Incidence of Dementia and Alzheimer Disease in 2 Communities

Yoruba Residing in Ibadan, Nigeria, and African Americans Residing in Indianapolis, Indiana

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Context Alzheimer disease (AD) represents a major and increasing public health problem. If populations were identified with significantly lower or higher incidence rates of AD, the search for risk factors in the genesis of AD could be greatly enhanced.

Objective To compare incidence rates of dementia and AD in 2 diverse, elderly community-dwelling populations.

Design The Indianapolis-Ibadan Dementia Project, a longitudinal, prospective population-based study consisting of a baseline survey (1992-1993) and 2 subsequent follow-up waves after 2 years (1994-1995) and 5 years (1997-1998). Each wave followed a 2-stage design, with an in-home screening interview followed by a full diagnostic workup of a subsample of participants based on screening performance.

Setting and Participants A total of 2459 community-dwelling Yoruba residents of Ibadan, Nigeria, without dementia, and 2147 community-dwelling African American residents of Indianapolis, Ind, without dementia (all aged 65 years or older). The cohorts were followed up for a mean of 5.1 years and 4.7 years, respectively.

Main Outcome Measures Incident cases of dementia and AD in each of the 2 populations.

Results The age-standardized annual incidence rates were significantly lower among Yoruba than among African Americans for dementia (Yoruba, 1.35% [95% confidence interval {CI}, 1.13%-1.56%]; African Americans, 3.24% [95% CI, 2.11%-4.38%]) and for AD (Yoruba, 1.15% [95% CI, 0.96%-1.35%]; African Americans, 2.52% [95% CI, 1.40%-3.64%]).

Conclusion This is the first report of incidence rate differences for dementia and AD in studies of 2 populations from nonindustrialized and industrialized countries using identical methods and the same group of investigators in both sites. Further explorations of these population differences may identify potentially modifiable environmental or genetic factors to account for site differences in dementia and AD.

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ALZHEIMER DISEASE (AD) REPREsents a major public health problem for developed countries, including the United States.[1,2] The impact of AD has not been studied as much in developing countries in which the growth of the proportion of elderly persons in the population is even greater than in developed countries.[3]

The assessment of rates of AD for different populations also could offer a powerful opportunity to explore risk factors for the disease. If populations could be identified with significantly different incidence rates of AD, the search for risk factors could be greatly enhanced by exploiting the diversity of their genetics and cultures, as well as their relative exposures to disease pathogens or environmentally noxious agents.

Considerable variations have been reported in prevalence and incidence rates of AD between countries,[4,5] but most investigators conclude that these variations in rates are mainly due to differences in study methods.[6]

Since 1992, research teams from Indiana University (Indianapolis) and the

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University of Ibadan (Ibadan, Nigeria) have been collaborating on studies of the prevalence and incidence of dementia in elderly African Americans and Yoruba using identical methods. We have reported significant differences in the age-adjusted prevalence rates of dementia and AD.[7] However, prevalence rates vary with factors other than actual rates of illness. Differences in life expectancy or in survival of individuals with and without dementia could alter these rates. Incidence rates are a better indication of true rates of illness than prevalence rates. In this article, we report the results of the 5-year incidence study of dementia and AD conducted at 2 sites.

METHODS
Populations of the Indianapolis-Ibadan Dementia Project

Ibadan, Nigeria. The study was carried out in the Idikan area and adjacent wards of the city of Ibadan. The city's population of about 3 million is fairly stable and comprises mainly Yoruba. A total population survey was carried out by means of door-to-door screening in a geographically defined area. Date of birth was estimated from a table of historical landmarks well known to the population, a well-tested, long-standing practice in Nigeria to assess ages of adults.[8]

Indianapolis, Ind. The geographic target area used in the study consisted of 29 contiguous census tracts in which African Americans represented 80% of the population in the 1990 US census. According to the US census, the distributions of age, sex, and socioeconomic status of the residents of these tracts are representative of all African Americans in Indianapolis and in the state of Indiana. Interviewers went door-to-door to randomly sampled addresses and to invite African Americans aged 65 years or older to participate.

