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Renovating Alzheimer's: "Constructive" Reflections on the New Clinical and Research Diagnostic Guidelines

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The development of disease concepts for conditions such as Alzheimer's disease (AD) is an ongoing social process that evolves over time. The biomedical paradigm about AD that has informed our culture's understanding of brain aging for the past several decades is currently undergoing a major and timely renovation in the early 21st century. This evolution is reflected in new guidelines issued by the National Institute on Aging and Alzheimer's Association (NIA/AA) for the diagnosis of AD and related conditions that aim at helping researchers identify and eventually treat AD in its presymptomatic stages. The purpose of this article is to offer the scientific, clinical, and ethics communities a critical analysis of the implications of proposed guidelines and prompt deeper reflection about the lessons learned from these new efforts both in terms of their actual content and the cultural context in which they were issued and will be used. From a social-constructivist perspective, we explore the gradual 100-year evolution of AD and summarize the proposed NIA/AA guidelines within this historical context, enumerating what we see as their main benefits and limitations. We then consider the potential implications of these guidelines in the clinical setting, and explore shifts in our cultural paradigm about brain aging that might be engendered by the logic of the guidelines.

Key Words: Alzheimer's disease, Dementia, Social factors, Guidelines, Biomarkers

"In some ways disease does not exist until we agree that it does—by perceiving, naming, and responding to it." ~ Dr. Siddhartha Mukherjee, *The Emperor of All Maladies*

> Lydia thought long and hard about whether to enroll in a research study of biomarkers for Alzheimer's disease (AD). On the one hand, she'd like to know her risk, but how will her life change if she is found to have a biomarker? Who will she tell? Will she prioritize her life roles and tasks differently? Knowing in your 40s that you are doomed

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> unless there's a major research breakthrough is pretty heavy. How would her sister handle it? Will she want to be tested too? What about her children? Will they start to watch her differently, checking closely for mistakes she is making and interpreting them as AD? Even risks for cancer are different from this—with cancer you can *do* something, but there seems to be nothing you can do to prevent AD. Hopefully, she will hear that she lacks the biomarker and be able to go home free of fear. Lydia decides to attend the feedback session alone, not even telling her partner that she is enrolled in the study. She'll figure out the implications later if she has to. Fascinating to think that none of these early screening options existed a decade ago, when her mother had started her decline.…

Lydia's dilemmas reflect the personal level at which the evolution of a disease construct can generate confusion and distress. The purpose of this article is to offer the scientific, clinical, and ethics communities a critical analysis of the implications of proposed guidelines recently issued by the National Institute on Aging (NIA) and Alzheimer's Association (AA) for the diagnosis of AD and related conditions (Albert et al., 2011; McKhann et al., 2011; Sperling et al., 2011). We begin by establishing a social-constructivist perspective that is useful for understanding the metamorphosis of disease concepts over time, and then turn to a closer consideration of AD, summarizing the proposed NIA/AA guidelines while enumerating what we see as their main benefits and limitations. We then consider the potential implications of these guidelines—which are now ostensibly intended for research—in the clinical setting, and explore shifts in our cultural paradigm about brain aging that might be engendered by the logic of the new guidelines.

A Social-Constructivist Perspective on Disease

In every society, disease concepts are constructed rather than simply discovered in nature (Jobst, Shostak, & Whitehouse, 2000; Gaines, 1992). All diseases have a biological basis in the sense that all human function and dysfunction has a manifestation in the body; however, our perceptions of the underlying processes are shaped by social, political, and economic beliefs, values, ideologies, assumptions, and practices that influence the way conditions are treated, understood, responded to, experienced, and lived by individuals (Kleinman, 1988). Hence, every disease is also socially constructed, and scientific study of a disease never operates in a value-free environment but is given meaning and creates new meaning in settings that are social, economic, and political as well as intellectual. Consequently, the gradual understanding of maladies such as AD is an ongoing social process that evolves over time (Fox, 1989; Gubrium, 1986; Herskovits, 1995; Whitehouse, Maurer, & Ballenger, 2000).

