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Lifetime risk and projected burden of dementia

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Understanding the lifetime risk of dementia can inform public health planning and improve patient engagement in prevention. Using data from a community-based, prospective cohort study (n = 15,043; 26.9% Black race, 55.1% women and 30.8% with at least one apolipoprotein E4 (*APOE* ε4) allele), we estimated the lifetime risk of dementia (from age 55 years to 95 years), with mortality treated as a competing event. We applied lifetime risk estimates to US Census projections to evaluate the annual number of incident dementia cases from 2020 to 2060. The lifetime risk of dementia after age 55 years was 42% (95% confidence interval: 41–43). Rates were substantially higher in women, Black adults and *APOE* ε4 carriers, with lifetime risks ranging from approximately 45% to 60% in these populations. The number of US adults who will develop dementia each year was projected to increase from approximately 514,000 in 2020 to approximately 1 million in 2060. The relative growth in new dementia cases was especially pronounced for Black adults. These results highlight the urgent need for policies that enhance healthy aging, with a focus on health equity.

The United States has experienced substantial population aging over the past century, resulting in a rise in late-life diseases[1]. Dementia, once an uncommon condition, now affects more than 6 million Americans[2]. It is a leading cause of disability among older adults and accounts for more than 100,000 deaths each year[3]. Dementia also carries a substantial economic burden, with total costs exceeding $600 billion annually in the United States[4].

The lifetime risk of dementia is a critical public health measure that can raise awareness, enhance engagement in prevention and inform policymaking[5,6]. Major health organizations, including the American Heart Association and the Alzheimer's Association, report this metric to educate patients and clinicians about dementia risk across the lifespan[5,7]. Lifetime risk estimates can also be used to generate and refine projections of dementia, which can help optimize public health planning[6].

Previous studies suggest that 11–14% of men and 19–23% of women in the United States will develop dementia during their lives[6,8,9]. However, these estimates were based on older data with limited dementia ascertainment, potentially resulting in underestimation. Racial disparities in the lifetime risk of dementia are also poorly characterized, as population-based analyses have typically been limited to Non-Hispanic White populations.

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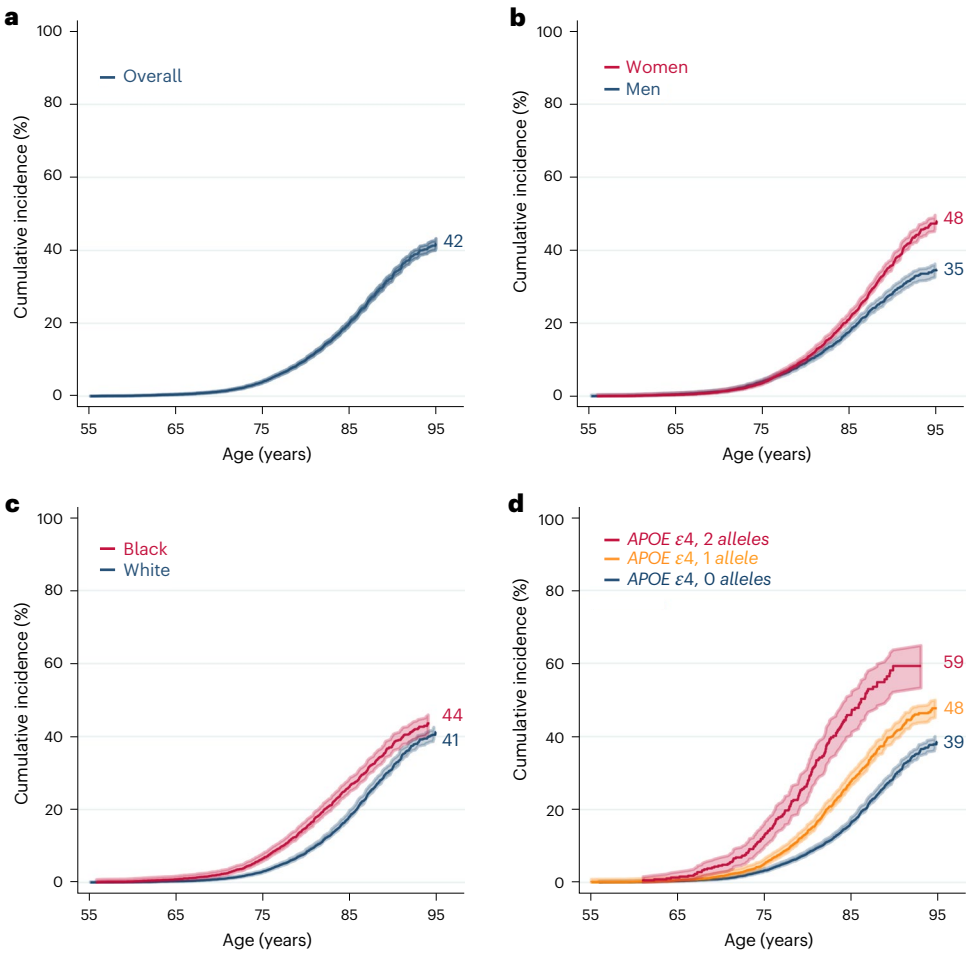

Fig. 1 | Lifetime risk of dementia (from age 55 years to 95 years), the ARIC study, overall and by sex, race and *APOE* ε4 status (*n* = 15,043). The cumulative incidence of dementia at a given age in the overall study population (**a**) and by sex (**b**), race (**c**) and *APOE* ε4 status (**d**). Estimates are expressed as percentages and account for the competing risk of death. The 95% CIs are indicated in the shaded area. The numbers on the right margins indicate the cumulative incidence at 95 years of age (94.2 years for Black adults and 93.3 years for those with two *APOE* ε4 alleles).

In the present study, our primary objective was to generate contemporary estimates of the lifetime risk of dementia, overall and across different population subgroups. We also characterized differences in the age of diagnosis and projected the number of new dementia cases that will develop in the United States over the next four decades. To achieve these aims, we analyzed over three decades of longitudinal data (1987–2020) from participants in the Atherosclerosis Risk in Communities (ARIC) study.

The study population included 15,043 participants free of dementia at age 55 years (26.9% Black race; 55.1% women). Approximately 31% of participants carried at least one apolipoprotein E4 (*APOE* ε4) allele (28.1% one copy; 2.7% two copies). Additional baseline characteristics are available in Extended Data Table 1.

Over a median follow-up of 23 years (interquartile range, 16–27 years), there were 3,252 incident cases of dementia, 5,803 deaths without dementia and 2,131 participants lost to follow-up. A total of 783 (24%) dementia cases were diagnosed at study visits with cognitive testing, 1,589 (49%) through phone interviews and 880 (27%) through review of hospital and death records (Extended Data Table 2). The crude incidence of dementia was higher in *APOE* ε4 carriers and Black adults but was similar across sex (Extended Data Table 3). In contrast, the incidence of death without dementia did not differ by *APOE* ε4 status but was higher in Black adults and men.

At age 55 years, the lifetime risk of dementia (up to age 95) was 42% (95% confidence interval (CI): 41–43) (Fig. 1a). The cumulative incidence of dementia remained low from age 55 to age 75 (3.9%) but increased substantially after age 75. There was a higher lifetime risk of dementia in women versus men (48% (95% CI: 46–50) versus 35% (95% CI: 33–36)) and Black versus White adults (44% (95% CI: 41–46) versus 41% (95% CI: 40–43)) (Fig. 1b,c). Differences in lifetime risk across race emerged by age approximately 75 years, whereas sex differences occurred starting at approximately 85 years. Adults with two copies of the *APOE* ε4 alle had a substantially higher lifetime risk of dementia (59% (95% CI: 53–65)) compared to those with one copy (48% (95% CI: 45–50)) and those with no copies (39% (95% CI: 37–40)), with differences beginning at age approximately 70 years (Fig. 1d). The cumulative incidence of dementia at each year of age corresponding to Fig. 1 are provided in Supplementary Table 1.

