AGING IN THE 21ST CENTURY: USING NEUROSCIENCE TO ASSESS COMPETENCY IN GUARDIANSHIPS

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Whether to remove a person's decision-making authority in a guardianship proceeding is one of society's most weighty determinations. As much as we value individual autonomy, we will strip that autonomy when a person is deemed legally "incompetent." This competency determination has traditionally relied, almost exclusively, on clinical assessments of cognitive and functional abilities, based mainly on observed behavior. But developments in neuroscience—and particularly the advent of physiological biomarkers of Alzheimer's disease—require us to think about a broader approach to competency determinations. Coupled with behavioral data, information from diagnostic biomarkers can add significant value to the competency determination. This Article discusses the potential benefits and risks of use of this evidence in the competency determination, concluding that we need to anticipate its introduction into the equation, but with care to avoid overvaluing the evidence.

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INTRODUCTION

Our population is aging. By 2030, more than seventy-one million American adults will be older than sixty-five, accounting for about twenty percent of the United States population.[1] This development will bring a commensurate increase in the number of individuals who will be afflicted with Alzheimer's disease ("AD"), a form of dementia that affects memory and other cognitive function.[2] It is predicted that by 2030, about 7.7 million will have dementia due to AD and by 2050, over fourteen million will be afflicted.[3] Dealing with a large swath of an aging population suffering cognitive decline will affect society in countless ways.

One important area of impact is the fundamental societal decision whether to remove an individual's decision-making authority. As a liberal democratic society, we have a powerful commitment to

1. PATRICIA A. TABLOSKI, GERONTOLOGICAL NURSING REVIEW AND RESOURCE MANUAL 11 (Am. Nursing Credentialing Ctr. ed., 3d ed. 2012). *See also* Alzheimer's Ass'n, *2016 Alzheimer's Disease Facts and Figures*, 12 ALZHEIMER'S & DEMENTIA 459, 471 (2016), https://www.alzheimersanddementia.com/article/S1552-5260(16)00085-6/pdf [https://perma.cc/7MQV-2QVR].

2. *See* 18 AM. JUR. PROOF OF FACTS 3D 185 § 1, Westlaw (Sept. 2018 update) [hereinafter ALZHEIMER'S AND MULTI-INFARCT DEMENTIA]. Dementia includes separate syndromes of neurodegenerative disease. Howard S. Kirshner, *Determination of Mental Competency, a Neurological Perspective*, 13 CURRENT NEUROLOGY AND NEUROSCIENCE REPS., no. 356, 2013, at 1. The most recent version of the Diagnostic and Statistical Manual of Mental Disorders ("DSM-5") eliminated the term "dementia" and subsumed it within the category of "Neurocognitive Disorders." AM. PSYCHIATRIC ASS'N, DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS 591 (5th ed. 2013) [hereinafter DSM-5]. The DSM-5 distinguishes between mild neurocognitive disorder, in which cognitive deficits do not interfere with independence, and major neurocognitive disorder, in which the cognitive deficits are sufficient to interfere with independence. *Id.* Alzheimer's disease accounts for about eighty percent of these neurocognitive disorders. *See* ALZHEIMER'S ASSOCIATION *supra* note 1, at 461.

3. Liesi E. Hebert et al., *Alzheimer's Disease in the United States (2010-2050) Estimated Using the 2010 Census*, 80 NEUROLOGY 1778, 1780 (2013), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3719424/. A recent study suggests, however, that the incidence of Alzheimer's disease may be declining in the United States due to an increase in educational attainment. *See* Kenneth M. Langa et al., *A Comparison of the Prevalence of Dementia in the United States in 2000 and 2012*, 177 JAMA INTERNAL MED. 51, 51 (2017), https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2587084?redirect=true [https://perma.cc/DH54-L4L8]. Even beyond disease, normal aging is often associated with a number of cognitive declines that can potentially influence a range of functional abilities.

individual autonomy.[4] This commitment is not absolute, however, and sometimes the law removes an individual's decision-making authority through civil guardianship proceedings. Legal guardianship, in which decision making authority is transferred to another individual,[5] may be imposed at any age, but the vast majority of guardianships are imposed on individuals over the age of sixty.[6] This consequential decision to deprive an individual of his autonomy turns on the crucial question of when to deem an individual legally "incompetent."[7]

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4. *See* THE DECLARATION OF INDEPENDENCE para. 2 (U.S. 1776) ("We hold these truths to be self-evident, that all Men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty, and the Pursuit of Happiness."). As the Supreme Court stated: "Before the turn of the century, this Court observed that '[n]o right is held more sacred, or is more carefully guarded, by the common law, than the right of every individual to the possession and control of his own person, free from all restraint or interference of others, unless by clear and unquestionable authority of law.'" *Cruzan v. Dir., Mo. Dep't of Health*, 497 U.S. 261, 269 (1990) (quoting *Union Pac. R. Co. v. Botsford*, 141 U.S. 250, 251 (1891)).

5. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(B) (2018); DEL. CODE ANN. tit. 12, § 3921 (2018); KAN. STAT. ANN. § 59-3075 (2018).

6. *See* ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 1. Most of these individuals show signs of what is commonly known as dementia. *Id. See also* Scott Y. H. Kim, Jason H. T. Karlawish & Eric D. Caine, *Current State of Research on Decision-making Competence of Cognitively Impaired Elderly Persons*, 10 AM. J. GERIATRIC PSYCHIATRY 151, 159 (2002) (stating that in comparative studies persons with dementia or cognitive impairment were more likely to be incompetent than elderly normal individuals without these diagnoses or impairment). We have seen a marked rise in contested guardianships, as older Americans as a group have amassed a considerable amount of wealth, while families are increasing blended and live farther apart from each other. These factors have given rise to increased family conflicts over a parent's health care management and financial dispositions. *See* Jennifer Moye, Daniel C. Marson & Barry Edelstein, *Assessment of Capacity in an Aging Society*, 68 AM. PSYCHOLOGIST 158, 163 (2013). Guardianship is frequently used in this context to place an elderly person involuntarily in a residential treatment facility, like a nursing home. *See* Jennifer L. Wright, *Protecting Who From What, and Why, and How?: A Proposal for an Integrative Approach to Adult Protective Proceedings*, 12 ELDER L.J. 53, 68 (2004).

7. A word on vocabulary. Technically, capacity is a medical term and competency a legal determination. Courts use these terms interchangeably in the sense of decision-making ability, however, and this Article will do this same, but will distinguish between "legal capacity" and "clinical capacity." AM. BAR ASS'N COMM'N ON LAW & AGING & AM. PSYCHOL. ASS'N, ASSESSMENT OF OLDER ADULTS WITH DIMINISHED CAPACITY: A HANDBOOK FOR LAWYERS 7 (2005) [hereinafter HANDBOOK FOR LAWYERS]; ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 1, at 191 (explaining that the concept of "incompetency" has "fallen into disfavor" and is now generally referred to as "incapacity"). Some states distinguish between "guardian," referring to a surrogate decision maker for health care and personal lifestyle, and "conservator," referring to a surrogate decision maker for finances and property. *See* James H. Pietsch, *Becoming a "Dementia-Capable" Attorney–Representing Individuals*

A legal finding of incompetency involves a value-driven judgment as to whether an individual has the minimal ability to care for oneself or one's property.[8] In making this judgment, the law strikes a balance between two core ethical principles, autonomy and protection.[9] Our conceptions of competency have evolved—and we have struck the balance differently—over time. Where we strike this balance reflects our social values, moral judgments, and legal principles. At the same time, assessing the competency of those in cognitive decline is a murky, complicated, and fast-changing area.

In making that assessment, the legal system relies heavily on expert clinical opinions regarding capacity.[10] Because an individual's competency can change over time,[11] experts play a particularly important role in predicting a person's future cognitive and functional abilities. While these opinions help the law make better decisions, they ultimately are just opinions—opinions about which competing experts may differ.[12]

Advances in neuroscience have the potential to assist in these clinical judgments and inform the legal finding of incompetency. They promise a more precise and sensitive method of assessing disease diagnosis and prognosis. In particular, scientists are discovering biological markers of AD, which identify early states of the disease,

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with Dementia, 19 HAW. B.J. 1, 27 & n.168 (2015). *See also* ARIZ. REV. STAT. ANN. § 14-5312(A); KY. REV. STAT. ANN. § 387.510(1), (3) (West 2018).

8. *See* Charles P. Sabatino & Suzanna L. Basinger, *Competency: Reforming Our Legal Fictions*, 6 J. MENTAL HEALTH & AGING 119, 119 (2000) (stating that "incapacity determinations for all but the clearest cases will depend on a malleable weighing process" including medical, social and practical variables). Determinations of incapacity pervade law. Courts have used separate, situation-specific standards for particular activities or transactions, such as capacity to marry, enter into a contract, vote, consent to treatment, or stand trial in a criminal proceeding. *See* HANDBOOK FOR LAWYERS, *supra* note 7, at 5; Laura J. Whipple, *Navigating Mental Capacity Assessment*, 29 TEMP. J. SCI. TECH. & ENVTL. L. 369, 373 (2010). Findings of incapacity in these specific contexts can nullify or prevent an act. HANDBOOK FOR LAWYERS, *supra* note 7, at 5. In contrast, guardianship proceedings traditionally cover general determinations of the ability to care for oneself or one's property, based on the status of the person. *See* Sabatino & Basinger, *supra*, at 121. Guardianship determinations are shaped by statute and not common law tests. *Id.*

9. *See* Paul S. Appelbaum & Thomas Grisso, *Assessing Patients' Capacities to Consent to Treatment*, 319 NEW ENG. J. MED. 1635, 1637 (1988); Wright, *supra* note 6, at 77.

10. *See* R. Ryan Darby & Bradford C. Dickerson, *Dementia, Decision Making and Capacity*, 25 HARV. REV. OF PSYCHIATRY 270, 272 (2017); Sabatino & Basinger, *supra* note 8, at 133.

11. Kirshner, *supra* note 2, at 2.

12. *See* Wright, *supra* note 6, at 83 ("our current legal procedures appear prone to error in the determination of incapacity, which is the sole basis on which deprivation of autonomy can be justified"); *infra* notes 116–130 and accompanying text.

even before observable outward behavioral changes occur. These biomarkers are proxies for neuropathological changes occurring in the brain.[13] Inevitably, these markers will be used in clinical practice.[14] And when they are, they will likely transform our diagnostic classification approach from one based mostly on clinical symptomology and neuro-psychological assessment tools to one that is based heavily on neurobiological metrics.[15] They will change our view of the disease as occurring in discrete stages to one of a process moving along a continuum, with outward clinical symptoms manifesting relatively late in the disease process.[16] These discoveries have profound implications for medicine, public policy, and law. But they will come with a set of risks. Biomarkers will offer objective, empirical data to assist in the competency assessment. But use of biomarkers will not avoid an error. They provide mathematical probabilities of the onset and progression of the disease—not absolute certainty. And they will never replace direct measures of cognitive performance in competency determinations.

We need to grapple now with how to use these measures in decisions about legal intervention. In particular, we need to examine whether the potential tension between performance-based assessment and use of neurobiological metrics can be reconciled. Should a brain state, independent of observable behavioral changes, even be considered in competency assessment, or should biomarker evidence only be incorporated into a traditional clinical diagnosis, after behavioral symptoms manifest, or used for a prognosis determination? Since changes to brain states as documented by biomarkers represent a continuum, rather than distinct stages, what weight should biomarker evidence be given? And how do we protect against the dangers of bias

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13. *See* Clifford R. Jack, Jr., et al., *NIA-AA Research Framework: Toward a Biological Definition of Alzheimer's Disease*, 14 ALZHEIMER'S & DEMENTIA 535, 537 (2018).

14. Paul S. Aisen et al., *On the Path to 2025: Understanding the Alzheimer's Disease Continuum*, 9 ALZHEIMER'S RESEARCH & THERAPY, no. 60, 2017, at 1. In fact, neuroimaging is already part of diagnostic and routine medical care with regard to certain dementias. Darby, *supra* note 10, at 274.

15. *See* Aisen et al., *supra* note 14, at 60; Jack et al., *supra* note 13, at 538 (calling for a research framework that defines AD by biomarkers and treats cognitive impairment as a symptom of the disease).

16. Aisen et al., *supra* note 14, at 60. Aisen states:

> Defining AD purely by its clinical presentation is artificial and efforts have been made to recognize the disease based on both clinical and biomarker findings . . . [which will lead to an] appreciation that AD should not [only] be viewed with discrete and defined clinical stages, but as a multifaceted process moving along a [seamless] continuum.

Id.

and over-diagnosis? This Article explores how these advances inevitably will and should affect the legal and clinical aspects of competency assessment in guardianship determinations.[17]

Part I briefly traces the evolution of our conceptions of competency in law from an initial focus on property management, to the use of vague status labels of mental illness, to the current emphasis on the value of self-determination. The prevailing approach strikes the balance in favor of the individual's autonomy interest, with appropriate due process protections, against the state interest in protection of the individual. Part II outlines typical guardianship proceedings. Although these proceedings vary by state, they exhibit several commonalities in procedure, principles, and goals. Nearly all state statutes list general, categorical factors for consideration. Most states require performance-based assessments, carried out by clinicians, and some states include medical diagnoses as a factor. The statutory standards are largely broad and vague, allowing room for more subjective decisions on whether an individual lacks competency to the degree that requires a guardian. Overall, the goal in guardianship determinations is to allow as much autonomy as possible under the individual circumstances, using current conceptions of competency.

Part III highlights some of the key neuroscience advances in discovering biomarkers of AD. Discovery of these markers represents a dramatic medical advance, potentially enabling us to better predict advancement from earlier to later states of AD, treat, and monitor progression of the disease. But use of these biomarkers has drawbacks. They may manifest in individuals who never actually develop clinical symptoms of AD.[18] Because of that risk, they will likely be used in conjunction with other diagnostics measures rather than as a stand-alone tool.

Part IV explores the potential impact of these biomarker discoveries on societal conceptions of competency and guardianship proceedings. What significance should courts attach to documentation of these brain changes in assessing competency? This Part concludes that we should anticipate the advent of biomarker diagnostics as an important tool in augmenting the civil competency assessment in older adults with cognitive impairment but we need to proceed with caution. Biomarkers will become an important screening tool. They will

17. Although this Article focuses on guardianship proceedings, a host of other legal issues arise with the advent of AD biomarkers. These scientific advances may affect questions of capacity in contract, tort and criminal law defenses, and discrimination in employment and insurance. *See* Joshua Preston et al., *The Legal Implications of Detecting Alzheimer's Disease Earlier*, 18 AMA J. ETHICS 1207, 1208, 1212–14 (2016).

18. *See* Jack et al., *supra* note 13, at 538.

reinforce the accuracy of the clinical diagnosis and prognosis of a patient with AD. When the biomarkers and traditional cognitive and behavioral measures disagree, that disagreement will alert decision makers to take a close and careful look at the individual. Although legal decision makers may consequently place more emphasis on AD diagnoses as the accuracy of biomarkers improves, we need to bear in mind that a medical condition should not by itself be conclusive of the competency judgment. And because experience suggests that we tend to overvalue objective measures, biomarker advances will both improve *and* complicate our judgments about capacity, autonomy, and independence. Science certainly should inform the law, but the legal decision to impose guardianship also entails a value judgment that cannot be reduced to a scientific formula. The stakes are too high to ignore the latest scientific advances – or their inevitable limitations.