To make the argument that diseases are socially constructed is not to invalidate conditions that cause real human suffering, such as AD. After all, it would be silly to doubt that a house is real because it underwent a process of human construction. However, like houses, disease constructs are built and demolished over time; some concepts are sturdy whereas others are hastily fabricated; some provide sufficient shelter for those who occupy them, and others create hazards. Both entities must be renovated over time if they are to best serve the human beings who inhabit them, and this truism takes on even greater meaning when one ponders the evolution of conditions such as hysteria, homosexuality, Asperger's syndrome, and countless others that have come and gone from societies over time.

The 100-year Construction of Alzheimer's

Alzheimer's disease is also subject to the vicissitudes of history, and the dominant molecular "construct" of AD is currently undergoing a major and urgently necessary renovation in the early 21st century. First identified by the German psychiatrist Dr. Alois Alzheimer in 1906, "Alzheimer's disease" was a terminology largely used to describe young onset dementia until the latter half of the 20th century when, due to a range of cultural forces—most notably an increase in longevity in developed countries, advances in scientific research technology, and astute political advocacy—AD replaced more vague terms like "senility" and came to be known as a specific late-life disease-event afflicting the elderly patients (Ballenger, 2006; Estes & Binney, 1989; George, Whitehouse, & Ballenger, 2011; Kral, 1962; Lyman, 1989; Whitehouse & George, 2008). In the past decade, hundreds of millions of research dollars have thus been invested in the amyloid cascade hypothesis and its promise to produce a pharmacological compound that would remove amyloid—the intracellular protein-based structure first documented by Dr. Alzheimer—and thus intercede in the neuronal death observed in AD (Castellani & Smith, 2011). However, multiple anti-amyloid compounds have failed in

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Phase 3 trials in the past decade (Selkoe, 2011), and these expensive, high-profile failures cast doubt on whether drugs that target amyloid pathways are a viable therapeutic option or whether amyloid-related biologies may actually play a protective role in the brain (Castellani et al., 2009; Castellani & Smith, 2011; Whitehouse, George, & D'Alton, 2011). Consequently, having failed to identify a singular causal or preventative pathway for a condition that emergently appears to be heterogeneous and age-related (Plassman, Williams, Burke, Holsinger, & Benjamin, 2010; Richards & Brayne, 2010; Whitehouse & George, 2008), scientists are rethinking the fundamental theories of specific causation that have dominated for a generation. Attempts are being made to rescue molecular conceptions by moving to more elusive and difficult-to-measure targets such as specific "oligomers" (small constituent proteins of amyloid) as the agents that do damage and need to be attacked. However, at some point the paradigm for any disease must shift and, with regards to AD, that shift is underway.

The AD field is now looking "upstream," conceding the fairly obvious: that the cluster of brain changes we now call "Alzheimer's" likely begins decades before symptoms appear, and hypothesizing that therapies administered earlier in the course of the condition might be more effective in forestalling neurodegeneration. As witnessed in the previous vignette about Lydia, AD guidelines are currently being restructured around this new theoretical framework of earlier causation and intervention. Specifically, in 2011, the NIA and AA issued new research guidelines for the diagnosis of AD and related conditions that ultimately aim at helping researchers establish biomarkers to identify AD in its presymptomatic stages and lead to hopeful prophylactic treatments.

It is imperative to think deeply about the lessons learned from these new efforts both in terms of their actual content and the cultural context in which they assume authority (Whitehouse & George, 2011). Guidelines for any medical condition can powerfully inform professional practice and public perception and thereby compose the scientific "scaffolding" of disease constructs. Therefore, critically engaging the current guidelines for a condition such as AD is not simply an academic exercise, but rather the responsibility of a civil and open society that must demand transparency and accountability from its scientific institutions. Not only do we owe circumspection to people who have dementia and must bear the immediate societal implications of new guidelines, or to physicians who may be putting guidelines into clinical practice in coming years, we also owe it to people like Lydia—not to mention ourselves—because we are all potentially at risk for age-related cognitive changes in coming decades.

