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Diversity and Disparity in Dementia: The Impact of Ethnoracial Differences in Alzheimer's Disease

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Abstract

Debate exists regarding differences in the prevalence of Alzheimer's disease (AD) in African Americans and Hispanics in the United States, with some evidence suggesting that the prevalence of AD may be considerably higher in these groups than in non-Hispanic whites. Despite this possible disparity, patients of minority ethnoracial groups often receive delayed diagnosis or inadequate treatment for dementia. This review investigates these disparities by conceptualizing the dementia disease process as a product of both biological and cultural factors. Ethnoracial differences in biological risk factors, such as genetics and cardiovascular disease, may help to explain disparities in the incidence and prevalence of AD, while race-specific cultural factors may impact diagnosis and treatment. Cultural factors include differences in perceptions about what is normal aging and what is not, lack of adequate access to medical care, and issues of trust between minority groups and the medical establishment. The diagnosis of AD in diverse populations may also be complicated by racial biases inherent in cognitive screening tools widely used by clinicians, but controlling for literacy level or using savings scores in psychometric analyses has the potential to mitigate these biases. We also suggest that emerging biomarker-based diagnostic tools may be useful in further characterizing diverse populations with AD. Recognizing the gap in communication that exists between minority communities and the medical research community, we propose that education and outreach are a critical next step in the effort to understand AD as it relates to diverse populations.

Keywords

Alzheimer's disease; ethnic groups; health disparities; literacy

Introduction

Afflicting approximately 30 million people worldwide[1,2], Alzheimer's disease (AD) is one of the leading causes of morbidity and disability among the elderly. With the continuing rise of the elderly population in the United States, dementia and AD in particular represent increasingly important public health concerns. Recent years have also witnessed a demographic shift in the United States, such that an increasing proportion of the population is comprised of minority ethnoracial groups. For instance, the U.S. Census Bureau reported in 2008 that "black persons" and "persons of Hispanic or Latino origin" represented 12.8 and 15.4 percent of the population, respectively, and these percentages have grown

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significantly in recent years.[3] While it still remains controversial whether substantial differences in the prevalence and incidence of AD exist between white and non-white populations, a growing body of evidence suggests that AD may disproportionately afflict minority ethnoracial groups in the U.S.[4-8]

This review seeks to clarify ethnoracial differences in AD by examining the disease process as a product of both biological and social factors. The pathophysiology of AD is defined by disease-specific biological changes in the brain that underlie symptomatology, but is also impacted by other biological risk factors that may predispose an individual to dementia. Evidence suggests that there may exist ethnoracial differences in risk factors associated with AD, such as genetics and co-morbid cardiovascular disease. Differences in these risk factors may help to explain some differences in the incidence and prevalence of AD with respect to race. However, they do not necessarily explain why Hispanics may present with more severe clinical symptoms at first onset [9] yet live longer with the disease,[10] or why African Americans may receive inadequate treatment for AD.[11-13] Social and cultural factors greatly influence the way in which AD is diagnosed and treated. As a result, the disease process manifests as a complex interaction between biology and culture that may differ greatly across ethnoracial groups.

Improved diagnosis and care for minority patients with AD will require a greater understanding of the complex interaction between these factors. Technological advances, such as the development of biomarkers for the early detection of pathological changes in the brain, may aid in the proper diagnosis of AD within diverse populations, while a greater understanding of certain patient and caregiver attitudes toward dementia may facilitate care. Given the shortage of primary care physicians (PCPs) in the U.S., especially for the elderly,[14] bridging ethnoracial disparities in dementia will depend upon interdisciplinary efforts between PCPs, nurses, neurologists, psychiatrists, and others.

Epidemiologic Differences and AD

Numerous studies have been conducted that examine differences in the prevalence and incidence of AD across ethnoracial groups, particularly whites, African Americans, and Hispanics or Latinos, with varied results. Although there does not yet exist a consensus, a growing body of evidence suggests that both the prevalence and the incidence of AD may vary substantially between different ethnoracial groups. Demirovic and colleagues found a significant difference in the prevalence of AD among African American men and white non-Hispanic men (14.4 vs. 5.4 percent) in a community-based study of one region of Florida.[4] In a separate seven-year community-based study, Tang and colleagues sampled and interviewed Medicare recipients ages 65 years and older in New York City.[5] They found that the cumulative incidence of AD to 90 years of age was approximately two times greater among African American and Caribbean Hispanic individuals than among white non-Hispanic individuals.[5] These analyses controlled for medical history, such as history of heart disease, stroke, and cardiovascular and cerebrovascular disorders, as well as other demographic factors, such as level of education and literacy. Nevertheless, the lack of a population-based sample in these studies hinders the generalizability of these results.

The Alzheimer's Association estimates that the prevalence of AD and other dementias in African Americans above the age of 65 years is about twice the rate among elderly whites, while the prevalence in Hispanics is approximately one and a half times greater than in whites.[6] In reaching these estimates, the Alzheimer's Association specifically used data from the Aging, Demographics, and Memory Study (ADAMS)[7] and the Washington Heights-Inwood Columbia Aging Project (WHICAP).[8] Findings from ADAMS show that 21.3 percent of African American subjects aged 71 years and older were diagnosed with

dementia, as compared to 11.2 percent of white subjects. Similarly, WHICAP reports dementia prevalence rates of 18.8 and 7.8 percent for African Americans and whites, respectively, aged 65 years and older. However, neither study unequivocally establishes ethnicity as a critical and independent predictor of AD. ADAMS only reports prevalence figures for the diagnosis of dementia unspecified. Therefore, it is possible that the increased prevalence of dementia in African Americans may be attributed to an increased prevalence of dementias other than AD. This would be consistent with findings that African Americans have a higher risk for vascular dementias as compared to whites.[15,16] In addition to demonstrating that rates of dementia were higher among African Americans and Hispanics than whites, the WHICAP study also found that the proportion of dementia cases diagnosed as AD was similar across ethnoracial groups, implying that AD was more prevalent in their minority populations. However, WHICAP raises other questions regarding the source of variability in prevalence figures. After controlling for age and education in its analyses, ethnoracial differences in the prevalence of AD were no longer statistically significant.

Furthermore, not all of the epidemiological data has been consistent or conclusive. In a study of individuals ages 68 years and over in the Piedmont area of North Carolina, Fillenbaum and colleagues reported no significant difference in the prevalence of AD among African American and white individuals – 7.0 and 7.2 percent, respectively.[17] In addition, Hendrie and colleagues found that the prevalence of AD in a similar cohort of African American subjects in Indianapolis, Indiana (including both community-dwelling and institutionalized patients) was 6.24 percent,[18] well within the confidence interval for the prevalence figure in whites reported by Fillenbaum and colleagues.[17] The Indianapolis/Ibadan studies also showed that the prevalence and incidence of AD were significantly lower among Africans in Ibadan, Nigeria than among age-matched African Americans in Indianapolis,[18,19] suggesting that differences in environmental factors, such as nutrition,[20] may play a larger role than race in influencing the development of AD. It is possible, however, that much of the variability in results across studies may be explained for by differences in experimental methodology.[21] In order to accurately compare prevalence and incidence figures between studies, investigations would need to be standardized with respect to a variety of factors, including criteria for ethnoracial grouping, inclusion criteria, diagnostic criteria, and others.