APOE ε4 carriage was associated with a marked increase in the lifetime risk of dementia for White men and women and for Black women but a modest increase for Black men (Extended Data Table 4). Lifetime risk of dementia increased progressively with older index ages (Extended Data Table 5). For example, among individuals alive and dementia free at age 75 years, lifetime risk exceeded 50% in the overall population and for nearly every population subgroup. Among participants with dementia identified through phone interviews, 50.4% also had dementia indicated on hospital records or death certificates. After excluding dementia cases identified by phone without further corroboration by medical or death records, the lifetime risk of dementia

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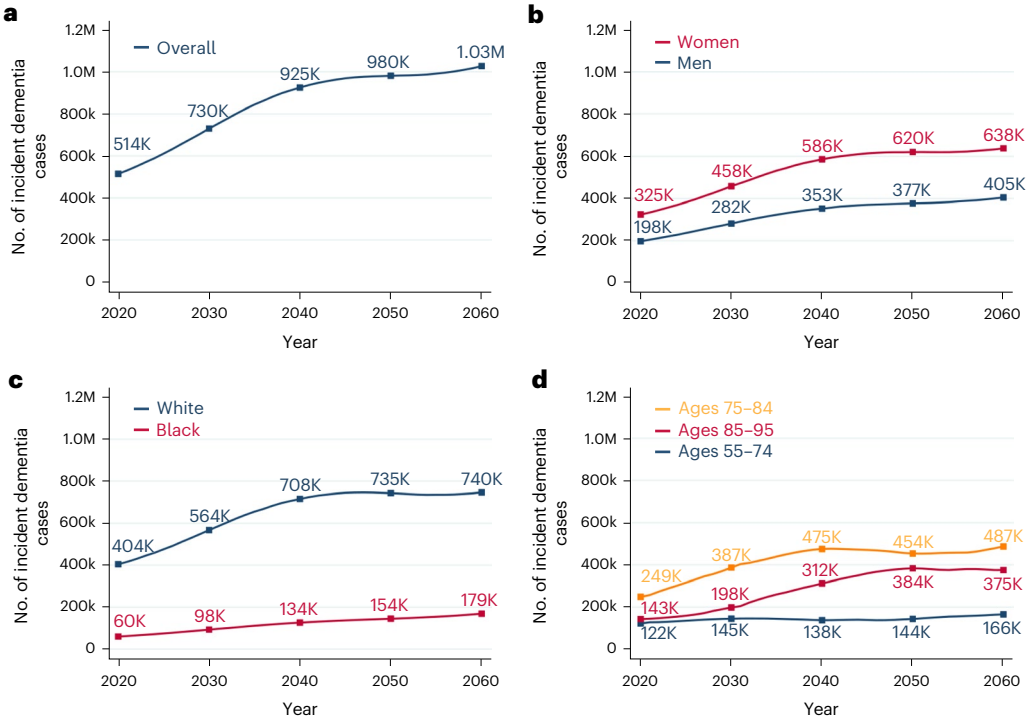

Fig. 2 | Projected number of incident dementia cases in US adults, 2020–2060, overall and by age, sex and race. Estimated number of US adults who will develop dementia each year from 2020 to 2060, overall (**a**) and by sex (**b**), race (**c**) and age (**d**). The projected number of total incident dementia cases in the overall population (**a**) may differ slightly from the total in stratified analyses (**b**–**d**) due to rounding and because incidence rates were calculated separately within each subgroup.

was 36%, with differences across subgroups that were similar to the primary analysis (Supplementary Table 2).

The median age of dementia diagnosis was 81 years (interquartile range: 77–86 years) (Extended Data Table 6). Dementia occurred at earlier ages for *APOE* ε4 carriers (median age: 79 years for two copies, 81 years for one copy and 82 years for no copies) and Black versus White adults (median age: 79 years versus 82 years). Overall, 17% of participants with dementia were diagnosed before the age of 75 years, with higher rates for men, Black adults and *APOE* ε4 carriers.

Applying our lifetime risk estimates to US Census population projections, the annual number of incident dementia cases is projected to increase from approximately 514,000 (2020) to approximately 1 million (2060) (Fig. 2). The largest absolute increase is expected to occur in individuals aged 85–95 years (increase of ~232,000) and 75–84 years (increase of ~238,000). The number of individuals who develop dementia each year is expected to nearly double in White adults and triple in Black adults.

In this large community-based cohort study, 42% of participants developed dementia after midlife. Lifetime dementia risk was highest in *APOE* ε4 carriers, women and Black adults, with lifetime risks in these groups ranging from approximately 45% to 60%. The annual number of incident dementia cases is expected to double over the next four decades, reaching approximately 1 million by 2060.

Our lifetime risk estimates are higher than those in previous population-based studies. In the Framingham Heart Study, 14% of men and 23% of women developed dementia from age 45–105 years[8]. The lifetime risk of dementia (age 45–95 years) in the Rotterdam Study was 19% and 31% for men and women, respectively[10]. The higher lifetime risk estimates in our analyses may reflect differences in dementia ascertainment. Previous research primarily relied on cognitive testing at study visits and a review of medical and death records to identify dementia. However, this may result in under-detection, because participants with cognitive impairment are less likely to attend in-person assessments, and administrative records lack sensitivity[11]. In contrast, the ARIC study combined cognitive evaluations at study visits with intensive surveillance (phone interviews and review of hospital and death records) to maximize dementia ascertainment. Ongoing phone interviews with participants and informants were especially important, as they identified approximately half of all dementia cases in our study.

The ARIC cohort is also more geographically, racially and socioeconomically diverse than cohorts in previous studies. Racial and ethnic minority adults and individuals from lower economic backgrounds have a higher burden of important risk factors, potentially contributing to differences in long-term dementia risk.

Our results suggest that the current lifetime risk of dementia may be substantially higher than previously thought, emphasizing the importance of prevention throughout the life course. Policies focused on optimizing cardiovascular health and preserving hearing may be particularly important[12]. Accumulating data from clinical trials have linked healthy lifestyle behaviors, the absence of vascular risk factors and hearing rehabilitation with improved cognitive outcomes[13–17]. However, only approximately 20% of US adults are meeting recommended lifestyle and cardiovascular health targets[18], and only approximately 30% of older adults with hearing loss are using a hearing aid[19]. These trends highlight broad opportunities for dementia risk reduction in the population.

We found that *APOE* ε4 carriers had a very high absolute risk of dementia. Roughly half of those with one *APOE* ε4 copy and approximately 60% with two copies developed dementia after midlife. Our estimates were similar to previous population-based research, which reported cumulative incidence rates ranging from 16% to 38% by age 80–85 years[20]. Consistent with previous studies[21,22], we also found that *APOE* ε4 carriers developed dementia substantially earlier than non-carriers. As a result, differences in the cumulative incidence of dementia between *APOE* ε4 carriers and non-carriers were evident by age 70 years. These findings align with clinical and basic research,

which suggests that *APOE* ε4 primarily increases Alzheimer's disease risk by causing earlier amyloid pathology in the brain[21,22].

We observed striking differences in dementia risk across race. Black adults had earlier dementia onset and a higher lifetime risk as compared to White adults. These findings extend previous studies, which have predominantly focused on racial/ethnic differences in prevalence or relative risk[2,23,24]. Racial disparities in dementia may reflect the cumulative effects of structural racism and inequality throughout the life course. For instance, poor access to education and nutrition may contribute to earlier differences in cognitive reserve, and socioeconomic disparities and limited access to care may lead to a higher burden of vascular risk factors at midlife. Reducing racial disparities will, therefore, require interventions that target high-risk individuals, along with reforms that address social determinants of health.

Consistent with previous studies, women had a substantially higher lifetime risk of dementia[6,8,10]. This pattern is thought to reflect women's higher life expectancy[25]. In our analyses, the incidence of death without dementia was nearly two times higher in men compared to women. Thus, men were less likely to survive to older ages, reducing their overall lifetime risk of dementia. These findings corroborate previous population-based research, which similarly found that sex differences in survival are a major contributor to the higher lifetime risk of dementia in women[8,26].

Similar to our results, the Global Burden of Disease Study estimated that approximately 516,000 US adults developed dementia in 2017 (ref. 27). We extended existing research by quantifying the growth of incident dementia over the next four decades. This trend will likely be driven by the large 'Baby Boom' generation reaching older age. The shifting racial composition of the United States may also contribute. Adults belonging to racial and ethnic minority groups have an increased long-term risk of dementia and are expected to make up the majority of the population by 2045 (ref. 28). In our projections, the relative increase in incident dementia cases was notably higher in Black versus White adults.

This study has several strengths. The ARIC study comprehensively captured dementia in all participants through cognitive testing, active surveillance and adjudication of dementia cases. ARIC is a diverse, contemporary, population-based cohort of adults followed from middle age.

There are also several study limitations. First, there may be some misclassification of dementia for participants identified through surveillance, because these were not adjudicated. Nonetheless, phone interviews were conducted using validated instruments, and diagnostic codes for dementia are highly specific[29]. Additionally, approximately half of dementia cases identified with phone interviews also had dementia documented in hospital or death records, indicating high reliability. Second, despite the comprehensive ascertainment of dementia, there still may be cases not captured in the ARIC study. This suggests that our analyses may be conservative and underestimate the true lifetime risk. Related to this, medical and death records may underestimate dementia, particularly in racial and ethnic minority adults[30]. However, differential ascertainment was mitigated by the use of multiple methods to identify dementia. Fourth, before study visit 5 (2011–2013, mean participant age 75 years), dementia was ascertained retrospectively with phone interviews and review of hospital and death records. As a result, there may be some underestimation of dementia before age 75 years. However, this bias may be minimal because most dementia cases develop at older ages. Fifth, we did not externally validate our results. Future population-based studies with long follow-up and comprehensive dementia ascertainment are needed to validate our lifetime risk estimates.