I. CHANGING CONCEPTIONS OF CAPACITY

Capacity generally is described as "a threshold requirement for persons to retain the power to make decisions for themselves."[19] Fundamentally, the concept of capacity reflects our legal, social, and moral view of human agency.[20] This view assumes that mature adults are rational actors, with a significant level of self-determination and autonomy in their lives.[21] The goal of competency determinations in guardianship proceedings is to allow individuals as much autonomy as possible, only interfering when cognitive and behavioral incapacity puts them at too great a risk of harm to themselves or their property.[22] At that level of incapacity, society permits courts to weigh the well-being of the individual over the individual's rights of self-determination in deciding that intervention is necessary.[23] The State's interest is commonly discussed as the state's power of *parens patriae*, which is

19. PAUL APPELBAUM & THOMAS GUTHEIL, CLINICAL HANDBOOK OF PSYCHIATRY AND THE LAW 218 (Michael F. Fisher ed., 1991).

20. *See* ROBERT F. SCHOPP, COMPETENCE, CONDEMNATION, AND COMMITMENT: AN INTEGRATED THEORY OF MENTAL HEALTH LAW 64, 66 (2001); Jennifer A. Drobac & Oliver R. Goodenough, *Exposing the Myth of Consent*, 12 IND. HEALTH L. REV. 471, 474 (2015); Sabatino & Basinger, *supra* note 8, at 119. Capacity determinations occur in many aspects of law, including competence to stand trial, to rights of silence and legal counsel, to parent, and to consent to medical treatment. Drobac & Goodenough, *supra*, at 474–75.

21. Drobac & Goodenough, *supra* note 20, at 476, 502.

22. *See* Raphael J. Leo, *Competency and the Capacity to Make Treatment Decisions: A Primer for Primary Care Physicians*, 1 PRIMARY CARE COMPANION J. CLINICAL PSYCHIATRY 131, 131 (1999).

23. *See* THOMAS GRISSO, EVALUATING COMPETENCIES 15 (Ronald Roesch ed., 2d ed. 2003); Wright, *supra* note 6, at 55.

the obligation of the State to protect its more vulnerable and less fortunate citizens.[24] Because competency determinations are made by the State, they are subject to constitutional safeguards. Due process demands that the State protect against erroneous deprivation of individual autonomy and self-determination interests.[25]

The law's conceptions of competency are operationalized through state statutory definitions. These have evolved, and the earliest state civil law guardianship statutes did not reflect our current view of competency.[26] Influenced by English law, states originally passed guardianship statutes that were focused on the protection of property and not on the rights or even care of the elderly—goals that were not introduced until later.[27] These early statutes used vague status tests, allowing a finding of incompetency when an individual was given an amorphous label such as idiot, lunatic, insane, or "of unsound mind."[28] The statutory tests "were very global, generalized determinations of one's ability to manage property and personal affairs,"[29] and gave judges enormous discretion over the finding of incompetency.[30]

By the middle of the 20th century states began to place greater reliance on disabling conditions.[31] Statutes required courts to find a disabling condition from lists of specified conditions, such as "mental illness," "mental disability," "advanced age," and "or other cause,"[32] but continued to give courts broad discretion in determining competency.[33] Many states began to add a second causal prong, requiring a finding that the condition caused a dysfunction in behavior.[34] Although requiring a causally connected dysfunctional behavior finding theoretically curtailed the discretion in the legal determination,[35] the behavioral standards, such as "incapable of taking

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24. *See* Sabatino & Basinger, *supra* note 8, at 120–21.

25. *See Mathews v. Eldridge*, 424 U.S. 319, 333–35 (1976) (describing three-factor due process analysis in weighing the government's interest against the individual liberty or property interest involved); Susan G. Haines & John J. Campbell, *Defects, Due Process, and Protective Proceedings*, 2 MARQ. ELDER'S ADVISOR 13, 13–15 (2000).

26. *See* Moye et al., *supra* note 6, at 161.

27. *See* Sabatino & Basinger, *supra* note 8, at 122.

28. *Id.*

29. *Id.* at 121. This is in contrast to adjudication standards developed for specific transactions, such as competency to execute a contract or will, marry, or stand trials for criminal prosecution. *Id.*

30. *See* Moye et al., *supra* note 6, at 163.

31. *See* Sabatino & Basinger, *supra* note 8, at 123.

32. *Id.*

33. *Id.*

34. *Id.*

35. *See id.* at 123–24.

care of himself," or "unable to provide for personal needs and/or property management," were still notoriously amorphous and subjective.[36]

A paradigm shift emerged in the 1980s, when approaches to competency began to emphasize specific functional abilities.[37] This view drew on the work of Dr. Thomas Grisso, a clinical and forensic psychologist whose writings deeply influenced conceptions of capacity.[38] In his seminal book, *Evaluating Competencies*, Grisso provided a conceptual model with six analytical characteristics for legal competency assessments, with functionality as the first characteristic.[39] He argued that a person's functional ability to carry out specific tasks is the most fundamental indication of capacity.[40] In Grisso's view, an expert in a competency proceeding should link a diagnosis of mental disorder (which Grisso referred to as the "causal factor") to the abilities and capacities in question.[41] He argued that a psychiatric diagnosis, without more, does not necessarily establish incapacity—we cannot assume that a particular mental disorder renders an individual incapable of specific intellectual, behavioral, and social functions.[42]

The Grisso model of capacity is reflected in an early version of a model guardianship statute, the Uniform Guardianship and Protective Proceedings Act (UGPPA).[43] The 1982 version of the UGPPA defined an incapacitated person as someone who was impaired "by reasons of mental illness, mental deficiency, physical illness or disability, chronic use of drugs, [or] chronic intoxication, . . . to the extent of lacking sufficient understanding or capacity to make or communicate responsible decisions."[44]

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36. *Id.* at 124. In addition, the distinction between medical incapacity and legal incapacity became increasingly blurred by the 1960s. *Id.* at 123. *See* GRISSO, *supra* note 23, at 317.

37. *See* Moye et al., *supra* note 6, at 163.

38. *See* GRISSO, *supra* note 23, at x–xi, 21–23.

39. *Id.* at 23. The original six characteristics Grisso proposed as common to all legal capacity assessments were: (1) functional; (2) contextual; (3) causal; (4) interactive; (5) judgmental; and (6) dispositional; but these were reduced to five in the second edition by combining the contextual and functional components. *Id.*

40. *Id.* at 25. *See* Moye et al., *supra* note 6, at 163 ("The preeminence of function in capacity is arguably the core contribution of [the Grisso] theoretical model and one that has deeply influenced a generation of subsequent capacity researchers . . . .").

41. *See* GRISSO, *supra* note 23, at 13.

42. *Id.* at 25.

43. UNIF. GUARDIANSHIP PROTECTIVE PROCEEDINGS ACT § 1-201(7) (NAT'L CONF. ON COMM'RS 1982).

44. *Id.*

Three public policy trends emerged to reinforce the Grisso model of specific, functional capacity: informed consent and the patients' rights movement; the push for deinstitutionalization of mentally ill patients; and the disability rights movement.[45] Although they developed in different contexts, these three trends brought attention to the rights of individuals with regard to autonomous decision making.

The first trend, the patients' rights movement and the doctrine of informed consent, shifted the legal and social focus from a physician-oriented view to a patient-oriented view. It emphasized individual autonomy and choice, putting the individual's right to self-determination at the forefront.[46] In moving away from the more paternalistic model of physician control, the common law now views choosing among treatment alternatives as a shared responsibility of physicians and patients.[47] The "right to choose" figures prominently in our conceptions of capacity, which weighs self-determination rights heavily in the balance against the need for surrogate decision making.

The second public policy trend began in the 1960s when community groups started advocating for integration of individuals with psychiatric illnesses into the community rather than keeping them in institutions.[48] Psychiatric treatment policy started emphasizing non-institutional and less restrictive treatment for mentally ill patients.[49] The movement led to enactment of The Community Mental Health Act of 1963, which provided federal funding for community mental health centers in the United States.[50] This Act gave rise to significant deinstitutionalization[51] and laid the foundation for assessing capacity in distinct areas such as managing finances and living in the community.[52]

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45. *See* Moye et al., *supra* note 6, at 161–62.

46. *See, e.g.*, DAN DOBBS ET AL., HORNBOOK ON TORTS § 21.9 (2d 2016). Thus, courts have recognized that the patient's right to self-determination includes the right to receive certain information about a medical procedure, including its risks, its necessity and available alternatives. *Id.*

47. *See Matthies v. Mastromonaco*, 733 A.2d 456, 463 (N.J. 1999) ("Physicians may neither impose their values on their patients nor substitute their level of risk aversion for that of their patients. . . . The choice is not for the physician, but the patient in consultation with the physician.").

48. Moye et al., *supra* note 6, at 162.

49. *Id.*

50. Community Mental Health Act of 1963, Pub. L. No. 88-164, 77 Stat. 282 (1963). *See also Community Mental Health Act*, MENTAL HEALTH FIRST AID NATIONAL COUNCIL FOR BEHAVIORAL HEALTH (2015), https://www.thenationalcouncil.org/about/national-mental-health-association/overview/community-mental-health-act/ [https://perma.cc/SWF9-77EU].

51. MENTAL HEALTH FIRST AID NATIONAL COUNCIL FOR BEHAVIORAL HEALTH, *supra* note 50.

52. *See* Moye et al., *supra* note 6, at 162.

The third influential public policy movement is the disability rights movement. The Americans with Disabilities Act of 1990,[53] which afforded significant protections for those with not just physical but also mental disabilities, represented a shift in policy from social welfare and perceived paternalism to recognition of individual rights.[54] With its emphasis on accommodation, the law reflected the view that people with disabilities were equal citizens entitled to participate in all areas of society.[55] This view influenced conceptions of capacity as well, turning the focus to the individual's preserved abilities rather than loss of ability.[56]

Following these trends, statutory definitions of capacity for guardianship purposes have shifted toward standards that focus on an individual's particular situation and capabilities, and emphasize rights to self-determination and autonomy.[57] States supplemented or replaced the two-pronged disabling condition and causation test with behavioral and functioning tests,[58] seeking to make the determinations less status driven and more tailored to individual needs.[59] The 1997 revision to the UGPPA, for example, removed the disabling condition language completely, replacing it with a cognitive functioning test: "'Incapacitated person' means an individual who . . . is unable to receive and evaluate information or make or communicate decisions to such an extent that the individual lacks the ability to meet essential requirements for physical health, safety, or self-care, even with appropriate technological assistance."[60]

Dr. Grisso supported this approach. As he noted in the second edition of his seminal work:

> The intent [of capacity assessment] is to require evidence of specific and significant functional incapacities that will:

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53. 42 U.S.C. §§ 12101–213 (2000).

54. *See* Samuel Bagenstos, *The Future of Disability Law*, 114 YALE L.J. 1, 3 (2004).

55. *Id.*

56. *See* Moye et al., *supra* note 6, at 162.

57. *See* ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 6.

58. HANDBOOK FOR LAWYERS, *supra* note 7, at 7. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D)(3) (2018); KAN. STAT. ANN. § 59-3064(b)(3) (2018); N.Y. MENTAL HYG. LAW § 81.09(c)(5)(vii) (McKinney 2018).

59. HANDBOOK FOR LAWYERS, *supra* note 7, at 7.

60. UNIFORM GUARDIANSHIP AND PROTECTIVE PROCEEDINGS ACT § 102(5) (UNIF. LAW COMM'N 1997), http://www.uniformlaws.org/shared/docs/guardianship%20and%20protective%20proceedings/UGPPA_2011_Final%20Act_2014sep9.pdf [https://perma.cc/Y4YE-GJMJ].

- protect individuals from guardianships based on the presence of a mental disorder alone
- install guardians and invoke the potentially sweeping loss of rights only when functional consequences are extreme
- require evaluations that provide the courts specific functional data to create limited rather than plenary guardianships.[61]

Current guardianship statutes incorporate this philosophy.[62] Accordingly, they have shifted focus from definitions based mostly on status and diagnosis to those based on function.[63] Generally they emphasize competency determinations based on observation evidence of the individual's ability to function in particular contexts, and seek to fashion limited guardianship tailored to specific deficits, rather than general guardianships.[64] The state statutes take a "mix-and-match" approach in their substantive standards, however, combining different tests in a variety of ways.[65] Some common approaches in these statutes, as well as the general framework of guardianship proceedings, are described below.

II. GUARDIANSHIP PROCEEDINGS

A guardianship occurs when a court entrusts a guardian with the custody and control of another person or his property, or both, because the court deems the person to be incompetent.[66] Although there have been several attempts to create national uniformity, we have never achieved a national consensus on the standard to declare an individual

61. GRISSO, *supra* note 23, at 316–17.

62. *See* Jalayne J. Arias, *A Time to Step In: Legal Mechanisms for Protecting Those with Declining Capacity*, 39 AM. J.L. & MED. 134, 136, 140, 149 (2013) (describing trend shifting focus of capacity evaluations from clinical diagnoses to functional and cognitive abilities).

63. *Id.*

64. *See* ARIZ. REV. STAT. ANN. § 14-5303(D)(3) (2018); KAN. STAT. ANN. § 59-3064(b)(3) (West 2018); N.Y. MENTAL HYG. LAW §§ 81.09(c)(5)(vii), 81.31 (McKinney 2018); ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 6. The ABA Commission on Aging & APA follows this model as well, emphasizing assessment of both cognitive and functional abilities. *See* HANDBOOK FOR LAWYERS, *supra* note 7, at 10; Moye et al., *supra* note 6, at 166.

65. *See* HANDBOOK FOR LAWYERS, *supra* note 7, at 7; Sabatino & Basinger, *supra* note 8, at 128–29.

66. ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 5.

incompetent. The UGPPA[67] lays out the standards and procedures for the appointment of a guardian for incapacitated individuals, but only about five states have adopted the model statute; another twenty states have adopted selected portions of the Act.[68] The American Bar Association and the American Psychological Association have collaborated on a series of capacity assessment handbooks for attorneys, judges, and psychologists.[69] These handbooks have not been especially influential, as states have not adopted the proposed definitions and procedures.[70] As a result, considerable variation remains in state definitions of and procedures for assessing capacity and the need for guardianship.[71]

Still, state guardianship proceedings display some commonalities, both procedurally and substantively. Usually, the person who seeks the guardianship ("the petitioner") is someone who has an interest in the allegedly incapacitated person's well-being, typically a family member, although incapacitated persons can initiate the proceedings themselves.[72] Once the petitioner has made the appropriate showing,[73] the court, usually a judge presiding in probate court, begins the proceedings. To

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67. UNIF. GUARDIANSHIP AND PROTECTIVE PROCEEDINGS ACT § 102(5) cmt. (UNIF. LAW COMM'N 1997), http://www.uniformlaws.org/shared/docs/guardianship%20and%20protective%20proceedings/UGPPA_2011_Final%20Act_2014sep9.pdf [https://perma.cc/Y4YE-GJMJ].

68. *Guardianship, Conservatorship, and Other Protective Arrangements Act*, UNIFORM L. COMMISSION, http://www.uniformlaws.org/Committee.aspx?title=Guardianship,%20Conservatorship,%20and%20Other%20Protective%20Arrangements%20Act [https://perma.cc/V5H9-G6Z9].

69. *See, e.g.*, HANDBOOK FOR LAWYERS, *supra* note 7; AM. BAR ASS'N COMM'N ON LAW & AGING & AM. PSYCHOL. ASS'N, ASSESSMENT OF OLDER ADULTS WITH DIMINISHED CAPACITY: A HANDBOOK FOR PSYCHOLOGISTS (2008), http://www.apa.org/pi/aging/programs/assessment/capacity-psychologist-handbook.pdf [hereinafter HANDBOOK FOR PSYCHOLOGISTS]; AM. BAR ASS'N COMM'N ON LAW & AGING, AM. PSYCHOL. ASS'N & NAT'L COLL. OF PROB. JUDGES, JUDICIAL DETERMINATION OF CAPACITY OF OLDER ADULTS IN GUARDIANSHIP PROCEEDINGS (2006), http://www.apa.org/pi/aging/resources/guides/judges-diminished.pdf [https://perma.cc/AB3G-64BB].

