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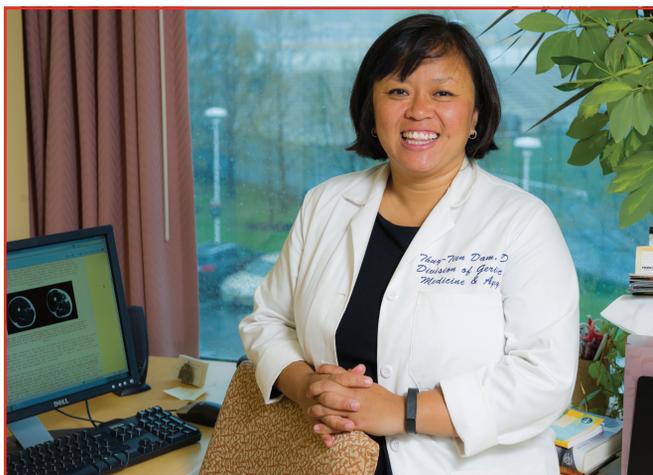
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Research Partnership Defines Diagnostic Criteria for Sarcopenia

Sarcopenia, age-related loss in muscle mass and strength, are important contributors to frailty. Frailty is a geriatric syndrome that identifies older adults who are vulnerable to hospitalizations, falls, fractures, and early death. “Sarcopenia is an early driver of the physical decline seen in frail older adults,” says Thuy-Tien L. Dam, MD, a geriatrician in the Division of Geriatric Medicine and Aging at New York Presbyterian/

The Allen Hospital and Columbia University College of Physicians and Surgeons. “Chronic diseases like diabetes can contribute to loss of muscle mass and function, leading to impaired mobility and physical inactivity. Impaired mobility, like poor walking, contributes to functional decline, which makes maintaining daily activities of living, such as cooking, dressing, and bathing, difficult for many older adults.”



Dr. Thuy-Tien L. Dam

In addition to its debilitating effects on older adults, sarcopenia impacts society at large. In the United States, the number of older adults (age 65 years and above) is expected to double to 86.7 million near 2050, resulting in a potential increase of comorbidities and the need for expensive institutionalization. “If you ask most people what’s really important for them, it’s not only to live longer, but to live longer with better quality of life,” says Dr. Dam.

According to Dr. Dam, researchers began studying sarcopenia in the early 1990s, and while diagnostic

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New Center Pointing the Way to Improvements in End-of-Life Care

In early 2014, the Office of Geriatric Research in the Division of Geriatrics and Palliative Medicine at Weill Cornell Medical College welcomed Holly G. Prigerson, PhD, and Paul K. Maciejewski, PhD, as Co-Directors of the newly established Center for Research on End of Life Care. Dr. Prigerson, an internationally recognized researcher on end-of-life care and bereavement, and Dr. Maciejewski, a biostatistician in medicine and radiology whose research expertise spans multiple disciplines, including statistics, philosophy, and biochemistry, bring expertise in the psychological, social, and cultural processes that influence end-of-life

medical decision-making and care. Dr. Prigerson joins Weill Cornell from the Dana-Farber Cancer Institute in Boston where she served as Director of Psycho-Oncology Research and Professor of Psychiatry, Brigham and Women’s Hospital, Harvard Medical School. Dr. Maciejewski, who collaborates on a number of research studies with Dr. Prigerson, most recently was Lecturer in Psychiatry at Harvard Medical School and on the staff at Brigham and Women’s Hospital.

Much of Dr. Prigerson’s research has focused on psychosocial factors that influence the quality of life and care received by terminally ill patients,

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criteria had been proposed, no consensus had been reached. In order for sarcopenia to be recognized as a clinical condition, criteria for diagnosis need to be based on clinically relevant thresholds and independently validated.

“Recent definitions for sarcopenia have been based on expert opinions without much evidence to support certain cutpoints for low muscle mass or muscle strength,” she says. “While these judgments were founded on some literature, they were not anchored to a clinically important outcome like poor mobility. Early definitions also focused only on the loss of muscle mass, but recent research suggests that strength and function may be better predictors of increased mortality.”

In order for sarcopenia to be recognized as a clinical condition, criteria for diagnosis need to be based on clinically relevant thresholds and independently validated.