Sixth, our projections may not be generalizable to the entire US population. Nonetheless, our estimates of incident dementia cases were very similar to the Global Burden of Disease Study, which generated estimates by combining a broad set of data sources in the United States[27]. This suggests that our projections may provide a useful approximation of the current and future burden of incident dementia in the United States. Seventh, we compared lifetime dementia risk only for Black and White adults because ARIC did not include a large number of participants from other racial and ethnic groups. More diverse studies are needed to understand how dementia risk differs across populations over the life course. Eighth, our projections assumed that the incidence of dementia will remain stable over the next four decades.

In conclusion, more than four in 10 adults developed dementia in this large, longstanding, community-based cohort study, with higher rates in *APOE* ε4 carriers, women and Black adults. Approximately 1 million US adults will develop dementia annually by 2060. Policies that enhance prevention and healthy aging are urgent public health priorities for reducing the substantial and growing burden of dementia[31].

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-024-03340-9.

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Methods

Study population

The ARIC study is a community-based cohort of 15,792 adults from four US communities (Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland). Participants aged 45–64 years were originally recruited from 1987 to 1989 and have undergone clinical examinations (including cognitive testing), laboratory testing and medical interviews (in-person and by phone) for the past three decades. Beginning at study visit 5 (2011–2013), ARIC investigators began conducting comprehensive neuropsychological testing (with expert adjudication) at study visits and semi-annual phone-based cognitive assessments. Phone-based assessments were administered to participants and informants (for example, relatives). All participants provided written informed consent, and the study was approved by institutional review boards at all research sites. Further details about the ARIC study are available elsewhere[32].

We excluded participants with prevalent dementia before age 55 years ($n = 4$), missing information for covariates ($n = 543$) and those who died or were lost to follow-up before the age of 55 years (the index age for our primary analyses, $n = 202$). These restrictions yielded an analytic sample of 15,043 participants.

Dementia ascertainment

Dementia ascertainment in ARIC is summarized in Supplementary Fig. 1 and was described in detail previously[33,34]. In brief, dementia status was determined in all participants, including those who did not return for clinical study visits or died during follow-up, using three broad approaches.

The first approach was based on cognitive testing at clinical study visits. A three-test neurocognitive battery was administered at visit 2 (1990–1992) and visit 4 (1996–1998), and an expanded 10-test neuropsychological battery was administered at visit 5 (2011–2013), visit 6 (2016–2017) and visit 7 (2018–2019)[35]. Due to the coronavirus disease 2019 (COVID-19) pandemic, a shortened six-battery test was administered at visit 8 (2020). The Clinical Dementia Rating scale, the Functional Activities Questionnaire, the Mini-Mental State Examination and the Blessed scale were used at visits 5–8, with the former two in only a subset of participants[36–39]. Dementia was initially diagnosed using an algorithm based on criteria recommended by the National Institute on Aging–Alzheimer's Association diagnostic guidelines workgroups and the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders*[40]. An expert panel subsequently reviewed and adjudicated cases of dementia identified by the algorithm.

For those who did not return for in-person study visits, dementia was identified through annual or semi-annual telephone interviews with participants and informants using validated instruments, including the Telephone Interview for Cognitive Status, the Clinical Dementia Rating scale, the Functional Activities Questionnaire, the Six-Item Screener and the Ascertain Dementia 8-item screener[36–38,41,42].

Dementia cases were identified by using diagnostic codes in hospital records or death certificates for all participants throughout the study (see Supplementary Table 3 for International Classification of Diseases (ICD) 9/10 codes used for ascertainment)[32]. Where possible, hospital or death certificate–based diagnoses were supported by interview informants using the Ascertain Dementia 8-item screener. Response rates for all three methods of dementia ascertainment (study visits, phone-interviews and medical and death records) are provided in Supplementary Table 4.

We used all available data (in-person testing, phone interviews and medical and death records) to classify participants. When multiple data sources were available, we used the following priority order to ascertain dementia: (1) expert diagnosis of dementia based on neuropsychological testing at study visits; (2) computer algorithm diagnosis based on neuropsychological testing at study visits; (3) low score on the Telephone Interview for Cognitive Status (adjusted for education level); (4) elevated score on the Clinical Dementia Rating scale and the Functional Activities Questionnaire; (5) low score on the Six-Item Screener and elevated score on the Ascertain Dementia 8-item screener; (6) two low scores on the Six-Item Screener; (7) one low score on the Six-Item Screener if participant was lost to follow-up or deceased; (8) dementia on hospital discharge codes; and (9) dementia on death certificate codes. The priority list was designed to classify participants with the most reliable data source available.

The date of dementia onset was defined as the earliest date dementia was diagnosed in any data source (study visit, phone interview or hospital or death records). For cases identified through informant interviews (for participants who were deceased), hospital records or death certificates, we subtracted 180 days from the date of diagnosis to account for a potential lag in reporting.

In sensitivity analyses, we re-estimated lifetime risk using a more conservative definition of incident dementia. In particular, participants were classified with dementia through phone interviews only if the diagnosis was also indicated in hospital records or death certificates. Participants with a phone-based diagnosis of dementia that was not 'confirmed' with medical records were classified as having no dementia and censored at the date of the phone interview. This conservative definition of dementia thus included cases identified through study visits, phone interviews that were subsequently confirmed through hospital or death records, or hospital or death records.

Sociodemographic characteristics and *APOE* ε4 status

Demographic characteristics (age, sex and race) were self-reported. Participants reported race from a list generated by the researchers (Asian, Black, American Indian/Alaskan Indian or White). *APOE* ε4 genotyping was performed using the TaqMan assay, and participants were classified by *APOE* ε4 status (zero, one or two alleles).

Statistical analyses

We examined baseline characteristics and the proportion of dementia cases identified through different ascertainment methods (study visits, telephone interviews or diagnostic codes). We estimated crude rates of dementia and death without dementia, overall and across subgroups.

We estimated non-parametric cumulative incidence function curves to calculate the lifetime risk of dementia (from age 55 years to age 95 years), overall and by sex, race and *APOE* ε4 status[43]. We treated death without dementia as a competing event to avoid overestimating lifetime dementia risk. We used age as the timescale and calculated lifetime risk for those who were alive and free of dementia at age 55 years (index age). Participants older than 55 years were included as late entries. We calculated person-time from age 55 years until dementia diagnosis, death free of dementia, loss to follow-up, age 95 years or administrative censoring (31 December 2020), whichever occurred first.

In secondary analyses, we re-estimated the lifetime risk of dementia with cumulative incidence function curves using (1) a more conservative definition of dementia and (2) older index ages (ages 65, 75 and 85). We also examined interactions between race and sex with the presence of *APOE* ε4.

Among individuals with incident dementia, we calculated the median age at diagnosis and the percentage of adults diagnosed between the ages of 55–74 years, 75–84 years and 85–95 years.

To project the burden of incident dementia, we generated smoothed cumulative incidence function curves for dementia using interpolation, overall and across subgroups. We then estimated age-specific incidence rates by calculating the increase in dementia incidence with each additional year of age. We multiplied these age-specific rates with corresponding population counts from the US Census to estimate the number of new dementia cases expected in

the United States[28] from 2020 to 2060, overall and by age categories (55–74 years, 75–84 years and 84–95 years), sex (men, women) and race (White, Black).

All analyses were conducted in Stata/SE 18.0 (StataCorp)[44].

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

ARIC data access procedures are in accordance with participant informed consent and NIH data-sharing policy. Anonymized data from the ARIC study are available at the NHLBI Biologic Specimen and Data Repository Information Coordinating Center and can be accessed through the website (https://biolincc.nhlbi.nih.gov/studies/aric/). Requests for access of ARIC data may also be submitted to the ARIC Publications Committee according to established study procedures, which include submission of a completed ARIC Manuscript Proposal Form (available at https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines) to the ARIC Publications Committee at aricpub@unc.edu. Review and approval of data access requests typically takes approximately 1 month.

Code availability

The analytic code used for analyses in this study is available from the corresponding author upon reasonable request.

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Author contributions

M.F. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: M.F. and J.C. Acquisition, analysis or interpretation of data: M.F., J.C., E.S. and J.H. Drafting of the manuscript: M.F. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: J.H. and J.W. Administrative, technical or material support: J.C. and E.S. Supervision: J.C.

Competing interests

D.S.K. has no disclosures relevant to the current work. D.S.K. serves on a Data Safety Monitoring Board for the Dominantly Inherited Alzheimer Network Treatment Unit study. He was an investigator in Alzheimer clinical trials sponsored by Biogen, Eli Lilly Pharmaceuticals and the University of Southern California and is currently an investigator in a trial in frontotemporal degeneration with Alector. He has served as a consultant for Roche, AriBio, Linus Health, Biovie and Alzeca Biosciences but receives no personal compensation. He receives funding from the NIH. The other authors declare no competing interests.

Additional information

Extended data is available for this paper at https://doi.org/10.1038/s41591-024-03340-9.

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41591-024-03340-9.