The association between race and AD still remains unclear for a variety of reasons. Perhaps the clearest reasons are the diversity within each ethnoracial group and the lack of understanding of the biological basis of race as well as the pathophysiologic basis of AD. In epidemiological studies of AD in diverse populations, race may be used as a surrogate marker for other, more important risk factors in the development of dementia. For example, differences in educational attainment between ethnoracial groups may account for much of the race-specific variability in prevalence figures.[8] Several researchers have even suggested that the biology of race may be entirely unrelated to the pathophysiology of AD,[22] while others contend that certain race-specific biological risk factors, such as vascular disease, may play a larger role in African American populations.[6]

Biological Basis of AD: Risk Factors in Diverse Populations

Epidemiological data suggests that certain risk factors for the development of AD may be more prevalent in African Americans and Hispanics than in whites, while other risk factors may play a smaller role. For example, differences in the prevalence of cardiovascular risk factors are often implicated in potentially accounting for some of the racial disparities in the prevalence and incidence of AD.[6,15] The Health and Retirement Study (HRS) found that high blood pressure was significantly more common in African Americans than in whites or Hispanics, while the prevalence of diabetes mellitus was higher in both African Americans

and Hispanics than in whites.[6] Since numerous studies have previously established cardiovascular diseases, including high blood pressure, diabetes, coronary artery disease, and stroke, as risk factors for AD and other dementias,[23-26] racial differences in cardiovascular health may contribute to racial disparities in AD.

Much research has also been conducted examining the potential contribution of genetics to AD risk, progression, and pathophysiology. Polymorphisms in the apolipoprotein E gene (APOE) have been found to play a significant role in the presentation of AD. The ε4 allele has been associated with increased risk of AD as well as earlier onset of the disease, while the ε2 allele has been associated with decreased risk of AD.[27] However, the role that ethnicity plays in influencing the effects of genetics on disease phenotype remains unclear. Population-based studies in New York, NY[28] and Chicago, IL[29] found that the APOE ε4 allele did not significantly increase the risk of AD among elderly African Americans, though the presence of the allele did increase risk in whites. In contrast to these findings, data from the population-based Indianapolis cohort found that the ε4 allele was a significant risk factor for AD in African Americans, while APOE ε2 had a protective effect.[30] These differences across studies may have resulted from differences in population characteristics. The frequency of the APOE ε4 allele varied within the African American control groups across studies, from 17.6 percent[30] in the Indianapolis cohort to 20.1[28] and 20.9 percent[29] in the New York and Chicago cohorts, respectively. The role of APOE in modifying risk of AD in non-white populations requires further clarification.

Other genes aside from APOE have also been identified that may represent independent risk factors for the development of AD. One of these genes of interest is the apolipoprotein D gene (APOD), which encodes a lipoprotein-associated glycoprotein involved in the transport of cholesterol, similar to the function of ApoE.[31,32] Researchers have found that levels of ApoD are significantly elevated in the CSF and hippocampi of AD patients.[31] Furthermore, research showing that ApoD deposits in the brain co-localize with dense fibrillar amyloid beta plaques suggest that ApoD may have a role in the pathogenesis of AD.[33] APOD gene polymorphisms may also have specific applications to the study of AD in diverse populations. Desai and colleagues[34] identified four polymorphisms of APOD not found in whites, but rather unique to populations of African ancestry, and found that one of these polymorphisms was associated with an increased risk of AD among African Americans in the population-based Indianapolis cohort described by Hendrie and colleagues.[18]

Recent studies have also identified an association between certain single-nucleotide polymorphisms in the neuronal sortilin-receptor gene (SORL1) and the risk of AD.[35-37] Furthermore, Lee and colleagues found that this association was significant in both African Americans and Hispanics in addition to whites,[37] though not all subsequent studies have supported this conclusion.[38] Researchers believe that the product of SORL1 mediates intracellular transport of the amyloid precursor protein (APP) and that deficiency of this protein may contribute to increased cleavage of APP leading to increased production of amyloid beta.[35] CSF levels of the SORL1 protein product are currently being studied as potential biomarkers for the early diagnosis of AD.[39]

AD is most likely a multifactorial disorder influenced by the interaction between numerous genes. For example, certain polymorphisms of the catechol-O-methyltransferase gene (COMT) and APOE ε4 have been found to have a synergistic effect on the risk of AD, even though COMT may not be an independent risk factor.[40,41] Epidemiologic studies support the presence of a genetic component in the development of AD regardless of race.

Green and colleagues found that first-degree relatives of African American probands were 1.6 times more likely to develop dementia by age 85 than first-degree relatives of white

probands.[42] However, even though first-degree relatives share similar genetics, they may also share similar environments, thus potentially confounding the effects of genetics with the impact of environment. The authors attempted to control for the effects of shared environment by using spouses as a surrogate control group, assuming that spouses shared similar environmental determinants with the probands without sharing any genetic information. The study found that spouses of African Americans with AD were 1.6 times more likely to develop AD than their white counterparts.[42] The additional risk conferred by being a first-degree relative as compared to being a spouse was similar among African Americans and whites (RR=2.4 and 2.6, respectively), suggesting that the AD risk attributable to genetics may be similar among both ethnoracial groups[42], even if the specific genes involved vary between groups.[28,29,34] These results also suggest that factors other than genetics may account for a large proportion of the increased risk of AD in non-white populations[28], and they may be explained for in part by differences in the prevalence of vascular disorders.[6]

The differences in the clinical presentation of AD in African Americans and Hispanics as compared to whites also remain poorly understood. Recent evidence from the Penn Memory Center (PMC) in Philadelphia suggests that Hispanics present with an earlier age of onset of AD and that both African Americans and Hispanics exhibit a greater severity of symptoms at the time of onset.[9] Hispanics presented with more cognitive impairment and greater severity of dementia, while both Hispanics and African Americans presented with more depression at the time of initial evaluation than white patients with AD. Also, similar to findings by Tang and colleagues,[28] Livney and colleagues did not find an association between APOE genotype and AD in the Hispanic cohort. Nevertheless, this study only examined a self-selected cohort of patients seeking treatment at the PMC. The cohort included 1,507 people who were self-referred, referred by their primary care providers, or recruited through outreach efforts in the West and North Philadelphia areas. Patients included in the study received a consensus diagnosis of either no cognitive impairment or AD from a group of experienced clinicians at the PMC, including neurologists, psychiatrists, and neuropsychologists. Since this cohort may not be reflective of the general population, larger population-based studies are needed to accurately characterize the differences in the clinical presentation of AD among different ethnoracial groups.