To provide the data-driven diagnostic criteria using an evidence-based approach, the Foundation for the National Institutes of Health (NIH) funded the Biomarkers Consortium Sarcopenia Project, a three-year study launched in 2010. Participants included representatives from the National Institute of Aging and the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the Center for Drug Evaluation and Research of the Food and Drug Administration, industry partners, and academic institutions, including NewYork-Presbyterian/Columbia, under the direction of Dr. Dam.

Just What is Sarcopenia?

Researchers combined data from nine sets of intervention and observational studies of older persons living in the community. The pooled sample included more than 26,000 participants – 57 percent female and 43 percent male – who already had data collected over the years. The median age was 78.6 years for women and for men, 75.2 years. Investigators examined the association between body mass index (a weight-to-height ratio), appendicular lean mass (the sum of lean mass in the arms and legs), grip strength, and walking speed. The study found that grip strength of less than 26 kilograms (approximately 57 pounds) for men or 16 kilograms (approximately 35 pounds) for women was low since these values best discriminated who had slow walking speed.

Recommendations for Cutpoints for Weakness and Low Lean Mass

CUTOPOINT WEAKNESS	MEN	WOMEN
Recommended: grip strength (GSMAX)	<26 kg	<16 kg
APPENDICULAR LEAN BODY MASS		
Recommended: ALM adjusted for BMI (ALM_{BMI})	<0.789	<0.512

Notes: ALM = appendicular lean mass; BMI = body mass index
Source: The Foundation for the National Institutes of Health Sarcopenia Project

Similarly, it proposed that low muscle mass, defined as the ratio of muscle mass to body mass index, be <0.789 in men or <0.512 in women. These values best discriminated adults who were weak. By pooling data from observational longitudinal studies and clinical trials, the researchers were able to arrive at a data-driven definition of what constitutes clinically important weakness and low lean mass. The recommendations provide specific characterizations of how low lean mass and low strength relate to mobility and disability.

The results of their work, which were published in a series of articles in the *Journals of Gerontology: Medical Sciences* in May 2014, are significant for several reasons, says Dr. Dam. “Why do we even care about sarcopenia? It’s because there are not many drugs available that can improve people’s strength and improve their muscle mass. In order for pharmaceutical companies and the FDA to move forward and test new drugs or initiate physical activity programs, we need to have a consistent agreed upon definition of sarcopenia. The Sarcopenia Project is one of the steps to do that.”

Dr. Dam notes that there are some new drugs in the pipeline that have the potential to impact muscle mass. “For example, there are serum antigen receptor modulators that are similar to testosterone, but without the negative effects. And there are Phase II studies that are looking at myostatin inhibitors, which may help to increase muscle mass and strength,” she says. “Providing a clear definition of sarcopenia will help promote not only drug development, but also help identify in the clinic a growing population of older adults who may benefit from interventions.”

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New Center Pointing the Way to Improvements in End-of-Life Care (continued from page 1)



Dr. Holly G. Prigerson

and factors influencing family caregivers both before and after the death of a loved one. For her work in the field, Dr. Prigerson received the National Hospice and Palliative Care Organization Distinguished Researcher Award, which recognizes an outstanding body of research that has contributed to the enhancement of hospice and palliative care.

In describing the goals of the Center for Research on End of Life Care, Dr. Prigerson says, “The Center consists of several cores. Among them is communication and medical decision making for patients and families confronting serious illnesses, including studies of comparative effectiveness of palliative treatments. Another is a mental health core that will encompass patients and families with anxiety disorders, depression, and anticipatory and prolonged grief. Other studies we have been conducting examine spirituality and ethnic disparities in care received at the end of life.” In addition, as part of the Center’s work, Dr. Maciejewski will pursue brain imaging studies to understand the neurobiology and neurosensory of loss and grief reactions.

Forging a New Field of Study

Dr. Prigerson has studied the quality of life and care received by terminally ill patients and factors influencing caregiver adjustment both before and after the death of a loved one since her dissertation work at Stanford University in the late 1980s. She completed a postdoctoral fellowship in the Epidemiology of Aging at Yale University and then was funded by the National Institute of Mental Health (NIMH) for a K-award to study psychosocial factors in bereavement-related depression while an Assistant Professor of Psychiatry at Western Psychiatric Institute and Clinic in Pittsburgh.