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Extended Data Table 1 | Participant characteristics at age 55 years, the ARIC study

	Overall (N=15,043)
Sex, %	
Men	44.9
Women	55.1
Race, %	
White	72.8
Black	26.9
Other	0.3
Study site	
Forsyth County, North Carolina	25.6
Jackson, Mississippi	23.4
Minneapolis, Minnesota	25.2
Washington County, Maryland	25.7
APOE ε4 status, %	
0 alleles	69.2
1 allele	28.1
2 alleles	2.7
Diabetes, %	
No	90.7
Yes	9.3
Smoking status, %	
Never	40.0
Former	35.8
Current	23.8
BMI, mean (SD), kg/m^2	28.2 (6)
BMI categories, %	
Normal (BMI <25 kg/m2)	30.0
Overweight (BMI 25-<30 kg/m2)	39.4
Obesity (BMI≥30 kg/m2)	30.6
Missing	0.1
Hypertension, %	
No	61.1
Yes	38.7
Missing	0.2

Diabetes, hypertension, smoking and body mass index (BMI) were based on available measurements from the clinical study visit closest to when participants were 55 years of age. Diabetes was defined as fasting glucose ≥ 126 mg dl^{-1}, non-fasting glucose ≥ 200 mg dl^{-1}, self-report of a diagnosis of diabetes by a physician or use of glucose-lowering medication. BMI was calculated as weight in kilograms divided by height in meters squared. Hypertension was defined as blood pressure ≥ 140/90 mmHg or self-reported use of blood pressure–lowering medication. Smoking status was self-reported.

 https://doi.org/10.1038/s41591-024-03340-9

Extended Data Table 2 | Number of participants with dementia by different diagnostic criteria, the ARIC study (*n*=3,252)

	Number of cases
Dementia identified at study visits	783 (24%)
1. Expert diagnosis of dementia based on neuropsychological testing	783
2. Computer algorithm diagnosis based on neuropsychological testing	
Dementia identified by phone interviews	1,589 (49%)
3. Low score on the TICS (adjusted for education level)	779
4. Elevated score on the CDR and FAQ	
5. Low score on the SIS and elevated score on the AD8	689
6. Two low scores on the SIS	82
7. One low score on the SIS if participant was loss to follow up or deceased	39
Dementia identified by administrative records	880 (27%)
8. Dementia on hospital discharge codes	685
9. Dementia on death certificate codes	195

AD8, Ascertain Dementia 8; CDR, Clinical Dementia Rating; Functional Activities Questionnaire, FAQ; SIS, Six-Item Screener; TICS, Telephone Interview for Cognitive Status.

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Extended Data Table 3 | Crude incidence for dementia and death free of dementia from age 55 years to age 95 years, the ARIC study, overall and by sex, race and *APOE* ε4 status (*n*=15,043)

	Number of participants	Number of incident dementia cases	Crude incidence for dementia, per 1,000 person-years	Number of deaths without dementia	Crude incidence for mortality without dementia, per 1,000 person-years
Overall	15,043	3,252	10.3	5,803	18.4
Sex					
Men	6,751	1,327	9.9	3,145	23.4
Women	8,292	1,925	10.7	2,658	14.8
Race					
White	10,958	2,233	9.5	4,103	17.4
Black	4,041	1,012	13.0	1,690	21.8
APOE ε4 status					
0 alleles	10,407	1,916	8.7	4,075	18.4
1 allele	4,234	1,164	13.5	1,597	18.5
2 alleles	402	172	22.7	131	17.3

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Extended Data Table 4 | Lifetime risk of dementia (from age 55 years to age 95 years), by *APOE* ε4 status, sex and race

	APOE ε4 status			Difference (2 alleles – 0 alleles)
	0 alleles	1 allele	*2* alleles	
White Women	45 (42, 48)	56 (51, 60)	64 (52, 73)	19
White Men	31 (29, 34)	40 (37, 44)	60 (49, 70)	29
Black Women	44 (39, 48)	53 (48, 58)	67 (56, 76)	23
Black Men	34 (29, 38)	38 (33, 43)	39 (26, 51)	5

Estimates are reported as percentages and indicate the cumulative incidence at the age of last observation (up to age 95 years) after accounting for the competing risk of death. The 95% CIs are reported in parentheses.

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Extended Data Table 5 | Lifetime risk of dementia after select index ages (ages 55, 65, 75 and 85) to 95 years, the ARIC study, overall and by sex, race and *APOE* ε4 status

	Index age			
	55 years (n=15,043)	65 years (n=13,830)	75 years (n=10,599)	85 years (n=2,940)
Overall	42 (41, 43)	45 (44, 47)	52 (50, 54)	56 (53, 59)
Sex				
Men	35 (33, 36)	38 (36, 40)	45 (43, 48)	51 (46, 55)
Women	48 (46, 50)	51 (49, 53)	57 (54, 59)	60 (56, 64)
Race				
White	41 (40, 43)	44 (42, 46)	50 (48, 52)	55 (51, 58)
Black	44 (41, 46)	49 (46, 51)	58 (55, 62)	63 (56, 69)
APOE ε4 status				
0 alleles	39 (37, 40)	42 (40, 43)	48 (46, 50)	53 (50, 57)
1 allele	48 (45, 50)	51 (49, 54)	60 (57, 63)	64 (58, 69)
2 alleles	59 (53, 65)	65 (59, 71)	74 (66, 81)	67 (47, 81)

Estimates are reported as percentages and indicate the cumulative incidence at the age of last observation (up to age 95 years) after accounting for the competing risk of death. The 95% CIs are reported in parentheses.

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Extended Data Table 6 | Median age at dementia diagnosis and distribution of diagnosis age, the ARIC study, overall and by sex, race and *APOE* ε4 status (*n*=3,252)

	Median age (IQR) at diagnosis, years	Percentage diagnosed between ages 55 and 74	Percentage diagnosed between ages 75 and 84	Percentage diagnosed between ages 85 and 95
Overall	81 (77, 86)	17%	53%	30%
Sex				
Men	81 (76, 85)	20%	53%	28%
Women	82 (77, 86)	15%	54%	31%
Race				
White	82 (78, 86)	14%	53%	34%
Black	79 (75, 84)	25%	55%	20%
APOE ε4 status				
0 alleles	82 (77, 86)	16%	49%	35%
1 allele	81 (77, 85)	17%	59%	24%
2 alleles	79 (75, 82)	28%	59%	13%

Percentages may not add up to 100% due to rounding. IQR, interquartile range.

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For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	N/A. Data was not collected using software.
Data analysis	All analyses were conducted in Stata/SE 18.0 (StataCorp, College Station, TX, USA)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

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Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

ARIC data access procedures are in accordance with participant informed consent and NIH data sharing policy. Anonymized data from the ARIC study are available at the NHLBI Biologic Specimen and Data Repository Information Coordinating Center and can be accessed through the website (https://biolincc.nhlbi.nih.gov/studies/aric/). Requests for access of ARIC data may also be submitted to the ARIC Publications Committee according to established study procedures which

includes submission of a completed ARIC Manuscript Proposal From (available at https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines) to the ARIC Publications Committee at aricpub@unc.edu. Review and approval of data access requests typically takes approximately one month.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Sex was self-reported. As reported in Supplemental Table 1, there were 15,043 total participants, of which 6,751 (44.9%) were men and 8,292 (55.1%) were women. Sex-specific estimates for the lifetime risk of dementia were reported in Figure 1, and sex-specific projections of incident dementia cases were reported in Figure 2. Data disaggregated by sex are available for researchers who obtain required permission to use the ARIC dataset.
Reporting on race, ethnicity, or other socially relevant groupings	Race was self-reported by participants during in-person interviews. Prior studies have reported large racial and ethnic differences in the prevalence of dementia, and current health policies have prioritized reducing these disparities. We sought to build on this literature by reporting race specific estimates of lifetime risk of dementia (in Figure 1) and race-specific projections of incident dementia cases (in Figure 2). Because our analyses were descriptive, we did not adjust for confounding. As reported in Supplemental Table 1, there were 15,043 total participants, of which 10,958 (72.8%) self-identified as White and 4,041 (27%) self-identified as Black. There were 44 participants (0.3% of total study population) that self-identified as belonging to other racial groups. Due to small sample size, we could not generate reliable race-specific estimates for these 44 participants. However, these participants were included in all other analyses.
Population characteristics	The study population included 15,043 participants free of dementia at age 55 years (26.9% Black race; 55.1% women). Approximately 31% of participants carried at least one APOE ε4 allele (28.1% one copy; 2.7% two copies). A detailed table of social and clinical participant characteristics is provided in Supplemental Table 1.
Recruitment	The ARIC Study is a community-based cohort of 15,792 adults from four US communities (Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland). Participants aged 45-64 years were originally recruited from 1987 to 1989 and have undergone clinical examinations (including cognitive testing), laboratory testing, and medical interviews (in-person and by phone) for the past three decades.
Ethics oversight	The ARIC Study was approved by institutional review boards at all research sites (Johns Hopkins University, Wake Forest University, University of Mississippi Medical Center, and University of Minnesota, New York University).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