Proposed Changes From the NIA/AA Guidelines

For full versions of the guidelines, readers are referred to earlier recommendations from the NIA–AA workgroups on diagnostic guidelines for Alzheimer's disease published in summer 2011 (Albert et al., 2011; Jack et al., 2011; McKhann et al., 2011; Sperling et al., 2011; these articles and accompanying commentaries can also be accessed by going to the web site of the national [U.S.] Alzheimer's Association [http://www.alz.org/research/diagnostic_criteria/]), as well as the articles "National Institute on Aging–Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease" (Hyman et al., 2012) and "National Institute on Aging–Alzheimer's Association Guidelines for the Neuropathologic Assessment of Alzheimer's Disease: A Practical Approach" (Montine et al., 2012).

The guidelines establish three defined stages in a clinical continuum: AD dementia, Mild Cognitive Impairment (MCI), and Preclinical AD. The least controversial of the new criteria is AD dementia. This criterion is met when there are clear deficits in two or more core cognitive domains, and activities of daily living are affected. AD dementia is characterized as either "Pathophysiologically proved" or "Clinical AD dementia." "Pathophysiologically proved AD dementia" is classified through meeting clinical and cognitive criteria for probable AD, and with the addition of "proof" through pathological examination. "Clinical AD dementia" is characterized by different degrees of certainty, including Probable AD Dementia, Possible AD dementia, and Not AD. The key differences between these categorizations and those from the past involve the expansion beyond a focus on memory impairment and the inclusion of biomarker evidence (in the form of amyloid and tau proteins in cerebral spinal fluid or visible with high-tech imaging) in making these classifications (McKhann et al., 2011).

Similarly, the criterion of MCI is met when there is concern regarding changes in cognitive functioning expressed by the individual, and when there is documented impairment greater than expected

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for a person's age and education in one or more cognitive domains although the person may function independently in social or occupational settings. However, this differs from the original formulations of MCI as now some degree of functional impairment is permitted, whereas previously activities of daily living were said to be intact (or relatively so). Probable etiology of MCI represents a subclassification scheme, and suggests various levels of probability that MCI is due to AD (Albert et al., 2011).

Finally, as illustrated in Lydia's story, the newest and most controversial criterion is that of "Preclinical AD." This category precedes MCI and encompasses the spectrum of presymptomatic autosomal dominant mutation carriers, asymptomatic biomarker-positive older individuals at risk for progression to MCI and AD dementia, as well as biomarker-positive individuals who have demonstrated subtle decline from their own baseline which exceeds that expected in typical aging, but would not yet meet criteria for MCI (Sperling et al., 2011).

At present, the guidelines are only intended for research. An earlier NIA/AA working group wrote: "This framework is not intended to serve as diagnostic criteria for clinical purposes. Use of these biomarkers in the clinical setting is currently unwarranted because many individuals who satisfy the proposed research criteria may not develop the clinical features of AD in their lifetime. Inappropriate use of this information in this context could be associated with unwarranted concern because there is currently insufficient information to relate preclinical biomarker evidence of AD to subsequent rates of clinical progression with any certainty" (Sperling et al., 2011, p. 287).

Benefits of the Guidelines

Scientifically, the new guidelines are claimed to offer greater precision than cognitive assessment tools in measuring the progression of AD, and may allow the inclusion of fewer research subjects studied over shorter intervals, thus lowering the cost of trials (Morris & Selkoe, 2011). In a broader sense, it is positive that scientists are abandoning failed "downstream" theories that have largely targeted plaques after clinical symptoms have appeared, and acknowledging that increased focus might be aimed "upstream" before neurological damage has been wrought. This essentially shifts AD from a "you have it or you don't" disease to a syndrome occurring along a continuum that encompasses normal, preclinical, MCI, and AD stages (Sperling & Johnson, 2012).

