interventions,

those groups were 36 percent less likely to experience an ADR regardless of setting.

"The bottom line is that a majority of ADRs are preventable, either through a focused intervention within a setting or through education of some sort, given how high the incidence of ADRs related to prescribing is. It probably seems intuitive, but interventions of any kind, and specifically those that are pharmacist-led, can have a really significant impact limiting ADRs. Yes, it's complicated given the disparate health care settings and fractured payments system in this country, but it's a problem that can be solved," says Dr. Hanlon.

References and Further Reading

References and a sample of published papers from Dr. Hanlon follow. For a complete listing of past works, please consult the PubMed.gov library.

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Welcome New Faculty

The Division of Geriatric Medicine continues its growth and expansion in 2018 with the appointment of several new faculty members. We are pleased to have the following individuals join our ranks and continue our mission of excellence in patient care and research.

Aditi U. Gurkar, PhD

Assistant Professor of Medicine



Dr. Gurkar's research interests revolve around the biology of aging and age-related diseases, and specifically how endogenous DNA damage and its molecular mechanisms and signaling pathways contribute to these processes of aging and related disease states.

Rachel Elizabeth Jantea, MD

Clinical Instructor of Medicine



Dr. Jantea joined the Division after completing her geriatric fellowship training and residency within the Division. She has a special focus on medical education and curriculum development, in addition to her clinical duties seeing outpatients within the Benedum Geriatric Center, and providing inpatient care and consultations at both UPMC Presbyterian and UPMC Shadyside.

Keisha Ward, MD

Clinical Assistant Professor of Medicine



Dr. Ward completed her geriatric fellowship at the University of Pittsburgh and joined the Division as a faculty member in 2017. Dr. Ward has a particular interest in dementia, especially in minority populations. In addition to seeing patients at the Benedum Geriatric Center and one of the UPMC long-term care sites, she also sees patients in their homes.

Geroscience: Frontiers in the Biology of Aging

(Continued from Page 2)

to repurpose existing FDA-approved compounds that we think might be beneficial or applicable in modifying processes of aging," says Dr. Finkel.

In the domain of basic science research, the laboratories of the Aging Institute are looking at such things as the connections between autophagy and mitophagy and their roles in removing or eliminating damaged proteins or organelles from the body and how this may contribute to aging itself. Other aspects of research will be focused on DNA damage repair, protein folding processes, mitochondrial and telomere research, and inflammation and its role in aging processes, among others.

For the testing of FDA-approved compounds, several projects are already in the planning phases, and the efforts from a broad perspective will be spearheaded by Anne B. Newman, MD, and Daniel Forman, MD. "Dr. Newman recently joined the Aging Institute as our clinical director, and she, along with Dr. Forman, who specializes in geriatric cardiology, will be leading many of our efforts to try and repurpose FDA-approved molecules for new, anti-aging uses," says Dr. Finkel.

The diabetes drug Metformin will be analyzed in an internally led study in the setting of elective surgery with older adults.

"The goal is to see if metformin taken prior to surgery provides benefits, including improved survival or reduced hospitalization time. There is also a large, multicenter, NIH-proposed study of metformin in aging in which we also will be part of here at Pitt."

Other areas of focus will likely look at reducing the nonspecific inflammatory responses seen in older adults.

"If you look at markers of inflammation, for example circulating interleukin-6 levels, it's probably one of the best predictors of who is or is not going to live as they become elderly. It's a marker of frailty and a sign of bad things to come. We are very interested in knowing whether biological agents that have been developed for other inflammatory conditions like rheumatoid arthritis or Crohn's disease can be repurposed in a safe and effective way in older adults. Our hope is to negate or modify frailty and the propensity for disease that this nonspecific inflammatory response belies."

The Emerging Paradigm of the Health Span

While a long life is generally desirable by most individuals, what is an extended length without commensurate quality? Much discussion is now focused on the idea of the health span — the length of time that one remains disease free and able to sustain a sufficient quality of life.

There is this observation that people who have incredibly long lives generally are relatively free from various morbidities. This theory, called the compression of morbidity, says that if as you extend life, you can also shrink the period of time an individual is suffering from morbidities.

