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A Meta-Analysis of Alzheimer’s Disease Incidence and Prevalence Comparing African-Americans and Caucasians

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Abstract

Background—Several studies have shown higher Alzheimer’s disease (AD) incidence rates are in African-Americans (AAs) than Caucasians (CCs). If this finding is consistent across studies, it raises important etiologic questions regarding factors responsible for this discrepancy. It also affects the likely public health burden of AD in the US in the future, as the non-Caucasian population becomes the majority.

Objective—Estimate the AA/CC rate ratio for AD incidence across all available studies.

Methods—We conducted a meta-analysis of population-based studies for the rate ratio (RR) of AD incidence for AAs versus CCs, after identifying six relevant studies from the literature. We calculated an AA/CC rate ratio across all studies using inverse-variance weighting, and assessed inter-study heterogeneity. Using these incidence data, as well as data on survival after diagnosis, and on all-cause mortality, we also estimated the US prevalence of AD among AAs and CCs.

Results—There were six population-based studies with data comparing AD incidence between AAs and CCs, with an estimated 370 AA and 640 CC incident cases. The meta-analysis RR showed that the AD rate for AAs was 64% higher than for CCs (RR = 1.64 (95% CI 1.35–2.00)), with no evidence of heterogeneity. We estimated the current US AD prevalence for ages 65–90 to be 5.5% for CCs, and 8.6% for AAs (prevalence ratio 1.56).

Conclusion—AAs have an increased risk of incident and prevalent AD compared to CCs for reasons which are unknown, but are hypothesized to reflect biological, psychological, and socioeconomic factors.

Keywords

African-American; Alzheimer’s disease; Caucasian; incidence; prevalence; race

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INTRODUCTION

While it is generally accepted that the incidence and prevalence of Alzheimer's disease (AD) is higher in African-Americans (AAs) than in Caucasians (CCs) in the US [1, 2], to date there has been no meta-analysis of AD incidence by race which combines the data from different studies to provide an overall estimate of racial differences in AD incidence. We were motivated to do this work for several reasons. Health disparities are an important issue for AD research. Incidence data by race are still relatively sparse, and a meta-analysis, if the data are consistent across studies, can add strength to existing individual studies. Data on incidence can provide valuable clues to disease etiology, while data on prevalence are more relevant to public health burden.

We conducted a meta-analysis of incident AD using population-based studies comparing rates between AAs and CCs.

We further used the incidence data, along with data on AD survival, to estimate US AD prevalence by race, and compared our results with the most recent data on prevalence [3].

METHODS

Meta-analysis of incidence for AAs and CCs

We searched PubMed and Ovid Medline databases for population-based studies published from 2000 onwards, using the search terms 'Alzheimer's', 'dementia', 'race', 'African-American', 'black', 'prevalence', and 'incidence', in various combinations. We also consulted the reference lists of articles published on this subject, including both review articles and individual studies. When there was more than one report for a cohort, we took the most recent one.

We found six US population-based studies regarding AD incidence by race, and used these to conduct a meta-analysis for the rate ratio (RR) for AAs versus CCs [4–9]. Several studies had data on dementia incidence for AAs versus CCs, but did not collect data on dementia type [10–12]. Katz et al. [6] reported the AA/CC RR only for dementia, but provided us with the AA/CC RR for AD (personal communication, April 30, 2015).

Each study's RR for AAs versus CCs AD incidence was weighted by the inverse of their variance, and a weighted average calculated; a test of heterogeneity between studies was also calculated [13].

Prevalence for AAs and CCs

To obtain estimated US AD prevalence for AAs and CCs, as well as the joint population, we combined race-specific data on AD incidence, AD mortality following disease occurrence, and all-cause mortality, following the general description in Brookmeyer et al. [14] for the 'forward method', considering competing risks. We constructed two hypothetical cohorts of AA and CC subjects, followed from ages 65–90.