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Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	We conducted a prospective cohort analysis using data from the Atherosclerosis Risk in Communities Study. Data were quantitative.
Research sample	Participants aged 45-64 years were recruited from 1987 to 1989 from four US communities (Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland). For the past three decades, participants have undergone clinical examinations (including cognitive testing), laboratory testing, and medical interviews (in-person and by phone). The study sample was designed to be representative of the four countries from which they were selected. The goal of this study sample was to select a large, diverse cohort of middle-aged adults from different regions in the US to study the national history of cardiovascular disease. In our analyses, we restricted our analytic sample to all participants in the ARIC study who were free of dementia at the study baseline. We chose this sample because we wanted to understand the lifetime risk of dementia using as much information as possible. We also included all participants in the study in order to generate lifetime risk estimate across different subgroups with precision. The analytic sample size was 15,043 (26.9% Black race, 55.1% women, 30.8% with ≥1 APOE ε4 allele).
Sampling strategy	Participants from each of the 4 ARIC sites were selected using stratified, probability sampling design. There was no formal power calculation used to determine the sample size. However, approximately 4,000 participants from each of the study. This sample size would deemed sufficient to achieve the study objective, which was to recruit a large sample of participants that was representative of each of the four communities and that would allow for comparison of different risk factors effects on cardiovascular disease. For our analysis (focused on dementia over the life course), the sample size (n=15,043) is among the largest in communities based

cohort studies examining the lifetime risk of dementia. Further, we had over 3 decades of follow up and extensive dementia ascertainment, allowing us to identify 3,252 incident dementia events. This allowed us to characterize the lifetime risk of dementia in our study sample with sufficient precision, overall and across subgroups.

Data collection

Detailed information about data collection are included in the manuscript.

For the past three decades, participants in the ARIC study have undergone clinical examinations (including cognitive testing), laboratory testing, and medical interviews (in-person and by phone) for the past three decades.

Dementia ascertainment in ARIC is summarized in Supplemental Figure 1. Briefly, dementia status was determined in all participants, including those who did not return for clinical study visits or died during follow-up, using three broad approaches.

Approach 1 - Clinical study visits
The first approach was based on cognitive testing at clinical study visits. A three-test neurocognitive battery was administered at visit 2 (1990-1992) and visit 4 (1996-1998). These tests were the 1) Delayed Word Recall; 2) Digit Symbol Substitution; 3) Word Fluency.

An expanded 10-test neuropsychological battery was administered at visit 5 (2011-2013), visit 6 (2016-2017), visit 7 (2018-2019). The 10 test were the: 1) Delayed Word Recall; 2) Digit Symbol Substitution; 3) Word Fluency; 4) Incidental Learning; 5) Animal Naming Score; 6) Logical Memory; 7) Trail Making A; 8) Trail Making B; 9) Digit Span Backwards; 10) Boston Naming.

Due to the COVID-19 pandemic, a shortened 6-battery test was administered at visit 8 (2020). These tests were the: 1) Word Fluency; 2) Animal Naming Score; 3) Digital Span Backwards; 4) Trail Making A; 5) Trail Making B; 6) Consortium to Establish a Registry for Alzheimer's Disease Word List.

The Clinical Dementia Rating scale, Functional Activities Questionnaire, Mini-Mental State Examination, and Blessed scale were used at visits 5-8, with the former two only in a subset of participants.

Assessments at study visits were completed by participants (with the help of proxies, as required). Dementia was initially diagnosed using an algorithm based on criteria recommended by the National Institute on Aging–Alzheimer's Association diagnostic guidelines workgroups and the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders. An expert panel subsequently reviewed and adjudicated cases of dementia identified by the algorithm.

Approach 2 - Telephone assessments
For those who did not return for in-person study visits, dementia was identified through annual or semiannual telephone interviews with participants and informants using validated instruments, including the Telephone Interview for Cognitive Status, Clinical Dementia Rating scale, Functional Activities Questionnaire, the Six Item Screener, and the Ascertain Dementia 8-item screener.

Approach 3 - Medical and death record review
Dementia cases were identified by using diagnostic codes in hospital records or death certificates for all participants throughout the study (see Supplemental Table 3 for ICD 9/10 codes used for ascertainment). Where possible, hospital or death certificate-based diagnoses were supported by interview informants using the Ascertain Dementia 8-item screener. Response rates for all three methods of dementia ascertainment (study visits, phone-interviews, and medical and death records) are provided in Supplemental Table 10.

The ARIC study is an observational study, and all analyses in the current study were descriptive. Therefore, there was no blinding of participants and research staff during any of the clinical assessments.

Timing

Data collected in the ARIC study began in 01-1987 and is still ongoing. Our analyses ended at 12-2020. Supplemental Figure 1 details the timing dementia ascertainment. As noted above, study visits occurred in 1987-1989 (visit 1), 1990-1992 (visit 2), 1996-1998 (visit 4), 2011-2013 (visit 5), 2016-2017 (visit 6), 2018-2019 (visit 7) and 2020 (visit 8). Telephone assessments began in 2011. Medical and death review took place from 01-1987 to 12-2020.

Data exclusions

We excluded participants with prevalent dementia prior to age 55 (n=4), missing information for covariates (n=543), and those who died or were lost to follow-up before the age of 55 (the index age for our primary analyses, n=202). These restrictions yielded an analytic sample of 15,043 participants.

Non-participation

All 15,043 participants had information about their dementia status available. Response rates for the three different methods of dementia are summarized below.

Response rate for dementia assessments at clinic study visits: 6,669 / 9,729 (68.5%) completed at least one adjudicated cognitive assessment at study visits among persons alive as of December 31st, 2013 (last day of study visit 5).

Response rate for dementia telephone assessments: 8,274 / 9,729 (85.0%) completed at least one phone-based assessment cognitive assessment among persons alive as of December 31st, 2013 (last day of study visit 5).

Response rate for medical and death records review: 13,942 / 15,043 (92.7%) had at least one ICD9/10 code from a medical record or death certificate.

Randomization

NA - ARIC is an observational cohort study, so participants were not randomized. Our analyses were descriptive so we did not adjust for confounders.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

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Supplementary information

https://doi.org/10.1038/s41591-024-03340-9

Lifetime risk and projected burden of dementia

In the format provided by the authors and unedited

Supplemental Table 1: Age-specific cumulative incidence of dementia (from starting age of 55 years), overall and by sex, race, and APOE ε4 status

		Sex		Race		*APOE* ε4 status		
Age	Overall	Men	Women	Black	White	0 alleles	1 allele	2 alleles
55	0.0 (0.0, 0.1)	0.0 (0.0, 0.2)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.2)	0*	0.1 (0.0, 0.3)	0*
56	0.0 (0.0, 0.1)	0.0 (0.0, 0.2)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.0 (0.0, 0.2)	0*	0.1 (0.0, 0.3)	0*
57	0.1 (0.0, 0.1)	0.1 (0.0, 0.2)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.1 (0.0, 0.3)	0.0 (0.0, 0.1)	0.1 (0.0, 0.3)	0*
58	0.1 (0.0, 0.1)	0.1 (0.0, 0.3)	0.0 (0.0, 0.1)	0.0 (0.0, 0.1)	0.2 (0.1, 0.4)	0.1 (0.0, 0.2)	0.1 (0.0, 0.3)	0*
59	0.1 (0.0, 0.2)	0.1 (0.0, 0.3)	0.1 (0.0, 0.2)	0.0 (0.0, 0.1)	0.2 (0.1, 0.4)	0.1 (0.0, 0.2)	0.1 (0.0, 0.3)	0*
60	0.1 (0.1, 0.2)	0.1 (0.1, 0.3)	0.1 (0.0, 0.2)	0.1 (0.0, 0.1)	0.2 (0.1, 0.5)	0.1 (0.0, 0.2)	0.1 (0.0, 0.4)	0*
61	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)	0.1 (0.1, 0.3)	0.1 (0.0, 0.2)	0.4 (0.2, 0.6)	0.1 (0.1, 0.3)	0.2 (0.1, 0.5)	0*
62	0.2 (0.1, 0.3)	0.2 (0.1, 0.4)	0.2 (0.1, 0.4)	0.1 (0.1, 0.2)	0.5 (0.3, 0.8)	0.2 (0.1, 0.3)	0.2 (0.1, 0.5)	0.3 (0.0, 1.6)
63	0.3 (0.2, 0.4)	0.4 (0.2, 0.6)	0.3 (0.2, 0.4)	0.2 (0.1, 0.3)	0.6 (0.4, 0.9)	0.3 (0.2, 0.4)	0.3 (0.2, 0.6)	0.6 (0.1, 1.9)
64	0.4 (0.3, 0.5)	0.5 (0.3, 0.7)	0.3 (0.2, 0.5)	0.3 (0.2, 0.4)	0.7 (0.5, 1.1)	0.4 (0.2, 0.5)	0.4 (0.2, 0.7)	0.8 (0.2, 2.3)
65	0.5 (0.4, 0.6)	0.5 (0.4, 0.8)	0.4 (0.3, 0.6)	0.3 (0.2, 0.4)	0.8 (0.6, 1.2)	0.4 (0.3, 0.5)	0.6 (0.4, 0.9)	1.1 (0.4, 2.6)
66	0.6 (0.4, 0.7)	0.7 (0.5, 0.9)	0.5 (0.3, 0.7)	0.4 (0.2, 0.5)	1.1 (0.8, 1.5)	0.4 (0.3, 0.6)	0.7 (0.5, 1.1)	1.3 (0.5, 2.9)
67	0.7 (0.5, 0.8)	0.8 (0.6, 1.0)	0.6 (0.4, 0.8)	0.4 (0.3, 0.6)	1.2 (0.9, 1.6)	0.6 (0.4, 0.7)	0.8 (0.6, 1.1)	1.8 (0.8, 3.6)