The paradigmatic focus on a continuum of severity and presymptomatic intervention is aligned with the general movement in U.S. health care towards greater emphasis on prevention. However, it is invariably the case that with the establishment of a preclinical phase to the illness, established risk factors for dementia—including toxic exposures, smoking, under- and over-nutrition, stress and depression, physical and cognitive activity, head injuries, etc.—become more relevant as contributors that may postpone or expedite one's progression along the continuum. While evidence is insufficient to support the association of any one modifiable factor with reduced risk of AD (Plassman et al., 2010; Williams, Plassman, Burke, Holsinger, & Benjamin, 2010), many believe that it will be more fruitful to study combinations of protective behaviors across the life course that can act directly on known contributors to neurodegeneration (i.e., inflammation, oxidative stress, hypoperfusion, impaired metabolism, physical injury, etc.; Centers for Disease Control and Prevention and the Alzheimer's Association, 2007; Hertzog et al., 2008; Whitehouse & George, 2008). Societally, taking a more aggressive approach to addressing known or presumed life-span risk factors for brain aging can shift therapeutic options away from an exclusive focus on drugs while illuminating the importance of investing in public health approaches and addressing socioeconomic disparities that perpetuate exposures to known risk factors for dementia. A renewed focus on prevention can provide hope that a new, more broadly conceived generation of therapeutic approaches can be more effective than the hitherto failed "downstream" interventions of the early 21st century. That said, there are prominent concerns and limitations about the proposed guidelines that deserve elaboration.

Limitations of the Guidelines

Downplaying Autopsy

Over the past several decades, it has been common wisdom that a definitive diagnosis of AD was possible only upon autopsy. Autopsy diagnosis was built upon findings of specific pathophysiological markers: cell loss, amyloid plaques, and neurofibrillary tangles. However, ample research from studies around the world has demonstrated that neuropathological markers of AD are

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heterogeneous and overlap with markers of normal aging and other dementias such as frontal lobe and vascular forms (Hachinski, 2008; Schneider et al., 2007; Snowdon, 1997; Snowdon et al., 1997), creating major doubt about the capacity of autopsies to provide "definitive" diagnosis. The new guidelines signal uncertainty by questioning the value of using neuropathological changes at autopsy as predictors of clinical symptoms. The new neuropathology guidelines essentially disengage autopsy findings from clinical features by creating a label "Alzheimer's disease neuropathological change" that can be applied without knowledge or reference to a clinical diagnosis of dementia.

In place of autopsy, the guidelines propose the consideration of less well understood and more difficult to validate early biomarkers that are justified through their linkages to later pathological features. It is not unreasonable to believe that future advances in accuracy using amyloid or tau, coupled with standardization, could eventually produce an effective (though imperfect) biomarker, and such a biomarker would be independent of the debate of whether amyloid is a marker of a "disease" or rather a marker of upstream neuronal damage (i.e., a marker of "brain health"). However, at present, it is still justifiable to ask if early biomarkers can be more accurate predictors of clinical course than those found in the supposed "disease-state" brains at autopsy? (Whitehouse & George, 2011). If autopsy examination is not suitable for validation, then couldn't inadequately understood biomarkers likewise be flawed? Indeed, many expert comments in the guidelines emphasize that we do not have early markers well standardized, nor do we understand which are best for which purposes and how they relate to each other. We can fairly ask whether these purportedly "new" guidelines are still largely trapped in the increasingly untenable "amyloid box" that assigns primary causative properties to amyloid (D'Alton & George, 2011). Fealty to old theories can be obscurant of new theoretical perspectives that might engender greater progress.

Blurring the Intended Audience

While the guidelines are nominally for researchers, there has been considerable confusion during their development as to whether the recommendations are just for researchers or clinicians, or both. Final drafts suggest that the asymptomatic guidelines are for researchers, the MCI in different forms (such as amnestic or multidomain types which can be preludes to different types of dementia) for both, and the dementia ones more for clinical use. Yet researchers may not be likely to accept the guidance of a small group of experts and may choose to take less conventional approaches in studying biomarkers that are not explicitly part of the new guidelines. Moreover, health care professionals wish to know much more about the clinical utility, public health, and economic implications of the recommended biomarkers before considering them for practice. As mentioned, the papers are full of caveats about the fact that biomarkers are not standardized, perhaps not even reliable except in narrow research settings, and certainly not validated. And even if biomarkers do eventually become validated, in the absence of an effective treatment for people like Lydia who would receive the stigmatizing diagnosis of preclinical AD, there is still major concern about potential clinical usage.

Creating Confusion in the Lay Public

Indeed, with regards to Lydia, the conversation in which researchers or health providers disclose diagnostic or prediagnostic information contains complex biomedical information that most lay people will struggle to understand (Rudd, Moeykens, & Colton, 1999). Diagnostic information typically contains a label along with a description of the entity referenced by the label, including etiology, associated symptoms, alternative interventions, and trajectory of the illness. In the case of biomarkers for AD, the information also contains probabilistic statements specific to many different biopsychosocial contexts, along with disclaimers regarding the validity of currently known biomarkers. Low rates of health information literacy (and numeracy) are significant challenges for consumers, researchers, and providers (Nielsen-Bohlman, Panzer, & Kindig, 2004), leading to a fairly high probability that accurate, carefully articulated and detailed information would be misunderstood.

Despite the potential for confusion, consumers desire information for their own planning purposes. Researchers have already investigated the interest among consumers in obtaining information about the presence of one marker of genetic risk for AD, apolipoprotein (ApoE) e4 allele on chromosome 19 in the Risk Evaluation and Education for Alzheimer's Disease (REVEAL) study (Roberts et al., 2003; Roberts & Tersegno, 2010).

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What do people take away from a disclosure about risk for dementia? Interestingly, in REVEAL, knowledge about the presence or absence of the ApoE allele was well retained, whereas knowledge about risk probabilities was poorly retained (Roberts et al., 2004). Furthermore, pretest intuitive risk estimates appeared to function as anchors for the actual information received, distorting memory for the data even among samples of educated, motivated volunteers. Little interaction has occurred between the biomarker and the genetic marker research communities, at least as has been expressed in the guidelines. But it is apparent from REVEAL that scientifically uncertain (e.g., estimates of risk vary depending on theoretical modeling and empirical data across different ethnic groups) and complicated health information may not be of clear value to prospective patients or their possible future caregivers. Lessons from REVEAL about consumer interpretation of complex information should be a consideration as biomarker research progresses.

Neglecting Economic Costs

It is peculiar that the guidelines give no consideration to any issues of an economic nature, and, given that the authors do not recommend a single well-defined package of tests, it is difficult to calculate the cost to society. However, a previous article (Whitehouse & George, 2011) used a modest (and probably low) estimate of approximately $5,000 per person added to the number of people with various forms of MCI and dementia in the United States alone (perhaps 20 million) and emerged with a projection of $10 billion. This raises concerns about opportunity costs. Every dollar spent on biomarkers represents money not spent on public health and education about prevention, or care, quality of life, and psychosocial wellbeing for persons with dementia, or support for caregivers, and so on.

Neglecting Social Costs

Even if we did spend this money on biomarkers for early diagnosis, what would we know and how would we use it to benefit individuals and society? Imagine a future in which people like Lydia would be told that their chances of late-life dementia are probably greater than they knew before they participated in the testing process. In reality, because AD syndrome has such variability, we may still have little idea of how much risk would be greater and even what set of conditions we are talking about being at risk for. And how many people would be given erroneous information (i.e., false positives/false negatives) because of our incomplete understanding of biomarkers? As Lydia ruminated over, stigma for AD is profound and pervasive. And the terror of the condition is invariably deepened by the lack of a viable treatment. These social costs are not given sufficient concern in the guidelines, but must be a deep consideration moving forward.

Considering Conflicts of Interest

Recent reports have demonstrated that the prevalence and under-reporting of conflicts of interest by members of guideline panels in the United States and Canada are high (Neuman et al., 2011). From an ethical perspective, it is imperative to think critically about who helped construct these guidelines and what conflicts of interest may exist. Both the NIA and the AA are dependent on funding from public and private sectors based on the sense of urgency they can create around the conditions they study. Many of the authors of the guidelines are consultants to drug companies, and the field itself is strongly influenced by the pharmaceutical industry, whose economic interests powerfully shape and influence human comprehension of biological processes. It is fair and necessary to ask whether these guidelines were constructed in an adequately unbiased and systematic way. Where was the representation of other (less politically positioned) experts on guideline construction, or the representation of people potentially most affected by the guidelines (caregivers and persons with dementia)? Any guidelines should be the focus of a serious attempt to evaluate validity, utility, and social implications before widespread introduction.

Potential Implications for the Clinical Setting

Sharing diagnostic information is an inherently social process that has broad implications for many lives. The initial clinical encounter is between provider (or researcher) and consumer (patient or participant) where information is relayed with mixed outcomes in understanding, memory, and impact. Consumers in the REVEAL study claimed motives that were not well addressed by the information disclosed (e.g., long-term planning is hard to do based on probabilities) which raises ethical issues regarding the

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critical material that needs to be covered in the informed consent document that participants sign when enrolling in research.

Inevitably, diagnostic risk information has interpersonal implications for the consumer's primary relationships as well. For preclinical AD risk statements, research on the familial impact of information sharing needs to be salient within the research agenda. With whom will consumers like Lydia share the information? Will the social sharing process vary based on the findings (e.g., are you more likely to share if you have the biomarker or if you do not have it?). How accurately will information be passed from consumer to others? How will primary family members discuss it among themselves, and with what effects on social relationships of consumers, such as Lydia's children, partner, friends, and co-workers?

Clinical observations have shown that families easily confuse the meaning of labels that cross over between technical terminology and lay language, such as "dementia" (Gray et al., 2009). Families may experience relief when labels other than the most feared appellations (e.g., AD) are used, regardless of the potentially more devastating meaning of the less familiar label (i.e., "She has dementia, but not Alzheimer's"). Further, it is reasonable to wonder how families will process imprecise probabilities about risk that might include difficult-to-understand data on biomarkers with other risks factor information such as age, family history, and lifestyle.

And, as Lydia worried about, how will families interact with adults known to have biomarkers for AD? We know that early behavioral signs of dementias are highly ambiguous for families to interpret (Teel & Carson, 2003). Post diagnosis, family members report having observed problem behaviors for years that they interpreted in benign ways or experienced as frustrating (Nichols & Martindale-Adams, 2006). Even troubling behavioral symptoms such as memory lapses and poorly executed familiar behavior sequences are not easy to interpret, leading primary caregivers to endorse multiple potential causes for signs of significant cognitive impairment. The constant confusion is experienced as stressful even at the level of MCI (Blieszner et al., 2007). The known presence of a biomarker may lead to earlier help seeking by families who interpret early behavioral signs of AD as symptoms. Alternatively, knowledge of the biomarkers may lead families to seek confirming behavioral evidence (Leventhal, Meyer, & Nerenz, 1980), including over-pathologizing of normative cognitive errors. In short, research is needed to determine how the known presence or absence of a biomarker influences common-sense symptom identification and help-seeking process (Leventhal, Forster, & Leventhal, 2007).

Further, the family system communicates information, presumably including health information, in nonlinear ways (Watzlawick, Beavin, & Jackson, 1967). Health care providers often presume that information will be shared accurately within families in a linear fashion that ensures the same information arrives to members in a logical, sequential manner of information-sharing. However, much like the children's game of "telephone," families communicate in nonlinear ways filled with feedback loops and revision of intentions and goals. They send messages from one person to another to another, with responses to the information feeding forward as well as backward. Such relational complexity needs to be considered when determining research of clinical protocols about complex biomarker information, especially genetic markers that may have direct implications for other family members.

Further, cultural variations in the role of families in the lives of patients and their care enhance the complexity of analyzing ethical approaches to disclosure of biomarker information, and pose challenges to clinicians seeking to ally with patients and families in assessment and intervention (Akinleye et al., 2011; Yeo & Gallagher-Thompson, 2006). Whereas health providers view relatives as circling but not touching the patient, families tend to view relatives as central in their own network (a more individualistic model), or as small, embedded members in a larger family system (a more familistic model). These variations imply that cultural rules for family structures will influence the impact of preclinical or clinical diagnostic information on many persons in the family system of older adults. Inclusion of family voices in the ethics conversations about biomarker research and use is critical.