70. *See* Arias, *supra* note 62, at 150.

71. *See, e.g.*, SALLY BARCH HURME, AM. BAR ASS'N COMM'N ON LAW AND AGING, CAPACITY DEFINITION & INITIATION OF GUARDIANSHIP PROCEEDINGS STATUTORY REVISIONS (AS OF AUGUST 7, 2018) (2018), https://www.americanbar.org/content/dam/aba/administrative/law_aging/chartcapacityandinitiation.authcheckdam.pdf [https://perma.cc/PZA9-GV3J] (providing fifty-state survey of capacity definition and guardianship proceedings).

72. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(A) (2018); KY. REV. STAT. ANN. § 387.530 (West 2018); N.Y. MENTAL HYG. LAW § 81.06 (McKinney 2018).

73. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5304 ; KAN. STAT. ANN. § 59-3067 (West 2018); N.Y. MENTAL HYG. LAW § 81.15.

protect the due process rights of the allegedly incapacitated person ("the respondent"), the court appoints an attorney and, in some states, a guardian ad litem.[74] The court also initiates an investigation to gauge the extent of the alleged incapacity, generally through an expert.[75] The court then conducts an evidentiary hearing, which is usually before the court, but may be before a jury.[76] The court determines whether the respondent is incompetent, based on whether the evidence meets the statutory standard.[77] Once the individual is deemed incompetent, the court appoints a guardian and issues an order describing the duration and scope of the guardian's duties.[78] The appointed guardian may have the authority to make all decisions regarding the personal care and finances of the respondent, or may be granted only limited guardianship in certain areas.[79] The court holds the guardian accountable through monitoring and reporting procedures for the duration of the guardianship.[80]

States differ in their approaches to these proceedings, but several overarching principles emerge in their standards that draw directly from the capacity concepts discussed above. First, guardianship law starts with the presumption that adults have full legal capacity in decision-making, and it is up to the petitioner to show otherwise.[81] Moreover, the paramount goal is to provide the least restrictive version of the guardianship, which means that a guardian can be appointed for a particular, limited purpose, as opposed to a general guardianship, in which all legal rights are transferred from the incapacitated person to

74. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(C); KAN. STAT. ANN. § 59-3063; N.Y. MENTAL HYG. LAW §§ 81.09–10.

75. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D); KAN. STAT. ANN. § 59-3064; N.Y. MENTAL HYGIENE LAW § 81.09.

76. *See* ARIZ. REV. STAT. ANN. § 14-5303(C); KAN. STAT. ANN. § 59-3067; KY. REV. STAT. ANN. § 387.580. Many states have statutes that confer upon the alleged incapacitated person a right to a jury trial. *See* HURME, *supra* note 71.

77. *See* ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 7.

78. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5304 (2018); KAN. STAT. ANN. § 59-3067(e) (2018); N.Y. MENTAL HYGIENE LAW § 81.15 (McKinney 2018).

79. At least half the states have created a limited guardianship option. *See* Whipple, *supra* note 8, at 393. *See also* ELEANOR CROSBY LAINER, AM. BAR ASS'N COMM'N ON LAW AND AGING, LIMITED GUARDIANSHIP OF THE PERSON AND PROPERTY (2017), http://www.americanbar.org/content/dam/aba/administrative/law_aging/chartlimitedguardianshipofthepresonandproperty.authcheckdam.pdf [https://perma.cc/QX8X-GFF6] (providing fifty-state survey of limited guardianship statutes).

80. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5315; KAN. STAT. ANN. § 59-3076; N.Y. MENTAL HYG. LAW § 81.31.

81. Whipple, *supra* note 8, at 376; *see* ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 6 (explaining that burden is on the petitioner for guardianship to present clear and convincing evidence of the need for guardianship).

the guardian.[82] Additionally, courts look for alternatives less restrictive than guardianship, such as powers of attorney, representation agreements, advance directives for health care, trust arrangements, and joint financial accounts.[83] The use of less restrictive alternatives is designed to maximize independence and self-reliance.[84]

The common objective among the states is to move away from broad, indefinite standards toward ones that allow a determination that will reflect the individual's specific needs.[85] The emphasis is on functionality.[86] The goal is to demand sufficient proof that an individual is incapable of managing his personal care or property. In addition to the functioning tests mentioned above,[87] many states incorporate two other factors to determine if an individual is incapacitated: necessity (a test balancing "interactive" factors like the risk of harm, the resources available to the individual, and the person's values and preferences); and any conditions, including diagnoses of illness, which could contribute to the need for a guardian.[88] States typically use a combination of these factors to make a determination of incompetency,[89] looking at the person as a whole.[90] Some states incorporate specific requirements, such as an analysis of the tasks the person is capable of performing,[91] an evaluation of the person's

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82. *See, e.g.*, N.Y. MENTAL HYG. LAW § 81.31 (stating legislative purpose that the least restrictive means of guardianship should be used). This is also evidenced by the high number of states that have enacted limited guardianship statutes. *See* Lainer, *supra* note 79.

83. *See* Pietsch, *supra* note 7, at 28; Wright, *supra* note 6, at 92.

84. *See generally* Lanier, *supra* note 79.

85. *See* HANDBOOK FOR LAWYERS, *supra* note 7, at 7; *supra* Part I.

86. *See* Arias, *supra* note 62, at 150.

87. *See* UNIFORM GUARDIANSHIP AND PROTECTIVE PROCEEDINGS ACT § 102(5) (UNIF. LAW COMM'N 1997), http://www.uniformlaws.org/shared/docs/guardianship%20and%20protective%20proceedings/UGPPA_2011_Final%20Act_2014sep9.pdf [https://perma.cc/Y4YE-GJMJ]; *supra* notes 62–64 and accompanying text.

88. *See* HANDBOOK FOR LAWYERS, *supra* note 7, at 7. The risk assessment seeks to balance the potential risks with the potential benefits of allowing an individual to maintain capacity for purposes of lifestyle, legal, medical or financial decision making. *See* Arias, *supra* note 62, at 140–41.

89. A fifty state survey of statutory definitions of incapacity showed that forty-three statutes contain the "functionality" test, thirty-six statutes contain the "necessity" test, and thirty-three statutes contain the "disabling condition" test. *See* HURME, *supra* note 71.

90. *See id.*

91. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D)(3) (2018); KAN. STAT. ANN. § 59-3064(b)(3) (2018); N.Y. MENTAL HYG. LAW § 81.09(c)(5)(vii) (McKinney 2018).

intellectual, physical, and social skills,[92] and a description of how disability or impairments (including disease diagnosis) affect the person,[93] but most states do not provide specific guidance on "functionality."[94] Generally, statutory standards are broad and do not give clarification on the level or breadth of impairment required to meet the determination of incompetency.[95] Instead, the standards allow for discretion, aiming to create a legal standard of incompetence that identifies functional incapacities "that exceed an unacceptable risk or harm threshold."[96]

Of all these factors, performance assessment is the paramount focus in competency evaluation.[97] This assessment seeks information about an individual's specific abilities to carry out the activity in question.[98] Thus, even if a person has a dementing illness, the emphasis is on a measurement of the person's abilities and preserved function rather than on the deficits associated with dementia.[99] If the statutory test incorporates a conditions factor, including a medical diagnosis such as AD, that factor is considered relevant but not dispositive to the determination of capacity.[100] Many states that incorporate a conditions factor also require a showing of a causal relationship between a diagnosed medical or psychological condition and specific deficits.[101]

In evaluating these factors, most states require an expert clinical opinion on capacity,[102] usually in the form of a written clinical

92. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D)(2); KAN. STAT. ANN. § 59-3064(b)(3); N.Y. MENTAL HYG. LAW § 81.09(c)(5)(vii).

93. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D)(1); KAN. STAT. ANN. § 59-3064(b)(2); N.Y. MENTAL HYG. LAW § 81.09(c)(5)(vii).

94. *See* Arias, *supra* note 62, at 150.

95. *Id.*

96. *See* GRISSO, *supra* note 23, at 316.

97. Functionality encompasses both performance of everyday tasks as well as cognitive abilities, such as planning, memory and judgment. *Id.* at 322. Some examples of these tasks that are tested are identifying and counting currency, grocery shopping, checking the mail, dressing, and eating. HANDBOOK FOR PSYCHOLOGISTS, *supra* note 69, at 159. *See also* Wright, *supra* note 6, at 68, 91 (explaining that focus in guardianship proceedings is on functional assessment in determining capacity).

98. *See* GRISSO, *supra* note 23, at 321–322; HANDBOOK FOR PSYCHOLOGISTS, *supra* note 69, at 25.

99. *See* GRISSO, *supra* note 23, at 316; Wright, *supra* note 6, at 91–92 & n.185 (explaining the crucial issue is whether the individual can function to meet the demands of his environment: "[t]he functional evaluator is less interested . . . in the cause of disability, the prognosis, or the potential for treatment.").

100. *See* ALZHEIMER'S AND MULTI-INFARCT DEMENTIA, *supra* note 2, § 7.

101. GRISSO, *supra* note 23, at 325.

102. HANDBOOK FOR PSYCHOLOGISTS, *supra* note 69, at 28 ("[T]he fulcrum of a capacity assessment is the clinical judgment."). *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D)(1) (2018); KAN. STAT. ANN. § 59-3064(b)(2) (West 2018).

evaluation.[103] Previously, psychologists would reach a conclusion about an individual's capacity after clinical interviews and general mental status evaluations,[104] but this methodology was criticized as overly subjective and unreliable.[105] In response, researchers developed standardized functional assessment instruments and neuropsychological tests to improve the validity (increased accuracy) and reliability (increased consistency) of results.[106] Neuropsychological tests are designed to measure psychological functions including cognitive deficiencies.[107] Functional assessment tests are designed to evaluate tasks associated with living independently.[108] A clinical evaluation will integrate test results with "interactive factors," which provide context of the individual's personal situation and lifestyle.[109] These standardized psychological tests and assessment instruments provide valuable information for capacity determinations and help "identify cognitive deficits relevant to a specific context and the degree of the deficits."[110] The tools have improved the reliability and validity of capacity judgments as compared to those made without such standardized tests.[111]

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103. ARIZ. REV. STAT. ANN. § 14-5303(D)(1); KAN. STAT. ANN. § 59-3064(b)(2).

104. HANDBOOK FOR PSYCHOLOGISTS, *supra* note 69, at 11.

105. *Id. See also* GRISSO, *supra* note 23, at 317.

106. *See* GRISSO, *supra* note 23, at 326–27.

107. *See* Lyn M. Gaudet et al., *Can Neuroscience Help Predict Future Antisocial Behavior?*, 85 FORDHAM L. REV. 503, 508 (2016); Philip D. Harvey, *Clinical Applications of Neuropsychological Assessment*, 14 DIALOGUES CLINICAL NEUROSCIENCE 91, 91 (2012). Clinicians typically use standardized tests such as the Mini-Mental State Exam (MMSE) and the Montreal Cognitive Assessment (MoCA), among others, to assess cognitive abilities. *See* Arias, *supra* note 62, at 138–39 (2013); Olivier Godefroy et al., *Is the Montreal Cognitive Assessment Superior to the Mini-Mental State Examination to Detect Poststroke Cognitive Impairment?: A Study with Neuropsychological Evaluation*, 42 STROKE 1712, 1712 (2011); Beau M. Ances, *Alzheimer Disease Diagnosis Using Biomarkers*, The American Academy of Neurology Institute (2017) (on file with author).

108. *See* Arias, *supra* note 62, at 139 (explaining that functional abilities are classified according to instrumental activities of daily living (IADLs), which are higher-functioning tasks such as managing a budget, and activities of daily living (ADLs), such as bathing and toileting).

109. HANDBOOK FOR LAWYERS, *supra* note 7, at 11. Examples of assessment tests for everyday living or financial decision making include the Assessment of Capacity for Everyday Decisionmaking and the Semi-Structured Clinical Interview for Financial Capacity (SFIC). Arias, *supra* note 62, at 146. *See generally* James M. Lai et al., *Everyday Decision-Making in Older Persons with Cognitive Impairment*, 16 AM. J. GERIATRIC PSYCHIATRY 693 (2008).

110. Arias, *supra* note 62, at 139.

111. *See* HANDBOOK FOR PSYCHOLOGISTS, *supra* note 69, at 12; *See* Kim et al., *supra* note 6, at 153 (reviewing literature on studies of decision making capacity of persons with dementia and finding varying and inconsistent definitions of and

Neuropsychological tests have high rates of accuracy. For example, one study found that the FR-FCSRT test[112] was the neuropsychological test "most strongly associated with incident AD," which was consistent with other studies that demonstrated the test's high validity in distinguishing dementia, especially AD, from other cognitive pathologies.[113] Another study found that an algorithm using the CERAD-NAB test,[114] in conjunction with a recollection and a verbal comprehension neuropsychological test, had an eighty-two percent accuracy in distinguishing AD patients from patients with other pathologies.[115]

Even with their strengths, both the functional assessment test and neuropsychological tests have limitations in the context of capacity determinations and neurodegenerative diseases like AD.[116] Functional assessment instruments may reach inconsistent results;[117] these tests are typically based on inventories (usually involving the ability to carry out activities of daily living) compiled by the individual and their families, which involve subjective judgments that may be subject to errors and biases in reporting.[118]

Despite their high rates of accuracy, neuropsychological tests have limitations in capacity determinations as well. Capacity determinations

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measurements of "capacity" and "competency"); Wright, *supra* note 6, at 80–81; Konstantine K. Zakzanis & Eliyas Jeffay, *Neurocognitive Variability in High-Functioning Individuals: Implications for the Practice of Clinical Neuropsychology*, 108 PSYCHOL. REP. 290, 290–92 (2011).

112. Free and Cued Selective Reminding Test. *See* Laura A. Rabin et al., *Predicting Alzheimer's Disease: Neuropsychological Tests, Self-Reports, and Informant Reports of Cognitive Difficulties*, 60 J. AM. GERIATRICS SOC'Y 1128, 1129 (2012).

113. *Id.* at 1132. As this study notes, other neuropsychological tests do not have a similar accuracy in distinguishing AD from other pathologies. *Id.* at 1132–33.

114. Consortium to Establish a Registry for Alzheimer's Disease—Neuropsychological Assessment Battery. *See* Pavel Gurevich et al., *Neuropsychological Testing and Machine Learning Distinguish Alzheimer's Disease from Other Causes of Cognitive Impairment*, 9 FRONTIERS AGING NEUROSCIENCE 1, 1 (2017).

115. *Id.* Patients in the early stage of disease were distinguished with 89 percent accuracy. *Id.* at 5. *But see* Aaron R. Ritter et al., *Neuropsychological Testing in Pathologically Verified Alzheimer Disease and Frontotemporal Dementia: How Well Do the Uniform Data Set Measures Differ Between Diseases?*, 31 ALZHEIMER DISEASE & ASSOCIATED DISORDERS 187, 187–89 (2017) (finding that neuropsychological tests were unable to accurately distinguish AD from FTLD patients, despite the "great interest in defining phenotypic signatures" for FTLD "in the absence of biomarkers").

116. *See* Arias, *supra* note 62, at 139–40.

117. Philip D. Harvey et al., *Performance-based and Observational Assessments in Clinical Trials Across the Alzheimer's Disease Spectrum*, 14 INNOVATIONS CLINICAL NEUROSCIENCE 30, 30–31 (2017).