68	0.8 (0.7, 1.0)	0.9 (0.7, 1.2)	0.8 (0.6, 1.0)	0.6 (0.4, 0.7)	1.5 (1.2, 2.0)	0.7 (0.5, 0.9)	1.0 (0.7, 1.4)	3.1 (1.7, 5.2)
69	1.0 (0.9, 1.2)	1.1 (0.9, 1.4)	0.9 (0.7, 1.2)	0.7 (0.6, 0.9)	1.8 (1.4, 2.3)	0.8 (0.6, 1.0)	1.3 (1.0, 1.7)	3.6 (2.1, 5.8)
70	1.2 (1.1, 1.4)	1.3 (1.0, 1.6)	1.2 (1.0, 1.5)	0.9 (0.8, 1.1)	2.1 (1.7, 2.6)	0.9 (0.8, 1.1)	1.7 (1.3, 2.1)	4.3 (2.6, 6.7)
71	1.5 (1.3, 1.8)	1.6 (1.4, 2.0)	1.5 (1.2, 1.7)	1.2 (1.0, 1.4)	2.5 (2.1, 3.1)	1.2 (1.0, 1.4)	2.1 (1.7, 2.6)	4.8 (3.0, 7.3)
72	2.0 (1.7, 2.2)	2.1 (1.7, 2.4)	1.9 (1.6, 2.2)	1.4 (1.2, 1.7)	3.4 (2.9, 4.0)	1.5 (1.3, 1.8)	2.6 (2.1, 3.1)	6.6 (4.4, 9.3)
73	2.5 (2.2, 2.7)	2.6 (2.3, 3.0)	2.3 (2.0, 2.7)	1.8 (1.6, 2.1)	4.1 (3.5, 4.8)	2.0 (1.7, 2.3)	3.2 (2.7, 3.8)	7.4 (5.1, 10.2)
74	3.1 (2.8, 3.4)	3.3 (2.9, 3.7)	2.9 (2.6, 3.3)	2.3 (2.0, 2.6)	5.2 (4.5, 5.9)	2.5 (2.2, 2.9)	3.8 (3.3, 4.5)	9.6 (7.0, 12.8)
75	3.9 (3.5, 4.2)	4.0 (3.6, 4.5)	3.7 (3.3, 4.1)	2.9 (2.6, 3.2)	6.5 (5.7, 7.3)	3.1 (2.8, 3.4)	4.9 (4.3, 5.6)	12.2 (9.2, 15.6)
76	4.9 (4.5, 5.2)	4.9 (4.4, 5.4)	4.9 (4.4, 5.4)	3.7 (3.4, 4.1)	8.0 (7.2, 8.9)	3.9 (3.5, 4.2)	6.5 (5.7, 7.2)	14.5 (11.2, 18.1)
77	6.0 (5.6, 6.4)	5.9 (5.3, 6.5)	6.1 (5.6, 6.6)	4.7 (4.3, 5.1)	9.5 (8.6, 10.4)	4.8 (4.4, 5.2)	7.9 (7.0, 8.7)	17.6 (14.0, 21.5)
78	7.1 (6.7, 7.6)	6.8 (6.2, 7.4)	7.4 (6.8, 8.0)	5.6 (5.2, 6.1)	11.2 (10.2, 12.2)	5.7 (5.2, 6.1)	9.4 (8.5, 10.3)	20.3 (16.4, 24.4)
79	8.5 (8.0, 8.9)	8.0 (7.4, 8.7)	8.8 (8.2, 9.5)	6.8 (6.3, 7.3)	13.0 (11.9, 14.1)	6.7 (6.2, 7.2)	11.5 (10.6, 12.6)	22.6 (18.5, 26.9)
80	9.9 (9.4, 10.4)	9.4 (8.7, 10.1)	10.3 (9.6, 11.0)	8.0 (7.5, 8.5)	15.1 (13.9, 16.2)	7.8 (7.2, 8.3)	13.4 (12.4, 14.6)	26.6 (22.2, 31.2)
81	11.7 (11.2, 12.3)	10.8 (10.1, 11.6)	12.4 (11.7, 13.2)	9.7 (9.1, 10.3)	17.3 (16.1, 18.6)	9.2 (8.6, 9.8)	15.9 (14.7, 17.1)	31.7 (26.9, 36.6)
82	13.5 (12.9, 14.1)	12.5 (11.6, 13.3)	14.3 (13.5, 15.2)	11.4 (10.8, 12.1)	19.4 (18.0, 20.7)	10.5 (9.8, 11.1)	18.9 (17.6, 20.2)	34.6 (29.6, 39.7)
83	15.4 (14.7, 16.0)	13.9 (13.0, 14.9)	16.6 (15.7, 17.5)	13.3 (12.6, 14.0)	21.3 (19.9, 22.7)	12.0 (11.3, 12.7)	21.3 (20.0, 22.7)	39.4 (34.0, 44.7)

84	17.7 (17.0, 18.4)	15.7 (14.8, 16.7)	19.3 (18.3, 20.3)	15.5 (14.7, 16.2)	24.0 (22.5, 25.5)	14.0 (13.2, 14.7)	24.3 (22.9, 25.8)	42.7 (37.2, 48.1)
85	19.9 (19.2, 20.7)	18.0 (16.9, 19.0)	21.6 (20.5, 22.6)	17.8 (17.0, 18.7)	26.0 (24.4, 27.6)	15.8 (15.0, 16.7)	27.5 (25.9, 29.1)	45.4 (39.7, 50.8)
86	22.5 (21.7, 23.3)	20.3 (19.2, 21.4)	24.3 (23.1, 25.4)	20.6 (19.6, 21.5)	28.0 (26.3, 29.6)	18.4 (17.5, 19.3)	29.9 (28.2, 31.5)	48.3 (42.5, 53.8)
87	25.1 (24.2, 26.0)	22.4 (21.2, 23.6)	27.3 (26.1, 28.6)	23.3 (22.3, 24.3)	30.3 (28.6, 32.1)	21.0 (20.0, 22.0)	32.4 (30.7, 34.2)	51.8 (45.9, 57.3)
88	28.0 (27.0, 28.9)	24.6 (23.3, 25.9)	30.8 (29.4, 32.1)	26.3 (25.2, 27.4)	32.9 (31.1, 34.8)	23.7 (22.6, 24.8)	35.9 (34.0, 37.7)	52.9 (47.0, 58.5)
89	30.7 (29.7, 31.7)	26.6 (25.2, 27.9)	34.2 (32.7, 35.6)	29.2 (28.0, 30.3)	35.3 (33.4, 37.2)	26.5 (25.4, 27.7)	38.4 (36.5, 40.3)	54.8 (48.9, 60.4)
90	32.9 (31.8, 33.9)	28.5 (27.1, 29.9)	36.6 (35.1, 38.1)	31.4 (30.1, 32.6)	37.5 (35.5, 39.5)	28.7 (27.5, 30.0)	40.4 (38.4, 42.3)	58.1 (52.0, 63.7)
91	35.4 (34.3, 36.5)	30.2 (28.7, 31.7)	39.8 (38.3, 41.4)	34.1 (32.8, 35.4)	39.3 (37.2, 41.3)	31.5 (30.1, 32.8)	42.7 (40.7, 44.7)	58.1 (52.0, 63.7)
92	37.8 (36.7, 39.0)	32.0 (30.5, 33.6)	42.7 (41.1, 44.4)	36.8 (35.5, 38.2)	40.7 (38.6, 42.8)	34.2 (32.8, 35.6)	44.5 (42.5, 46.6)	58.1 (52.0, 63.7)
93	39.4 (38.2, 40.6)	33.2 (31.6, 34.9)	44.6 (42.9, 46.3)	38.5 (37.1, 39.9)	42.1 (39.9, 44.2)	35.8 (34.3, 37.2)	46.2 (44.0, 48.3)	58.1 (52.0, 63.7)
94	40.4 (39.2, 41.7)	33.6 (32.0, 35.3)	46.3 (44.5, 48.1)	39.6 (38.1, 41.1)	42.9 (40.7, 45.1)	37.2 (35.6, 38.7)	46.4 (44.2, 48.5)	59.3 (53.2, 64.9)
95	41.8 (40.5, 43.2)	34.7 (33.0, 36.5)	47.9 (46.0, 49.9)	41.3 (39.7, 42.9)	43.6 (41.3, 45.9)	38.6 (37.0, 40.3)	47.7 (45.4, 49.9)	59.3 (53.2, 64.9)

* = No participants in cell; could not estimate dementia incidence

Note: Estimates correspond to Figure 1, are reported as percentages, account for the competing risk of death, and use 55 years as the baseline age. The age of last observation was 94.2 years for Black adults and 93.3 years for those with 2 APOE $\varepsilon 4$ alleles The 95% confidence intervals are indicated in paratheses.

