Preclinical Alzheimer’s: Study Examines Consequences of Documenting Biomarker Test Results

Tests for biomarkers that can identify preclinical Alzheimer’s disease (AD) are raising hopes for earlier treatments but also concerns about consequences associated with test results, according to Jalayne J. Arias, JD, MA, Associate Director of Cleveland Clinic’s NeuroEthics Program. She is principal investigator of a three-year study exploring the legal and ethical consequences of AD biomarker testing in asymptomatic individuals.

“Initially, we wondered what the consequences would be if a research study tested participants for amyloid biomarker status and if that information were disclosed. Then we expanded our view to consider what the consequences would be if biomarker testing began in the clinical setting and was documented in patients’ medical records,” says Ms. Arias.

Her study, supported by a Mentored New Investigator Research Grant to Promote Diversity from the Alzheimer’s Association, focuses on potential employment and insurance discrimination.

The potential: clinical use of biomarkers

In 2011, the National Institute on Aging and Alzheimer’s Association’s clinical diagnosis update recognized three stages of AD: preclinical, mild cognitive impairment and dementia due to AD.

The guidelines also noted two biomarker categories: amyloid beta (Aβ) accumulation (via amyloid PET imaging or low cerebrospinal fluid Aβ42) and neurodegeneration or injury (such as elevated CSF tau and specific PET patterns).

These biomarkers are being used in research into preclinical AD, and “one may assume they will inevitably be approved for clinical use,” says Ms. Arias.

Limited protection with existing laws

In 2014, Ms. Arias and Jason Karlawish, MD, Professor of Medicine, Medical Ethics & Health Policy at the University of Pennsylvania, published a paper in Neurology outlining concerns that existing laws may not protect individuals from discrimination based on biomarker testing in Alzheimer’s research.

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Dear Colleague,

Welcome to the 2015 issue of Bioethics Reflections. As bioethicists, we feel privileged to work at one of the nation’s leading academic medical centers, where the drive to provide quality, affordable and innovative care is fully matched by the mission to put Patients First. To support Cleveland Clinic in these endeavors, the Department of Bioethics provided consultations in over 500 cases last year, engaged in hundreds of educational initiatives and continued to pursue critical research.

In this issue of Reflections, you will read about two such research initiatives. Jalayne Arias, JD, MA, has received a generous three-year grant from the Alzheimer’s Association for her study, “Legal, Ethical & Social Analysis of Preclinical Biomarker Tests in Alzheimer’s Disease.” Susannah Rose, PhD, has received a substantial grant from The Greenwall Foundation for her study, “Physician Disclosures in the Real World of Conflicting Interests and Off-Label Prescribing.”

This issue also provides an opportunity for us to welcome Patricia Mayer, MD, new Director of Clinical Ethics for Cleveland Clinic Florida-Weston, and new bioethics fellows Johan Bester, MB, ChB, and Jessie DeWeese, JD. We also spotlight Transplant Ethics Fellow Jed Gross, JD, MPhil.

You’ll also find a roundup of Bioethics faculty accomplishments over the past year, and a profile of Tom Harter, JD, a former Cleveland Fellow in Advanced Bioethics who is now at Gundersen Health System in La Crosse, Wisconsin.

We hope you enjoy this issue of Bioethics Reflections. Stay well, and keep in touch!

Eric Kodish, MD  
F.J. O’Neill Professor and Chairman, Cleveland Clinic Bioethics Department  
Director, Center for Ethics, Humanities and Spiritual Care, Cleveland Clinic
Their concerns included the following:

- The Genetic Information Nondiscrimination Act (GINA), which prohibits insurers and employers from discriminating against individuals with an APOE e4 allele, does not extend to biomarker tests.

- Protections under the Americans with Disabilities Act (ADA) are unclear because case law has not tested whether preclinical Alzheimer’s (based on biomarker status) constitutes a “disability” under the ADA.

- The Patient Protection and Affordable Care Act prohibits health insurers from denying coverage based on pre-existing conditions but contains no protections related to disability or long-term care insurance.

Confidentiality protections are included in research protocols, such as assigning code numbers for anonymity, and by the federal Health Insurance Portability and Accountability Act (HIPAA).

“Yet even with these protections, there is potential risk that information could inadvertently be disclosed,” Ms. Arias says. An individual might tell a work colleague about biomarker status, and the employer might then learn this information. As a result of their paper, Ms. Arias and Dr. Karlawish identified a need for additional research exploring the potential consequences associated with preclinical biomarkers.