Research Design

The design consisted of a prevalence study at baseline followed by 2 incidence waves after 2 and 5 years. Each wave followed a 2-stage design (**FIGURE 1**) in which there was first an in-home screening followed by a full diagnostic workup of a subsample of participants selected on the basis of the performance on the screening test. Before the start of each wave of the study, informed consent was obtained from the participants and informants. The institutional review boards at both universities approved the study.

The prevalence study was conducted from 1992 to 1993. The first incidence wave was conducted 2 years later from 1994 to 1995 and the second incidence wave was conducted approximately 5 years after the prevalence study from 1997 to 1998. The mean follow-up time for subjects in Ibadan was 5.1 years and for subjects in Indianapolis was 4.7 years.

The study cohort consisted of 2459 community-dwelling Yoruba and 2147 community-dwelling African Americans. This excluded the participants diagnosed as having dementia in the prevalence study (65 African Americans and 28 Yoruba). The prevalence study also included an additional 106 nursing home residents in Indianapolis who were not included in the incidence studies as the great majority (72) were diagnosed as having dementia in the prevalence study, the remainder being very ill and frail.

At each incidence wave, study participants were divided into 3 performance groups (good, intermediate, and poor) based on their current screening scores and their changes in scores from previous waves. To ensure that participants with the highest probability of having dementia would be clinically assessed, 100% of the poor performance group was invited to be clinically assessed. Participants were randomly sampled from the intermediate performance group until 50% had clinical assessments and from the good performance group (weighted to obtain a sample for which 75% would be aged ≥75 years) until 5% had clinical assessments. The percentages of the participants in Indianapolis and in Ibadan in each of these performance groups were quite comparable for both incidence 1 and incidence 2.

Each clinically assessed participant received a diagnosis of normal, cognitively impaired, or demented, with the individuals with dementia further subtyped (see "Diagnostic Criteria"). All individuals diagnosed as having dementia were excluded from subsequent incidence waves. All participants who were diagnosed as cognitively impaired in a previous wave proceeded directly to the clinical assessment stage without any screening procedure (the overall scheme is depicted in the Figure).

Screening Instruments

The Community Screening Interview for Dementia (CSID) was developed by our group specifically for use in comparative epidemiological studies of dementia in culturally disparate, nonliterate and literate populations.[9,10] This screening interview consists of a cognitive assessment of the study participant and an interview with a close relative (informant) evaluating the daily functioning of the participant. The development of the CSID placed great emphasis on making each item harmonious with the local language and culture. Pilot studies were conducted at both sites prior to the initial prevalence study to establish normative values and optimum cut-off scores at each site. Details of its content and development are described elsewhere.[9,10]

Clinical Assessment Instruments

All clinically assessed participants at both sites received the same examination, which included a structured interview with an informant; neuropsychological testing; examination by a physician; and laboratory and imaging studies, when deemed clinically appropriate. All clinical assessments were conducted in the participant's home. The research nurse and psychometrician first visited the participants and completed the informant interview and neuropsychological testing. The physician then reviewed the data, made a home visit to conduct the physical and

neurological examination, collected blood for laboratory tests, and ordered a head computed tomographic scan whenever possible and when deemed clinically appropriate. In addition, in Ibadan, a sample of nondemented subjects were scanned in an effort to establish a database of elderly subjects across a spectrum of cognitive function for comparative purposes and future prospective studies. A total of 65 demented subjects in Indianapolis were scanned. In Ibadan, a total of 62 scans were performed on 19 healthy subjects, 28 cognitively impaired subjects, and 15 subjects with dementia.