118. *Id.*; *see* Ances, *supra* note 107 ("Capturing the history . . . of progressive cognitive and functional loss can be time-consuming and sometimes is inexact.").

are based on the individual's capabilities at the time of the examination,[119] and elders may display better decision-making skills at certain times than others.[120] Even experienced clinicians can be inaccurate in the clinical diagnostic process.[121] Primary care physicians may fail to recognize dementia in more than fifty percent of affected patients.[122] Among clinicians, there is a "widespread disagreement regarding the independent and joint contribution of . . . various assessment domains and the optimal strategy for measurement of each domain."[123] Furthermore, although clinicians and other professionals have developed numerous instruments to conduct capacity evaluations, they "have not yet reached a general consensus on a single set of tools to implement universally" in determining capacity.[124] And even with the increase in reliability and validity of measurements, individual competency determinations can be inconsistent for a number of reasons.[125] Studies demonstrate that clinicians provide inadequate reports for competency determinations by focusing on the wrong factors, applying the wrong tests, or providing incomplete information.[126] Clinicians may not receive sufficient training in conducting capacity evaluations.[127] The discrepancies may be due to a clinician's focus on different cognitive and decisional abilities or even holding different values from those of the patient or other clinicians.[128]

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119. *See* Arias, *supra* note 62, at 139.

120. *See id.* (explaining that individuals may experience good days and bad days and moments of lucidity); Drobac & Goodenough, *supra* note 20, at 485–86 (describing "sundowning" condition in elders).

121. *See* T.G. Beach, et al., *Accuracy of the Clinical Diagnosis of Alzheimer Disease at National Institute on Aging Alzheimer Disease Centers, 2005–2010*, 71 J. NEUROPATHOLOGY & EXPERIMENTAL NEUROLOGY 266, 266 (2012).

122. *See* Soo Borson et al., *Improving Identification of Cognitive Impairment in Primary Care*, 21 INT'L. J. GERIATRIC PSYCHIATRY 349, 349 (2006).

123. Laura A. Rabin et al., *Predicting Alzheimer's Disease: Neuropsychological Tests, Self-Reports, and Informant Reports of Cognitive Difficulties*, 60 J. AM. GERIATRIC SOC'Y 1128, 1128 (2012).

124. Arias, *supra* note 62, at 142–43, 145–46.

125. *See* Moye et al., *supra* note 6, at 165.

126. *See* Laura Gibson, *Giving Courts the Information Necessary to Implement Limited Guardianships: Are We There Yet?*, 54 GERONTOLOGICAL SOC. WORK 803, 806 (2011).

127. Wright, *supra* note 6, at 80–81 (describing study of guardianship proceedings in three states indicating clinical inconsistencies and lack of adequate clinical basis for competency determinations).

128. *See* Moye et al., *supra* note 6, at 165. Personal values, age discrimination, background and experience of the clinician can influence capacity judgments. HANDBOOK FOR PSYCHOLOGISTS, *supra* note 69, at 12. Potential measurement errors include limitations in hearing, vision, or processing speed, fear of examination, as well as susceptibility to fatigue. GRISSO, *supra* note 23, at 326–27.

Clinical interviews may vary in quality.[129] Moreover, both the neuropsychological tests and functional assessment tests were designed to detect changes in patients with the last stage of AD (dementia), and may not be sensitive enough to identify the more subtle impairment associated with earlier stages of AD or sufficiently assess progression over time to later stages.[130]

Developments in neuroscience hold promise to supplement and enhance the accuracy of neuropsychological and assessment test results, particularly with regard to diagnosing early stages of AD, and thereby assist in capacity measurements and assessment. They also hold promise for achieving more exact prognoses. The next section turns to some of these developments.

III. DISCOVERY OF BIOMARKERS OF EFFECT AND SUSCEPTIBILITY TO ALZHEIMER'S DISEASE

Alzheimer's disease is a progressive, severe neurodegenerative disorder of the brain characterized by cognitive decline and loss of memory.[131] Currently, diagnosis of AD depends on medical clinical assessment and neuropsychological testing, with definitive verification through autopsy.[132] Scientists are searching for reliable surrogate physiological markers of AD.[133] These biomarkers, which are discrete and quantifiable biological parameters that can serve as an indicator of health and disease, can help diagnose and monitor the progression of the disease.[134] In this way, they can offer a more accurate diagnosis in the living brain.[135] Although these biomarkers are mostly at the research stage, a sea change is occurring in the research framework to

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129. *See* Moye et al., *supra* note 6, at 166.

130. Harvey et al., *supra* note 117, at 31, 34; *see* Ances, *supra* note 107 (finding that dementia screening tools provide a "snapshot" of an individual's cognitive status at a point in time and do not assess individual decline; may be subject to false positives and false negative findings).

131. Christian Humpel, *Identifying and Validating Biomarkers for Alzheimer's Disease*, 29 TRENDS BIOTECHNOLOGY 26, 26 (2011).

132. *Id.*

133. *Id.*; *see Earlier Diagnosis*, ALZHEIMER'S ASS'N, http://www.alz.org/research/science/earlier_alzheimers_diagnosis.asp#Brain [https://perma.cc/WJ79-S8D5] [hereinafter *Earlier Diagnosis*].

134. Kaj Blennow et al., *Fluid Biomarkers in Alzheimer's Disease*, COLD SPRING HARBOR PERSP. MED., Sept. 2012, at 1, 2 ("Biomarkers are objective measures of a biological or pathogenic process that can be used to evaluate disease risk or prognosis, to guide clinical diagnosis, or to monitor therapeutic interventions."); Humpel, *supra* note 131, at 26; *Earlier Diagnosis*, *supra* note 133.

135. Rebecca Craig-Schapiro et al., *Biomarkers of Alzheimer's Disease*, 35 NEUROBIOLOGY DISEASE 128, 129 (2009).

implement a biological definition of AD, based on neuropathological verification through biomarkers, independent from clinical symptoms.[136] These advances have the potential to significantly affect the capacity assessments at the heart of the guardianship proceedings. To demonstrate this, I review the clinical stages of AD, and then highlight some of the scientific advances in discovering biomarkers in bodily fluid, structural and functional brain changes, and genes.

A. Clinical Stages of Alzheimer's Disease

AD has three recognized clinical stages,[137] reflecting a spectrum of symptom severity: (1) Preclinical AD ("PCAD"); (2) Mild Cognitive Impairment (MCI) due to AD; and (3) Dementia due to AD or "clinical AD."[138] In individuals with Preclinical AD, changes to the brain occur, often years or decades before outward symptoms of cognitive impairment are detectable,[139] or they may manifest subtle cognitive impairments that do not meet the diagnostic criteria for MCI or AD.[140] In the second stage of AD (MCI due to AD), individuals exhibit cognitive impairment that is pronounced enough to be observable to the individual (or close friends and family) but not so pronounced as to

136. *See* Jack et al., *supra* note 13, at 536, 538. Given the huge strides that have been made in AD biomarker research, the National Institute on Aging and the Alzheimer's Association (NIAA-AA) have called for a biological, rather than a syndrome-based definition of AD. *Id*. at 538. The NIAA-AA recognized that biomarkers now exist that are proxies for AD neuropathological changes and should be used to define AD in living persons. They cautioned, however, that this recommendation should be used for research purposes and is not yet intended for general clinical practice. *Id.* at 537. They envision eventual reliance on diagnoses based on pathological processes, as we currently approach other medical conditions such as diabetes, bone density, and hypertension. *Id.* at 537–38.

137. A shift is occurring in the research framework—although not yet in the medical domain—viewing the disease as a continuum rather than three distinct clinical phases. *Id.* at 537, 545.

138. Reisa A. Sperling et al., *Toward Defining the Preclinical Stages of Alzheimer's Disease: Recommendations from the National Institute on Aging–Alzheimer's Association Workgroups on Diagnostic Guidelines for Alzheimer's Disease*, 7 ALZHEIMER'S & DEMENTIA 280, 281 (2011).

139. *Id.*

140. Sperling et al., *supra* note 138, at 281. Preclinical AD breaks down into subsets. The National Institute on Aging-Alzheimer's Association (NIA-AA) proposed three stages of Preclinical AD: (1) amyloid pathology present only; (2) amyloid pathology and presence of signs of neuronal injury; and (3) amyloid and neuronal injury pathologies plus subtle cognitive decline (SCD). Luka Kulic & Paul G. Unschuld, *Recent Advances in Cerebrospinal Fluid Biomarkers for the Detection of Preclinical Alzheimer's Disease*, 29 CURRENT OPINION NEUROLOGY 749, 750 (2016).

interfere with independent daily functioning.[141] Studies suggest that MCI individuals are three times more likely than healthy controls to develop AD over a 4.5 year period.[142] The final stage (Clinical AD), is diagnosed when there are cognitive or behavioral symptoms that reflect impairment of various abilities, including the ability to function at work or other usual activities, the ability to acquire and remember new information, impairment of language functions, and changes in personality or behavior.[143] Scientists are searching for biomarkers of all three of these stages.[144]

As noted, a diagnosis of AD only can be verified accurately in autopsy.[145] The brains of post-mortem AD patients are characterized by the presence of: (1) amyloid plaques;[146] (2) neurofibrillary tangles (NFTs);[147] and (3) neurodegeneration.[148] Scientists are eager to

141. Marilyn S. Albert et al., *The Diagnosis of Mild Cognitive Impairment due to Alzheimer's Disease: Recommendations from the National Institute on Aging–Alzheimer's Association Workgroups on Diagnostic Guidelines for Alzheimer's Disease*, 7 ALZHEIMER'S & DEMENTIA 270, 271 (2011).

142. *See* Christoffer Rosén et al., *Fluid Biomarkers in Alzheimer's Disease—Current Concepts*, MOLECULAR NEURODEGENERATION, June 2013, at 1, 4.

143. This diagnosis is inherently a clinical judgment based on the individual circumstances of the patient and information from knowledgeable informants, and may include neuropsychological testing. Guy M. McKhann, et al., *The Diagnosis of Dementia Due to Alzheimer's Disease: Recommendations from the National Institute on Aging-Alzheimer's Association Workgroup on Diagnostic Guidelines for Alzheimer's Disease*, 7 ALZHEIMER'S & DEMENTIA 263, 265 (2011). Prodromal AD is considered the first phase of clinical AD. *See* William G. Britt III et al., *Mild Cognitive Impairment: Prodromal Alzheimer's Disease or Something Else?*, 27 J. ALZHEIMER'S DISEASE 543, 543, 548; Rosén et al., *supra* note 142, at 3. There are multiple interpretations of "prodromal AD" in the clinical field; for purposes of this paper, "prodromal AD" will be defined as the first stage of AD following progression from MCI to AD.

144. *See* Howard Chertkow et al., *Definitions of Dementia and Predementia States in Alzheimer's Disease and Vascular Cognitive Impairment: Consensus from the Canadian Conference on Diagnosis of Dementia*, 5 ALZHEIMER'S RESEARCH & THERAPY, no. S2, 2013, at 1.

145. Humpel, *supra* note 131, at 26.

146. These are aggregated amyloid-beta (Aβ) peptides that form insoluble deposits in the brain. Shannon L. Risacher & Andrew J. Saykin, *Neuroimaging and Other Biomarkers for Alzheimer's Disease: The Changing Landscape of Early Detection*, 9 ANN. REV. CLINICAL PSYCHOL. 621, 623 (2013). Amyloid biomarkers are widely viewed as the earliest detectable evidence of AD. *See* Jack et al., *supra* note 13, at 539.

147. These are insoluble helical filament structures formed from the hyper-phosphorylation of microtubule-associated tau. Risacher & Saykin, *supra* note 145, at 623.

148. *See* Jack et al., *supra* note 13, at 536, 538; Katharina S. Goerlich et al., *Neuroanatomical and Neuropsychological Markers of Amnestic MCI: A Three-Year Longitudinal Study in Individuals Unaware of Cognitive Decline*, FRONTIERS AGING NEUROSCIENCE, Feb. 22, 2017, at 1, 2; Risacher & Saykin, *supra* note 146, at 623.

determine whether these post-mortem characteristics can be detected in the living brain and at the different stages of AD. The research generally targets bodily fluid (like cerebral spinal fluid and blood), structural and functional brain changes, and genes.[149] An ideal biomarker for AD will provide an accurate and early diagnosis of AD, distinguish AD from other dementias and pathologies, indicate disease severity, demonstrate reproducible results over time, and exhibit clear cut-off values (used to define positive and negative diagnoses), while being inexpensive, non-invasive, and easy to use.[150] "Biomarkers ideally could move the diagnosis of AD from the current syndromic 'black box' to an etiological diagnosis based on molecular pathology."[151] The discussion below highlights some of the research in this area.[152]

B. Fluid Biomarkers

Cerebrospinal fluid (CSF) is an optimal source of biomarkers for AD since it comes in close contact with the brain.[153] The most studied CSF biomarkers for identifying AD are levels of Aβ42 (a protein found in amyloid plaques), levels of total tau (t-tau) (a protein specific to the brain), and levels of phosphorylated-tau (p-tau) (a tau protein associated with neurofibrillary tangles).[154]

Aβ42 is the main protein component of amyloid plaques, and researchers widely believe that aggregation of the protein into amyloid deposits is associated with decreased Aβ42 levels in the cerebral spinal fluid.[155] Scientists think this decrease in Aβ42 levels is one of the

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The third category, neurodegeneration, appears to be less specific to AD and can also occur in other dementia conditions. *See* Jack et al., *supra* note 13, at 539.

149. *See generally* Harald Hampel et al., *Development of Biomarkers to Chart All Alzheimer's Disease Stages: The Royal Road to Cutting the Therapeutic Gordian Knot*, 8 ALZHEIMER'S & DEMENTIA 312, 317–23 (2012).

150. Humpel, *supra* note 131, at 26; Mario Riverol & Oscar L. López, *Biomarkers in Alzheimer's Disease*, FRONTIERS NEUROLOGY, July 14, 2011, at 1, 1; Neeti Sharma & Anshika Nikita Singh, *Exploring Biomarkers for Alzheimer's Disease*, 10 J. CLINICAL & DIAGNOSTIC RES., July 2016, at 1, 1–2.

151. *See* Ances, *supra* note 107.

152. For an overview of the research in this area, see Jack et al., *supra* note 13, at 538-544.

153. Blennow et al., *supra* note 134, at 2.

154. *Id.* at 2–3.

155. *Id.* at 2. AD patients exhibit significantly lower CSF Aβ42 levels, approximately fifty percent of healthy control levels in the CSF. *Id.* at 3.

earliest detectable signs of AD, even detectable as early as early middle age (45–54 years).[156]

Another area of research focuses on tau, which is a protein specific to the brain.[157] T-tau measures the total amount of the tau protein in the brain, and scientists believe that certain levels can indicate neuronal injury or degeneration.[158] AD patients have significantly higher CSF t-tau levels than in cognitively normal individuals, and higher levels are also associated with a faster rate of cognitive decline.[159] T-tau is thought to be a marker for predicting the likelihood of progression from MCI to AD.[160] P-tau levels reflect the total amount of phosphorylated tau, a type of tau that is associated with the formation of neurofibrillary tangles in AD patients.[161] P-tau in the CSF has been shown to distinguish AD from other dementias—such as Frontotemporal Dementia, Lewy Body Dementia, and Vascular Dementia—and from major depression.[162] Many other CSF biomarkers are also being studied to improve the accuracy of AD diagnoses and to distinguish AD from other neuropathologies.[163]

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156. In one study, decreased Aβ levels were found in the CSF even before a PET scan could detect plaque deposits. Kulic & Unschuld, *supra* note 140, at 751.

