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Abstract

Alzheimer's disease confronts us with an ethical challenge: How do we live with dignity and quality of life in the face of progressive disability and, ultimately, death? Patients' cognitive and decision-making impairments often make them unable to answer this question, and when professionals who provide services for older adults fail to recognize and accommodate these impairments, patients suffer. Patients and their caregivers need a health care system that fosters caregiving so that each will live with dignity and well-being. Another way to answer this question is to discover treatments that prevent disabling cognitive impairments, but this strategy will require expanding the Alzheimer's label to include people who do not have dementia or who are even cognitively normal. Controversies are likely to occur over how best to describe the Alzheimer's problem, measure the value of early diagnosis and treatment, and live with a brain at risk.

Keywords

elderly, ethical issues, legal/regulatory issues

Disciplines

Bioethics and Medical Ethics | Health Policy | Neuroscience and Neurobiology | Neurosciences | Other Legal Studies

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Abstract

Alzheimer's disease confronts us with an ethical challenge: How do we live with dignity and quality of life in the face of progressive disability and, ultimately, death? Patients' cognitive and decision-making impairments often make them unable to answer this question, and when professionals who provide services for older adults fail to recognize and accommodate these impairments, patients suffer. Patients and their caregivers need a health care system that fosters caregiving so that each will live with dignity and well-being. Another way to answer this question is to discover treatments that prevent disabling cognitive impairments, but this strategy will require expanding the Alzheimer's label to include people who do not have dementia, or who are even cognitively normal. Controversies are likely to occur over how best to describe the Alzheimer's problem, measure the value of early diagnosis and treatment, and live with a brain at risk.

Rising prevalence, increasing costs, and persistent failure to discover effective pharmacologic treatments have made Alzheimer's disease a national problem that evokes disaster images such as "silver tsunami" and "epidemic." The United

States is responding. In 2011 President Obama signed the National Alzheimer's Project Act into law. Commonly called NAPA, it has led to an integrated national plan.(1)

As policy makers develop and implement this plan, they should recognize that Alzheimer's disease confronts patients with an ethical challenge--"How do I live with dignity and quality of life in the face of progressive disability and, ultimately, death?" A system of laws, ethics, and social norms grants each of us the freedom to answer this question and to respect each other's autonomy to do the same, but patients with Alzheimer's disease face challenges in their ability to participate in this system.

Over time, patients not only develop disabilities performing daily tasks, such as taking their medications safely, but also develop impairments in deciding how best to manage these problems, a phenomena that reflects how patients often underestimate or even do not recognize their disabilities.(2) They also develop impairments in their decision-making abilities.(2-4) The failure to recognize and accommodate these complex disabilities can cause a patient to suffer harms; such as losses of dignity and respect, abuse, neglect, and exploitation. Our national plan for Alzheimer's disease therefore requires an ethical response.

First, early in the disease, patients vary in whether they retain the ability to make day-to-day decisions about matters such as money management and living arrangements. Professionals who provide services for older adults, especially in long-term care, and the legal, banking, and financial services industries need methods to assess and monitor their clients' decision-making abilities, and, when they detect impairments, take appropriate action. Secondly, as cognitive and functional impairments worsen, patients need other people, typically a family member or friend, to care for them. As these caregivers witness the person "die twice," first in mind and then a few years later in body, they make day-to-day and often ethically charged decisions for the patient as they themselves experience notable morbidity, especially depression.(5) Patients and their caregivers need a health care system that fosters caregiving so that each will live with dignity and well-being.

Another response to prevent the harms of losses of dignity and respect, as well as abuse, neglect, and exploitation, is to prevent Alzheimer's disease, and one of goals of the US national Alzheimer's plan (released in 2012) is that by 2025, the United States will discover a treatment that prevents, halts, or even reverses the onset of disabling cognitive impairments. Partnerships between the NIH, academia, and the pharmaceutical

industry have launched large-scale studies to reach this ambitious goal.(6,7) Discovering an effective treatment requires a diagnosis prior to dementia or even mild cognitive impairments, an approach that will need to accommodate a new understanding of the label "Alzheimer's disease:" It does not necessarily equate to having dementia or even any symptoms of cognitive impairment.

This understanding will present new ethical and policy challenges. As the number of people with Alzheimer's disease expands along a diverse continuum that includes people at risk of disability to those who are extremely disabled, controversies are likely to occur over how best to describe the Alzheimer's disease problem, how big it is, how to demonstrate the value of early diagnosis and treatment, and how to live with a brain at risk.