In 1997, she returned to Yale where she received three National Institutes of Health R01 grants: 1) to conduct a *Diagnostic and Statistical Manual* field trial of consensus criteria for Prolonged Grief Disorder, 2) a psychiatric epidemiologic study of advanced cancer patients and the caregivers that survived them, and 3) a study of psychosocial factors influencing ethnic disparities in end-of-life care and bereavement adjustment.

“We’re doing research that we see is making a difference clinically. We’re not promoting a drug. We’re not promoting palliative care. We’re conducting research to figure out how to reduce the pain and suffering of patients and families confronting one of life’s most challenging periods – the death of a loved one.”

— Dr. Holly G. Prigerson

Prior to joining Harvard Medical School and Brigham and Women’s Hospital, Dr. Maciejewski served as Director of Statistics, Women’s Health Research, and Assistant Professor of Psychiatry and a member of the Magnetic Resonance Research Center at Yale University School of Medicine. He received his PhD from Stanford University.

Their bereavement research has focused on answering the question, “How do we know if someone has clinically significant difficulty adjusting to the death of a loved one?” To answer this question, their research has comprised a broad range of study, including DSM-5 field trials for Prolonged Grief Disorder (PGD). Dr. Prigerson, as principal investigator, and Dr. Maciejewski, as chief statistician, served as advisors to the *Diagnostic and Statistical Manual for Mental Disorders* (DSM-5) and International Classification of Diseases (ICD)-11 on the inclusion of PGD in the DSM-5. Their publication “*Prolonged Grief Disorder: Psychometric Validation of Criteria Proposed for DSM-5 and ICD-11*” in *PLoS Medicine* in 2009, was the final report from their National Institute of Mental Health-supported study. “It tested and refined consensus criteria for this syndrome,” says Dr. Prigerson. “Prolonged Grief Disorder is now slated for inclusion as a type of stress-response syndrome like post-traumatic stress disorder, and the criteria based on our studies will appear in the ICD-11.”



Dr. Paul K. Maciejewski

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New Center Pointing the Way to Improvements in End-of-Life Care (continued from page 3)

Dr. Prigerson plans to continue this research in PGD at Weill Cornell. “We have a commitment for pooling data from thousands of PGD assessments administered all over the world by independent investigators who have used our scale,” she notes. “We want to look at causes of death, cultural variations, and kinship relationships as they relate to grief severity.”

Dr. Prigerson’s work has also included an NCI- and NIMH-funded multi-site prospective cohort study of advanced cancer patients and their family caregivers who survive them (the Coping with Cancer study). The Coping with Cancer study has generated a program of research that has included the examination of ethnic disparities in and mediators of end-of-life care. And she and Dr. Maciejewski serve as principal investigators for the NCI-funded R01 grant – *Black-White Differences in Advanced Cancer Communication, Acceptance, and Care* – awarded in April 2014.

“There is a huge disparity in black, white, and Latinos in the intensity of care at the end of life,” says Dr. Prigerson. “Our studies are showing that particular religious beliefs are explaining a significant amount of the inequalities in care. For example, we find black patients tend to use religion to cope with cancer more than their white counterparts. Black patients are more likely than white patients to believe in miracles and that it is their duty to stay alive as long as possible until the miracle occurs – a disincentive to agreeing to a Do Not Resuscitate order. We have NCI-funded studies that will enable us to identify particular beliefs such as these that we can target for interventions to reduce disparities in end-of-life care.”

Additional research projects focus on:

- comparative effectiveness of palliative treatments (e.g., palliative chemotherapy) to determine when these interventions do and don’t benefit patients
- addressing ways to improve terminally ill patients’ and family caregivers’ prognostic understanding and knowledge of the intent and likely outcomes of treatments
- improving clinical communication and medical decision-making to promote superior care of patients and their family members
- development and testing of online self-management tools to reduce bereavement-related distress, and tailor these tools to diverse bereaved populations
- testing interventions to reduce the cardiovascular risks posed by bereavement, and more specifically Prolonged Grief Disorder

At the Center for Research on End of Life Care, Drs. Prigerson and Maciejewski plan to continue to focus on issues of end-of-life care primarily affecting cancer patients. “There’s still quite a lot to be done,” says Dr. Prigerson. “It’s been very rewarding to see the impact our research has had on the field, and results translated into ways to improve care, reduce disparities in care, and improve the health and well-being of bereaved family survivors. We are enormously grateful for the support of this work and believe that Cornell has created an environment that will enable us to accomplish research that aims to substantially improve care of patients and families who confront serious illness.”

For More Information

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