Supplemental Table 2: Lifetime risk of dementia (from age 55 to 95 years) based on a conservative defintion (N=15,043) the ARIC Study

	Lifetime risk (95% CI)
Overall	36 (35, 38)
Sex	
Men	30 (28, 33)
Women	41 (39, 44)
Race	
White	36 (33, 38)
Black	39 (36, 42)
APOE ε4 status	
0 alleles	34 (31, 36)
1 allele	41 (38, 44)
2 alleles	56 (48, 63)

Abbreviations: ARIC = Atherosclerosis Risk in Communities; CI = confidence interval

Note: Dementia cases were identified through study visits, phone interviews (only if subsequently confirmed through hospital or death records), or hospital or death records. Estimates are reported as percentages and indicate the cumulative incidence at 95 years of age (94.2 years for Black adults and 93.3 years for those with 2 APOE $\varepsilon 4$ alleles) after accounting for the competing risk of death. The 95% confidence intervals are reported in paratheses.

Supplemental Table 3: ICD-9/10 codes used for dementia diagnosis

Code source	Code[1]
ICD-9 CM	Starting with or equal to 290 (including: 290.0, 290.1x, 290.2x, 290.3, 290.4x, 290.8, 290.9); 294 (including 294.0, 294.1x, 294.2x, 294.9); 331 (including 331.0, 331.1x, 331.2, 331.7, 331.8x, 331.9; but excluding 331.83 - mild cognitive impairment)
ICD-10 CM	Starting with or equal to F01 (including: F01.5x); F02 (including: F02.8x); F03 (including: F03.9x); F04; F06.8; G30 (including G30.1, G30.8, G30.9); G31 (including G31.0x, G31.1, G31.8x, G31.9; but excluding G31.84 - mild cognitive impairment); G94 R41 (including R41.8x, R41.9)

1 Code with a suffix "x" can have one subsequent digit from 0 to 9 in the place of "x" when applicable.

Supplemental Table 4: Response rates by dementia ascertainment method, the ARIC study

No. of participants (%) that completed at least one adjudicated cognitive assessment at study visits among persons alive as of December 31st, 2013 (last day of study visit 5)	6,669 / 9,729 (68.5%)
No. of participants (%) that completed at least one phone-based assessment cognitive assessment among persons alive as of December 31st, 2013 (last day of study visit 5)	8,274 / 9,729 (85.0%)
No. of participants (%) that had at least one ICD9/10 code from a medical record or death certificate.	13,942 / 15,043 (92.7%)
No. of participants (%) that had at least one source of data for dementia ascertainment (study visit assessment, phone interview assessment, or medical or death records)	15,043 / 15,043 (100%)

Abbreviations: ARIC = Atherosclerosis Risk in Communities

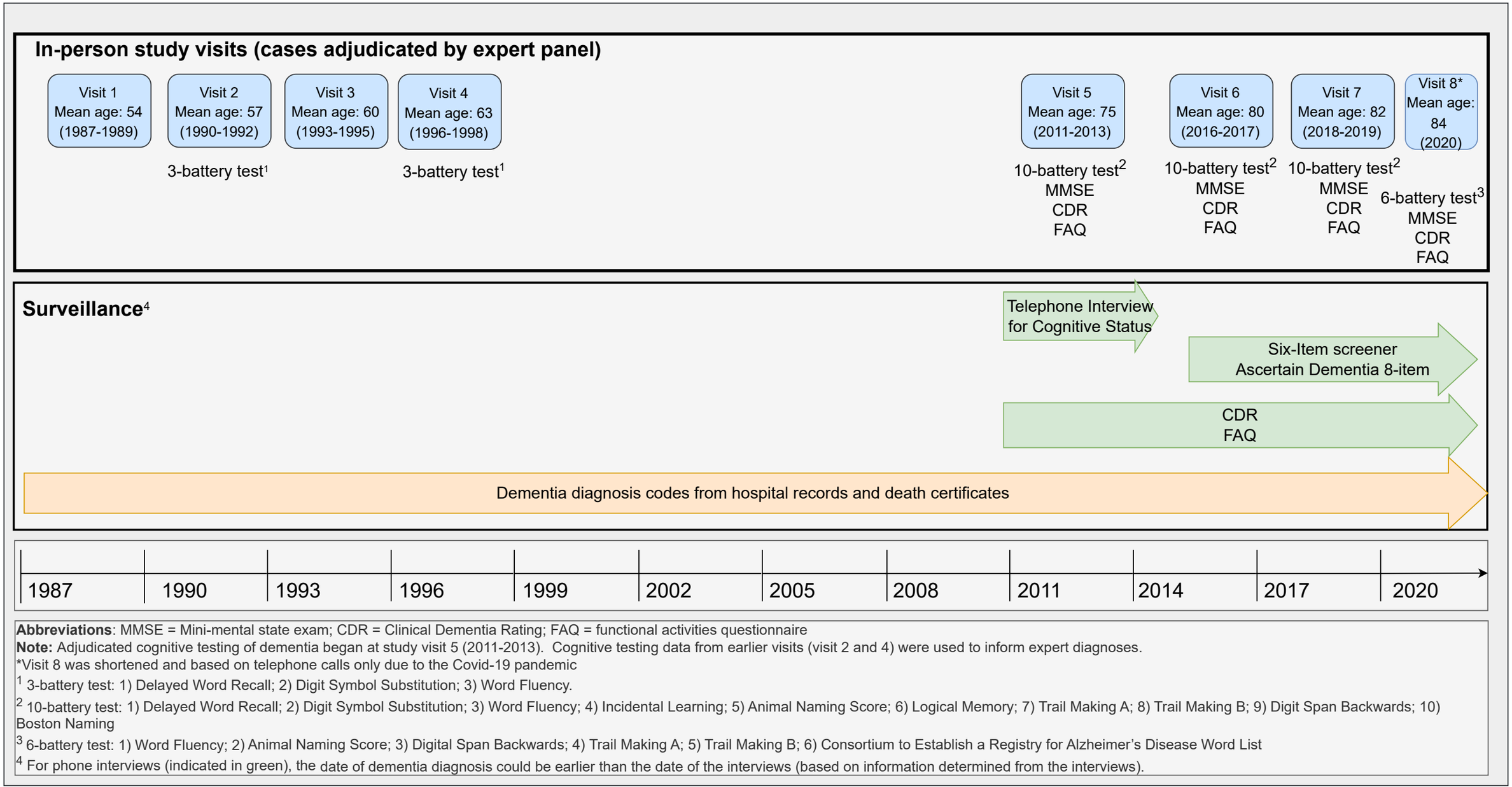
Note: Adjudicated cognitive assessments and phone-based assessments began at study visit 5 (2011-2013). For these two ascertainment methods, response rates were calculated among persons who were alive at the end of 2013.

Supplemental Figure 1: Ascertainment of dementia in the ARIC Study, 1987-2020

[Attached below]

Caption: Supplemental Figure 1 describes the three major approaches (in-person neuropsychological testing, with expert adjudication; telephone assessments; and medical and death record review) used to ascertainment dementia in the ARIC study

Abbreviations: ARIC = Atherosclerosis Risk in Communities



Abbreviations: MMSE = Mini-mental state exam; CDR = Clinical Dementia Rating; FAQ = functional activities questionnaire

Note: Adjudicated cognitive testing of dementia began at study visit 5 (2011-2013). Cognitive testing data from earlier visits (visit 2 and 4) were used to inform expert diagnoses.

*Visit 8 was shortened and based on telephone calls only due to the Covid-19 pandemic

[1] 3-battery test: 1) Delayed Word Recall; 2) Digit Symbol Substitution; 3) Word Fluency.