Facilitating Decision-Making

Medicine, psychology, and the law have made substantial progress developing and translating a conceptual model of decision-making capacity. The model requires that for a given decision, the clinician assess the person's decision-making abilities. This assessment informs the clinician's judgment whether the person is able to provide informed consent, or instead, needs assistance, or even someone else, to provide

consent. (8,9) Studies show that patients with very mild to moderate stage Alzheimer's disease have substantial variability in their decision-making abilities. They are able to express a choice, meaning they can state what they do or do not want, such as declining to attend an adult day-care program, but they often have clinically significant impairments in their abilities to understand relevant facts and appreciate how an intervention such as adult care will help them. (4,10) Comparing patients' capacity to make different decisions shows that they may retain the capacity to make one kind of decision, such as appointing a surrogate, but lack the capacity to make a more complex decision, such as whether to join a research study that involves a neurosurgical intervention. (11)

These findings explain why most very mild to moderate stage patients either make a decision with someone else or someone else makes decisions for them, (12) and that neither the diagnostic label of Alzheimer's disease dementia nor the scores on cognitive and functional measures from very mild to moderate stage disease can substitute for an assessment of decision-making capacity.

Medical decisions are, of course, just one kind of important and often ethically charged decision patients make. They also make decisions about long-term care, and legal,

banking, and other financial matters. Although the professionals in these fields may not know whether their clients have Alzheimer's disease, cognitive changes that impact everyday decision-making are common among older adults.(13) It would be very beneficial if these professionals had the skills to assess older adults' decisional abilities. The more they possess these skills, the better they can decide whether an older adult's decision is a decision to be respected, or instead, signals a problem in need of monitoring or even intervention.

These skills are especially important for professionals working in the financial services and banking industries. They are essentially on the front lines of screening for cognitive impairment because declines in financial decision-making capacity are among the earliest functional changes seen in people with Alzheimer's disease.(14) These professionals need professional standards and regulatory guidance that set out their obligations to identify people with impaired financial decision-making capacity, training in how to do this, and, how to address people with impaired capacity.(15,16)

However, it might be argued that non-medical professionals should not assess older adults' decision-making abilities because such assessments are medical matters. Certainly, in high stakes or contested decisions such as a major asset transfer or

whether to move from one home to another, medical consultation may well be essential, but as a matter of daily practice, physicians and the courts cannot be brought into adjudicating whether a patient has capacity to make each and every daily decision.

Older adults should at least expect that professionals who work with them are skilled in effectively communicating with them and their caregivers. The ability to assess capacity is among the skills of a good teacher. When, for example, an adult protective services caseworker asks an older adult who has had several emergency department visits for medication errors, "Do you think that using a weekly pill box for your medications could benefit you?" the caseworker is assessing the client's ability to appreciate the benefits of an intervention, which is one of the decision-making abilities physicians use to judge capacity. The caseworker is also engaging in good communication with someone whose problem managing medications suggests the presence of a cognitive impairment.(4) Caseworkers and discharge planners may find an instrument such as the Assessment of Capacity for Everyday Decisionmaking useful to assess and document a person's decision-making abilities.(3,4)

Enduring The Unendurable

This section's title is taken from one of Arthur Kleinman's essays about his wife's decline and ultimate death from Alzheimer's disease.(17,18) Kleinman, a psychiatrist and anthropologist, has studied the ways patients make sense of disease and the role clinicians have in eliciting patients' illness experiences.(19) Turning these skills to understanding his experiences caring for his spouse, he arrived at insights of substantial ethical and policy importance.

Kleinman came to see how the person with the disease and the person who cares for them essentially exchange roles. "She is happy much of the time. It is me, the caregiver, who, more often, is sad and despairing."(17) Studies reinforce this. Patients consistently rate their quality of life and functional abilities better than caregivers rate patients' quality of life and functional abilities,(2,20) and caregivers experience notable symptoms of depression.(5) In short, not only patients but their caregivers have an illness experience.

Kleinman's solution to endure this gradual exchange of roles is caregiving, a deeply interpersonal practice that resonates with matters of living, self, and dignity.(17) Because caregiving is an indelible part of what it means to be human, it is therefore among the foundations of our common moral experience. People such as Kleinman use this experience to make

day-to-day and often ethically charged decisions. Unfortunately, medicine and the health care system have largely neglected this foundation; for example, caregivers do not have ready access to education and training. In the care of people with Alzheimer's disease, this is a notable shortcoming because patients often underestimate or even entirely deny that they have functional problems, and, as a result, may decline care. In such a situation, the *caregiver* is the ethically appropriate means to provide *patient-centered* care. What follows are initiatives that policy makers can take to foster caregiving.