157. Humpel, *supra* note 131, at 28.

158. Blennow et al., *supra* note 134, at 2. In patients with temporary cognitive conditions such as traumatic brain injury (TBI) and stroke, t-tau levels are increased and correlate with amount of damaged neural tissue. *Id.* In chronic conditions, CSF t-tau levels are highest in conditions that experience the most rapid cognitive decline, such as Creutzfeldt-Jakob Disease (CJD). *Id.* In AD patients, CSF t-tau levels are correlated with post-mortem tangle load, suggesting that tau levels increase as the protein is released into the CSF by tangle-bearing neurons. *Id.* at 3.

159. *Id.* at 2–4. AD patients had CSF t-tau levels 300 percent higher than controls. *Id.* at 4. *See* Harald Hampel et al., *Total and Phosphorylated Tau Protein as Biological Markers of Alzheimer's Disease*, 45 EXPERIMENTAL GERONTOLOGY 30, 34 (2010) (showing that p-tau231 declined longitudinally with individual disease progression from mild to moderate AD).

160. Humpel, *supra* note 131, at 27. As opposed to patients that remain in the MCI stage (stable MCI), 90 percent of MCI patients that progressed to AD exhibited high CSF t-tau levels. *Id.* Furthermore, higher CSF levels of t-tau and p-tau 181 are associated with a faster rate of progression from MCI to AD. Blennow et al., *Fluid Biomarkers*, *supra* note 134, at 2–3. One study found that individuals that converted from MCI to AD within five years had significantly higher t-tau and p-tau levels than individuals that converted within five to ten years, even though both groups had similar Aβ42 levels. Rosén et al., *supra* note 142, at 4.

161. Rosén et al., *supra* note 142, at 2.

162. Humpel, *supra* note 131, at 27. P-tau differentiated AD patients from LBD and FTD with approximately ninety-two percent sensitivity and sixty-four percent specificity. Rosén et al., *supra* note 142, at 5. However, one study of AD, VaD, LBD, and Parkinson's Dementia patients noted that an AD biomarker profile was present in many non-AD patients. *Id.*

163. Blennow et al., *supra* note 134, at 7, 10 (VILIP-1, a calcium sensor protein that is associated with neuronal death may be useful in predicting individual

Although an optimal source for biomarkers, CSF has many disadvantages. The lumbar puncture required to acquire CSF is highly invasive and can result in individual side effects.[164] Many CSF biomarkers for AD can overlap with other pathologies, such as traumatic brain injury.[165] Also, CSF Aβ42 levels can vary between individuals and over time within one individual.[166] Using a panel of biomarkers rather than just one could mitigate some of these problems.[167]

C. Blood Plasma

Approximately 500 mL (about 18 ounces) of CSF normally is absorbed into the blood every day, and movement of proteins from the brain to the blood is increased when there is damage to the blood-brain barrier, a symptom found in AD.[168] Blood plasma is a desirable source of biomarkers for AD because the procedure to acquire it is less invasive, can be used more frequently, and with fewer adverse effects, than the lumbar puncture needed to acquire CSF.[169] Despite these

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progression from cognitively normal to mild dementia); Craig-Schapiro et al., *YKL-40: A Novel Prognostic Fluid Biomarker for Preclinical Alzheimer's Disease*, 68 BIOLOGICAL PSYCHIATRY 903, 909–11 (2010) [hereafter Craig-Schapiro et al., *YKL-40*] (stating that YKL-40, a protein associated with inflammation near amyloid plaques found to positively correlate with plaque and cortical burden in AD-relevant brain regions and CSF t-tau/p-tau levels in AD individuals); Geneviève Evin et al., *BACE: Therapeutic Target and Potential Biomarker for Alzheimer's Disease*, 42 INT'L J. BIOCHEMISTRY & CELL BIOLOGY 1923, 1923–25 (2010) (stating that BACE1, an enzyme that is highly expressed in the brain and generates Aβ, found to significantly increase in the CSF of MCI patients and has the potential to predict progression from MCI to AD); Kulic & Unschuld, *supra* note 140, at 753; Jin-Moo Lee et al., *The Brain Injury Biomarker VLP-1 Is Increased in the Cerebrospinal Fluid of Alzheimer Disease Patients*, 54 CLINICAL CHEMISTRY 1617, 1622 (2008).

164. Humpel, *supra* note 131, at 27.

165. Aβ pathology is seen in LBD and infectious CNS diseases such as acute bacterial meningitis. Kaj Blennow et al., *Amyloid Biomarkers in Alzheimer's Disease*, 36 TRENDS PHARMACOLOGICAL SCI. 297, 304 (2015) [hereinafter Blennow et al., *Amyloid Biomarkers*]. Aβ plaques are present in the brains of TBI patients. *Id.* Healthy controls experience an increase in t-tau with age, and t-tau levels are also significantly increased in CJD. Humpel, *supra* note 131, at 26–27.

166. Blennow et al., *supra* note 165, at 300. Some non-AD individuals are naturally low producers of Aβ42, which could result in a false positive diagnosis for AD. *Id.* Similarly, some AD individuals are naturally high producers of Aβ, which could result in a false negative. *Id.*

167. *But see* Kulic & Unschuld, *supra* note 140, at 750 (noting study that found a concordance of less than sixty percent between imaging and CSF measures in PCAD individuals).

168. A. Hye et al., *Proteome-Based Plasma Biomarkers for Alzheimer's Disease*, 129 BRAIN 3042, 3042–43 (2006).

169. Humpel, *supra* note 131, at 27–28.

advantages, developing blood plasma as a source for biomarkers has several challenges and drawbacks.[170]

Scientists have focused on Aβ42 as a marker in blood plasma, but they have not yet found a correlation between Aβ42 found in plasma and Aβ42 found in the CSF of AD patients,[171] or a correlation between Aβ42 levels in plasma and plaque build-up or "burden."[172] However, several longitudinal studies found significantly increased baseline plasma Aβ42 levels in cognitively normal individuals who later progressed to AD.[173] Other blood plasma biomarkers are being studied as well.[174]

D. Structural and Functional Neuroimaging Biomarkers

1. ANATOMICAL CHANGES

Brain atrophy, both in the whole brain and in specific regions, is a classic biomarker of AD.[175] By the time an individual warrants a

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170. There are lower concentrations of neuronal proteins in blood plasma than in CSF. Rosén et al., *supra* note 142, at 7. Brain-derived proteins are also diluted in plasma and are subject to degradation. *Id.* Moreover, Aβ is naturally elevated in plasma because the Aβ protein aids in platelet aggregation. Humpel, *supra* note 131, at 28. And Aβ levels in plasma are unstable and can vary due to factors such as medication, age, and lifestyle. *Id.*; Sharma & Singh, *supra* note 150, at 3. In addition, it is difficult to isolate the proteins being studied; the attempt to remove other proteins from the blood plasma samples that they are not studying may unintentionally remove proteins they are interested in. Hye et al., *supra* note 168, at 3047. Furthermore, abundant proteins that are targeted for removal may themselves be biomarkers. *Id.*

171. Humpel, *supra* note 131, at 28.

172. Craig-Schapiro et al., *supra* note 135, at 132. With regard to MCI, plasma Aβ42 levels were increased in female MCI patients when compared to healthy controls, but the same result was not found in male MCI patients. Humpel, *supra* note 131, at 27.

173. Craig-Schapiro et al., *supra* note 135, at 132. But one study found no association between plasma Aβ42 levels and AD progression after adjusting for individual factors such as age. *Id.*

174. One study found that Complement Factor H, a plasma protein present in plaques, was significantly increased in AD patients but not in those with other neurodegenerative disorders. Hye et al., *supra* note 168, at 3048. Levels of desmosterol (a molecule similar to cholesterol) and the desmosterol/cholesterol ratio in blood plasma may prove to be a biomarker as well. Yoshiaki Sato et al., *Identification of a New Plasma Biomarker of Alzheimer's Disease Using Metabolomics Technology*, 53 J. LIPID RES. 567, 575 (2012) (finding levels of desmosterol significantly decreased in MCI and AD patients). Another example of blood plasma biomarkers is Cystatin C (Cys C), which is associated with anti-inflammation and is found in all bodily fluids. Rui Wang et al., *Plasma Cystatin C and High-Density Lipoprotein Are Important Biomarkers of Alzheimer's Disease and Vascular Dementia: A Cross-Sectional Study*, FRONTIERS AGING NEUROSCIENCE, Feb. 7, 2017, at 1, 2.

175. Risacher & Saykin, *supra* note 146, at 622–23.

clinical AD diagnosis, widespread atrophy typically can be seen in the neocortex and subcortical regions, especially in the temporal, parietal, and frontal cortices.[176] In MCI individuals, whole-brain atrophy rates were found to predict the progression from MCI to AD.[177] Atrophy of specific brain regions, such as hippocampal atrophy,[178] grey matter atrophy,[179] and degeneration in the medial temporal lobe[180] also predicted progression. One study of AD patients found that hippocampal and whole-brain atrophy rates correlated with cognitive performance and disease severity.[181]

Measuring brain atrophy for biomarker purposes has limitations. Brain volume may naturally decrease with age and thus cannot easily distinguish AD patients from healthy controls.[182] Also, measuring atrophy rates and volumes of brain regions is labor intensive and is currently limited to research studies.[183] Finally, researchers have not agreed on standard brain volume values that could determine the significance of particular region shrinkage for an individual.[184]

Studying anatomical changes in the eye, especially in the retina, also holds promise.[185]

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176. *Id.* at 623. The occipital and sensory-motor regions of the brain are typically spared from neurodegeneration in AD patients. *Id.*

177. Riverol & López, *supra* note 150, at 4. Whole-brain atrophy rates in MCI individuals mirrored atrophy rates in AD individuals and, at 1 percent per year, are between AD (approximately 1.9–2.2 percent per year) and healthy control rates (approximately 0.5-0.7 percent). *Id.* However, another study found that the rate of atrophy in the hippocampus of HCs was approximately 1 percent per year compared to 4.5 percent per year in AD patients. Risacher & Saykin, *supra* note 146, at 627.

178. Risacher & Saykin, *supra* note 145, at 632 (finding hippocampal atrophy in MCI patients shown to predict progression from MCI to AD).

179. Goerlich et al., *supra* note 148, at 6 (finding grey matter atrophy in early MCI patients was present even before noticeable cognitive decline and correlated with impaired verbal memory).

180. *See* Risacher & Saykin, *supra* note 146, at 624 (finding degeneration in medial temporal lobe, associated with memory, linked to earliest clinical symptoms of AD in AD patients).

181. Riverol & López, *supra* note 150, at 4. Moreover, AD patients possessed smaller hippocampal volumes compared to healthy controls. *Id.*

182. *Id.*

183. *Id.*

184. *Earlier Diagnosis*, *supra* note 133.

185. Jeremiah K. H. Lim et al., *The Eye as a Biomarker for Alzheimer's Disease*, FRONTIERS AGING NEUROSCIENCE, Nov. 17, 2016, at 1, 1–4, 8 (finding that Retinal Nerve Fiber Layer decreases with thickness in AD patients; AD individuals showed significant narrowing of retinal veins and reduced blood flow to healthy controls, and a decrease in the velocity of eye movement, associated with memory function).

2. MAGNETIC RESONANCE IMAGING

Magnetic Resonance Imaging (MRI) can be used to detect the amount of blood flow to the brain (cerebral perfusion); perfusion is reduced in AD individuals.[186] Estimates of perfusion from MRI scans demonstrate significant brain atrophy in specific regions that reflect the distribution of neurofibrillary tangles.[187] This measure tracks disease severity as well.[188] Functional MRI (fMRI) studies, which measure blood oxygen levels and blood flow in the brain during tasks and rest, showed decreased activation during episodic memory encoding and recall tasks in AD individuals.[189]

E. Positron Emission Topography

Positron Emission Topography (PET) measures metabolism and neurochemical processes in the brain using radioactive tracers, or ligands, that bind to molecules.[190] Two main types of ligands are used in AD research: a glucose tracer called ^{18}F-FDG and amyloid tracers such as ^{11}C PiB and ^{18}F Florbetapir.[191]

The brain relies on glucose for energy, so PET is used to determine the brain's metabolism by observing its use of fluorodeoxyglucose ("FDG").[192] ^{18}F-FDG measures have been demonstrated to distinguish AD from normal individuals and distinguish AD from other dementias.[193] Results from using the ligand ^{18}F-FDG can distinguish patients who will progress from MCI to AD from those who will not; it can also identify asymptomatic individuals who are at a higher risk for developing AD.[194]

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186. Risacher & Saykin, *supra* note 146, at 626–27. This is also known as hypoperfusion. *Id.* at 627.

187. *Id.*; Riverol & López, *supra* note 150, at 4. These regions included the medial temporal lobe, the lateral temporal lobe, the medial and lateral parietal lobe, and frontal lobe. *Id.*

188. Riverol & López, *supra* note 150, at 4.

189. Risacher & Saykin, *supra* note 145, at 627.

190. *Id.* at 626–27.

191. *Id.* ^{18}F-FDG is utilized to measure brain metabolism via glucose consumption, and amyloid tracers bind to amyloid plaques in the brain. *Id.*; Riverol & López, *supra* note 150, at 4.

192. *See* Keith A. Johnson et al., *Brain imaging in Alzheimer's Disease*, COLD SPRING HARBOR PERSP. MED., Jan. 31, 2012, at 1, 8.

193. Riverol & López, *supra* note 150, at 5 (showing sensitivity of eighty-nine percent and specificity of eighty-five percent).

194. *Id.*

When the ligand ^{11}C PiB binds to plaques in the brain, it correlates with other biomarker measures of AD.[195] In AD individuals, PiB binding correlated with a finding of post-mortem amyloid plaques.[196] Moreover, PiB binding was significantly elevated in brain regions known for amyloid deposits.[197]

PET imaging has a number of limitations. First, using the ligand ^{18}F-FDG only shows general patterns of reduced metabolism in the brain and cannot provide individual diagnostic information for patients.[198] Second, the radioactive isotopes used in the ligands have short half-lives; ^{11}C specifically has a very short half-life and thus cannot be used outside of expert research centers.[199] Third, cognitively normal adults also have Aβ deposits that show up on PiB PET imaging.[200] Finally, PiB binding was shown to occur in other pathologies such as Lewy Body Dementia, demonstrating that PiB binding is not specific to AD.[201]

F. Genetic Biomarkers

The majority of AD cases are sporadic, with a small population (less than 2.5%) attributed to genetic disposition.[202] The most widely studied genetic variant that relates to AD is the apolipoprotein E epsilon

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195. *Id.* (showing correlation with whole-brain atrophy rates and CSF Aβ42 levels).

196. Blennow et al., *supra* note 165, at 300; Risacher & Saykin, *supra* note 146, at 627.

197. Risacher & Saykin, *supra* note 146, at 630. Research suggests that amyloid deposition occurs mostly in the early phases of AD and that accumulation slows down by the time of the typical AD diagnosis. *Id.* One study found that cognitively normal individuals who were PiB positive (meaning that the ligand bound to some significant plaque deposition in the brain) were five times more likely to progress to AD; twenty-five percent of the PiB-positive individuals progressed to MCI or AD within three years. Riverol & López, *supra* note 150, at 6.

198. *Earlier Diagnosis*, *supra* note 133.

199. Blennow et al., *supra* note 165, at 300. ^{18}F has a shorter half-life than ^{11}C but ^{18}F does not have as high of a binding affinity to plaques as ^{11}C. *Id.*; Riverol & López, *supra* note 150, at 5.