"This is sort of the Holy Grail — to extend a person's life span but compress the time period where they are incapacitated or debilitated. We think that it has to do with what's driving the aging process, and again we are very optimistic about this approach and the research contributing to it. This is a new way of thinking about diseases, not in a disease-specific context but one whereby you modify aging itself," says Dr. Finkel.

A Selection of Recent Publications

Robinson AR, Yousefzadeh MJ, Rozgaja TA, Wang J, Li X, Tilstra JS, Feldman CH, Gregg SQ, Johnson CH, Skoda EM, Frantz MC, Bell-Temin H, Pope-Varsalona H, **Gurkar AU**, Nasto LA, Robinson RAS, Fuhrmann-Stroissnigg H, Czerwinski J, McGowan S, Cantu-Medellin N, Harris JB, Maniar S, Ross MA, Trussoni CE, LaRusso NF, Cifuentes-Pagano E, Pagano PJ, Tudek B, Vo NV, Rigatti LH, Opresko PL, Stoltz DB, Watkins SC, Burd CE, Croix CMS, Siuzdak G, Yates NA, Robbins PD, Wang Y, Wipf P, Kelley EE, Niedernhofer L. Spontaneous DNA Damage to the Nuclear Genome Promotes Senescence, Redox Imbalance and Aging. *Redox Biol.* 2018 Jul; 17: 259-273.

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Awards and Accomplishments



Susan L. Greenspan, MD, became president of the National Osteoporosis Foundation in 2018. Dr. Greenspan is dually trained in geriatrics and endocrinology and has, among other accomplishments, led the research efforts as principal investigator of the Pittsburgh Claude D. Pepper Older Americans Independence Center since 2012, as well as leading the Division's NIH-funded T32 training program.



Anne B. Newman, MD, MPH, was appointed to be the new clinical director of the Aging Institute of UPMC Senior Services and the University of Pittsburgh. Dr. Newman will oversee the translational research efforts of the Institute. Among other appointments, Dr. Newman is a professor of medicine and chair of the Department of Epidemiology at the University of Pittsburgh.



Adele Towers, MD, MPH, FACP, associate professor of medicine and psychiatry, was elected president of the Allegheny County Medical Society in 2018.

ABOUT THE UPMC DIVISION OF GERIATRIC MEDICINE

Ranked among the nation's top hospitals for geriatric care by *U.S. News & World Report*, UPMC Presbyterian Shadyside offers older adult patients access to a multidisciplinary network of comprehensive clinical care. Our geriatricians, all specialists in internal medicine, have additional subspecialty training in geriatrics.

- We focus on the prevention, diagnosis, and treatment of geriatric syndromes, including:
 - Memory loss/dementia
 - Falls or unsteadiness
 - Decreased appetite or weight loss
 - Multiple medical issues
 - Osteoporosis
 - Depression or agitation
 - Incontinence
 - Generalized weakness
 - Multiple medications with possible side effects
 - Functional decline
- Our physicians provide integrated care to patients in acute care, ambulatory care, home and community-based care, and long-term care.
- Each year, the Division hosts the Clinical Update in Geriatric Medicine, a three-day seminar featuring timely, relevant topics from a range of experts in geriatric medicine.

To learn more about the UPMC Division of Geriatric Medicine, please visit
UPMCPhysicianResources.com/Geriatrics.



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A \$19 billion world-renowned health care provider and insurer, Pittsburgh-based UPMC is inventing new models of patient-centered, cost-effective, accountable care. UPMC provides more than \$900 million a year in benefits to its communities, including more care to the region's most vulnerable citizens than any other health care institution. The largest nongovernmental employer in Pennsylvania, UPMC integrates 85,000 employees, 40 hospitals, 600 doctors' offices and outpatient sites, and a 3.4 million-member Insurance Services Division, the largest medical insurer in western Pennsylvania. As UPMC works in close collaboration with the University of Pittsburgh Schools of the Health Sciences, *U.S. News & World Report* consistently ranks UPMC Presbyterian Shadyside on its annual Honor Roll of America's Best Hospitals. UPMC Enterprises functions as the innovation and commercialization arm of UPMC, and UPMC International provides hands-on health care and management services with partners around the world. For more information, go to UPMC.com.