A 2012 NAPA-commissioned review of interventions to support caregivers found multiple randomized and controlled trials and translational studies that show psychosocial and environmental interventions and training can foster caregiving that, in turn, benefits both patients and their caregivers.(21) The Resources for Enhancing Alzheimer's Caregiver Health (REACH) studies, for example, show that intervention strategies such as education, problem solving, and telephone support groups can improve caregiver mood and well-being and reduce patient morbidity.(22) Unfortunately, interventions such as REACH are not part of the routine care of a person with Alzheimer's disease in the same manner as prescriptions for mildly effective symptomatic medications. A prescription for caregiver training should be as

available as, for example, nutritional consultation and education are part of the routine care of a patient with diabetes.

Other interventions that can foster caregiving include redesigning the electronic medical record (EMR).⁽²³⁾ The default design records the care of an individual patient who, via a "patient portal," remotely accesses it to check results and to communicate with providers. For patients who need caregivers, this design is insufficient. Caregivers need access to this exchange of patient information.. Medicare requirements for how clinicians should use the EMR need to include a record of the patient's caregivers and their roles, and allow them access to the patient's portal.

As patients decline, they have increasing needs for both palliative and hospice care, but delivering hospice care to them faces structural problems. Predicting that a patient with dementia has a six-months or less life expectancy and is therefore eligible for the Medicare hospice benefit is challenging.⁽²⁴⁾ Patients often live beyond this life expectancy, putting them at great risk of being discharged from hospice care. A sensible reform would be to allow patients with severe stage dementia to enroll and remain in hospice as long as it fits their goals of care, rather than their life expectancy.

"Enduring the unendurable" has been about the ethics of living with progressive and disabling cognitive impairments; that is, living with dementia. For much of the 20th century, Alzheimer's disease and dementia were tightly linked concepts. (25) Now, at the beginning of the 21st century, that link is beginning to fracture. In its place is a new concept of Alzheimer's disease, that it is a continuum of decline beginning when a person is cognitively normal. This presents novel challenges to living with Alzheimer's disease.

Preparing For The 'Brain At Risk'

Our approaches to Alzheimer's disease diagnostics and treatment as well as our understandings of its prevalence, costs, and personal and family burdens have relied on diagnostic criteria issued in 1984. (26) Often called the "McKhann criteria," shorthand for their lead author Guy McKhann, the criteria define Alzheimer's disease as a clinical diagnosis explained by a characteristic pathology. The clinical diagnosis describes a person whose history of cognitive and functional impairments follows a stereotypical pattern. The pathology that explains this dementia is commonly called "plaques and tangles of Alzheimer's disease," because between the neurons are dense deposits of a protein called amyloid (amyloid plaques) and

within the deceased neurons, there are tangles of fibrils (tau tangles).

By the close of the 20th century, researchers argued that numerous inconsistencies between what the 1984 criteria suggested researchers should observe versus what they actually did observe required new criteria. Their most provocative observations came from studies performing serial measures of older adults' cognition, function, brain structure and function, and tissues such as spinal fluid; and post-mortem brain autopsy. (27) First, Alzheimer's plaque and tangle pathology can be found post-mortem in older adults who were cognitively *normal*. Second, older adults with dementia typically have not only Alzheimer's pathology, but other pathologies as well, most notably vascular disease. Third, distinct measures of brain pathophysiology, commonly called "biomarkers," seem to predict which older adults start out cognitively normal, but, over time, develop disabling cognitive impairments.

In 2011, three National Institute on Aging-Alzheimer's Association workgroups revised the criteria for dementia caused by Alzheimer's disease and added two non-dementia stages to the disease: a mild cognitive impairment stage characterized by measurable impairments in cognition without dementia and a stage defined entirely by biomarkers and their connection to future

cognitive impairment, called "preclinical Alzheimer's disease." (28-30) The International Working Group for New Research Criteria for the Diagnosis of Alzheimer's Disease has also proposed similar criteria for "asymptomatic at risk for Alzheimer's disease." (31) Their *lingua franca* are the biomarkers and genes that might identify who will progress from cognitive normality or mild cognitive impairment to Alzheimer's disease dementia.