200. Yang Jiang et al., *Alzheimer's Biomarkers are Correlated with Brain Activity in Older Adults Differentially During Resting and Task States*, FRONTIERS AGING NEUROSCIENCE, Feb. 8, 2016, at 1, 2 (finding 20-50 percent of cognitively normal adults have Aβ deposits that are shown on PiB PET imaging). Even if no plaque pathology is present, PiB may give a positive result if vascular deposits are detected. *Id.* Furthermore, some patients that were diagnosed as mild AD yielded a negative PiB result had low levels of plaques at autopsy. Riverol & López, *supra* note 150, at 6.

201. Riverol & López, *supra* note 150, at 5.

202. *See* Guerreiro et al., *The Genetic Architecture of Alzheimer's Disease; Beyond PSENs and APOE*, 33 NEUROBIOLOGY AGING 437, 437 (2012).

4 (APOE ε4) allele.[203] Individuals who carry the APOE ε4 allele are more likely to develop AD than individuals without the allele and the risk increases with the number of copies of the allele the person has.[204] This elevated risk correlates with other markers: individuals with the APOE ε4 allele are more likely to be PiB positive, have higher baseline level of brain atrophy and increased rates of atrophy, greater amyloid accumulation levels, and higher CSF t-tau/p-tau levels.[205] But because not all individuals who carry the APOE ε4 allele develop AD, the presence of the allele only indicates an increased risk of developing AD.[206] This means that the best use of this marker may be to monitor such individuals and find early signs of AD.[207] Other genes are being studied as well.[208]

G. Limitations and Implications

AD biomarkers under study are not yet ready for widespread implementation in medical practice.[209] Although the research is

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203. *See* Risacher & Saykin, *supra* note 146, at 635.

204. *See id.*

205. *Id.*; Riverol & López, *supra* note 150, at 3–6.

206. *Earlier Diagnosis*, *supra* note 133. Individuals with Familial AD who were pre-symptomatic carriers of the presenilin 1 E280 A mutation had detectable decreases in Aβ42 in CSF up to twenty years before an MCI diagnosis and up to four years before amyloid tracer binding evidence on PET imaging. Kulic & Unschuld, *supra* note 140, at 751; *see* Jack et al., *supra* note 13, at 551 ("gene variants do not measure pathologic change but rather indicate risk for developing pathologic change.").

207. In a longitudinal study of AD cases with dominantly inherited mutations of the allele, for example, amyloid accumulation on PET imaging was the earliest detectable difference between pre-symptomatic carriers and noncarriers, which occurred up to fifteen years before the estimated onset of Clinical AD symptoms. Risacher & Saykin, *supra* note 146, at 636. Dominantly inherited mutations include mutations in the amyloid precursor protein (APP), presenilin 1, and presenilin 2 genes. *Id.* Other biomarkers such as CSF Aβ42, tau, and MRI brain volume, did not show changes until ten to fifteen years before estimated onset of symptoms, and some observable cognitive decline occurred approximately five years before the estimated onset of symptoms. *Id.*

208. Individuals with a mutation on the MPT gene, the gene associated with producing tau protein, are more likely to have higher CSF t-tau and p-tau levels. Blennow et al., *supra* note 134, at 16. Individuals who possessed a mutation on the CR1 gene, associated with AB metabolism, were more likely to have elevated AB deposition and have a greater likelihood of developing AD. Xi-Chen Zhu et al., *Effect of* CR1 *Genetic Variants on Cerebrospinal Fluid and Neuroimaging Biomarkers in Healthy, Mild Cognitive Impairment and Alzheimer's Disease Cohorts*, 54 MOLECULAR NEUROBIOLOGY 551, 558–59 (2017).

209. Riverol & López, *supra* note 150, at 2. Even so, some neuroimaging is already routine in diagnosing certain dementias. *See* Darby, *supra* note 10, at 274. And biomarkers have been included in recent sets of diagnostic criteria for AD. *See* Bruno Dubois et al., *Advancing Research Diagnostic Criteria for Alzheimer's Disease: The*

promising, we do not yet have a biomarker that can diagnose clinical AD, predict conversion from MCI to AD, detect preclinical AD, and distinguish AD from other pathologies with sufficient accuracy to use clinically. Several factors inhibit standardized usage.[210] Even as biomarkers with acceptable levels of validity are developed, they are likely to be probabilistic rather than determinative and used in conjunction with other diagnostic measures rather than in isolation.[211]

Most significant for purposes of this article, AD pathology can be present in individuals who do not show cognitive symptoms, demonstrating that biomarker evidence does not always correspond to manifested clinical symptoms.[212] One possible explanation for this phenomenon is what is known as cognitive reserve. Thought to be related to educational or occupational attainment, individuals with a higher cognitive reserve exhibit better cognitive performance than individuals with a lower cognitive reserve, even in the presence of similar amyloid accumulation.[213] This could possibly lead to difficulties

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IWG-2 Criteria, 13 LANCET NEUROLOGY 614, 614 (2014) (stating that International Working Group requires biomarker evidence for diagnosis of AD); McKhann et al., *supra* note 143 (suggesting that biomarkers could be used to support a clinical diagnosis of AD but are not required).

210. Researchers have not yet developed standardized cut-off values for biomarkers, thus preventing universal reference points that can be used in diagnosis. *See* Rosén et al., *supra* note 142, at 7; Jack et al., *supra* note 13, at 550-551. Sample analysis varies from institution to institution. *Earlier Diagnosis*, *supra* note 133. Another complication is the amount of conflicting data reported, which may be due to differences in research study sampling procedures as well as the difficulty in gathering healthy controls of the same age, sex, educational level, and lifestyle as the MCI/AD patients. Humpel, *supra* note 131, at 30. Assays of CSF proteins are currently very expensive to generate, *id.*, and most insurers do not cover the cost of imaging and biomarker tests. STEVEN D. PEARSON ET AL., INST. FOR CLINICAL & ECON. REVIEW, DIAGNOSTIC TESTS FOR ALZHEIMER'S DISEASE: GENERATING AND EVALUATING EVIDENCE TO INFORM INSURANCE COVERAGE POLICY 5 (2012). ELISA assays for CSF biomarkers cost about $72 per patient, and the ideal expense would be approximately $11 per patient. *See* Humpel, *supra* note 131, at 30. *See also* Jack et al., *supra* note 13, at 555 (stating that current AD biomarkers are either expensive or invasive).

211. *See* Jack et al., *supra* note 13, at 544, 555 ("None of the biomarkers are as sensitive as direct examination of tissue at autopsy."). *See generally* Preston et al., *supra* note 17.

212. PEARSON ET AL., *supra* note 210, at 10. Plaque and tangle pathologies do not necessarily indicate dementia; elderly non-demented individuals can exhibit these changes in their brains. Blennow et al., *supra* note 134, at 4; *see* Jack et al., *supra* note 13, at 538, 552.

213. Daniel Ferreira, et al., *Cognitive Variability during Middle-Age: Possible Association with Neurodegeneration and Cognitive Reserve*, Frontiers Aging Neuroscience, June 9, 2017, at 1, 1; Kenneth M. Langa, *supra* note 3, at 51 (finding age-specific risk of dementia may have declined over the past 25 years due to an increase in educational attainment); Risacher & Saykin, *supra* note 146, at 635.

in establishing a diagnosis for those with higher cognitive reserve, especially in capacity testing.[214]

And yet, discovery of and clinical use of these types of biomarkers are on the horizon. What are the implications of discovering these biomarkers of AD susceptibility, diagnosis, and prognosis for guardianship proceedings?

IV. THE IMPACT OF AD BIOMARKERS ON CAPACITY ASSESSMENT AND GUARDIANSHIP DECISIONS

The law traditionally relies on changes in observed behavior before it acts, so the availability of biomarker evidence, and its ability to look at brain states, has the potential to unsettle all kinds of legal assessments.[215] The potential impact could include competency assessments in guardianship proceedings, which, in line with the traditional view, generally rely upon behavioral data such as performance-based tests and clinical observation to determine whether the law should act to remove an individual's decision making authority. Because the statutory schemes governing these assessments were enacted well before biomarker research in this area advanced, they do not anticipate use of biomarker evidence or documentation of brain states of AD. Use of AD biomarkers in capacity assessments has not yet been introduced in court, so it is unclear how biomarker evidence will affect these determinations.

Several challenges lie ahead. First and foremost, should the law even consider biomarker evidence of AD, most especially pre-behavioral symptomatology, in this context, or would its consideration be antithetical to our conceptions of competency? Even if it does allow consideration, the use of markers would have to pass evidentiary muster; establishing the probity of tests indicating a higher probability for developing or having AD will present significant evidentiary and interpretive challenges. If biomarker diagnostic evidence does not come into evidence directly, either because its consideration would be impermissible under the statutory scheme, would not pass evidentiary standards, or fundamentally would violate due process concerns, we need to anticipate that its availability will likely have indirect effects,

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214. One possible solution to these problems is to use a panel of many biomarkers. *See* Annie M. Racine et al., *Biomarker Clusters are Differentially Associated with Longitudinal Cognitive Decline in Late Midlife*, 139 BRAIN 2261, 2262 (2016).

215. *See* Preston et al., *supra* note 17, at 1207; *cf.* Stephen Morse, *Criminal Law and Common Sense: An Essay on the Perils and Promise of Neuroscience*, 99 MARQ. L. REV. 39, 64 (2015) (arguing that in most cases, neuroimaging is likely to add little value beyond behavioral data to legal decisions).

both positive and negative, on the guardianship decision. This section examines these key issues.

A. Should the Law Consider Diagnostic Biomarkers Evidence in Guardianship Decisions?

Relying on individualized assessment and judgments based on outwardly manifested behavior in guardianship decisions is designed to protect the respondent's due process rights and prevent wrongful intervention and subsequent loss of rights.[216] Homing in on a person's performance abilities in a capacity assessment—what a person understands, or can do, in relation to the competency question at issue—presumably creates a more objective, tailored, and therefore fairer assessment of the individual's capacity.[217] Relatedly, we do not want experts or courts to infer solely from a medical or psychiatric diagnosis that an individual will be unable to carry out certain specific tasks.[218] Drawing on the Grisso model of capacity, this view—that a "diagnosis of dementia does not imply incapacity,"[219]—requires, at the very least, a demonstration of a causal connection between the diagnosis and a particular deficit to satisfy due process concerns.[220] It requires a showing that the individual is cognitively impaired *and* behaving in ways that puts him at significant risk.[221] As a result, we need to act cautiously in relying on evidence that documents brain states of AD, especially early brain states, to make sure that the evidence is not used for illegitimate purposes.

Recognizing these concerns, this section addresses the benefits and risks of using biomarker diagnostics in competency decisions.

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216. *See* Haines & Campbell, *supra* note 25, at 15 ("It is not the deprivation of a liberty interest that is subject to due process scrutiny. Rather, it is the erroneous deprivation of that liberty interest that must be protected with due process."); Wright, *supra* note 6, at 61, 74 ("Accurate determination of mental incapacity is essential to justify the infringement of autonomy rights.").

217. *See* Wright, *supra* note 6, at 68, 91 (explaining that focus in guardianship proceedings is on functional assessment in determining capacity); *supra* notes 18–25 and accompanying text.

218. *See* Wright, *supra* note 6, at 67; notes *supra* 97–101 and accompanying text.

219. Kim et al., *supra* note 6, at 159; *see* Paul S. Appelbaum, *Consent in Impaired Populations*, 10 CURRENT NEUROLOGY & NEUROSCIENCE REP. 367, 368 (2010).

220. GRISSO, *supra* note 23, at 29; Wright, *supra* note 6, at 67.

221. Wright, *supra* note 6, at 67.

1. BENEFITS OF DIAGNOSTIC BIOMARKERS USAGE

Although behavioral data will remain the paramount consideration in assessing capacity, use of biomarker diagnostics can offer significant value in competency determinations.

In general, when diagnoses are considered in guardianship decisions, they can play an important role by offering more information to confirm or challenge a finding of incompetency. Diagnostics can provide a likely explanation for the individual's apparent deficits in functioning abilities.[222] This is especially important when dementia is suspected, since an individual's decision making abilities may fluctuate with AD, especially during earlier stages of the disease.[223] There may be other explanations for observed behavior: individuals may manifest a functional deficit at a particular time, but it may be temporary due to circumstances surrounding that particular examination, such as use of medication or lack of sleep the previous night.[224] Moreover, using a diagnosis can also help prevent the "evaluation of an individual's ability to make autonomous decisions from being reduced to an evaluation of the social acceptability of the decisions made."[225] Thus, the diagnostic component of the competency determination remains very important in ensuring that the finding of incompetence is not made in error or for inappropriate reasons[226] and can play a key role in competency assessments.[227]

Having a diagnosed condition also can assist courts with prognosis, an important consideration in guardianship decisions. The diagnosis can guide the court in predicting future behaviors in certain settings, since the guardianship determination does not focus on a single task at a definite point in time, but rather on how the individual will fare on performing many tasks over the longer term.[228] It can help courts determine whether the deficit is a permanent or reversible condition. A diagnosis of AD, for example, suggests that the deficits will progress and can indicate a likely pattern of symptoms.[229] This is in contrast,

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222. *See id.*

223. *See* Panagiota Voskou et al., *Testamentary Capacity Assessment: Legal, Medical, and Neuropsychological Issues*, 31 J. GERIATRIC PSYCHIATRY & NEUROLOGY 3, 6 (2018).

224. GRISSO, *supra* note 23, at 30.

225. Wright, *supra* note 6, at 67 ("The evaluation of rationality must focus on the nature of the decision making process, not on the outcome of that process.").

226. *Id.*

227. GRISSO, *supra* note 23, at 27.

228. *Id.* at 31, 384.

229. *See* Sperling et al., *supra* note 138.

say, to a diagnosis of major depression, which may be treatable and offers promise of improvement.[230]

Given that a significant number of guardianship cases involve patients with dementia, the availability of AD diagnostic biomarkers will only enhance the benefits of using diagnoses in guardianship determinations for those respondents. Of paramount importance, biomarker diagnostics can offer validation of a clinical diagnosis of AD. As noted, psychiatric diagnoses like dementia are currently clinical;[231] and AD can only be definitively diagnosed through autopsy.[232] Use of biomarkers will be used to confirm an already strong clinical suspicion and move the psychiatric diagnosis from relying solely on behavioral data to include "hard," more objective, empirical data of an altered brain state. As biomarkers improve, this may become critical in providing a system of checks and balances to professional opinions on capacity, which are not infallible using our current assessment tools,[233] especially when symptoms fluctuate in a disease like AD.[234] Biomarkers will function as a screening instrument: a disparity in results may indicate the need for a more intensive evaluation.[235] When the results both support each other, we will be more confident about making a decision—and when the measures disagree, this will alert the system to take a close and careful look at the competency determination.

Usage of AD biomarker diagnostics inevitably will increase in the practice of medicine. As development of biomarker testing provides a clearer understanding of the correct diagnosis, it will likely become a significant part of the standard of care for diagnosing and treating AD in the living brain. The medical community has already begun to adopt some biomarker tests[236] and likely will adopt more as it becomes common practice to use this measure of assessment. This usage will increase when studies demonstrate sufficient levels of reliability and

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230. *See* Sönke Arlt, *Non-Alzheimer's Disease-Related Memory Impairment and Dementia*, 15 DIALOGUES CLINICAL NEUROSCIENCE 465, 470 (2013).

231. *See supra* note 134 and accompanying text. Some clinicians have also begun to use neuroimaging tests through MR scans to assist in diagnosis. *See Earlier Diagnosis*, *supra* note 133.

232. *See Humpel*, *supra* note 131.

233. *See* GRISSO, *supra* note 23, at 28; Moye et al., *supra* note 6, at 165 ("[C]linicians arrive at significantly discrepant judgments of capacity in dementia."); *supra* notes 118–130 and accompanying text.

234. *See* Voskou, *supra* note 223, at 6.