Potential Shifts in the Cultural Paradigm

Moving Towards Life Span, Intergenerational Approaches to Brain Health

Certainly, by focusing decades earlier in the neurodegenerative process than had previously been

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within the ambit of the amyloid cascade hypothesis, the guidelines appear to be supporting the view that AD is a heterogeneous set of life-span conditions rather than an end-of-life disease event (Whitehouse & George, 2008, 2011). With the increasing global prevalence of dementia, and the realization that disease-modifying drugs may not be available in the foreseeable future (or ever), the guidelines can serve as a watershed moment in which our society questions the promise of a pharmacological fix. Our multiage communities can use drug failures that have marked the past decade as a stimulus for growing more reflective about the myriad modifiable risk factors—dietary patterns, exercise, stress levels, toxic exposures, health care access, head injuries, lifelong learning, and other risk factors present in our shared built and natural environments—that affect brain aging processes from in utero through the end stages of our lives (Ferraro & Shippee, 2009; Gubrium, 1972; Stein, 2008), and more open to evidence-based nonpharmacological community programs for dementia care (Teri et al., 2012).

Viewed in this way, the quality of life enjoyed by elders depends on how they have been taken care of and educated as children and across the life span: a reality that can inform a shared intergenerational ethic (Chambre, 1993; George, Whitehouse, & Whitehouse, 2011). What can follow from this powerful ethic are actions taken by people such as Lydia that encompass: eating more fruits and vegetables and less red meat (and making healthy foods more available in one's community, particularly to the underserved), wearing bike helmets (and making sure neighbors have access to good quality helmets), reducing pollutants and toxins in our homes and neighborhoods (and recognizing the pressing need to address this problem in our poorest areas), and volunteering—steps that protect community members who are all susceptible to age-related changes. Although evidence for particular interventions is limited (as alluded to above), healthy, multigenerational, egalitarian communities with greater human capital will produce healthier brains, and it will be the responsibility of science and other sectors of society to not just beat the drum for molecular biology, but to better communicate the worth of life-span preventative measures to the public.

Empowering Patients and Families in the Clinic

Giving patients and families the choice to self-determine the labels and stories they take forward can be empowering. Some prefer a clinical approach that medicalizes memory loss; others do not feel as comfortable with biomedical jargon and would benefit from a less medicalized approach, for instance speaking about the condition as "brain aging" or "senility" rather than a specific disease. In moving society away from the "You have it or you don't" paradigm of AD, the guidelines validate the uncertainty and contingency of clinical diagnosis. Out of this ambiguity can emerge a renewed understanding that illness narratives matter (Kleinman, 1988), and that patients and their families need not merely acquiesce to the labels suggested by their doctors. We have written elsewhere of our preference for using the language of "aging-associated cognitive challenges" in clinical settings, because a "challenge" is something that can be risen to and perhaps even serve as a source of growth (Whitehouse & George, 2008). Clearly, empowered patient choice will be a function of increased public knowledge about AD, and it is therefore imperative to continue educating the public—people like Lydia and her family members—about this condition, and identifying clinical strategies that encourage self-determination.

Conclusion

After a century of existence following the initial case study shared by Dr. Alzheimer in 1906, the dominant cultural paradigm about AD is changing once again, as evinced in the conceptual renovations embodied by the NIA/AA guidelines. Depending on how our culture constructs this new paradigm, we can recapitulate the scientific, social, and ethical errors of the past 30 years, or we can amend our conceptual understanding so that it is ballasted by new theories, ideas, values, metaphors, language patterns, and vignettes that have the potential to reinvigorate public health: creating a new ethos of solidarity among the generations, emphasizing quality of life over sheer length, and fortifying us with the strength to accept certain realities about our mortal bodies and brains over time. In bringing about this future, we would do well to remember that a long history of critique about concepts of AD exists, and that the march to progress is by no means straightforward and the ultimate goals not certain. Ironically, this critical process began with the words of Dr. Alzheimer, who, in 1911 reflected on his early observations of AD and perhaps presaged our current scientific predicament, writing: "There is, then, no tenable

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reason to consider these cases as caused by a specific disease process" (Alzheimer, 1911).

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