To determine the number of deaths in the CC cohort for each year of follow-up, we multiplied the population at risk (alive) in that year by age-specific US CC all-cause

mortality rates (using the same age categories), based on the year 2013 (<http://wonder.cdc.gov/>). To determine the number of new AD cases for each year of follow-up for the CC cohort, we applied AD incidence rates for CCs from the five of the six population-based incidence studies (omitting Plassman et al. [9], which did not provide age-specific AD incidence rates by race), for the age categories 65–74, 75–84, and 85+, averaged across the five studies, with rates weighted by the number of cases in each study. Although Kukull et al. [7] did not provide age-specific AD rates by race, we included the combined rates here as CC rates, given that their cohort was 90% CC. When necessary, we grouped data on incidence from different age categories into the aforementioned age-specific categories since these were most available across studies. To obtain the post-diagnosis mortality rate for CC AD cases, we multiplied the CC age-specific all-cause mortality rate by 3.20, based on the data from Wilson et al. [14], which was adjusted for age, race, education, and gender. Wilson et al. [14] is a population-based study from the Chicago Study of Health and Aging (CHAP), a cohort which was also used in one of the five population-based studies of AD incidence [4]. We then multiplied the number of AD cases occurring during each year, and those surviving from any prior year, by the CC age-specific AD mortality rate following diagnosis. This enabled us to estimate the number of CC AD cases who were still alive at the end of each year of follow-up, which was in turn needed for prevalence estimates.

We conducted similar analyses for the AA cohort. To obtain age-specific AA AD incidence rates, we multiplied the age-specific CC rates from the five incidence studies, as described above, by the AA/CC RR obtained in our meta-analysis. To obtain post-diagnosis mortality rates for AAs, we multiplied the AA age-specific all-cause mortality rate by 2.59, taken from Wilson et al. [14].

We calculated an overall US estimated age-adjusted prevalence for AAs and CCs separately, and combined, from age 65–90, by weighting each year's prevalence by the number of AAs and CCs in the US population of that age, from census data for 2013 (<http://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=bkmk>, accessed May 7, 2015).

RESULTS

Table 1 shows the RRs for incident AD in the six population-based cohorts; RRs ranged from 1.2 to 2.4. A fixed effects meta-analysis of these studies yielded a combined RR of 1.64 (95% CI 1.35–2.00), with no evidence of heterogeneity across studies ($p = 0.53$). Caution needs to be exercised with the inclusion of Fitzpatrick et al. as the RR is age-adjusted only, while other RRs are adjusted minimally for age, gender, and education. However, exclusion of Fitzpatrick et al. [8] yielded very similar results (meta-analysis RR 1.60, 1.29–2.00). The number of total AD cases and the average follow-up time are approximations based on the data available, as noted in the footnote to Table 1.

Our estimated US prevalence for the combined population of AAs and CCs ages 65–90 was 5.7%; the prevalence for AAs ages 65–90 was 8.6%, compared to 5.5% for CCs (prevalence ratio 1.56). Restricting to ages 71–90 resulted in an estimated prevalence of AD for both races combined of 8.3%; 13.1% for AAs and 7.8% for CCs (prevalence ratio 1.68).

DISCUSSION

To our knowledge, this is the only meta-analysis reporting incidence of AD (and derived prevalence) for both AAs versus CCs. Results of our incidence analyses suggest that AAs are 64% (95% confidence interval 35% to 100%) more likely to develop AD than CCs. The six studies on which our meta-analysis is based are all community-based studies, in different areas of the US, and may be reasonably representative of the US population as a whole. Nonetheless, the overall sample size remains limited, and our results from a relatively small number of communities could be non-representative. There are also issues of adequate adjustment for socioeconomic status (SES) and the inclusion of Hispanics among whites in most studies, factors which add to uncertainty (see discussion below).

The higher incidence for AAs may be the result of a combination of biological, psychological, and socioeconomic influences [15, 16]. For example, AAs have higher rates of hypertension [17], obesity [18], and diabetes [19] compared to CCs, all of which are linked to AD [20]. Vascular risk factors such as hypertension may increase oxidative stress or activate a neuroinflammatory response, triggering amyloid production [21], or act directly to influence brain amyloid levels [22–25]. These variables, as well as depression and stress (see below), could be acting as confounders, as they were not included in the models in the six studies we consider here; their inclusion might have reduced the AA/CC rate ratio.