235. *See* Kim et al., *supra* note 6, at 159–60 ("The main challenge in studying [measurement of decisional abilities] has been the lack of a clear criterion or reference standard of incompetence."); Andrew Peterson, *Should Neuroscience Inform Judgment of Decision-Making Capacity*, NEUROETHICS, May 9, 2018, at 12.

236. *See* Darby, *supra* note 10 at 274.

validity for clinicians to adopt these biomarker tests into their routine practice.[237] The increasing adoption of biomarker diagnostics will move the medical community toward earlier, and presumably more accurate, diagnoses.

The potential for enhanced accuracy and earlier diagnosis in medicine will spill over into the civil capacity assessment arena.[238] If the state competency test allows use of diagnosis as a factor in the capacity assessment, use of biomarker evidence will be incorporated in that way as it becomes part of the standard of care.[239]

But not all states recognize the use of diagnosis as a factor in competency determinations.[240] As clinicians incorporate biomarker diagnostics into standard procedure, it may become difficult for those states to ignore their widespread usage and their added benefits in the guardianship context. The broader acceptance of biomarker usage may cause more states to expand the factors enumerated in their current

237. *See* Jack et al., *supra* note 13, at 537 (calling for longitudinal cohort studies and randomized placebo controlled studies before adopting biological definition of AD in general clinical practice); Ances, *supra* note 107. One problem with validation is that biomarker results are tested by reference to conventional measures. The biomarkers being developed do not yet answer the question whether an individual has AD; the researcher must look to other indicia. Most of the biomarker studies thus far have only been validated when compared to healthy controls and those with AD verified by neuropsychological or other conventional testing, which is based on clinical observation, or through autopsy. *See, e.g.*, Keun-A Chang et al., *Plasma Soluble Neuregulin-1 as a Diagnostic Biomarker for Alzheimer's Disease*, 97 NEUROCHEMISTRY INT'L 1, 2 (2016) (describing that both healthy controls and AD-verified participants were recruited for the study, in which AD patients were verified via neuropsychological tests such as the MMSE); *id.* at 1 ("Presently, a definitive diagnosis of AD can only be made postmortem . . . [and] [c]urrent methods for diagnosing AD involve taking a detailed history and neuropsychological testing to establish the presence of dementia."). In other words, we validate our new tools with our old tools. We have not yet reached (and may never reach) the point at which biomarkers are an independent measure of AD in the living brain. *See* Humpel, *supra* note 131, at 30 ("[I]t is important to collect healthy controls who are age-matched and have a similar lifestyle, sex and education. This is extremely difficult to achieve . . . ."). This is new research, and we need further longitudinal studies to tie validity to longer term outcomes. Another problem is that we have begun to measure physiological changes that have no (or not yet any) manifestation in cognition or behavior. *See, e.g.*, Kulic & Unschuld, *supra* note 140, at 749 ("Alzheimer's disease-related pathophysiological changes can be detected as early as 10–20 years before overt cognitive impairment.").

238. *See* Kim et al., *supra* note 6, at 159–61, 163.

239. Some states may not permit psychologists to testify about the cause of cognitive deficits or a medical diagnosis; that testimony may need to come from a neurologist or psychiatrist. *See, e.g.*, ARIZ. REV. STAT. ANN. § 14-5303(D) (2018) (stating that the report on the alleged incapacitated person's diagnosis must be filed by a "physician, psychologist or registered nurse *acting within that person's scope of practice*") (emphasis added).

240. *See supra* notes 88–89 and accompanying text.

statutes to include diagnoses. In this way, the increased usage of biomarkers may lead to greater standardization of the factors considered in guardianship determinations nationally. And as more states adopt diagnosis as a factor for consideration, some state statutes may even specify the employment of biomarkers, requiring their use in the guardianship determination (as well as requiring professionals who are trained in the use of biomarkers and qualified to interpret them).[241] Eventually, the increased acceptance and usage of biomarkers may even result in greater weight given to the pathology of AD and its progression in the competency determination.

Even if a state test does not (yet) include diagnoses as a factor, the development of biomarker diagnostics will still affect and enhance capacity assessment indirectly. Biomarkers may help strengthen the accuracy of current behavioral assessment and capacity assessment instruments, particularly as we learn more about differentiating between different stages of AD through physiological evidence. Neuropsychological tests rely on comparison of the individual's data with a normative database derived from control subjects who do not exhibit neurological or psychiatric dysfunction, as well as data from other patient populations.[242] In other words, the results of neuropsychological tests can tell doctors how a subject is performing relative to others of the same age, sex, and education level. Biomarker data should bolster these instruments by providing additional relevant comparison group data to enhance the normatively derived cutoff scores. Comparison data are critical—even purely individual clinical evaluations necessarily rely on comparison to other groups.[243] Biomarker evidence can strengthen the group data comparison by providing empirical evidence of others who suffer from a similar disease or condition at similar stages.[244] In general, this enhancement should help lead to more standardized approaches to and results in competency determinations, even indirectly. This is significant in an

241. *See generally* Francis X. Shen, *Neurolegislation: How U.S. Legislators Are Using Brain Science*, 29 HARV. J.L. & TECH. 495, 498 (2016) (discussing increase in legislation partly based on brain science in health, education, and criminal justice; brain science has been mentioned in nearly 1,000 bills proposed in state legislatures from 1992–2009).

242. Gaudet, *supra* note 107, at 509; Harvey, *supra* note 107, at 92; Peterson, *supra* note 235, at 12.

243. For example, a clinician will reach a diagnosis by drawing on the clinician's previous experience with other patients. *See* Carl Thompson, *Clinical Experience as Evidence in Evidence-Based Practice*, 43 J. ADVANCED NURSING 230, 230 (2003); Peterson, *supra* note 235.

244. *See* Moye et al., *supra* note 6, at 167 ("most capacity instruments . . . lack fundamental normative data . . . to [help] establish . . . range and limits of their use").

area like capacity assessment, where accuracy and consistency are critical.[245]

More generally, biomarker diagnostics have the potential to spark a paradigm shift in the way we look at the competency determination. Biomarker evidence may move the legal system to redefine the binary choice between competent and incompetent in a demented patient. As use of biomarker diagnostics of dementia becomes generally accepted in the medical community, and the medical community becomes more sensitive to the view of AD as a spectrum, the ability to detect changes in brain states may argue in favor of a guardianship model that includes legal protections for those who do not yet meet the legal threshold for incompetence. As Professor Jalayne Arias advocates, we may need to recognize a "gap" category to protect individuals with declining capacity, but who do not yet meet the criteria for incompetency.[246] Biomarkers will become part of the inquiry to identify individuals along the spectrum of AD.[247] In this context, even pre-behavioral symptomatic biomarker evidence may be useful for screening purposes. It may assist in reinforcing the need for a clinical assessment and provide a quick and efficient way to identify individuals whom we should examine more carefully for "quasi" competency under this gradient model.[248]

Finally, biomarker evidence will provide an additional baseline to measure the progression of the disease, allowing us to reach back earlier in the continuum of the multiple stages of AD. A baseline enhances scientific rigor in determining when the loss of capacity likely has occurred,[249] helping to avoid an approach of "I know it when I see

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245. *See* Kim et al., *supra* note 6, at 163.

246. Arias, *supra* note 62, at 151–55 (recommending recognition of a "gradient" model of incompetency that better reflects the realities of capacity).

247. *Cf.* Jamie A. Grodsky, *Genomics and Toxic Torts: Dismantling the Risk-Injury Divide*, 59 STAN. L. REV. 1671, 1712–14 (2007) (arguing in the context of toxic torts that courts need to rethink the concept of "physical injury" as advances in genetic science make it easier to detect the consequences of toxic exposure before the manifestation of clinical symptoms of disease).

248. Others have argued persuasively that we should no longer view capacity as an "on-off" switch and adjust our legal standards accordingly. *See* Arias, *supra* note 62, at 136–37 (arguing for revised model with levels of protection tailored toward individual deficits to capture gap between competent and incompetent); Drobac & Goodenough, *supra* note 20, at 473 (arguing that neuroscience can offer a more nuanced view of capacity and we should adjust our legal standards accordingly).

249. It will help, for example, in determining an individual's testamentary capacity at the time of signing a will. Testamentary capacity will likely invoke a different legal standard, but the lack of testamentary capacity may be considered in the guardianship proceeding. Typically, at the time of executing a will, the testator must "have capacity to know the natural objects of his . . . bounty, to understand the nature and extent of his . . . property, and to interrelate these elements sufficiently to make a

it." The availability of additional empirical measurements for baselines will be particularly important with individuals with mild cognitive impairment, the period with the most variation. Different individuals decline at different rates, and biomarker identification will help track the rate of decline more accurately. Not only will this help give precision to when a guardianship is appropriate, it can also help determine its scope.

2. RISKS OF BIOMARKER DIAGNOSTICS USAGE

As we gain confidence in biomarker diagnostics and prognostics, the availability of the evidence may prove to be a double-edged sword; increased use of biomarker diagnostics poses significant risks. Even if biomarker diagnostics are not admitted into evidence, their availability increases the potential for misrepresentation and manipulation. Would family members press an individual not to contest guardianship proceedings after brain alterations are identified or a genetic predisposition found, but while the individual still thinks he is competent? Would members of a family-run business take advantage of the biomarker findings to pressure the individual to turn to surrogate decision-making? Courts will need to take precautions to guard against these undue influences and new potential for elder abuse and financial exploitation once biomarkers come into the picture.[250]

Another risk with the advent of biomarkers is that the lack of AD biomarkers in a respondent could make the showing of incapacity harder to demonstrate. As use of biomarker diagnostics becomes more commonplace, courts may come to expect a showing that the individual has a detectable biomarker indication of AD before assigning a guardian. Courts may assign too much importance to the presence or absence of biomarker evidence, which is intended for supplemental purposes. Furthermore, although it accounts for the biggest cause of dementia, AD is not the only source of impaired cognitive function. Cognitive decline occurs with normal aging, as well as with other

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disposition of property according to a rational plan." HANDBOOK FOR LAWYERS, *supra* note 7, at 5. The standard for testamentary capacity "does not require that the person be capable of managing all of his . . . affairs or making day-to-day business transactions," but whether the person is capable of managing all of his affairs may be considered in a guardianship proceeding. *Id.; see supra* Part II.

250. *See generally* Sheena M. Horning et al., *A Case of Elder Abuse and Undue Influence*, 12 CLINICAL CASE STUD. 373, 374–75 (2013); Ashley E. Rathbun, *Marrying into Financial Abuse: A Solution to Protect the Elderly in California*, 47 SAN DIEGO L. REV. 227 (2010). The American Bar Association has issued guidelines for dealing with elder abuse. *See Elder Abuse*, AM. BAR ASS'N, https://www.americanbar.org/groups/law_aging/resources/elder_abuse.html [https://perma.cc/65P8-GBMJ].

forms of dementia, which can contribute to impaired capacity.[251] It is likely that biomarkers for AD will be developed first, before biomarkers of other forms of dementia, since AD is the main focus of research.[252] Thus, the absence of AD biomarkers in an individual suspected of being demented may not be significant. But will the lack of AD biomarkers in individuals who may suffer cognitive decline due to other forms of dementia involving these scientific laggards unduly affect the determination of competency?

The biggest challenge with biomarker evidence may be to guard against undue consideration of biomarker evidence when behavioral symptoms are manifesting at their earliest stages. We need to proceed slowly and cautiously in introducing these test results, especially as we shift our view of AD from staged to a continuum. Under all these scenarios, however, it is important to resist the imposition of de facto categorical rules on the significance of biomarker findings. We do not want incapacity to be defined by a diagnosis of AD based solely on biomarker evidence; nor do we want it to be ignored. Instead, it can be probative evidence in competency proceedings, depending on how predictive the biomarker evidence is shown to be and the other evidence submitted. We can assume that the biomarker results will be supplemental to functionality and behavioral tests, and never used without those measures. They will be used as a tool to explain functional deficits or challenge inconsistent findings. In order to guard against misinterpretation, misuse, and unintended consequences, we will need to educate courts and caretakers about the significance and limitations of the biomarker test results, as we have done in other areas where scientific measures have been introduced into courts.[253]

B. Evidentiary Hurdles

A proffer of biomarker evidence, with its inherent potential for bias and prejudice, will inevitably lead to evidentiary disputes in guardianship proceedings. Rules of evidence will govern whether the

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251. *See* Moye et al., *supra* note 6, at 162.

252. *See* Jack et al., *supra* note 13, at 545 (explaining that use of biomarkers for AD should not be delayed until discovery of biomarkers of other possible causes of dementia).

253. *See* PRESIDENT'S COUNCIL OF ADVISORS ON SCI. & TECH., REPORT TO THE PRESIDENT—FORENSIC SCIENCE IN CRIMINAL COURTS: ENSURING SCIENTIFIC VALIDITY OF FEATURE-COMPARISON METHODS, 1, 40 (2016), https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST/pcast_forensic_science_report_final.pdf [https://perma.cc/T3J5-V5Y6] [hereinafter REPORT TO THE PRESIDENT] (forensic evidence); *Regulation of Genetic Tests*, NIH NAT'L HUM. GENOME RES. INST., https://www.genome.gov/10002335/regulation-of-genetic-tests/ [https://perma.cc/X4XU-7LMV] (providing guidelines on genetic testing).

factfinder is permitted to consider it. Under the balancing analysis typified by Federal Rule of Evidence 403, the judge will weigh the relative probity of the evidence against its prejudicial effect on the respondent.[254] The main concern in admitting the biomarker evidence is that it may lend overly persuasive credibility to the claim that State intervention is needed and surrogate decision-making should be imposed, based on misunderstood data. The apprehension is that the scientific evidence will overpower arguments based on individualized behavioral data and performance assessments.[255] This may elevate the biomarker-based diagnosis to a greater significance than the state guardianship statute intends or that offends fundamental due process concerns.

Even if the biomarker evidence is not unduly prejudicial, however, it still must meet the requirements for admissibility of scientific evidence.[256] Under the federal *Daubert* test (which has been adopted by most states), the trial judge serves a gate-keeping function to determine admissibility of expert evidence.[257] The judge must use a three-pronged test to determine admissibility: (1) the evidence must be relevant; (2) the expert must be qualified to present the evidence; and (3) the evidence must be scientifically valid.[258] Although courts generally do

254. Rule 402 states that all relevant evidence is admissible, unless it is subject to a special exclusion. FED. R. EVID. 402. Under Rule 403, the court must weigh the probity of the evidence against its prejudicial impact: "The court may exclude relevant evidence if its probative value is substantially outweighed by a danger of one or more of the following: unfair prejudice, confusing the issues, misleading the jury, undue delay, wasting time, or needlessly presenting cumulative evidence." FED. R. EVID. 403. State evidence codes also impose similar requirements for admissibility of evidence, although sometimes they impose a more restrictive standard for admitting expert testimony. *See* A. C. Pustilnik, *Imaging Brains, Changing Minds: How Pain Neuroimaging Can Inform the Law*, 66 ALA. L. REV. 1099, 1147 (2015).

255. *See, e.g.*, Jessica R. Gurley & David K. Marcus, *The Effects of Neuroimaging and Brain Injury on Insanity Defenses*, 26 BEHAV. SCI. & L. 85, 85–86, 93 (2008); Deena Skolnick Weisberg et al., *The Seductive Allure of Neuroscience Explanations*, 20 J. COGNITIVE NEUROSCIENCE 470, 474–76 (2008). *But see* Adina L. Roskies et al., *Neuroimages in Court: Less Biasing Than Feared*, 17 TRENDS COGNITIVE SCI., 99, 99 (2013); Michael J. Saks et al., *The Impact of Neuroimages in the Sentencing Phase of Capital Trials*, 11 J. EMPIRICAL LEGAL STUD.105, 105 (2014).

256. *See Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 589–90 (1993) (holding that courts should consider the validity of a proffered theory or technique by considering many factors, including whether it has been subjected to peer review, whether it has a known error rate, and whether it has garnered widespread acceptance within its field); 1 JAMES T. O'REILLY, TOXIC TORTS PRACTICE GUIDE § 3:8, Westlaw (2018).

257. *Daubert*, 509 U.S. at 592–93.

258. *Id.* at 587–93.

not subject psychiatric expert testimony to *Daubert* testing,[259] the use of more objective evidence will trigger challenges under *Daubert* and will lead to greater judicial scrutiny of the basis for the diagnosis. Biomarker evidence will need to meet judicial standards for sufficient reliability and have sufficient sensitivity, specificity, and predictive value for use in court.[260]

In discussing scientific validity, the *Daubert* Court focused on the scientific methodology used rather than the conclusions generated.[261] The *Daubert* Court identified several factors to consider in evaluating the validity of the methodology, including: (1) testability; (2) peer review and publication; and (3) error rate.[262] A number of factors affect the methods of scientific research and the information that it generates.[263] These factors include sample size, the comparison group, and outcome measures.[264] Moreover, scientists generally do not reach a conclusion on a hypothesis until multiple studies have replicated the result.[265]

Although there is an abundance of research in biomarkers of AD, including studies aimed at replication, conducting AD biomarker research is not easy.[266] It requires considerable effort to enroll a sufficient number of patients, representative of the general older population, to draw a valid conclusion.[267] Even with appropriate sample sizes, other problems exist. The methods of research used are not consistent, and scientists use variable outcome measures.[268] Predictive measures for AD will require long term studies.[269] As yet, there are no

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259. *See* Bruce D. Sales & Daniel W. Shuman, *Science, Experts, and Law: Reflections on the Past and the Future*, *in* EXPERT PSYCHOLOGICAL TESTIMONY FOR THE COURTS 9, 24–25 (Mark Constanzo et al. eds., 2007) (noting that courts do not apply *Daubert* criteria "rigorously" to "clinical opinion testimony"); Deidre M. Smith, *The Disordered and Discredited Plaintiff: Psychiatric Evidence in Civil Litigation*, 31 CARDOZO L. REV. 749, 772–73, 776 (2010) (noting that courts readily admit psychiatric diagnoses into evidence).

260. *Daubert*, 509 U.S. at 589–90.

261. DAVID L. FAIGMAN ET AL., 1 MODERN SCIENTIFIC EVIDENCE: THE LAW AND SCIENCE OF EXPERT TESTIMONY § 1:18, at 57–58 (2014); *cf. Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997) ("[C]onclusions and methodology are not entirely distinct from one another.").

262. *Daubert*, 509 U.S. at 593–95.

263. FAIGMAN ET AL., *supra* note 261, § 1:22, at 67.

264. *Id.*

265. *Id.* § 1:22, at 68.

266. *See supra* notes 208–214 and accompanying text.

267. *See* Sperling et al., *supra* note 138, at 286–87.

268. *See id.* at 287; *supra* note 210.

269. *See* Sperling et al., *supra* note 138, at 287 (discussing limitations of biomarker AD research; proposing research and criteria model for refining research with longitudinal clinical research studies). *See also* Jack et al., *supra* note 13, at 537.

large scale population studies to suggest that the association between any biomarkers of dementing diseases and diagnoses is sufficiently robust to be used in clinical practice or the courts, which would make it problematic to meet the *Daubert* requirements. To translate biomarker research into use in the courtroom, these problems will need to be addressed and more consistency achieved.[270]

The third and potentially most important *Daubert* factor—"known or potential rate of error"[271]—was not specifically defined by the Court.[272] Much ink has been spilled over defining the term.[273] It is generally understood that tests will make mistakes; the relevant inquiry is the percentage of mistakes that is acceptable.[274] "A scientist's judgment of the value of a technique will depend on both the amount and kind of error associated with the technique."[275]

The two types of errors that scientists focus on are false positives (the test results suggest that individual has a disease when in fact an individual does not have the disease) and false negatives (the test results suggest that the individual does not have a disease when in fact he does have the disease).[276] The *Daubert* decision does not discuss whether the error rate should focus on the rate of false positives, false negatives or both. A leading treatise on scientific evidence applauds this omission: "the costs of making an error are different in different contexts."[277]

Setting the appropriate error rate for clinical use of biomarkers will be challenging and subject to many variables.[278] The predictive

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270. *See* Jack et al., *supra* note 13, at 537.

271. *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594 (1993).

272. FAIGMAN ET AL., *supra* note 261, § 1:21, at 66.

273. *Id.* at 67 (stating definition should be context driven; "the costs of making an error are different in different contexts"); REPORT TO THE PRESIDENT, *supra* note 253, at 18 (distinguishing between foundational validity and validity as applied); Andrew Jurs, *Judicial Analysis of Complex & Cutting-Edge Science in the* Daubert *Era: Epidemiologic Risk Assessment as a Test Case for Reform Strategies*, 42 CONN. L. REV. 49, 84–88 (2009); Erin Murphy, *The New Forensics: Criminal Justice, False Certainty, and the Second Generation of Scientific Evidence*, 95 CALIF. L. REV. 721, 792–93 (2007).

274. FAIGMAN ET AL., *supra* note 261, § 1:20, at 65.

275. *Id.* § 1:21, at 66.

276. *Id.*

277. *Id.* at 67 (citing examples of psychiatric predictions of violence: a judge may require a lower error rate before admitting prediction in a capital case, but permit higher error rates in a probation setting).

278. *See* Henry T. Greely, *Predicting Alzheimer Disease: Potential Ethical, Legal, and Social Consequences*, NEUROETHICS BLOG (June 30, 2014), http://www.theneuroethicsblog.com/2014/06/predicting-alzheimer-disease-potential.html [https://perma.cc/Y9S7-73QP] (explaining that predictive values may differ depending on the test, age of individual, or whether behavioral symptoms have

value of individual biomarker tests for AD will vary; some markers may be highly predictive of pre-clinical and clinical AD while others may simply indicate risk levels above those of the general population. Furthermore, at this point biomarkers are not meant to be used alone as a diagnostic test. Instead, it is assumed that the test will be used with several different kinds of tests to diagnose AD. And clinical adoption of different biomarkers may be gradual, increasing over time. All of these factors will affect admission of biomarker evidence in guardianship proceedings.

This raises the overarching problem of applying group data to the individual level, or what is known as the group-to-individual ("G2i") inference problem.[279] Marker results are generally based on group averages and statistics.[280] These group averages provide basic research data to associate an individual with a given disease, or "framework evidence."[281] But even if a patient's profile is consistent with group averages showing abnormalities in marker diagnostics for dementia, it is not conclusive with regard to application to a specific individual and specific behaviors and capacities, or "diagnostic evidence."[282] This means we may need to turn to other measures like behavioral data to complete a diagnosis.

More significantly, no single assessment instrument will ever capture all the medical, legal, and social aspects of a competency determination. Beyond the issues of acceptable error rates, validity, reliability, and G2i inferences, the key to use of this evidence in the guardianship setting will be determining the strength of the link between biomarker diagnostics, clinical capacity assessment, the statutory factors and the legal definition of competency. The expert who introduces this evidence in court will need to testify about how likely it is that an individual suffers from or will suffer from clinical dementia given certain biomarker and other testing results, which may be valid for informing a relevant factual issue, such as diagnosis or prognosis, but the question remains whether that individual is legally competent even with those indications.

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begun to manifest; calling for public assessment of biomarker testing similar to FDA approval before clinical use is allowed).

279. *See* Carl E. Fisher, et al., *Toward a Jurisprudence of Psychiatric Evidence: Examining the Challenges of Reasoning from Group Data in Psychiatry to Individual Decisions in the Law*, 69 U. MIAMI L. REV. 685, 688 (2015).

280. *See* Owen D. Jones, et al., *Brain Imaging for Legal Thinkers: A Guide for the Perplexed*, 2009 STAN. TECH. L. REV. 5, 8.

281. *See* Fisher, *supra* note 279, at 694.

282. *Id.* at 694, 708 (stating that "what is true in the aggregate for members of a large group may not be equally valid for a single person").

These considerations will need to be understood by the judge and jury. Ensuring this understanding will be a challenge; jurors may lack ability to interpret statistical evidence[283] and may have difficulty weighing probabilities.[284] Some judges may have difficulty interpreting the results as well.[285] This suggests that we need to consider developing guidelines for use of this evidence in court, as we have done in other areas like forensic evidence.[286]

Even with a bench trial, and with a judge more practiced in interpreting such evidence, the impact of biomarker diagnostics evidence in the proceeding remains a concern. Both the expert and the judge may be overly prejudiced by the evidence. The expert preparing the report may be unduly influenced by the biomarker findings and be subject to confirmation bias (the tendency to interpret evidence as confirmation of one's own findings). The court will need to grapple with the uncertainty about the significance of the results as well. If biomarkers become part of the expert report, the judge may be affected by confirmation bias in determining incompetency. This is the concern about use of diagnostics in competency generally—that a diagnosis does not necessarily translate to incompetency—and these biases may be strengthened when the diagnosis is supported by seemingly more objective, empirical data. Protecting against this bias will be particularly challenging when the biometric data is not determinative but instead represents a range of likely outcomes.

C. Privacy Concerns

Assuming that the biomarker evidence is admissible, there is yet another hurdle to overcome. The use of biomarker test results raises significant confidentiality and privacy questions. The Health Insurance Portability and Accountability Act of 1996 (HIPAA)[287] offers strong protections for patient medical records.[288] In the face of those

283. *See*, *e.g.*, FAIGMAN ET AL., *supra* note 261, § 4.18, at 252–53. *See also* Bradley D. McAuliff et al., *Can Jurors Recognize Missing Control Groups, Confounds, and Experimenter Bias in Psychological Science?*, 33 LAW & HUM. BEHAV. 247 (2009).

284. McAuliff et al., *supra* note 283, at 248.

285. *See* Sophia Gatowski, et al., *Asking the Gatekeepers: A National Survey of Judges on Judging Expert Evidence in a Post-*Daubert *World*, 25 L. & HUM. BEHAV. 433, 444–47 (2001) (finding that, of judges surveyed, only six percent exhibited sufficient understanding of falsifiability and only four percent exhibited sufficient understanding of error rates).

286. *See* REPORT TO THE PRESIDENT, *supra* note 253.

287. Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104–191, 110 Stat. 1936 (1996).

288. Standards for Privacy of Individually Identifiable Health Information, 45 C.F.R. §§ 160, 164 (2000).

protections, will the results of testing be discoverable? A petitioner could request the test results, but the respondent may refuse to authorize release of the medical records. In that case, a judge must decide whether the petitioner can gain access to the biomarker data.[289] In so doing, the judge will likely balance the need for the test results against the need for privacy protection, and issue protective orders allowing for discovery of the evidence when appropriate.[290] But even the potential for discoverability of the medical records may create a disincentive to get tested.[291] This may call for special legislative protections for biomarker testing, the model developed in the genetic testing area.[292] Such legislation may inhibit use of biomarker evidence in contested guardianship proceedings.[293]

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289. *See* FED. R. CIV. P. 35 (authorizing courts to order physical and mental examination of party where that condition is in controversy).

290. *See id.*; FED. R. EVID. 403.

291. Another question is whether a court would order a respondent to submit to biomarker testing, given the intrusiveness of the test, considering that current typical tests (clinical and neuropsychological evaluations) are noninvasive.

292. The Genetic Information Nondiscrimination Act (GINA) prohibits employers and health insurers from accessing or utilizing genetic information, but it does not apply to non-genetic information, such as brain scans. *See* Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, 122 Stat. 881, 884, 907 (2008). It is unlikely that GINA would apply to AD biomarker information and protect against discovery in guardianship proceedings, unless the test involved using genetic methods. *See* Greely, *supra* note 278; Shaheen E. Lakhan et al., *Biomarkers in Psychiatry: Drawbacks and Potential for Misuse*, 3 INT'L ARCHIVES MED. 1, 4 (2010).

293. Beyond the sensitive privacy interests of the individual, the availability of biomarker testing may have powerful indirect effects on all the stakeholders in the guardianship proceedings. Some will be positive in motivating individuals and families toward better planning; more negative effects may also occur. Although some individuals will refuse to be tested or receive the results, JENNIFER S. LIN ET AL., SCREENING FOR COGNITIVE IMPAIRMENT IN OLDER ADULTS: AN EVIDENCE UPDATE FOR THE U.S. PREVENTATIVE SERVICES TASK FORCE 57 (2013), https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0063382/pdf/PubMedHealth_PMH0063382.pdf [https://perma.cc/H89Y-TUET], those that receive the results may be spurred to modify their approach to life and life planning. *See* Holly C. Gooding et al., *Genetic Susceptibility Testing for Alzheimer Disease: Motivation to Obtain Information and Control as Precursors to Coping with Increased Risk*, 64 PATIENT EDUC. & COUNSELING 259, 265 (2006). This may even include arranging for later initiation of guardianship proceedings. This may give the patient, as well as the family, greater peace of mind, and even give the individual greater control over the choice of the guardian. If the individual has significant business dealings, taking the initiative may enable them to have a greater say in the succession of responsibility for business decisions. It may also give the individual the opportunity to seek targeted interventions short of guardianship, such as transferring power of attorney, creating joint financial accounts and trust arrangements. At the other extreme, identification of biomarkers may lead to depression or even attempts at suicide, which may hasten the guardianship proceedings as well. *See* Richard J. Caselli et al., *Predictive Testing for Alzheimer's Disease: Suicidal Ideation in Healthy Participants*, 29 ALZHEIMER DISEASE &

CONCLUSION

We have a strong societal interest in being able to accurately discriminate between intact from impaired cognitive functioning. As our population ages, the need to evaluate decision making capacity will become even more prevalent than it is today. On one hand, core societal, moral, or due process commitments demand that we give sufficient weight to individual autonomy in decision-making; it is critical to avoid premature determinations of incapacity. On the other hand, biomarker diagnostics of AD are on the near horizon and we need to anticipate their impact on the guardianship proceeding now.

Ultimately, the determination of how much of a deficit in functioning is sufficient to justify the restriction of individual liberties is a legal, social, and moral judgment, not a scientific or clinical one. However, this value judgment about competency is informed heavily by the capacity evaluation of an expert. The empirical foundation offered by biomarkers will only strengthen these evaluations. Although it is not meant to replace less quantitative measures in the assessment, biomarker evidence will become a significant tool that will assist courts in addressing the legal competency question. Diagnostics strengthened by biomarkers will become more prominent in our evaluation: how people behave should be informed by why people behave.[294] The objectivity and supplemental data offered by this evidence may eventually force us to reevaluate our tests for capacity or their relative significance.

At the same time, we need to recognize that while biomarker evidence offers large benefits, it also raises the possibility of misuse. This requires caution, as we consider uncertainty, biases, and privacy concerns. But that does not mean we should categorically reject the evidence. Instead, we will need to provide sufficient education to lawyers and judges to be able to scrutinize the methodology and soundness of the conclusions reached. We should take a lesson from other evidence-based measures used in law and develop guidelines for their use and interpretation in court.

ASSOCIATED DISORDERS 252, 252 (2015). And family members may be more observant in looking for indications of incapacity and may seek guardianship sooner, as well as pressure the individual to allow surrogate decision making at an earlier stage. *See* Greely, *supra* note 278.

294. Owen D. Jones & Timothy H. Goldsmith, *Law and Behavioral Biology*, 105 COLUM. L. REV. 405, 414 (2005).