**Preclinical test’s impact on stakeholders explored**

A prior study Ms. Arias conducted during her Cleveland Clinic Fellowship in Advanced Bioethics with Paul J. Ford, PhD, Director of NeuroEthics; Alexander Rae-Grant, MD; and Jeffrey Cummings, MD, Director of Cleveland Clinic’s Lou Ruvo Center for Brain Health, informed her current research.

In the study, 17 family members of individuals diagnosed with mild cognitive impairment were interviewed about the perceived benefits and harms of preclinical biomarker testing. Potential benefits identified included the ability to prepare for future financial needs; potential harms included worry and anxiety about future health. An analysis of the family member interviews, “Stakeholders’ Perspectives on Preclinical Testing for Alzheimer’s Disease,” has been accepted for publication in the *Journal of Clinical Ethics*.

**Study aims to guide policy-making**

Ms. Arias’ three-year study is examining federal and state laws that affect how insurers and employers may use medical information to make decisions. She and her team are interviewing clinicians, human resource managers and insurance underwriters to explore physicians’ responsibilities when offering preclinical AD biomarker testing, including the potential for inadvertent disclosure. Their findings will be reported to the Alzheimer’s Association in 2017.

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**NEW STAFF**

We welcome Patricia Mayer, MD, MS

On Sept. 1, Patricia Mayer, MD, MS, became Director of Clinical Ethics at Cleveland Clinic Florida-Weston. Dr. Mayer earned her medical degree from the University of Arizona and completed a fellowship in rheumatology. She practiced rheumatology in northern Colorado, where she also served as a palliative care consultant and as Medical Director for Hospice of Northern Colorado. Dr. Mayer is board-certified in internal medicine, rheumatology, and hospice and palliative medicine. She recently completed a two-year Fellowship in Advanced Bioethics at Cleveland Clinic. Her areas of interest include end-of-life issues, moral distress in caregivers and psychiatric ethics.
Do financial relationships between medical institutions and industry automatically represent a wrongful conflict of interest?

“Not necessarily,” says Susannah Rose, PhD, Director of Bioethics Research and Policy in the Department of Bioethics and a member of the Innovation Management and Conflicts of Interest Committee at Cleveland Clinic.

“Those relationships may in fact benefit patients, enhance medical research and help advance patient care,” she says. Yet these financial relationships are complex, she notes, and the nuances of different types of relationships among physicians, hospitals, researchers and for-profit industries must be closely evaluated and properly managed by hospitals and universities.

How industry relationships impact patient care

“The tension lies in weighing the potential benefits of connections with industry against the potential risk of harm to patients and to the research,” Dr. Rose says. “We want to make sure it’s not just money exchanged but that a true benefit may be realized.”

For example, to improve patient outcomes, the joint-replacement device industry must work with a joint replacement surgeon who knows how to improve a device. Unless the surgeon is involved in design and testing, the new device might never be created.

Conversely, some types of industry relationships may increase the risk of harm to patients, such as when physicians rely solely on industry for funding and information about drug products. Not only might the money unconsciously bias clinical decision-making, but the situation may also bias the information the physician receives about the drug’s risks and benefits.

How transparency affects patient trust

Preserving patient trust is central to patient care and to medical research, says Dr. Rose. She believes that institutions should be fully transparent about financial relationships, possibly even disclosing the amount of money involved and why it was provided. “However, we need more research on what type of information is necessary for transparency, and how, when and by whom it should be presented,” she says.

“Truth-telling is a critical component of developing patient-physician trust,” notes Dr. Rose. Research suggests that disclosure may indicate trust and has positive effects. However, transparency can create a false sense of trust that may lead patients to trust people who might not be trustworthy.
Susannah Rose, PhD, appointed Director of Bioethics Research and Policy in the Department of Bioethics on Oct. 1, 2014, focuses her research on conflict of interest in healthcare and patient decision-making at the end of life. She holds joint appointments in Cleveland Clinic’s Taussig Cancer Institute and Medicine Institute, and serves on the faculty in Cleveland Clinic Lerner College of Medicine at Case Western Reserve University (CWRU).

She also teaches health policy and health policy ethics at CWRU’s Weatherhead School of Management and at Harvard University’s School of Public Health.

Dr. Rose completed a master’s degree in social work from Columbia University in New York City, a master’s in bioethics at Union College/Albany Medical Center and a PhD through Harvard University’s Health Policy Program. She joined Cleveland Clinic in 2011.

“Several studies show that patients may falsely trust a professional who discloses a conflict but does not act in their best interest,” Dr. Rose says. Furthermore, such disclosure may merely shift responsibility to the patient, who may not know how to use the information in medical decision-making, she says.

Analyzing data nationwide

Dr. Rose is analyzing national disclosure data related to conflict of interest at academic medical centers across the country. “We really don’t know much about disclosure practices or their effects on clinical decision-making,” she notes.

Most academic medical centers have a conflict of interest management committee, but policies throughout the nation vary widely in levels of restrictiveness, permissions and transparency.

“The point of future research is to understand how disclosure of conflict of interest can help or hinder patient care,” she says. “We need to create institutional protections and management plans that protect the integrity of patient care and medical research.”

Congratulations to Our Staff

Ruth Farrell, MD, received a three-year grant from The Enhancing Life Project. It will combine conceptual and empirical analyses of factors and forces driving the development of prenatal genetic technologies.

Paul J. Ford, PhD, participated in two NIH Brain Research through Advancing Innovative Neurotechnologies workshops: “Industry Partnerships to Facilitate Early Access to Neuro-modulation and Recording Devices for Human Clinical Studies” in June and “Ethical Issues in Neuroscience Research” last November. In March, he took part in “Panel Discussion of Approaches to Evaluating Institutional Ethics Programs” at the Joint Centre for Bioethics in Toronto and was asked to speak on “Ethics and Invasive Brain Stimulation Programs: An Overview and Updates from Research on Patient Perspectives” at Institut de Recherches Cliniques de Montréal. Last August, Dr. Ford presented “Neuroscience Research — Clinical Innovation and Applications” to the Presidential Commission for the Study of Bioethical Issues.

Eric Kodish, MD, was invited to speak at the National Cancer Institute (NCI) Think Tank on Bioethics Research on July 14. The meeting was co-organized by former Cleveland Clinic bioethics fellow E. Charlisse F. Caga-Anan, JD, MA, now Program Director in the Division of Cancer Control and Population Sciences at the National Cancer Institute.

Martin Kohn, PhD, received the Arts and Culture Lab Arts Fellowship sponsored by the Mandel Jewish Community Center of Cleveland, the Cleveland Jewish Arts & Culture Lab and the Cleveland Jewish Federation. The fellowship promotes the arts as a Jewish source of expression and inspiration for artists, culturalists and the broader community.

Susannah L. Rose, PhD, presented a peer-reviewed paper, “Patient Advocacy Groups: Their Roles in Health Policy and Research,” at the 2015 Academy of Health Annual Research Meeting in Minneapolis in June. That month she also presented her research, “Transparency, Trust, and Survival: Patient Advocacy Groups and Institutional Conflicts of Interest” at a national conference at Harvard’s Edmond J. Safra Center for Ethics in Cambridge, Massachusetts.

Kathryn Weise, MD, MA, was recognized for concluding her three terms on the American Academy of Pediatrics Committee on Bioethics at the organization’s May 28-29 meeting in Chicago.
Former Fellow Profile: Thomas D. Harter, PhD

During his first weeks as an undergraduate, Tom Harter, PhD, knew he would become a philosopher. “I figured I’d teach ethics at a university,” says Dr. Harter, who concentrated on ethics during his doctoral program at the University of Tennessee.

But a career in clinical bioethics? It wasn’t on the radar until a friend suggested he apply for the Cleveland Fellowship in Advanced Bioethics (CFAB).

Captivated by clinical bioethics

“Cleveland Clinic changed everything,” he says. “During the interview, I became even more captivated by bioethics. The most fascinating conversations I had enjoyed with colleagues in grad school were just like those that professionals in the Department of Bioethics had every day.”

Dr. Harter moved to Cleveland and began his fellowship in 2010. Two months later, “I had no interest in going back to academia,” he says.

Impacting lives at the bedside

Today, Dr. Harter is the Associate Clinical Ethicist for Gundersen Health System in La Crosse, Wisconsin. He and a co-worker provide nearly 100 consults per year. He also offers ethics education for residents and staff, and lectures at local universities. Research and administrative work, including co-chairing the system’s ethics committee and serving as alternate chair of the institutional review board, round out his responsibilities.

“I was drawn to bioethics by the theory and the riveting questions,” says Dr. Harter. “But it wasn’t until I began practicing at the bedside that I realized the joy of using ethics to help people — learning about their struggles and helping them find some kind of resolution. Many of my academic colleagues don’t realize the rich impact ethicists can immediately make on individual lives.”

Dr. Harter credits Cleveland Clinic with molding him into not only a clinical ethicist but also a worthy professional. “The Bioethics staff’s mentorship and friendship cannot be overstated,” he says.

Meet Our Transplant Ethics Fellow

Jed Gross, JD, MPhil, says that interviewing potential living organ donors was a highlight of the first year of his Fellowship in Transplant Ethics. “My interactions with patients and transplant professionals have affirmed that, with proper safeguards, living donation is an admirable thing,” he says. This year, he is exploring communication and perceptions of increased risks for cadaveric liver transplant among wait-listed patients.

“Working in a field where the appropriate use of medical technology can help patients regain capabilities and flourish is profoundly rewarding,” says Mr. Gross.

A Yale PhD candidate, he has been invited to join an NIH-funded working group to assess the best regulatory approach to microbiota transplantation.

Immersive Bioethics Training Offered

The Department of Bioethics’ Clinical Ethics Immersion Program (CLEIP) offers unique training in clinical ethics consultation through a skill-building curriculum and immersion experience. CLEIP capitalizes on the Bioethics faculty’s depth of expertise and collaborative relationships across Cleveland Clinic. Our faculty welcomed 12 participants into CLEIP 2015, beginning with a successful intensive weekend in March. CLEIP 2016 begins the weekend of April 1, 2016, and applications are due Dec. 15, 2015. Please direct any inquiries to Margot Eves, JD, MA, at evesm@ccf.org.

Connect with your Cleveland Fellowship in Advanced Bioethics colleagues. Contact Bioethics Alumni Network co-chairs Margot Eves or Courtenay Bruce at evesm@ccf.org or crbruce@bcm.edu.
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**Giving to Bioethics**

Many services in Cleveland Clinic’s Department of Bioethics are supported by the generous donations of individuals, groups and institutions. Those who recognize the importance of bioethics at Cleveland Clinic may wish to offer their financial support for these programs. If you would like to help or receive more information, please contact Barbara Goulden at 216.444.8720 or Amy Kubacki at 216.636.5024.

**e-Ethics Cleveland Clinic**

Cleveland Clinic bioethicists provide face-to-face remote ethics consults, as well as ethics training and assistance with policy development.

To learn more about e-Ethics Cleveland Clinic, contact Anne Lederman Flamm, JD, at 216.444.8720 or at flamma@ccf.org.

**Recognized for Exceptional Care**

In 2015, Cleveland Clinic was ranked one of the top five hospitals in America in the *U.S. News & World Report* Best Hospitals survey. Cleveland Clinic is ranked among the top 10 hospitals in 13 specialty areas and is the top hospital in heart care for the 21st consecutive year.

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**The Cleveland Clinic Way**

by Toby Cosgrove, MD, CEO and President of Cleveland Clinic

Great things happen when a medical center puts patients first. Visit clevelandclinic.org/ClevelandClinicWay for details or to order a copy.

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Bioethics Department Welcomes New Fellows

Johan Bester, MB, ChB, received his medical degree from the University of Stellenbosch in South Africa, where he earned a master's degree in philosophy. He is currently completing his doctorate in applied ethics with a specialization in bioethics. Dr. Bester most recently served as Clinical Assistant Professor in Family Medicine at the University of Calgary, where he was responsible for developing several bioethics workshops. His interests include research on the ethics of mandatory immunization.

Jessie DeWeese, JD, graduated from Loyola University Chicago School of Law and received a bachelor's degree in philosophy from Purdue University. She developed an interest in bioethics by participating in Yale University's Summer Bioethics Program, interning in Yale's Bioethics Department and pursuing a Certificate in Health Law at Loyola, where she is working on a master's in bioethics and health policy.

Ms. DeWeese was a poster presenter at the International Neuroethics Society Annual Meeting in November 2014. Her research projects include incidental findings in fMRI research and the use of memory-dampening drugs for PTSD, particularly in combat veterans.

Applying for Advanced Bioethics Fellowships

The Cleveland Fellowship in Advanced Bioethics (CFAB) is a two-year, full-time program designed to train the next generation of leaders in the field of bioethics. Applications will be considered from professionals with terminal postgraduate degrees in medicine, philosophy, nursing, social work, religious studies, law and other fields related to the practice of clinical and academic bioethics.

Applicants with strong potential for leadership in the field and who will most benefit from the rich clinical environment this program offers will receive priority. Completed applications must be received by Nov. 1, 2015. For more information about the CFAB and the application process, visit clevelandclinic.org/bioethics.