Genetic differences may also contribute to higher AD rates for AAs. Evidence has been mixed whether the $\epsilon 4$ allele is as strong a risk factor for AD in AAs as in CCs [26–29]. More recent data in two large studies indicates that APOE $\epsilon 4$ was a strong risk factor for AD among AAs (odds ratios of 2.31 and 2.60), as it is known to be for CCs [30, 31]. Kaup et al. [32] have also recently shown that that cognitive decline was similar in AA and CC APOE $\epsilon 4$ carriers. Data are mixed on whether the prevalence of the APOE $\epsilon 4$ variant is similar in AAs and CCs [31].

Existing data do not indicate neuropathological differences between racial groups in AD upon autopsy [33, 34], although data remain sparse.

Independent of race, both depression and stress have been linked to increased AD risk [35, 36]. AAs are more likely to report higher levels of stress [37, 38]. African-Americans in a national survey have been shown to have higher levels of both current and major depression [39], or higher levels of severe and chronic depression [40].

Our results for prevalence are similar to the most recent study by Plassman et al. [3] for both overall and race-specific AD prevalence. Based on national survey data, Plassman et al. [3] estimated the prevalence of AD for all races combined between ages 71–90 to be 9.7%, similar to our own estimate of 8.3%, based on a nationally representative sample. Plassman et al. [3] estimated an AD prevalence ratio of 1.77 (ages 71–90) for AAs versus CCs, adjusted for age, gender, and education (decreasing for 1.50 after adjustment for APOE4). Our corresponding prevalence ratio was similar (1.68), although adjusted for age only.

It should be noted that a higher estimated prevalence of AD in AAs versus CCs is consistent not only with higher incidence rates but also higher survival after AD diagnosis for AAs

versus CCs. Four studies have found consistent evidence of an approximately 20% longer survival after AD diagnosis for AAs versus CCs [14, 34, 41, 42].

Our data may be important in light of US population projections (<http://www.census.gov/population/projections/data/national/2014/summarytables.html>). The US Census Bureau projects that the population age 65 and older will more than double by 2060. Over the same time period, the AA population is expected to increase from 14% to 18% of the total population, while the non-Hispanic white population is expected to decrease from 62% to 44%, and the Hispanic population will increase from 18% to 29%. Although data on Hispanic incidence are rare [5] and data on Hispanic prevalence remains sparse, Hispanics have a reported 50% higher prevalence of AD than non-Hispanic whites [2], and one study indicates the age of onset for Hispanics is younger by four years than for non-Hispanic whites [43]. The projected population numbers suggest, then, that the future increase in the AD public health burden will not only be driven by individuals living longer, but also by an overall shift in demography as higher risk individuals (both AAs and Hispanics) will constitute the majority of the US population.

A limitation of the data we used from the six studies is that only two of them [5, 6] explicitly separated out Hispanic versus non-Hispanic CC, such that the RRs reported are for AAs and non-Hispanic CCs. In the other four studies, an unknown percentage of CCs would have been of Hispanic origin. However, the percent Hispanics among CCs in these studies is likely to be small, and given that (as noted above) Hispanics may have higher AD risk than non-Hispanic whites, their inclusion among CCs in these studies is likely to—if anything—cause an underestimation of the AA versus CC RR.

We believe that it is unlikely that the present results are explained by confounding by education; all the studies were adjusted for education level as a measure of SES, which is known to be different between AAs and CCs. Yaffe et al. [10] have pointed out that socioeconomic status may not be well controlled by a variable for years of education, and noted that in their data (Health ABC study in Memphis and Pittsburg) a combination of years of education, income, and an adult literacy test, greatly reduced the AA to CC rate ratio for dementia; no data were available on AD incidence *per se*. Hence it is possible that residual confounding by SES may have contributed to the higher AD incident rates for AAs. On the other hand, Schwartz et al. [43] found markedly worse cognition for AAs versus CCs in Baltimore, which remained substantial even after extensive adjustment for multiple measures of SES (education, occupation, income, and wealth).

In summary, our results stress the need for further research investigating etiological risk factors across the AD process among AAs. There is evidence that AAs seek health care for cognitive problems later than CCs, and are then not evaluated by specialists, posing major obstacles for early deployment of disease-modifying therapies [44, 45]. Future research efforts should target AAs at high risk for AD due to parental history and vascular factors during middle age, before the AD neuropathological cascade begins and when there is time to stage an intervention.

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References

1. Dilworth-Anderson P, Hendrie HC, Manly JJ, Khachaturian AS, Fazio S. Social, Behavioral and Diversity Research Workgroup of the Alzheimer's Association. Diagnosis and assessment of Alzheimer's disease in diverse populations. *Alzheimers Dement*. 2008; 4:305–309. [PubMed: 18631983]
2. Alzheimer's Association. 2015 Alzheimer's disease facts and figures. *Alzheimers Dement*. 2015; 11:332–384. [PubMed: 25984581]
3. Plassman BL, Langa KM, Fisher GG, Heeringa SG, Weir DR, Ofstedal MB, Burke JR, Hurd MD, Potter GG, Rodgers WL, Steffens DC, Willis RJ, Wallace RB. Prevalence of dementia in the United States: The aging, demographics, and memory study. *Neuroepidemiology*. 2007; 29:125–132. [PubMed: 17975326]
4. Hebert LE, Bienias JL, Aggarwal NT, Wilson RS, Bennett DA, Shah RC, Evans DA. Change in risk of Alzheimer disease over time. *Neurology*. 2010; 75:786–791. [PubMed: 20805524]
5. Tang MX, Cross P, Andrews H, Jacobs DM, Small S, Bell K, Merchant C, Lantigua R, Costa R, Stern Y, Mayeux R. Incidence of AD in African-Americans, Caribbean Hispanics, and Caucasians in northern Manhattan. *Neurology*. 2001; 56:49–56. [PubMed: 11148235]
6. Katz MJ, Lipton RB, Hall CB, Zimmerman ME, Sanders AE, Verghese J, Dickson DW, Derby CA. Age-specific and sex-specific prevalence and incidence of mild cognitive impairment, dementia, and Alzheimer dementia in blacks and CCs: A report from the Einstein Aging Study. *Alzheimer Dis Assoc Disord*. 2012; 26:335–343. [PubMed: 22156756]
7. Kukull WA, Higdon R, Bowen JD, McCormick WC, Teri L, Schellenberg GD, van Belle G, Jolley L, Larson EB. Dementia and Alzheimer disease incidence: A prospective cohort study. *Arch Neurol*. 2002; 59:1737–1746. [PubMed: 12433261]
8. Fitzpatrick AL, Kuller LH, Ives DG, Lopez OL, Jagust W, Breitner JC, Jones B, Lyketsos C, Dulberg C. Incidence and prevalence of dementia in the Cardiovascular Health Study. *J Am Geriatr Soc*. 2004; 52:195–204. [PubMed: 14728627]
9. Plassman BL, Langa KM, McCammon RJ, Fisher GG, Potter GG, Burke JR, Steffens DC, Foster NL, Giordani B, Unverzagt FW, Welsh-Bohmer KA, Heeringa SG, Weir DR, Wallace RB. Incidence of dementia and cognitive impairment, not dementia in the United States. *Ann Neurol*. 2011; 70:418–426. [PubMed: 21425187]
10. Yaffe K, Falvey C, Harris TB, Newman A, Satterfield S, Koster A, Ayonayon H, Simonsick E. Health ABC Study. Effect of socioeconomic disparities on incidence of dementia among biracial older adults: Prospective study. *Brit Med J*. 2013; 347:f7051. [PubMed: 24355614]
11. Perkins P, Annegers JF, Doody RS, Cooke N, Aday L, Vernon SW. Incidence and prevalence of dementia in a multiethnic cohort of municipal retirees. *Neurology*. 1997; 49:44–50. [PubMed: 9222168]
12. Fillenbaum GG, Heyman A, Huber MS, Woodbury MA, Leiss J, Schmader KE, Bohannon A, Trapp-Moen B. The prevalence and 3-year incidence of dementia in older Black and White community residents. *J Clin Epidemiol*. 1998; 51:587–595. [PubMed: 9674666]
13. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986; 7:177–188. [PubMed: 3802833]
14. Brookmeyer R, Evans DA, Hebert L, Langa KM, Heeringa SG, Plassman BL, Kukull WA. National estimates of the prevalence of Alzheimer's disease in the United States. *Alzheimers Dement*. 2011; 7:61–73. [PubMed: 21255744]
15. Wilson RS, Aggarwal NT, Barnes LL, Bienias JL, Mendes de Leon CF, Evans DA. Biracial population study of mortality in mild cognitive impairment and Alzheimer disease. *Arch Neurol*. 2009; 66:767–772. [PubMed: 19506138]

16. Chin AL, Negash S, Hamilton R. Diversity and disparity in dementia: The impact of ethnoracial differences in Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2011; 25:187–195. [PubMed: 21399486]
17. Barnes LL, Bennett DA. Alzheimer's disease in African Americans: Risk factors and challenges for the future. *Health Aff (Millwood)*. 2014; 33:580–586. [PubMed: 24711318]
18. Centers for Disease Control and Prevention. Prevalence of Hypertension and Controlled Hypertension — United States, 2007–2010. *Morbidity and Mortality Weekly Report*. 2013; 62:144–148.
19. Centers for Disease Control and Prevention. Prevalence of Obesity Among Adults Aged 20 Years, by Race/Ethnicity and Sex — National Health and Nutrition Examination Survey, United States, 2009–2010. *Morbidity and Mortality Weekly Report*. 2012; 61:130.
20. Centers for Disease Control and Prevention. Diabetes — United States, 2006 and 2010. *Morbidity and Mortality Weekly Report*. 2013; 62:99–104. [PubMed: 23407125]
21. Deckers K, van Boxtel MP, Schiepers OJ, de Vugt M, Muñoz Sánchez JL, Anstey KJ, Brayne C, Dartigues JF, Engedal K, Kivipelto M, Ritchie K, Starr JM, Yaffe K, Irving K, Verhey FR, Köhler S. Target risk factors for dementia prevention: A systematic review and Delphi consensus study on the evidence from observational studies. *Int J Geriatr Psychiatry*. 2015; 30:234–246. [PubMed: 25504093]
22. Helzner EP, Scarmeas N, Cosentino S, Tang MX, Schupf N, Stern Y. Survival in Alzheimer disease: A multiethnic, population-based study of incident cases. *Neurology*. 2008; 71:1489–1495. [PubMed: 18981370]
23. Wharton W, Stein JH, Korcarz C, Sachs J, Olson SR, Zetterberg H, Dowling M, Ye S, Gleason CE, Underbakke G, Jacobson LE, Johnson SC, Sager MA, Asthana S, Carlsson CM. The effects of ramipril in individuals at risk for Alzheimer's disease: Results of a pilot clinical trial. *J Alzheimers Dis*. 2012; 32:147–156. [PubMed: 22776970]
24. Wharton W, Goldstein FC, Zhao L, Steenland K, Levey AI, Hajjar I. Modulation of renin-angiotensin system may slow conversion to mild cognitive impairment to Alzheimer's disease. *J Am Geriatr Soc*. 2015; 63:1749–1756. [PubMed: 26389987]
25. Miners JS, Ashby E, Van Helmond Z, Chalmers KA, Palmer LE, Love S, Kehoe PG. Angiotensin-converting enzyme (ACE) levels and activity in Alzheimer's disease, and relationship of perivascular ACE-1 to cerebral amyloid angiopathy. *Neuropathol Appl Neurobiol*. 2008; 34:181–193. [PubMed: 17973905]
26. Hajjar I, Brown L, Mack WJ, Chui H. Impact of Angiotensin receptor blockers on Alzheimer disease neuropathology in a large brain autopsy series. *Neurology*. 2012; 69:1632–1638.
27. Reitz C, Mayeux R. Genetics of Alzheimer's disease in Caribbean Hispanic and African American populations. *Biol Psychiatry*. 2014; 75:534–541. [PubMed: 23890735]
28. Goldstein FC, Ashley AV, Gearing M, Hanfelt J, Penix L, Freedman LJ, Levey AI. Apolipoprotein E and age at onset of Alzheimer's disease in African American patients. *Neurology*. 2001; 57:1923–1925. [PubMed: 11723294]
29. Tang MX, Stern Y, Marder K, Bell K, Gurland B, Lantigua R, Andrews H, Feng L, Tycko B, Mayeux R. The APOE-epsilon4 allele and the risk of Alzheimer disease among African Americans, whites, and Hispanics. *JAMA*. 1998; 279:751–755. [PubMed: 9508150]
30. Farrer LA, Cupples LA, Haines JL, Hyman B, Kukull WA, Mayeux R, Myers RH, Pericak-Vance MA, Risch N, van Duijn CM. Effects of age, sex, and ethnicity on the association between apolipoprotein E genotypes and Alzheimer disease. *JAMA*. 1997; 278:1349–1356. [PubMed: 9343467]
31. Reitz C, Jun G, Naj A, Rajbhandary R, Vardarajan BN, Wang LS, Valladares O, Lin CF, Larson EB, Graff-Radford NR, Evans D, De Jager PL, Crane PK, Buxbaum JD, Murrell JR, Raj T, Ertekin-Taner N, Logue M, Baldwin CT, Green RC, Barnes LL, Cantwell LB, Fallin MD, Go RC, Griffith P, Obisesan TO, Manly JJ, Lunetta KL, Kamboh MI, Lopez OL, Bennett DA, Hendrie H, Hall KS, Goate AM, Byrd GS, Kukull WA, Foroud TM, Haines JL, Farrer LA, Pericak-Vance MA, Schellenberg GD, Mayeux R. Alzheimer Disease Genetics Consortium. Variants in the ATP-binding cassette transporter (ABCA7), apolipoprotein E 4, and the risk of late-onset Alzheimer disease in African Americans. *JAMA*. 2013; 309:1483–1492. [PubMed: 23571587]

32. Logue MW, Schu M, Vardarajan BN, Buross J, Green RC, Go RC, Griffith P, Obisesan TO, Shatz R, Borenstein A, Cupples LA, Lunetta KL, Fallin MD, Baldwin CT, Farrer LA. Multi-Institutional Research on Alzheimer Genetic Epidemiology (MIRAGE) Study Group. A comprehensive genetic association study of Alzheimer disease in African Americans. *Arch Neurol*. 2011; 68:1569–1579. [PubMed: 22159054]
33. Kaup AR, Nettiksimmons J, Harris TB, Sink KM, Satterfield S, Metti AL, Ayonayon HN, Yaffe K. Cognitive resilience to apolipoprotein E ε4: Contributing factors in black and white older adults. Health, Aging, and Body Composition (Health ABC) Study. *JAMA Neurol*. 2015; 72:340–348. [PubMed: 25599330]
34. Wilkins CH, Grant EA, Schmitt SE, McKeel DW, Morris JC. The neuropathology of Alzheimer disease in African American and white individuals. *Arch Neurol*. 2006; 63:87–90. [PubMed: 16401740]
35. Mehta KM, Yaffe K, Pérez-Stable EJ, Stewart A, Barnes D, Kurland BF, Miller BL. Race/ethnic differences in AD survival in US Alzheimer's Disease Centers. *Neurology*. 2008; 70:1163–1170. [PubMed: 18003939]
36. Diniz BS, Butters MA, Albert SM, Dew MA, Reynolds CF 3rd. Late-life depression and risk of vascular dementia and Alzheimer's disease: Systematic review and meta-analysis of community-based cohort studies. *Br J Psychiatry*. 2013; 202:329–335. [PubMed: 23637108]
37. Machado A, Herrera AJ, de Pablos RM, Espinosa-Oliva AM, Sarmiento M, Ayala A, Venero JL, Santiago M, Villarán RF, Delgado-Cortés MJ, Argüelles S, Cano J. Chronic stress as a risk factor for Alzheimer's disease. *Rev Neurosci*. 2014; 25:785–804. [PubMed: 25178904]
38. Williams DR. The health of men: Structured inequalities and opportunities. *Am J Public Health*. 2003; 93:724–731. [PubMed: 12721133]
39. Clark R, Anderson NB, Clark VR, Williams DR. Racism as a stressor for African Americans. A biopsychosocial model. *Am Psychol*. 1999; 54:805–816. [PubMed: 10540593]
40. Centers for Disease Control and Prevention. Current Depression Among Adults – United States, 2006 and 2008. *Morbidity and Mortality Weekly Report*. 2010; 59:1229–1235. [PubMed: 20881934]
41. Williams DR, González HM, Neighbors H, Nesse R, Abelson JM, Sweetman J, Jackson JS. Prevalence and distribution of major depressive disorder in African Americans, Caribbean blacks, and non-Hispanic whites: Results from the National Survey of American Life. *Arch Gen Psychiatry*. 2007; 64:305–315. [PubMed: 17339519]
42. Steenland K, MacNeil J, Seals R, Levey A. Factors affecting survival of patients with neurodegenerative disease. *Neuroepidemiology*. 2010; 35:28–35. [PubMed: 20389122]
43. Fitten LJ, Ortiz F, Fairbanks L, Bartzokis G, Lu P, Klein E, Coppola G, Ringman J. Younger age of dementia diagnosis in a Hispanic population in southern California. *Int J Geriatr Psychiatry*. 2014; 29:586–593. [PubMed: 24478258]
44. Schwartz BS, Glass TA, Bolla KI, Stewart WF, Glass G, Rasmussen M, Bressler J, Shi W, Bandeen-Roche K. Disparities in cognitive functioning by race/ethnicity in the Baltimore Memory Study. *Environ Health Perspect*. 2004; 112:314–320. [PubMed: 14998746]
45. Hinton L, Franz C, Friend J. Pathways to dementia diagnosis: Evidence for cross-ethnic differences. *Alzheimer Dis Assoc Disord*. 2004; 18:134–144. [PubMed: 15494619]
46. Mukadam N, Cooper C, Livingston G. A systematic review of ethnicity and pathways to care in dementia. *Int J Geriatr Psychiatry*. 2011; 26:12–20. [PubMed: 21157846]

Table 1

Study-specific and combined rate ratios (RRs) for AD incidence, AAs versus CCs

Study	cases AA	cases CCs	RR AA/CCs	Mean y follow-up	Location and confounder adjustment
Hebert et al. [4]	213 ^a	147	1.76 (1.19–2.63)	7.1	Chicago; adjusted for age, race, gender, education; 65+; tri-annual visits over 11 years (1997–2008)
Tang et al. [5]	64	22	2.4 (1.5–4.0) ^b	2.9	New York City; adjusted for age, gender, education; bi-annual visits over a 7 year period (1992–1999)
Katz et al. [6]	29	68	1.27 (0.82–1.98)	3.9	New York City; adjusted for age, gender, education, referent non-Hispanic CCs; annual follow-up, all subjects had 2+ follow-ups, rolling recruitment 1993–2004+.
Kukull et al. [7]	7	140	1.54 (0.73–3.29)	4.5	Seattle; adjusted for age, gender, education, APOE; enrollment in 1994–1996, bi-annual follow-up, end of follow-up not stated, all had at least one follow-up visit, 15% died and 6% dropped out during follow-up (1990–1999)
Fitzpatrick et al. [8]	39	203	1.81 (0.98–2.41) ^c	5.4	3 counties in NC, Maryland, California, and Pittsburgh; adjusted for age only; annual visits over 10 years national sample; adjusted for age, gender, education, and APOE, age 72+, RR estimated via logistic regression; 3 follow-up visits approximately 2 years apart from 2001/2003 through 2008/2009
Plassman et al. [9]	18 ^d	59 ^d	1.22 (0.58–2.57)	4.9	
Combined	370	639	1.64 (1.35–2.00)	5.5 ^e	

^aNumbers of AA and CC cases provided by personal communication, Sept 29, 2015.

^bRR for AAs versus Caucasians, excluding Hispanics.

^cRR derived from age-adjusted rates for AAs (34.7/100,000), and CCs (19.2/100,000), std. error of log RR calculated from p-value of 0.06 for rate ratio.

^dData on number of AA versus CC cases estimated from race-specific numbers of dementia cases and percentage AD cases among dementia cases.

^eWeighted average of follow-up times from six studies with available data; weights are the sum of AD cases in each study.