Informant Interview

A research nurse conducted a structured interview with an informant, usu-

Figure 1. Design and Participant Flow Chart for Incidence Study
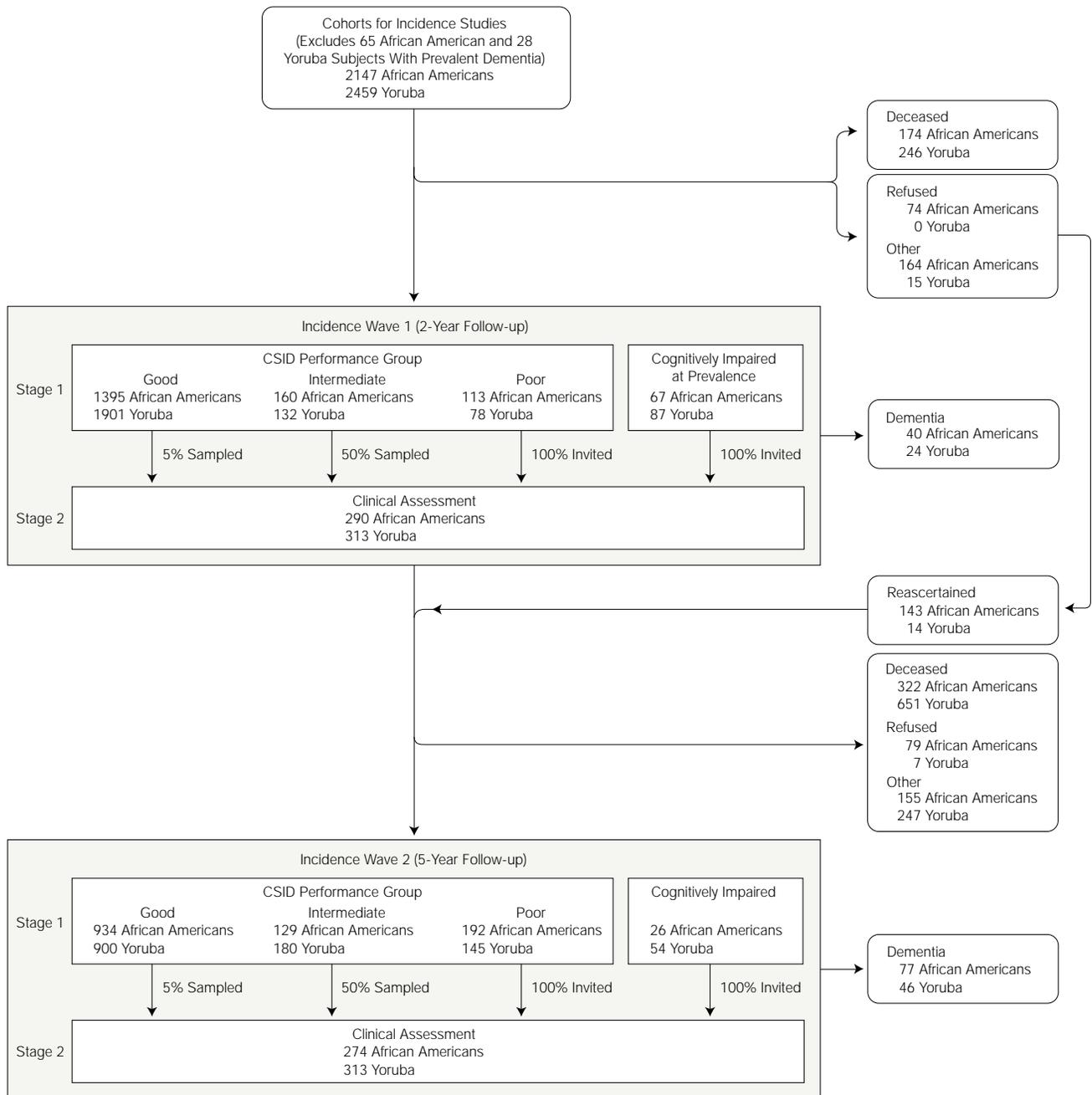
CSID indicates Community Screening Interview for Dementia.[9,10]

ally a relative of the participant. The interview has 4 components consisting of (1) a historical review of the participant's cognitive function, memory, language, judgment, reasoning, and personality function; (2) a review of the participant's performance in the various domains of activities of daily living; (3) a review of the participant's medical history and medications; and (4) a history of possible dementia-associated conditions. The interview was based on the Cambridge Mental Disorders of the Elderly Examination.[11] The nurses obtained a high degree of reliability after training, agreeing on 98.6% of the items.

Neuropsychological Battery

Cognitive testing in the clinical assessment was done with a slightly modified version of the Consortium to Establish a Registry for Alzheimer Disease neuropsychological battery,[12] which was translated into Yoruba for use in Ibadan.

Physician Examination

The physical and neurological examinations were conducted and recorded according to the Consortium to Establish a Registry for Alzheimer Disease procedures.[12]

Diagnostic Criteria

Both *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition (DSM-III-R)*[13] and *International Classification of Diseases, 10th Revision (ICD-10)*[14] criteria were used to diagnose dementia and to rate dementia severity. Participants had to satisfy both sets of criteria to be counted as having dementia. There were no participants who satisfied *ICD-10* criteria who did not also satisfy *DSM-III-R* criteria.

The National Institute for Neurological and Communicative Diseases and Stroke–Alzheimer Disease and Related Disorders Association criteria[15] were used for probable and possible AD; *ICD-10* criteria were used for vascular dementia and other secondary dementias. Criteria for cognitive impairment were similar to those published by the Aging-Associated Cognitive Decline Working Party.[16]

Diagnostic Process

Every attempt was made to ensure diagnostic consistency across sites. The diagnostic process involved senior experienced members of the faculties of medicine at the University of Ibadan and at Indiana University familiar with both the criteria for dementia and with the local culture. All available information from the clinical assessment(s) was reviewed in determining the diagnosis. No information from the screening interview was used in making a diagnosis. Local normative data from each site were used to interpret Consortium to Establish a Registry for Alzheimer Disease neuropsychological test battery raw scores and change scores.[17,18] The information was first reviewed by the site clinicians in a consensus conference and a site diagnosis was made. Later, 1 or more clinicians from the other site reviewed all of the clinical data while blinded to the local team's diagnosis, and recorded an independent diagnosis. A consensus conference, involving clinicians from both sites, was held to review cases with discrepant diagnoses between sites and a final consensus diagnosis was made.

Statistical Analysis

Variables between participants with and without clinical assessment in the poor performance group were compared using *t* tests for continuous variables and χ^2 tests for categorical variables.

To identify factors associated with various attrition patterns, all study participants were divided into 4 mutually exclusive groups: (1) individuals who completed both incidence waves, (2) individuals who had died since the prevalence study, (3) individuals who participated in the first incidence wave but not the second, and (4) individuals who were lost to follow-up after the prevalence phase. Comparisons of continuous baseline characteristics (age, years of education, and screening scores) were conducted using 1-way analysis of variance with 4 groups for India-napolis and 3 groups for Ibadan (the lost-to-follow-up group was excluded because of small sample size). Scheffe multiple comparison procedure was used to compare the complete follow-up group with the other 3 groups. Categorical baseline variables (sex and education) were compared using χ^2 tests.

To examine any differential mortality between sites, χ^2 tests were used to compare mortality rates between the 2 populations by age and by baseline diagnosis. Comparisons of mortality rates between participants with and without dementia from study baseline within each population were also performed using χ^2 tests.

The person-years method of estimating incidence rates[19] was extended to take into account sampling for clinical assessment and attrition due to death. Since only a subset of participants was clinically diagnosed, the probability of disease for any participant was estimated from weighted logistic regression based on the clinically diagnosed individuals using disease as the binary outcome variable with age, sex, and performance groups as predictors; the weights were the reciprocals of sampling probability. The total number of participants with dementia or AD for each of the 2 study populations was estimated by summing predicted probabilities of disease over all participants. To estimate the number of incident cases, the estimated total number of participants with disease was further adjusted by the estimated number of participants with dementia among those not clinically evaluated in the previous waves. The person-years at risk for an individual with dementia were calculated as the follow-up time from prevalence baseline to the midpoint between a previous evaluation without a dementia diagnosis to the time of the dementia diagnosis. Person-years at risk for participants with dementia were derived as the time lapse between study baseline to the time of last clinical assessment if the participant was clinically evaluated, or the time of the last screen-

ing interview if the participant was not clinically assessed.

We adjusted our incidence rates for mortality to provide a fair comparison of the disease rates. Probabilistic models for death were derived for baseline demented and nondemented participants, separately, for both the Yoruba and the African Americans using logistic regression models controlling for age, sex, and most current performance group. Probability of dementia and AD was then calculated for the deceased participants using Bayes theorem based on the participant's age at death, sex, and most recent performance group standing. The estimated total number of incident demented (AD) participants then included the estimated number with incident dementia (AD) among the deceased participants.

The incidence rates for a specific age group were calculated as the total estimated number with incident disease (dementia or AD) divided by the total person-years at risk for the age group. Since the incidence rates were derived from complex models, we chose to use a nonparametric method, the jackknife variance estimator, for the derivation of SEs of the rate estimates. Age-standardized overall incidence rate for each population was obtained by applying the estimated age-specific rates to the age distribution of African-American residents in Indianapolis observed in the 1990 census: 60% aged 65 to 74 years, 30% aged 75 to 84 years, and 10% aged 85 years or older. The variance of the overall age-standardized rate was calculated as a weighted mean of the variances of the age-specific rates. Ninety-five percent confidence intervals (CIs) for the incidence rates were constructed based on asymptotic normality of the estimates.

RESULTS

The number of participants at each incidence wave, including the number in each performance category, the total number of clinically assessed at each site, the number of participants lost, and the reasons for attrition, are shown in the Figure.

TABLE 1 shows comparisons of baseline-prevalent demographic characteristics and screening scores between participants with and without clinical assessment in the poor performance group by CSID at each study wave in Yoruba and African Americans. Participants in both populations in the poor performance category who were not clinically assessed did not differ significantly from participants who were clinically assessed on age, sex, education, and informant scores. African Americans without clinical assessment scored slightly but significantly lower on cognitive scores than those with clinical assessment in the second incidence wave. Yoruba had no significant difference in cognitive scores. These results indicate that the clinically assessed among those in the poor performance groups were comparable with those not assessed, except that in Indianapolis those not clinically assessed had slightly lower cognitive scores and thus might have been more likely to have dementia.

TABLE 2 compares the baseline demographic characteristics and screening scores for 4 groups of participants: individuals who completed both incidence waves; individuals who had died since prevalence determination; individuals who participated in the first incidence wave but not the second; and individuals who were lost to follow-up after the prevalence phase.

In both populations, the major significant differences were between the participants who had died during the course of the study and the participants who completed both stages of the study. In both sites, the deceased participants were significantly older and scored more poorly, both cognitively and functionally, in the screening evaluation. The African American participants who died also had fewer years of education. There were few significant

Table 1. Comparisons of Baseline Demographic Characteristics and Screening Scores Between Participants With and Without Clinical Assessment in the Poor Performance Group*

Baseline Variable	Study Wave 1			Study Wave 2		
	With Clinical Assessment	Without Clinical Assessment	P Value	With Clinical Assessment	Without Clinical Assessment	P Value
	African Americans					
	(n = 65)	(n = 48)		(n = 135)	(n = 57)	
Age	76.2 (7.7)	78.9 (8.0)	.08	76.8 (7.2)	77.1 (8.4)	.75
Women, %	63.1	60.4	.77	71.2	75.4	.61
Education, y	8.6 (3.3)	8.1 (3.2)	.42	9.1 (3.0)	8.5 (3.2)	.17
Cognitive score	29.5 (2.8)	29.3 (2.9)	.74	30.3 (2.4)	29.4 (2.7)	.02
Informant score	3.7 (3.5)	4.5 (3.5)	.40	3.3 (3.0)	3.3 (2.4)	.91
	Yoruba					
	(n = 61)	(n = 17)		(n = 119)	(n = 26)	
Age	74.2 (6.8)	76.8 (9.2)	.19	73.7 (8.4)	73.5 (6.1)	.90
Women, %	75.4	76.5	.93	77.3	61.5	.10
Any education, %	8.2	23.5	.10	9.2	15.4	.47
Cognitive score	27.5 (3.8)	27.1 (2.8)	.73	28.3 (2.6)	28.9 (2.4)	.29
Informant score	2.3 (2.6)	2.8 (2.3)	.49	2.4 (2.2)	2.7 (2.4)	.59

*Scores are based on responses to the Community Screening Interview for Dementia and are presented as mean (SD) unless otherwise indicated.

Table 2. Comparisons of Baseline Characteristics for 4 Outcome Groups*

Baseline Variables†	Completed Follow-up	Died During Follow-up	Partial Follow-up	Lost to Follow-up	Analysis of Variance P Value‡
		African Americans			
	(n = 1321)	(n = 496)	(n = 181)	(n = 149)	
Age, y	73.0 (6.5)	75.7 (7.5)	74.0 (6.2)	74.0 (7.3)	<.001§
Women, %	68.4	57.3	66.9	57.7	.001
Education, y	9.9 (3.0)	9.2 (3.2)	9.4 (3.0)	9.6 (3.2)	<.001§
Cognitive score	31.0 (2.1)	30.2 (2.5)	30.4 (2.2)	30.0 (3.2)	<.001§‖¶
Informant score	2.4 (2.6)	3.1 (3.3)	2.4 (2.5)	2.9 (3.6)	<.001§
		Yoruba			
	(n = 1303)	(n = 897)	(n = 254)	(n = 5)	
Age, y	71.3 (6.7)	74.2 (8.4)	69.9 (5.5)	73.6 (7.0)	<.001§‖
Women, %	64.6	63.3	71.7	80.0	.05
Any education, %	16.7	13.2	14.6	40.0	.08
Cognitive score	28.7 (2.7)	27.5 (4.2)	29.1 (2.5)	29.2 (2.4)	<.001§
Informant score	2.2 (1.9)	3.0 (2.9)	2.0 (1.6)	4.2 (4.6)	<.001§

*Participants in the complete follow-up group were either followed up at study wave 2 or had dementia at study wave 1. Participants in the partial follow-up group were followed up at study wave 1, but lost to follow-up at study wave 2. Participants in the lost-to-follow-up group provided no information beyond baseline.
†Values are expressed as mean (SD) unless otherwise indicated.
‡Derived using analysis of variance comparing all 4 groups for Indianapolis, Ind, and the first 3 groups for Ibadan, Nigeria. Scheffe multiple comparison procedure was used to compare the group of participants who completed follow-up vs the other 3 groups.
§P<.05 for comparison of the completed follow-up group with the group who died during follow-up.
‖P<.05 for comparison of the completed follow-up group with the partial follow-up group.
¶P<.05 for comparison of the completed follow-up group with the lost-to-follow-up group.

Table 3. Comparisons of Mortality Rates by Age Groups and Baseline Diagnosis

	Yoruba		African Americans		
	Total	No. (%) Died	Total	No. (%) Died	P Value*
Age group, y					
65-74	1780	565 (31.7)	1297	240 (18.5)	.001
75-84	461	206 (44.7)	667	182 (27.3)	.001
≥85	218	126 (57.8)	183	74 (40.4)	.001
Overall	2459	897 (36.5)	2147	496 (23.1)	.001
Baseline diagnosis					
Dementia	28	17 (60.7)	65	34 (52.3)	.46
No dementia	395	165 (41.8)	287	90 (31.4)	.01

*P values are derived from χ^2 tests comparing the mortality rates.

differences between the other groups and the group that completed all phases of the study. Among African Americans, the partial follow-up and lost-to-follow-up participants scored significantly poorer in the cognitive portion of the prevalence screening test. The Yoruba participants with partial follow-up were significantly younger than those who remained in the study.

The mortality rates of the Yoruba and African Americans by age group and baseline diagnosis are presented in TABLE 3. Yoruba had significantly higher mortality rates than African Americans for all age groups. The Yoruba participants without dementia at baseline also had a significantly higher mortality rate than the African

Americans without dementia. In both populations, those with dementia at baseline had significantly higher mortality rates than those without dementia at baseline (P=.05 for Yoruba and P=.001 for African Americans).

TABLE 4 shows the results of the clinical assessments for each incidence wave by performance group. A total of 117 African Americans were diagnosed as having incident dementia (40 in the first wave and 77 in the second wave). Of these, 89 (76%) met criteria for probable or possible AD and 16 (14%) met criteria for vascular dementia. Other diagnoses in African Americans included alcoholism-related dementia (7 individuals), and Parkinson dementia (1 individual). Four developed demen-

tia in association with multiple, severe chronic illnesses. A total of 70 Yoruba were diagnosed as having incident dementia (24 in the first wave and 46 in the second wave). Of these, 62 (88%) Yoruba met criteria for probable or possible AD and 4 (5.7%) were diagnosed as having vascular dementia. One Yoruba had Parkinson dementia, 2 had dementia associated with severe chronic illnesses, and 1 had an unspecified dementia.

The age-specific, age-standardized, mortality-adjusted annual incidence rates for Yoruba and African Americans are shown in TABLE 5. The overall age-standardized incidence rates for both dementia and AD were significantly lower in the Yoruba than in the African Americans (for dementia: Yoruba, 1.35% [95% CI, 1.13-1.56], African Americans, 3.24% [95% CI, 2.11-4.38]; for AD: Yoruba, 1.15% [95% CI, 0.96-1.35], African Americans, 2.52% [95% CI, 1.40-3.64]). The age-specific incidence rates for both dementia and AD were lower in all age categories in the Yoruba than in the African Americans, although in most age categories 95% confidence limits overlap. The association between increasing age and incidence rates was similar in both populations.

Table 4. Number of Participants With Dementia and Alzheimer Disease (AD) by Sampling Group

| | Yoruba | | | | | | | | | | | | African Americans | | | | | | | | | | | |
| | Wave 1 | | | Wave 2 | | | Wave 1 | | | Wave 2 | | |
Performance	Total*	Dementia	AD	Total*	Dementia	AD	Total*	Dementia	AD	Total*	Dementia	AD
Good†	32	0	0	11	0	0	20	0	0	10	1	1
Good‡	68	0	0	37	0	0	57	2	1	39	2	0
Intermediate	65	0	0	92	5	4	81	3	2	64	6	3
Poor	61	10	7	119	37	33	65	18	14	135	59	48
Cognitively impaired	87	14	14	54	4	4	67	17	14	26	9	6
Total	313	24	21	313	46	41	290	40	31	274	77	58

*Total numbers of participants with clinical evaluation in each group.
†Participants younger than 75 years.
‡Participants 75 years or older.

COMMENT

In the Indianapolis-Ibadan Dementia Project, the age-standardized annual incidence rates for both dementia and AD were significantly lower for Yoruba in Ibadan (1.35% with dementia and 1.15% with AD) than for African Americans living in Indianapolis (3.24% with dementia and 2.52% with AD). To our knowledge, this is the first report of incidence rate differences for AD and dementia between populations in developed and developing countries in studies that used identical methods and groups of investigators.

The Indianapolis-Ibadan incidence rates for dementia and AD for African Americans are in the higher range of previously published incidence rates,[5,20-33] but similar to other published rates from African American populations[34,35] (**FIGURE 2**). The incidence rates for both dementia and AD for Yoruba are among the lowest of previously reported rates. Methodological issues may account for some of the differences in reported incidence rates, including whether adjustments had been made for mortality.

Although there are a number of major potential sources of bias in large-scale, comparative epidemiological studies, we have attempted to minimize these biases. Special attention has been paid to screening and sampling procedures, cohort attrition, and diagnostic issues.

The samples in both sites were population-based and followed strict sampling rules. Our screening instrument, the CSID, was designed specifically for use in nonliterate as well as literate populations and has performed well in pre-

Table 5. Age-Specific Annual Incidence Rate of Dementia and Alzheimer Disease, Adjusted for Mortality*

	Age Group, y	Yoruba Rate, % (95% Confidence Interval)†	African Americans Rate, % (95% Confidence Interval)†
Dementia	65-74	0.45 (0.30-0.60)	1.74 (0.15-3.32)
	75-84	1.69 (1.29-2.10)	4.29 (2.52-6.06)
	≥85	5.71 (4.19-7.22)	9.12 (5.97-12.28)
	Age-standardized overall rate	1.35 (1.13-1.56)	3.24 (2.11-4.38)
Alzheimer disease	65-74	0.38 (0.24-0.52)	1.38 (0-2.99)
	75-84	1.41 (1.04-1.77)	3.29 (1.56-5.01)
	≥85	5.02 (3.62-6.42)	7.07 (4.54-9.61)
	Age-standardized overall rate	1.15 (0.96-1.35)	2.52 (1.40-3.64)

*The overall rates (standardized for age) were derived using the age distributions of African Americans in Indianapolis, Ind, according to the 1990 US Census Bureau data.
†The 95% confidence intervals are narrower in Yoruba than in African Americans' incidence rate because the incidence rate in Yoruba was lower.

vious studies in different populations. Our sampling procedure involved clinically assessing a 5% sample of the good performance category of participants to protect against verification bias.

A major problem in all epidemiological studies, particularly in the elderly, is cohort attrition.[36,37] In our study, the main reason for cohort attrition at both sites was death. Individuals who died were older, had poorer cognitive scores, and lower levels of functioning in activities of daily living. Since the mortality rate was higher in Ibadan, we adjusted the incidence rates for mortality for a fair comparison between sites. Refusal rates were low in both populations, and there were few differences between subjects who did and did not complete the study. If there was any bias due to subjects in the poor performance category not participating in clinical assessments, the inclusion of

these participants would have increased the difference in rates between sites because African American nonparticipants scored lower than participants, wheras Yoruba participants and nonparticipants scored similarly.

Establishing comparable diagnoses is always a major issue in cross-cultural research, but great care was taken to ensure that diagnostic consistency was maintained within and between the sites as described in the diagnostic procedure. Although we were unable to blind the investigators as to the site at which participants resided, the objective criteria used and having the same investigators evaluating both groups should help to minimize bias.

In summary, we do not believe that methodological issues account for our findings of different incidence rates for dementia and AD between the 2 sites,

although we acknowledge that there may be other factors associated with mortality and the dementia process that were not adjusted for and that remain to be investigated further in our ongoing longitudinal study. Advances in molecular genetics now allow the opportunity for international studies such as ours to explore etiological hypotheses involving specific genes rather than simple comparisons between races or ethnic groups. One of the most consistent findings in AD research has been the association of the possession of the apolipoprotein E (*APOE*) ε*4* allele to increased susceptibility for AD.[38] In contrast to reports from other populations, we have found only a marginally significant association between possession of the ε*4* allele and AD in the African American population[39] similar to other study reports.[40] In the Yoruba, we have found no significant association between the possession of the ε*4* allele and dementia or AD in either the heterozygous or homozygous states.[41] As the frequencies of the 3 major *APOE* alleles are

almost identical in the 2 populations, this variation in the strength of the association between ε*4* and AD may account for some of the differences in incidence rates between the populations, although it is not likely to explain all of it. It also raises the possibility that some other genetic or environmental factor affects the association of the ε*4* allele to AD and reduces incidence rates for dementia and AD in Yoruba.

Another major difference between the sites is the much lower prevalence of factors often associated with vascular risk in Yoruba as compared with African Americans (ie, lower cholesterol levels, lower body mass index, less hypertension, and less diabetes).[42] Vascular disease may contribute both to dementia and to the development, progression, and clinical severity of AD.[43-45] It is possible that the lower rates of vascular disease risk factors, in addition to or in combination with the difference in the lower association of the *APOE* ε*4* with AD in Yoruba, may account for our reported differences in AD.

This is the first time a study using the same methods in 2 different populations has shown a significant difference in incidence rates of dementia and AD. The findings presented in this article will enable us to pursue the elusive risk factors for AD in these 2 disparate populations. However, it would be premature to conclude from this 1 study that incidence rates of AD would generally be lower in the developing world. It is hoped that this report will encourage more research into AD in these countries. The very strong relationship between AD and increasing age in the Yoruba and the African Americans also suggests, despite the lower incidence rates in Yoruba, that AD is going to present a major public health problem for all countries in the 21st century.

Figure 2. Annual Incidence Rates of Dementia and Alzheimer Disease

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