"Preclinical" or "asymptomatic at risk for Alzheimer's disease" are *not* concepts ready for clinical practice, but they are eligibility criteria for ongoing studies whose results will standardize biomarkers, distinguish normal from abnormal biomarker levels, and identify people in need of treatment. McKhann, some twenty-seven years after the publication of the criteria that informally bear his name, explains a view echoed by his fellow NIA workgroup members, that the most important of these studies are clinical trials. "The ultimate goal of these recommendations is to realign the clinical and research diagnostic approach with potential therapies... Waiting for the appearance of dementia would be tantamount to physicians trying to prevent heart disease in only those who have had a myocardial infarction." (32)

The National Institutes of Health (NIH), in cooperation with pharmaceutical industry partners, has committed at least \$100 million to four clinical trials whose goal is to identify cognitively normal people with either a genetic or biomarker-defined risk of cognitive decline in order to intervene with a pharmacological intervention that will slow this decline. The Anti-Amyloid in Asymptomatic Alzheimer's Study (the A4 Study), for example, a joint NIH- and Eli Lilly-sponsored randomized and controlled trial, is enrolling cognitively normal adults ages 65-85 who have elevated amyloid as detected on a PET scan to test whether three-and-a-half years of treatment with an anti-amyloid drug slows the rate of cognitive decline.(7) Similar studies are ongoing or are soon to start in cognitively normal people who are at heightened genetic risk of developing Alzheimer's disease dementia. If the studies are successful, they will begin to redefine Alzheimer's disease into a biomarker-based diagnosis that is largely independent of the clinical expression of the disease.

The conceptual model of these studies comes from clinical trials for other diseases of aging whose results established tight links among a biomarker, a drug that targets the biomarker, and an outcome measuring the chance of a future clinical event.(33) Clinical trials have transformed diseases

such as heart disease and osteoporosis from clinical to biomarker-based diagnoses, as, for example, the biomarker of cholesterol engenders statin treatment to reduce the risk of heart attack. Diagnosing and treating Alzheimer's disease in a preclinical stage has tremendous appeal to both an individual's health and the public health, but this also presents ethical and policy challenges.

A common feature of chronic diseases of aging is that they unfold slowly and insidiously, and then, in a thunderclap, the patient is sick. Stroke, heart attack, hip fracture, and acute congestive heart failure are dramatic events that share common features. They are easily measured and therefore easily quantified. These events are also readily understood by researchers, clinicians, patients, and policy makers. These features are of substantial advantage to translating into clinical practice the results of trials in diabetes, cardiovascular disease, and osteoporosis.

Alzheimer's disease prevention trials do not measure these kinds of events. Their primary endpoint is the slope of decline in a measure of cognition. This measure is a composite of several cognitive tests, most of which are not used in clinical practice. This endpoint presents a pressing problem: how to translate it into clinical practice and treatment guidelines?

This problem will have substantial importance and urgency because the number of people who are "biomarker positive" and therefore potentially eligible for a prevention therapy could be in the millions. For example, among adults age sixty-five and older who are cognitively normal, about one-third are amyloid positive on PET scans.(28)

Addressing this problem will require approaches that use the results of clinical trials and longitudinal cohort studies to create prediction models, also called algorithms, that demonstrate the kinds of patients who will benefit from interventions.(34) What data will be used, and how the models will be designed, interpreted, and updated are matters of interrelated scientific, ethical, and public policy importance. Unlike the Food and Drug Administration-regulated drug approval process, treatment algorithms and guidelines are typically developed by professional societies. They are more likely to experience the conflicts of interest that arise when professional, private, and scientific interests compete.(35)

As one or more combinations of biomarkers defines the disease, the prevalence of people with Alzheimer's disease will increase, but as it increases, it will begin to encompass a diverse spectrum of patients, ranging from those who have dementia, to persons who are cognitively normal but "biomarker

positive." These different kinds of people with the disease will undermine the ability of having one prevalence number to express the magnitude of the problem and therefore its costs.

As people are labeled with biomarker-defined Alzheimer's disease, they will have to live with and make sense of a label that renegotiates the boundaries between a healthy brain versus a brain at risk for a disease Americans fear even more than cancer. (36,37) People in the preclinical stage of the disease may well be working and want to purchase long-term care insurance, so legal reforms and professional initiatives will be needed to minimize discrimination in employment and insurability. Over time, despite treatment, some patients may develop symptoms and signs of cognitive impairment. This reiterates the importance of training professionals in law, banking, and finance on how to assess decision-making abilities and, if they detect impairments, the actions they should take.

Conclusion

One afternoon at the Memory Center where I care for patients, a caregiver interrupted his narrative of his wife's decline and insisted, "I have Alzheimer's disease!" In a sense, he's right. As researchers unleash Alzheimer's disease from the category of people with dementia to a continuum of cognitive decline, each of us is even more likely to have it. Short of a

cure, prevention will delay but not eliminate cognitive impairment. As this impairment slowly degrades a patient's autonomy, the disease will inevitably engage others and these caregivers will suffer as well. Whether as patients or as caregivers, we all have Alzheimer's disease. The question we must engage is how should we live with it?

Notes

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