Screening and Diagnostic Techniques in Diverse Populations

One of the greatest challenges in studying ethnoracial differences in the epidemiology, risk factors, and clinical presentation of AD is establishing an accurate diagnosis of AD in diverse populations. In order to make appropriate inferences across studies, researchers must find ways to validate and standardize the diagnosis of AD across ethnoracial groups. The core diagnostic criteria for AD employed by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer Disease and Related Disorders (NINCDS-ADRDA) focus on the presence of progressive impairment of episodic memory that is demonstrable on testing, with or without other cognitive deficits.[43] Although efforts are underway to revise these diagnostic criteria to more fully incorporate biological markers of the disease,[44] the clinical diagnosis of AD continues to rely primarily on the evaluation of cognitive symptoms, such that the sensitivity and specificity of diagnosis often rely heavily on clinicians' expertise with measures of cognition. Although diagnosis in the research setting typically includes a battery of neuropsychologic tests and neuroimaging procedures, AD is still very much defined by a clinical phenotype. Considering that the clinical presentation of AD may vary across ethnoracial groups and may be further complicated by other forms of dementia, current psychometric diagnostic techniques may be less sensitive and/or specific in certain populations.

Although the Mini-Mental Status Exam (MMSE) is not a specific instrument for the diagnosis of AD, it is commonly used by physicians in various clinical practice settings to screen for deficits in cognition suggestive of dementia.[45,46] Recent studies have suggested that the MMSE may have low specificity within minority populations, with up to a 42 percent false-positive rate for cognitive impairment among African Americans as compared to a 6 percent rate among whites.[47] Although age, education, and socioeconomics status may affect MMSE scores, racial bias often persists even after controlling for these factors.[48] A potential explanation for this finding is that there may exist ethnoracial group-specific factors not controlled for by traditional demographic data that influence scores on neuropsychological assessments.[22] For example, low education has previously been established as a significant risk factor for the development of dementia,[49] but there exists only a relatively weak association between years of education and dementia risk among African Americans.[50] Research has shown that quality of education, as measured through literacy, is more sensitive than number of years of education in predicting the rate of memory decline in minority populations.[51,52] Therefore, performance on neuropsychological assessments should perhaps be adjusted for literacy level instead of years of education to compensate for differences in the quality of education across ethnoracial groups.

Another possibility might be to monitor changes in neuropsychological scores instead of using absolute scores as a screening method for dementia. For example, serial MMSE scores could be recorded over a period of years to document progression of cognitive decline. This would theoretically eliminate racial biases involved in obtaining the baseline score. However, this method would require early neuropsychological testing while the patient is still cognitively normal as well as regular follow-ups to monitor changes in cognition. Given the diverse cultural beliefs about dementia and the mistrust of health care professionals within minority communities,[53,54,55] early screening and regular follow-ups may prove especially difficult. Another potentially useful approach is to employ cognitive instruments that are known to be affected by education, literacy, and cultural appropriateness in ways that allow for further interpretation of performance in other cognitive domains, such as memory. For example, Whitfield and colleagues demonstrated that after controlling for demographics and health factors, cognitively normal African Americans named significantly fewer items on the Boston Naming Test (BNT) than whites.[56] However, when these previously named items were employed as targets in a verbal recall task, there were no racial differences in the proportion of items recalled either immediately or after a delay, underscoring the notion that differences in familiarity with memory task stimuli may underlie much of the performance difference observed between white and non-white populations.

Although neuropsychological instruments could be made more specific to AD in minority populations, such instruments are imperfect in their ability to disambiguate the underlying pathophysiology of AD from other neurodegenerative conditions. It remains true that the definitive diagnosis of AD can only be made at autopsy, when the pathological hallmarks of amyloid β (Aβ) plaques and tau neurofibrillary tangles can be observed. However, a growing body of evidence suggests that a variety of biological markers may prove useful for signifying the presence of AD. For example, measures of Aβ and tau protein levels in cerebrospinal fluid have emerged as potentially informative indicators of disease.[57-60] Neuroimaging techniques such as PET imaging with ^{11}C-labeled Pittsburgh compound-B (PiB)—a compound retained in cortical regions that contain significant Aβ—also hold promise as tools for assessing the presence and progression of AD.[61] Several studies have shown that the prevalence of tau and Aβ in post-mortem brain tissue is similar between African Americans and whites diagnosed with AD.[62-64] This suggests that neuroimaging techniques or CSF assays that evaluate these biomarkers may be of similar diagnostic value

across diverse populations, and thus may someday be instrumental in mitigating or eliminating racial biases that exist in current screening and diagnostic techniques.

Biomarkers have the potential to disambiguate AD from other forms of dementia, such as vascular dementia especially in African Americans. Given the higher prevalence of vascular risk factors[6] and vascular dementia[15,16] in African Americans, it is important to understand how or if vascular pathology contributes to the development of AD. Biomarkers could contribute to our understanding of how vascular and neurological factors interact to produce the constellation of symptoms associated with AD and may help to explain why African Americans and Hispanics seem to present with more severe clinical symptoms at time of onset.[9] The use of biomarkers could also alter differences in prevalence and incidence rates between ethnoracial groups if a proportion of dementia cases currently diagnosed as AD in African Americans is in fact a form of vascular dementia. Advances in biomarker development may be instrumental in advancing the study of ethnoracial differences in the biology of AD. Nevertheless, biology is only one component of the disease process, and extrinsic social factors, including cultural differences, may also significantly contribute to differences in clinical presentation, treatment modalities, and treatment outcomes.

Differences in Cultural Factors: Effect on Treatment and Outcomes

Hispanics and African Americans often receive delayed or inadequate health care services, especially for dementia.[65] Any effort to narrow this health disparity will require a greater understanding of how different cultural beliefs influence the understanding of dementia in minority populations. For example, dementia may be stigmatized more strongly in a certain population, leading to delayed diagnosis and/or inadequate treatment.[66] If so, culturally specific interventions have the potential to bridge this gap in understanding and improve outcomes. Clinicians must not only understand potential differences in the clinical presentation of AD in different ethnoracial populations, but must also understand the different ways in which dementia, or the perception of dementia, impacts the daily lives of patients and caregivers.

To date, there has been relatively sparse research in the area of differences in knowledge and beliefs about AD between ethnoracial groups and their affect on health outcomes. Roberts and colleagues surveyed a small, diverse sample consisting of predominantly white and African American middle-aged adults.[54] They found that African American respondents were significantly more likely than white respondents to express beliefs that AD symptoms are a normal part of aging. In addition, African American respondents were more optimistic that a cure for AD would be available in the near future, less worried about their risk of developing AD, and less knowledgeable about certain facts regarding AD, such as the availability of current treatments. These findings may help to explain part of the reason why African Americans often receive delayed care for dementia. Given the possibly increased prevalence of AD within African American and Hispanic populations,[4-6] it has become increasingly important to understand and address these differences in knowledge and beliefs.

Differing expectations with respect to cognition in normal aging may significantly impact the time it takes for an individual with symptoms of AD to seek treatment. A recent survey, predominantly of caregivers and first-degree relatives of individuals with AD, found that significantly more African American respondents than white respondents believed substantial memory loss to be a normal aspect of aging,[55] while qualitative research conducted through interviews of African Americans, Hispanics, and Chinese found similar beliefs.[53] These data suggests that educational efforts focused on teaching the facts of AD may have a positive impact on increasing awareness and decreasing time to diagnosis,

especially within minority populations. Initial recognition of symptoms of dementia by caregivers or family members is the most important step toward the treatment of AD.

Research also suggests that, in certain communities, beliefs about dementia may be tied to deeply held convictions that transcend the conventional medical model of disease. For instance, Connell and colleagues found that religious and spiritual beliefs may differentially impact perceptions of dementia among African Americans as compared to whites.[55] A significantly higher proportion of African Americans indicated that they believed “God’s will” had a hand in determining who developed AD and who did not. Some of these patients may be more prone to believe that medicines will be ineffective in treating a disease that stems from a spiritual cause, while others may feel that aggressively seeking treatment to fight a disease like AD may be acting in opposition to a divine plan. Although one must be careful in drawing generalized conclusions from a small sample drawn from only two metropolitan areas, this survey suggests that religion and spirituality may play a stronger role in the conceptualization of health and wellbeing for African Americans than for whites.

Clinicians, researchers, and educators must be cognizant of potential connections between health and spirituality for patients. On the one hand, spiritual beliefs are a powerful and often integral coping mechanism for patients and caregivers dealing with the difficult diagnosis of AD, often giving rise to hope even in grim clinical scenarios. It is well known that mood and affect impact outcomes in dementia,[67,68] and a positive outlook engendered by spiritual beliefs may help patients in the long run. On the other hand, the spiritual belief that diseases like AD have metaphysical causes may lead patients and caregivers to delay seeking a diagnosis for symptoms, and to a subsequent delay in treatment. Moreover, conviction that physical illness is related to spiritual causes may lead to increased skepticism about the efficacy of medical interventions and perhaps to differences in medical compliance. Outreach efforts within minority communities should seek to better understand the impact of religion on the conceptualization of health.

In addition to expressing differences in the perception of dementia, individuals within minority communities may also hold different opinions of the medical establishment and of the health care system than their white counterparts. For many of these patients, opinions regarding the medical field have been powerfully shaped by historic events in which minority groups have either been denied equal medical treatment or have suffered in the wake of unethical and discriminatory biomedical research practices, such as the Tuskegee Syphilis Study.[69-71] Although the legacy and impact of these historical events may be fading in the minds of the public,[72] there exists evidence that racism may still play a role in the treatment of AD received by minority patients. Specifically, several large studies have found that African Americans and Hispanics are significantly less likely than whites to receive medications, such as acetylcholinesterase inhibitors (AChEIs) or memantine, for dementia treatment.[11-13] This racial disparity in the management of AD may lead to greater cognitive decline and suffering for minority patients.

Whether or not a patient trusts his or her doctor undoubtedly impacts whether or not he or she will report symptoms of dementia, regardless of his or her knowledge of the disease process. In one study, Mahoney and colleagues gathered data through interviews of African American, Hispanic, and Chinese caregivers of individuals with AD.[53] The authors found that the African American caregivers expressed feelings of disappointment with and disrespect from health care providers who oftentimes dismissed caregiver concerns about a spouse’s or a family member’s memory loss. Community education and outreach programs focused on AD will have little impact if primary care physicians are unable, or unwilling, to recognize expressed concerns about the disease. Research has also shown that different family dynamics within minority communities may influence how an individual interacts

with the health care system. Mahoney and colleagues found that Hispanic respondents were fearful of institutionalized or nursing home-based care, viewing it as an attack on traditional family-centered care.[53] As a result, Hispanic caregivers may be more reluctant to bring their spouse or family member to the doctor, perhaps out of fear that the doctor will destroy the role of the family in the care of the individual. If the doctor-patient relationship lacks trust and respect, diagnosis and treatment of any disorder will be greatly hindered.

Differences between ethnoracial groups exist with respect to nursing home placement, although the overall clinical impact of these differences is unclear. Using data from the National Alzheimer's Coordinating Center, Mehta and colleagues found that African American and Hispanic patients with AD were less likely than white patients to live in a skilled nursing or assisted living facility.[10] Non-white patients in this investigation had significantly lower hazards for mortality as compared to white patients over the duration of their follow-up at an Alzheimer's Disease Center. This finding is consistent with some evidence that suggests that nursing home placement is associated with an increased mortality risk for dementia patients,[73], and that a focus on family-centered care[53] of individuals with AD may improve survival time. However, other investigators have not found nursing home placement to be associated increased mortality risk among patients with dementia.[74-76] Whether the lower mortality rate of African American and Hispanic patients with AD is related to differences in how, where, and by whom these patients are cared for remains to be detemined.

It seems contradictory then that African Americans and Hispanics present with a greater severity of symptoms at time of diagnosis,[9] yet they live longer with AD than their white counterparts.[8] Cultural factors may have a role in explaining this discrepancy. Patient distrust of the health care system[53] coupled with racial differences in physician prescribing practices[9] most likely contribute to less aggressive treatment for AD in minority populations. However, it remains unclear whether more aggressive treatment with such drugs as AChEIs has a beneficial effect on long-term outcomes or overall survival.[77] More aggressive treatment for any disease may be theoretically associated with poorer outcomes due to increased incidence of iatrogenic adverse events. Nevertheless, studies have found AChEIs to be efficacious for the symptomatic treatment of AD[78] and all patients should be treated with the standard of care regardless of race.

Although it is difficult to measure the impact of culture on disease, it is likely that race-specific cultural factors influence the way in which AD is recognized and subsequently treated in minority populations. Whether ethnoracial differences in outcomes partially stem from disparities in knowledge about AD, certain spiritual beliefs concerning health and well being, or distrust of the health care system, physicians should consider that biology is only one aspect of disease and that social factors may be just as important. Encouragingly, evidence suggests that modification of some social factors may have a positive impact on the lives of patients with AD. [79, 80] Improving the treatment of cognitive disorders in minority populations will require greater appreciation of factors that include but are not limited to education, socioeconomic status, family dynamics, faith and spirituality, and the subtleties of the doctor-patient relationship. In short, the pharmacological treatment of the biological manifestations of disease is only one piece of a larger picture in the treatment of dementia, particularly in minority populations.

Differences in Access to and Engagement in Clinical Research

Clinical research with human subjects is paramount to uncovering answers to many of the questions surrounding the pathophysiology of AD. Furthermore, the research into diverse populations has become increasingly important due to the possibility of differences in the

prevalence and incidence of dementia between white and non-white populations and due to the relative lack of scientific information regarding dementia within diverse groups. Despite the need for more research, overall participation in clinical research trials of AD is often lacking, and recruitment efforts within non-white populations have been met with even more challenges.[81]

Many studies have previously examined potential reasons for low recruitment rates, as well as low retention rates, in clinical trials of AD. For example, Schneider and colleagues found that strict inclusion and exclusion criteria typically used in phase III clinical trials of AD may result in a sample that is not demographically or clinically representative of the overall clinic population.[82] In particular, they found that female and non-white patients were underrepresented in samples selected using typical eligibility criteria. Another factor found to influence retention in clinical trials of AD was the research setting (i.e. in-home vs. in-clinic assessments).[83] Researchers found that in-home assessments may reduce withdrawal rates as compared to in-clinic assessments. A variety of additional factors that may influence participation in AD research have also been reported, including clinic accessibility, transportation costs and availability, caregiver and patient attitudes toward medical establishments, concerns about personal safety, and the belief that research trials will not directly benefit the study subjects.[84] Some of these barriers to participation in research are common between white and non-white populations. Nevertheless, a greater understanding of the barriers that are specific to or more significant for diverse populations will aid in the research of dementia and its differential effects across ethnoracial groups.

Lack of access to health care for African Americans and Hispanics almost certainly contributes to lower rates of participation in clinical research trials of AD. A recent meta-analysis found significant evidence to suggest that African Americans and Hispanics with dementia access diagnostic services later in the course of their illness than non-Hispanic whites.[85] Disparities in access may either stem from an inability to visit a qualified health professional or an unwillingness to do so given the opportunity. Furthermore, while most adults in the United States over age 65 have access to health in insurance through Medicare, additional barriers may contribute to inadequate access to care for minorities, including inadequate understanding of health insurance (including poorer familiarity with Medicare)[86] and lack of AD clinics in minority communities.[87] Through interventions that enhance care for minorities, knowledge of and desire to participate in clinical research studies of AD may subsequently increase.

Minority populations should also have adequate access to AD clinics in or near their communities. At a recent meeting of the “Diagnosis and Assessment of Alzheimer’s Disease in Diverse Populations” workshop in Chicago, IL, members identified the need for AD clinics to establish closer ties with local communities and primary care facilities.[87] Given that cultural and religious beliefs often play such a prominent role in the perception of AD within minority communities, AD clinics should also work to establish ties with churches and other faith-based institutions. These ties are necessary to cultivate a relationship based on trust between health care providers and minority communities. Researchers working in AD clinics must promote their clinics as sites where minority patients will be treated with the utmost respect and dignity while having the opportunity to contribute to the development of novel diagnostic techniques and treatment options.

In a study of African American psychiatric patients, Thompson and colleagues found that African Americans tended to harbor higher levels of distrust toward clinical research,[88] perhaps perpetuated by the history of social injustice and institutional racism in the United States.[89] This distrust was especially evident toward research conducted by whites. In addition, the authors found that higher levels of stigma surrounding mental illness within

African American communities also hampered recruitment efforts. Surprisingly though, their results also showed that matching interviewers and patients on the basis of ethnicity did not significantly impact participation rates.[88] All of the study's interviewers, regardless of ethnicity, had experience working with low-income patients from urban settings and received training in culturally sensitive interview techniques. These results add hope to the belief that some of the barriers to participation in research for diverse populations may be overcome with careful planning and appropriate investigator training.

One considerable challenge in pursuing AD research in minorities is that of accurately diagnosing AD in non-white populations. Minorities are often underrepresented in AD biomarker research,[90] such that diagnosis of AD is principally based upon clinical evaluation. However, current understanding of the differences in clinical presentation across ethnoracial groups is limited. In turn, this limited understanding likely affects the ability to accurately diagnose AD in diverse populations. For instance, some evidence suggests that personality and functional changes associated with AD may precede signs of cognitive impairment in African Americans more often than in Anglo patients in the early stages of AD.[91] Alternatively it may be the case that personality and functional impairments occur equally often in both groups but are interpreted differently by caregivers and clinicians when they occur in African American patients compared to white patients. In either case, it may be that more African Americans than whites are inappropriately labeled as normal or misdiagnosed with a primary psychiatric disturbance, and thus excluded from clinical studies. In addition, aforementioned cultural factors that may influence delayed diagnosis of AD in minority populations may also contribute to poor recruitment rates in research. Without a more thorough understanding of how race, ethnicity, and culture interact with biological factors to affect the clinical presentation of AD, this disease may not be adequately identified in minority populations.

Conclusions

AD should be conceptualized as a multifactorial process in which clinicians and researchers have the opportunity to unravel the complex contributions of biology and culture. A better understanding of these factors and of how their interactions differ across ethnoracial groups may allow clinicians to more effectively diagnose and treat AD in patients of all races. Certain pathological changes in the brain fundamentally define AD as a disease. Whether the amyloid plaque, the neurofibrillary tangle, or some other molecule is the toxic agent, it is likely that the pathophysiology of AD follows a final common pathway regardless of race. Therefore, differences in epidemiology, diagnosis, clinical presentation, treatment, and outcomes across ethnoracial groups are most likely accounted for by differences in the prevalence of certain biological risk factors as well as social and cultural factors unique to certain populations.

As the population of the U.S. ages and becomes more diverse, the burden of dementia may be falling disproportionately on elderly minorities, both in terms of prevalence and severity. Many important aspects of AD, including genetic and cardiovascular risk factors, differ according to race. The reasons for these differences and their implications remain poorly understood. Minority patients with AD oftentimes present with greater cognitive impairment than their white counterparts. However, the degree to which these differences in disease severity may be attributed to racial biases of the neuropsychologic tests used to screen for dementia also remains unclear. Importantly, unaccounted for differences in literacy level may contribute substantially to differences in psychometric performance determined by race, and may therefore be an important consideration in the evaluation of AD and other dementias. In addition, diagnosis using biologically based criteria with biomarkers has the

potential to provide clearer estimates of AD rates in diverse populations as well as to disambiguate AD from other forms of dementia.

A complex combination of social and cultural factors also contributes to delayed diagnosis and care of AD in minority populations. Some of these influences include differences in perceptions about normal and abnormal aging, lack of adequate access to medical care, and issues of trust between minority groups and the medical establishment. Similar factors also contribute to the dearth of minorities participating in clinical research related to AD and other dementias. Efforts to address ethnoracial disparities in dementia may call for novel approaches in which clinicians and clinical researchers partner closely with local civic leaders and organizations to raise awareness about the burden of AD among minorities, draw attention to the signs and symptoms that patients and their loved ones should recognize, and cultivate trust and understanding between minority communities and the medical community. Importantly, addressing these disparities also requires that physicians be made aware of the disproportionate impact that dementia has in minority communities and recognize the biases of the medical establishment in the diagnosis and care of these underserved individuals.

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References

1. Brookmeyer R, Johnson E, Ziegler-Graham K, et al. Forecasting the global burden of Alzheimer's disease. Alzheimers Dement. 2007; 3(3):186–91. [PubMed: 19595937]
2. Alzheimer's Disease International. World Alzheimer Report 2010. London: Alzheimer's Disease International; 2010.
3. [April 22, 2010] United States Census Bureau: State and County QuickFacts [U S Census Bureau web site]. Feb 23. 2010 Available at: http://quickfacts.census.gov/qfd/states/00000.html
4. Demirovic J, Prineas R, Loewenstein D, et al. Prevalence of dementia in three ethnic groups: the South Florida program on aging and health. Ann Epidemiol. 2003; 13:472–8. [PubMed: 12875807]
5. Tang MX, Cross P, Andrews H, et al. Incidence of AD in African-Americans, Caribbean Hispanics, and Caucasians in northern Manhattan. Neurology. 2001; 56:49–56. [PubMed: 11148235]
6. Alzheimer's Association. 2010 Alzheimer's disease facts and figures. Alzheimers Dement. 2010 Mar; 6(2):158–94. [PubMed: 20298981]
7. Potter GG, Plassman BL, Burke JR, et al. Cognitive performance and informant reports in the diagnosis of cognitive impairment and dementia in African Americans and whites. Alzheimers Dement. 2009; 5:445–53. [PubMed: 19896583]
8. Gurland BJ, Wilder DE, Lantigua R, et al. Rates of dementia in three ethnoracial groups. Int J Geriatr Psychiatry. 1999; 14:481–93. [PubMed: 10398359]
9. Livney MG, Clark CM, Karlawish JH, et al. Ethnoracial differences in the clinical presentation of Alzheimer's disease at an urban Alzheimer's Disease Center. American Journal of Geriatric Psychiatry. In press.
10. Mehta KM, Yaffe K, Pérez-Stable EJ, et al. Race/ethnic differences in AD survival in US Alzheimer's Disease Centers. Neurology. 2008; 70:1163–70. [PubMed: 18003939]
11. Hernandez S, McClendon MJ, Zhou XH, et al. Pharmacological treatment of Alzheimer's disease: effect of race and demographic variables. J Alzheimers Dis. 2010; 19:665–72. [PubMed: 20110610]
12. Mehta KM, Yin M, Resendez C, et al. Ethnic differences in acetylcholinesterase inhibitor use for Alzheimer disease. Neurology. 2005; 65:159–62. [PubMed: 16009909]

13. Zuckerman IH, Ryder PT, Simoni-Wastila L, et al. Racial and ethnic disparities in the treatment of dementia among Medicare beneficiaries. J Gerontol B Psychol Sci Soc Sci. 2008; 63:S328–33. [PubMed: 18818454]
14. Cohen SA. A review of demographic and infrastructural factors and potential solutions to the physician and nursing shortage predicted to impact the growing US elderly population. J Public Health Manag Pract. 2009; 15:352–62. [PubMed: 19525780]
15. Fitzpatrick AL, Kuller LH, Ives DG, et al. Incidence and prevalence of dementia in the Cardiovascular Health Study. J Am Geriatr Soc. 2004; 52:195–204. [PubMed: 14728627]
16. Froehlich TE, Bogardus ST Jr, Inouye SK. Dementia and race: are there differences between African Americans and Caucasians? J Am Geriatr Soc. 2001; 49:477–84. [PubMed: 11347796]
17. Fillenbaum GG, Heyman A, Huber MS, et al. The prevalence and 3-year incidence of dementia in older Black and White community residents. J Clin Epidemiol. 1998; 51:587–595. [PubMed: 9674666]
18. Hendrie HC, Osuntokun BO, Hall KS, et al. Prevalence of Alzheimer's disease and dementia in two communities: Nigerian Africans and African Americans. Am J Psychiatry. 1995; 152:1485–92. [PubMed: 7573588]
19. Hendrie HC, Ogunniyi A, Hall KS, et al. Incidence of dementia and Alzheimer disease in 2 communities: Yoruba residing in Ibadan, Nigeria, and African Americans residing in Indianapolis, Indiana. JAMA. 2001; 285:739–47. [PubMed: 11176911]
20. Hall K, Murrell J, Ogunniyi A, et al. Cholesterol, APOE genotype, and Alzheimer disease: an epidemiologic study of Nigerian Yoruba. Neurology. 2006; 66:223–7. [PubMed: 16434658]
21. Corrada M, Brookmeyer R, Kawas C. Sources of variability in prevalence rates of Alzheimer's disease. Int J Epidemiol. 1995; 24:1000–5. [PubMed: 8557432]
22. Manly JJ. Deconstructing race and ethnicity: implications for measurement of health outcomes. Med Care. 2006; 44(Suppl 3):S10–6. [PubMed: 17060816]
23. Breteler MM. Vascular risk factors for Alzheimer's disease: An epidemiologic perspective. Neurobiol Aging. 2000; 21:153–60. [PubMed: 10867200]
24. Newman AB, Fitzpatrick AL, Lopez O, et al. Dementia and Alzheimer's disease incidence in relationship to cardiovascular disease in the Cardiovascular Health Study cohort. J Am Geriatr Soc. 2005; 53:1101–7. [PubMed: 16108925]
25. Skoog I, Kalaria RN, Breteler MM. Vascular factors and Alzheimer disease. Alzheimer Dis Assoc Disord. 1999; 13(Suppl 3):S106–14. [PubMed: 10609689]
26. Luchsinger JA, Reitz C, Honig LS, et al. Aggregation of vascular risk factors and risk of incident Alzheimer disease. Neurology. 2005; 65:545–51. [PubMed: 16116114]
27. Graff-Radford NR, Green RC, Go RC, et al. Association between apolipoprotein E genotype and Alzheimer disease in African American subjects. Arch Neurol. 2002; 59:594–600. [PubMed: 11939894]
28. Tang MX, Stern Y, Marder K, et al. The APOE-epsilon4 allele and the risk of Alzheimer disease among African Americans, whites, and Hispanics. JAMA. 1998; 279:751–5. [PubMed: 9508150]
29. Evans DA, Bennett DA, Wilson RS, et al. Incidence of Alzheimer disease in a biracial urban community. Arch Neurol. 2003; 60:185–189. [PubMed: 12580702]
30. Murrell JR, Price B, Lane KA, et al. Association of apolipoprotein E genotype and Alzheimer disease in African Americans. Arch Neurol. 2006; 63:431–4. [PubMed: 16533971]
31. Terrisse L, Poirier J, Bertrand P, et al. Increased levels of apolipoprotein D in cerebrospinal fluid and hippocampus of Alzheimer's patients. J Neurochem. 1998; 71:1643–50. [PubMed: 9751198]
32. Chen Y, Jia L, Wei C, Wang F, et al. Association between polymorphisms in the apolipoprotein D gene and sporadic Alzheimer's disease. Brain Res. 2008; 1233:196–202. [PubMed: 18671953]
33. Desai PP, Ikonomovic MD, Abrahamson EE, et al. Apolipoprotein D is a component of compact but not diffuse amyloid-beta plaques in Alzheimer's disease temporal cortex. Neurobiol Dis. 2005; 20:574–82. [PubMed: 15916898]
34. Desai PP, Hendrie HC, Evans RM, et al. Genetic variation in apolipoprotein D affects the risk of Alzheimer disease in African-Americans. Am J Med Genet B Neuropsychiatr Genet. 2003; 116B: 98–101. [PubMed: 12497622]

35. Rogaeva E, Meng Y, Lee JH, et al. The neuronal sortilin-related receptor SORL1 is genetically associated with Alzheimer disease. Nat Genet. 2007; 39:168–77. [PubMed: 17220890]
36. Lee JH, Cheng R, Schupf N, et al. The association between genetic variants in SORL1 and Alzheimer's disease in an urban, multiethnic, community-based cohort. Arch Neurol. 2007; 64:501–506. [PubMed: 17420311]
37. Lee JH, Cheng R, Honig LS, et al. The association between genetic variants in SORL1 and autopsy-confirmed Alzheimer's disease. Neurology. 2008; 70:887–889. [PubMed: 17978276]
38. Liu F, Ikram MA, Janssens AC, et al. A study of the SORL1 gene in Alzheimer's disease and cognitive function. J Alzheimers Dis. 2009; 18:51–64. [PubMed: 19584446]
39. Ma QL, Galasko DR, Ringman JM, et al. Reduction of SorLA/LR11, a sorting protein limiting beta-amyloid production, in Alzheimer disease cerebrospinal fluid. Arch Neurol. 2009; 66:448–57. [PubMed: 19364929]
40. Wang PN, Liu HC, Liu TY, et al. Estrogen-metabolizing gene COMT polymorphism synergistic APOE epsilon4 allele increases the risk of Alzheimer disease. Dement Geriatr Cogn Disord. 2005; 19:120–5. [PubMed: 15591802]
41. Martínez MF, Martín XE, Alcelay LG, et al. The COMT Val158 Met polymorphism as an associated risk factor for Alzheimer disease and mild cognitive impairment in APOE 4 carriers. BMC Neurosci. 2009; 10:125. [PubMed: 19793392]
42. Green RC, Cupples LA, Go R, Benke KS, et al. Risk of dementia among white and African American relatives of patients with Alzheimer disease. JAMA. 2002; 287:329–36. [PubMed: 11790212]
43. McKhann G, Drachman DA, Folstein M, Katzman R, et al. Clinical diagnosis of Alzheimer's disease—report of the NINCDS–ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology. 1984; 34:939–44. [PubMed: 6610841]
44. Dubois B, Feldman HH, Jacova C, DeKosky S, et al. Research criteria for the diagnosis of Alzheimer's disease: revising the NINCDS-ADRDA criteria. Lancet. 2007; 6:734–46.
45. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975; 12:189–98. [PubMed: 1202204]
46. Tombaugh TN, McIntyre NJ. The mini-mental state examination: a comprehensive review. J Am Geriatr Soc. 1992; 40:922–35. [PubMed: 1512391]
47. Stephenson J. Racial barriers may hamper diagnosis, care of patients with Alzheimer disease. JAMA. 2001; 286:779–80. [PubMed: 11497517]
48. Wood RY, Giuliano KK, Bignell CU, et al. Assessing cognitive ability in research: use of MMSE with minority populations and elderly adults with low education levels. J Gerontol Nurs. 2006; 32:45–54. [PubMed: 16615712]
49. Kawas, CH.; Katzman, R. Epidemiology of dementia and Alzheimer's disease. In: Terry, RD.; Katzman, R.; Bick, KL., et al., editors. Alzheimer's Disease. 2. Vol. 95. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 116
50. Hall KS, Gao S, Unverzagt FW, et al. Low education and childhood rural residence: risk for Alzheimer's disease in African Americans. Neurology. 2000; 54:95–9. [PubMed: 10636132]
51. Manly JJ, Touradji P, Tang MX, et al. Literacy and memory decline among ethnically diverse elders. J Clin Exp Neuropsychol. 2003; 25:680–90. [PubMed: 12815505]
52. Manly JJ, Schupf N, Tang MX, et al. Cognitive decline and literacy among ethnically diverse elders. J Geriatr Psychiatry Neurol. 2005; 18:213–7. [PubMed: 16306242]
53. Mahoney DF, Cloutterbuck J, Neary S, et al. African American, Chinese, and Latino family caregivers' impressions of the onset and diagnosis of dementia: cross-cultural similarities and differences. Gerontologist. 2005; 45:783–92. [PubMed: 16326660]
54. Roberts JS, Connell CM, Cisewski D, et al. Differences between African Americans and whites in their perceptions of Alzheimer disease. Alzheimer Dis Assoc Disord. 2003; 17:19–26. [PubMed: 12621316]
55. Connell CM, Scott Roberts J, McLaughlin SJ, et al. Racial differences in knowledge and beliefs about Alzheimer disease. Alzheimer Dis Assoc Disord. 2009; 23:110–6. [PubMed: 19474569]

56. Whitfield KE, Fillenbaum GG, Pieper C, et al. The effect of race and health-related factors on naming and memory. The MacArthur Studies of Successful Aging. J Aging Health. 2000; 12:69–89. [PubMed: 10848126]
57. Clark CM, Xie S, Chittams J, et al. Cerebrospinal fluid tau and beta-amyloid: How well do these biomarkers reflect autopsy-confirmed dementia diagnoses? Arch Neurol. 2003; 60:1696–1702. [PubMed: 14676043]
58. Shaw LM, Vanderstichele H, Knapik-Czajka M, et al. Cerebrospinal fluid biomarker signature in Alzheimer's Disease Neuroimaging Initiative subjects. Ann Neurol. 2009; 65:403–413. [PubMed: 19296504]
59. Blennow K, Hampel H, Weiner M, et al. Cerebrospinal fluid and plasma biomarkers in Alzheimer disease. Nat Rev Neurol. 2010; 6:131–44. [PubMed: 20157306]
60. Britschgi M, Wyss-Coray T. Blood protein signature for the early diagnosis of Alzheimer disease. Arch Neurol. 2009; 66:161–5. [PubMed: 19064741]
61. Klunk WE, Engler H, Nordberg A, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. Ann Neurology. 2004; 55:306–19.
62. Wilkins CH, Grant EA, Schmitt SE, et al. The neuropathology of Alzheimer disease in African American and white individuals. Arch Neurol. 2006; 63:87–90. [PubMed: 16401740]
63. Riudavets MA, Rubio A, Cox C, et al. The prevalence of Alzheimer neuropathologic lesions is similar in blacks and whites. J Neuropathol Exp Neurol. 2006; 65:1143–8. [PubMed: 17146288]
64. Sandberg G, Stewart W, Smialek J, et al. The prevalence of the neuropathological lesions of Alzheimer's disease is independent of race and gender. Neurobiol Aging. 2001; 22:169–75. [PubMed: 11182466]
65. Manly, JJ.; Jacobs, D.; Mayeux, R. Alzheimer's disease among different ethnic and racial groups. In: Terry, RD.; Katzman, R.; Bick, KL., et al., editors. Alzheimer's Disease. 2. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 117-31.
66. Espino DV, Lewis R. Dementia in older minority populations. Issues of prevalence, diagnosis, and treatment. Am J Geriatr Psychiatry. 1998; 6(Suppl 1):S19–25. [PubMed: 9581217]
67. Appleby BS, Roy P, Valenti A, et al. Diagnosis and treatment of depression in Alzheimer's disease: impact on mood and cognition. Panminerva Med. 2007; 49:139–49. [PubMed: 17912149]
68. Robert PH, Berr C, Volteau M, et al. Importance of lack of interest in patients with mild cognitive impairment. Am J Geriatr Psychiatry. 2008; 16:770–6. [PubMed: 18757769]
69. Wasserman J, Flannery MA, Clair JM. Raising the ivory tower: the production of knowledge and distrust of medicine among African Americans. J Med Ethics. 2007; 33:177–80. [PubMed: 17329393]
70. Byrd, WM.; Clayton, LA. An American health dilemma: a medical history of African Americans and the problem of race. Vol. 1 and 2. New York, New York: Routledge; 2000. p. 2002
71. Shavers VL, Lynch CF, Burmeister LF. Knowledge of the Tuskegee study and its impact on the willingness to participate in medical research studies. J Natl Med Assoc. 2000; 92:563–72. [PubMed: 11202759]
72. Katz RV, Green BL, Kressin NR, et al. Exploring the "legacy" of the Tuskegee Syphilis Study: a follow-up study from the Tuskegee Legacy Project. J Natl Med Assoc. 2009; 101:179–83. [PubMed: 19378637]
73. Aneshensel CS, Pearlin LI, Levy-Storms L, et al. The transition from home to nursing home mortality among people with dementia. J Gerontol B Psychol Sci Soc Sci. 2000; 55:S152–62. [PubMed: 11833983]
74. McClendon MJ, Smyth KA, Neundorfer MA. Long-term-care placement and survival of persons with Alzheimer's disease. J Gerontol B Psychol Sci Soc Sci. 2006; 61(4):P220–7. [PubMed: 16855034]
75. Schäufele M, Bickel H, Weyerer L. Predictors of mortality among demented elderly in primary care. Int J Geriatr Psychiatry. 1999; 14:946–56. [PubMed: 10556866]
76. Suh G-H, Yeon BK, Lee J-Y. Mortality in Alzheimer's disease: a comparative prospective Korean study in the community and nursing homes. Int J Geriatr Psychiatry. 2005; 20:26–34. [PubMed: 15578675]

77. Suh GH, Ryu SH, Lee DW, et al. Cholinesterase Inhibitors for Alzheimer Disease: Do They Provide More Than Symptomatic Benefits? Am J Geriatr Psychiatry. 2010 Epub ahead of print.

78. Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev. 2006; (1) CD005593.

79. Littlewood C, Seymour J, Owen V. Does treating Alzheimer's disease early, delay institutionalisation? Int J Geriatr Psychiatry. 2010; 25(12):1307–09. [PubMed: 21086542]

80. Mittelman MS. Psychosocial intervention research: Challenges, strategies and measurement issues. Aging & mental health. 2008; 12(1):1–4. [PubMed: 18297474]

81. Olin JT, Dagerman KS, Fox LS, et al. Increasing ethnic minority participation in Alzheimer disease research. Alzheimer Dis Assoc Disord. 2002; 16(Suppl 2):S82–5. [PubMed: 12351920]

82. Schneider LS, Olin JT, Lyness SA, et al. Eligibility of Alzheimer's disease clinic patients for clinical trials. J Am Geriatr Soc. 1997; 45:923–928. [PubMed: 9256842]

83. Bedard M, Molloy DW, Standish T, et al. Clinical trials in cognitively impaired older adults: home versus clinic assessments. J Am Geriatr Soc. 1995; 43:1127–1130. [PubMed: 7560704]

84. Connell CM, Shaw BA, Holmes SB, et al. Caregivers' attitudes toward their family members' participation in Alzheimer disease research: implications for recruitment and retention. Alzheimer Dis Assoc Disord. 2001; 15:137–45. [PubMed: 11522931]

85. Cooper C, Tandy AR, Balamurali TB, et al. A systematic review and meta-analysis of ethnic differences in use of dementia treatment, care, and research. Am J Geriatr Psychiatry. 2010; 18:193–203. [PubMed: 20224516]

86. Morgan RO, Teal CR, Hasche JC, et al. Does poorer familiarity with Medicare translate into worse access to health care? J Am Geriatr Soc. 2008; 56:2053–60. [PubMed: 19016939]

87. Dilworth-Anderson P, Hendrie HC, Manly JJ, et al. Diagnosis and assessment of Alzheimer's disease in diverse populations. Alzheimers Dement. 2008; 4:305–9. [PubMed: 18631983]

88. Thompson EE, Neighbors HW, Munday C, et al. Recruitment and retention of African American patients for clinical research: an exploration of response rates in an urban psychiatric hospital. J Consult Clin Psychol. 1996; 64:861–7. [PubMed: 8916612]

89. Byrd WM, Clayton LA. Race, medicine, and health care in the United States: a historical survey. J Natl Med Assoc. 2001; 93(Suppl):11S–34S. [PubMed: 12653395]

90. Williams MM, Scharff DP, Mathews KJ, et al. Barriers and facilitators of African American participation in Alzheimer disease biomarker research. Alzheimer Dis Assoc Disord. 2010; 24(Suppl):S24–9. [PubMed: 20711059]

91. Holston EC. Stigmatization in Alzheimer's disease research on African American elders. Issues Ment Health Nurs. 2005; 26:1103–27. [PubMed: 16284001]