[2] 10-battery test: 1) Delayed Word Recall; 2) Digit Symbol Substitution; 3) Word Fluency; 4) Incidental Learning; 5) Animal Naming Score; 6) Logical Memory; 7) Trail Making A; 8) Trail Making B; 9) Digit Span Backwards; 10) Boston Naming

[3] 6-battery test: 1) Word Fluency; 2) Animal Naming Score; 3) Digital Span Backwards; 4) Trail Making A; 5) Trail Making B; 6) Consortium to Establish a Registry for Alzheimer's Disease Word List

[4] For phone interviews (indicated in green), the date of dementia diagnosis could be earlier than the date of the interviews (based on information determined from the interviews).

nature portfolio

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For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

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☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
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☒	☐ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	N/A. Data was not collected using software.
Data analysis	All analyses were conducted in Stata/SE 18.0 (StataCorp, College Station, TX, USA)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

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- For clinical datasets or third party data, please ensure that the statement adheres to our policy

ARIC data access procedures are in accordance with participant informed consent and NIH data sharing policy. Anonymized data from the ARIC study are available at the NHLBI Biologic Specimen and Data Repository Information Coordinating Center and can be accessed through the website (https://biolincc.nhlbi.nih.gov/studies/aric/). Requests for access of ARIC data may also be submitted to the ARIC Publications Committee according to established study procedures which

includes submission of a completed ARIC Manuscript Proposal From (available at https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines) to the ARIC Publications Committee at aricpub@unc.edu. Review and approval of data access requests typically takes approximately one month.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	Sex was self-reported. As reported in Supplemental Table 1, there were 15,043 total participants, of which 6,751 (44.9%) were men and 8,292 (55.1%) were women. Sex-specific estimates for the lifetime risk of dementia were reported in Figure 1, and sex-specific projections of incident dementia cases were reported in Figure 2. Data disaggregated by sex are available for researchers who obtain required permission to use the ARIC dataset.
Reporting on race, ethnicity, or other socially relevant groupings	Race was self-reported by participants during in-person interviews. Prior studies have reported large racial and ethnic differences in the prevalence of dementia, and current health policies have prioritized reducing these disparities. We sought to build on this literature by reporting race specific estimates of lifetime risk of dementia (in Figure 1) and race-specific projections of incident dementia cases (in Figure 2). Because our analyses were descriptive, we did not adjust for confounding. As reported in Supplemental Table 1, there were 15,043 total participants, of which 10,958 (72.8%) self-identified as White and 4,041 (27%) self-identified as Black. There were 44 participants (0.3% of total study population) that self-identified as belonging to other racial groups. Due to small sample size, we could not generate reliable race-specific estimates for these 44 participants. However, these participants were included in all other analyses.
Population characteristics	The study population included 15,043 participants free of dementia at age 55 years (26.9% Black race; 55.1% women). Approximately 31% of participants carried at least one APOE ε4 allele (28.1% one copy; 2.7% two copies). A detailed table of social and clinical participant characteristics is provided in Supplemental Table 1.
Recruitment	The ARIC Study is a community-based cohort of 15,792 adults from four US communities (Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland). Participants aged 45-64 years were originally recruited from 1987 to 1989 and have undergone clinical examinations (including cognitive testing), laboratory testing, and medical interviews (in-person and by phone) for the past three decades.
Ethics oversight	The ARIC Study was approved by institutional review boards at all research sites (Johns Hopkins University, Wake Forest University, University of Mississippi Medical Center, and University of Minnesota, New York University).

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

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Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	We conducted a prospective cohort analysis using data from the Atherosclerosis Risk in Communities Study. Data were quantitative.
Research sample	Participants aged 45-64 years were recruited from 1987 to 1989 from four US communities (Forsyth County, North Carolina; Jackson, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland). For the past three decades, participants have undergone clinical examinations (including cognitive testing), laboratory testing, and medical interviews (in-person and by phone). The study sample was designed to be representative of the four countries from which they were selected. The goal of this study sample was to select a large, diverse cohort of middle-aged adults from different regions in the US to study the national history of cardiovascular disease. In our analyses, we restricted our analytic sample to all participants in the ARIC study who were free of dementia at the study baseline. We chose this sample because we wanted to understand the lifetime risk of dementia using as much information as possible. We also included all participants in the study in order to generate lifetime risk estimate across different subgroups with precision. The analytic sample size was 15,043 (26.9% Black race, 55.1% women, 30.8% with ≥1 APOE ε4 allele).
Sampling strategy	Participants from each of the 4 ARIC sites were selected using stratified, probability sampling design. There was no formal power calculation used to determine the sample size. However, approximately 4,000 participants from each of the study. This sample size would deemed sufficient to achieve the study objective, which was to recruit a large sample of participants that was representative of each of the four communities and that would allow for comparison of different risk factors effects on cardiovascular disease. For our analysis (focused on dementia over the life course), the sample size (n=15,043) is among the largest in communities based

cohort studies examining the lifetime risk of dementia. Further, we had over 3 decades of follow up and extensive dementia ascertainment, allowing us to identify 3,252 incident dementia events. This allowed us to characterize the lifetime risk of dementia in our study sample with sufficient precision, overall and across subgroups.

Data collection

Detailed information about data collection are included in the manuscript.

For the past three decades, participants in the ARIC study have undergone clinical examinations (including cognitive testing), laboratory testing, and medical interviews (in-person and by phone) for the past three decades.

Dementia ascertainment in ARIC is summarized in Supplemental Figure 1. Briefly, dementia status was determined in all participants, including those who did not return for clinical study visits or died during follow-up, using three broad approaches.

Approach 1 - Clinical study visits
The first approach was based on cognitive testing at clinical study visits. A three-test neurocognitive battery was administered at visit 2 (1990-1992) and visit 4 (1996-1998). These tests were the 1) Delayed Word Recall; 2) Digit Symbol Substitution; 3) Word Fluency.

An expanded 10-test neuropsychological battery was administered at visit 5 (2011-2013), visit 6 (2016-2017), visit 7 (2018-2019). The 10 test were the: 1) Delayed Word Recall; 2) Digit Symbol Substitution; 3) Word Fluency; 4) Incidental Learning; 5) Animal Naming Score; 6) Logical Memory; 7) Trail Making A; 8) Trail Making B; 9) Digit Span Backwards; 10) Boston Naming.

Due to the COVID-19 pandemic, a shortened 6-battery test was administered at visit 8 (2020). These tests were the: 1) Word Fluency; 2) Animal Naming Score; 3) Digital Span Backwards; 4) Trail Making A; 5) Trail Making B; 6) Consortium to Establish a Registry for Alzheimer's Disease Word List.

The Clinical Dementia Rating scale, Functional Activities Questionnaire, Mini-Mental State Examination, and Blessed scale were used at visits 5-8, with the former two only in a subset of participants.

Assessments at study visits were completed by participants (with the help of proxies, as required). Dementia was initially diagnosed using an algorithm based on criteria recommended by the National Institute on Aging–Alzheimer's Association diagnostic guidelines workgroups and the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders. An expert panel subsequently reviewed and adjudicated cases of dementia identified by the algorithm.

Approach 2 - Telephone assessments
For those who did not return for in-person study visits, dementia was identified through annual or semiannual telephone interviews with participants and informants using validated instruments, including the Telephone Interview for Cognitive Status, Clinical Dementia Rating scale, Functional Activities Questionnaire, the Six Item Screener, and the Ascertain Dementia 8-item screener.

Approach 3 - Medical and death record review
Dementia cases were identified by using diagnostic codes in hospital records or death certificates for all participants throughout the study (see Supplemental Table 3 for ICD 9/10 codes used for ascertainment). Where possible, hospital or death certificate-based diagnoses were supported by interview informants using the Ascertain Dementia 8-item screener. Response rates for all three methods of dementia ascertainment (study visits, phone-interviews, and medical and death records) are provided in Supplemental Table 10.

The ARIC study is an observational study, and all analyses in the current study were descriptive. Therefore, there was no blinding of participants and research staff during any of the clinical assessments.

Timing

Data collected in the ARIC study began in 01-1987 and is still ongoing. Our analyses ended at 12-2020. Supplemental Figure 1 details the timing dementia ascertainment. As noted above, study visits occurred in 1987-1989 (visit 1), 1990-1992 (visit 2), 1996-1998 (visit 4), 2011-2013 (visit 5), 2016-2017 (visit 6), 2018-2019 (visit 7) and 2020 (visit 8). Telephone assessments began in 2011. Medical and death review took place from 01-1987 to 12-2020.

Data exclusions

We excluded participants with prevalent dementia prior to age 55 (n=4), missing information for covariates (n=543), and those who died or were lost to follow-up before the age of 55 (the index age for our primary analyses, n=202). These restrictions yielded an analytic sample of 15,043 participants.

Non-participation

All 15,043 participants had information about their dementia status available. Response rates for the three different methods of dementia are summarized below.

Response rate for dementia assessments at clinic study visits: 6,669 / 9,729 (68.5%) completed at least one adjudicated cognitive assessment at study visits among persons alive as of December 31st, 2013 (last day of study visit 5).

Response rate for dementia telephone assessments: 8,274 / 9,729 (85.0%) completed at least one phone-based assessment cognitive assessment among persons alive as of December 31st, 2013 (last day of study visit 5).

Response rate for medical and death records review: 13,942 / 15,043 (92.7%) had at least one ICD9/10 code from a medical record or death certificate.

Randomization

NA - ARIC is an observational cohort study, so participants were not randomized. Our analyses were descriptive so we did not adjust for confounders.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging