

Supplementary Online Content

Qiao Y, Suri FK, Zhang Y, et al. Racial differences in prevalence and risk for intracranial atherosclerosis in a US community-based population. *JAMA Cardiol*. Published online November 1, 2017. doi:10.1001/jamacardio.2017.4041

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Statistical Methods Used for Adjusting for Selection and Survival Bias in ARIC Studies

With respect to bias, probably the most important source of bias that may affect estimates in our study is age-related selection bias (a combination of survival and non-response bias). A major advantage of ARIC (as compared to *de novo* surveys in elderly participants), is that we can track the ARIC sample for over 25 years, and we can use estimates that take into account cohort attrition. In addition, our study was based in the ARIC Neurocognitive Study (NCS), an ancillary study conducted in ARIC Visit 5 to obtain 2,000 brain MRIs from study participants. In the ARIC NCS study, participants with evidence of cognitive impairment were oversampled as it was thought that these participants would provide more information for neurocognitive outcomes (the primary objective of the ARIC NCS study). In our analysis, we used a combination of survey sampling methods and inverse probability attrition weighting (IPAW) to take these factors into account, as follows:

- 1) For the main analysis, we used survey sampling methods to obtain prevalence estimates that could be applicable to ARIC Visit 5 (Stage 1) participants. Of 10,749 original cohort members deemed alive at the start of visit, 713 (6.6%) died during the 15-month recruitment period without having visit 5, leaving 10,036 who were either examined or not examined but alive through August 2013. Of these, 6,538 (age range=66 to 90 years) took part in visit 5 (5,918 full clinic exams, 228 abbreviated clinic exams, 392 home or care facility exams) (https://www2.csc.unc.edu/atic/Visit_5_NCS_Stage_1_Cohort_Description). From this initial sample, the objective was to obtain 2,000 brain MRIs (ARIC NCS) as follows: Cohort Visit 5 (Stage 1) participants were selected under a probability sampling plan designed to oversample for participants with evidence of cognitive impairment (“atypical”). In brief, 100% of atypical participants (low MMSE score, or low Z-score on any of 5 cognitive domains and definite cognitive decline) as well as 100% of ARIC Brain MRI participants were invited to Stage 2 (the ARIC Brain MRI study was an ancillary study conducted at Visit 3 in the Jackson and Forsyth County sites that performed brain MRIs in 1,927 Visit 3 participants). A random sample of the remaining participants, with selection probabilities varied by field center and age group (<80, ≥80 years), was also invited (Stage 2). Participants were invited to Stage 3 if they were selected to Stage 2, had no contraindications to MRI and (initially) if they attended a clinic visit. This was later revised so that participants completing home visits were invited to Stage 3 as well, but only 10 such participants completed a Stage 3 exam. The goal was to achieve a sample size of 2,000 Stage 3 participants. Selection probabilities were adjusted periodically to achieve that goal; updated selection probabilities were then applied retrospectively so that all participants within a given stratum had an equal probability of selection, regardless of timing of the Stage 1 visit. These weights and the associated survey sampling methods were developed by the ARIC study and have been applied to multiple ARIC NCS MRI analyses. The main analyses of the paper are thus weighted to represent the ARIC Visit 5 (Stage 1) sample.
- 2) As sensitivity analyses, we further applied a second type of weights also developed by the ARIC study and applied in multiple papers (i.e., Gottesman, JAMA Neuro 2014, 71 (10)). This second set of weights was developed for use in IPAW to address selection bias in Visit 5 due to underrepresentation of individuals who died or were lost-to-follow-up between ARIC Visit 1 and Visit 5 (these weights were also estimated as inverse estimated probabilities of selection). These set of weights are applied to Visit 5 analyses and provide the prevalence of ICAD in the counterfactual situation that all participants in Visit 1 had remained alive and attended Visit 5 exam.

eTable 1. Plaque Distributions in Intracranial Vessels.

| | Number of plaques | Number of participants |
|-------|--------------------------|-------------------------------|
| MCA | 257 | 146 |
| ICA | 469 | 337 |
| ACA | 93 | 70 |
| PCA | 401 | 239 |
| BA | 232 | 170 |
| VA | 255 | 204 |
| Total | 1707 | 637 |

MCA, M1, M2 and M3 segments of the middle cerebral artery; ICA, cavernous and supraclinoid internal carotid artery; ACA, A1, A2 and A3 segments of the anterior cerebral artery; PCA, P1, P2 and P3 segments of the posterior cerebral artery; BA, basilar artery; VA V3 and V4 segments of the vertebral artery.

eTable2. Risk Ratios for Intracranial Plaque Number per Participant with 95% Confidence Intervals Adjusted for CVD Risk Factors

| | Overall | | Black | | White | |
|---|--------------------------|--------------------------|---------------------------|-------------------|--------------------------|--------------------------|
| | Vsit-1 & Visit-5 factors | | Vsit-1 & Visit-5 factors | | Vsit-1 & Visit-5 factors | |
| Age (5-year increments) | 1.49 (1.32, 1.68) | | 1.33 (1.13, 1.56) | | 1.53 (1.33, 1.76) | |
| Gender (men vs women) | 1.32 (1.03, 1.69) | | 1.62 (1.15, 2.28) | | 1.17 (0.87, 1.58) | |
| Race (blacks vs whites) | 1.46 (1.14, 1.86) | | | | | |
| Smoking status | Visit-1 | Visit-5 | Visit-1 | Visit-5 | Visit-1 | Visit-5 |
| Current vs Never | 1.03 (0.66, 1.61) | 1.03 (0.55, 1.93) | 1.57 (1.06, 2.33)* | †† | 0.65 (0.39, 1.10)* | 1.59 (0.75, 3.38) |
| Former vs Never | 0.92 (0.60, 1.42) | 0.98(0.65, 1.47) | 0.91 (0.61, 1.38) | †† | 0.78 (0.48, 1.25) | 1.21 (0.78, 1.89) |
| Hypertension (Yes vs No) | 1.39 (1.07, 1.80) | 1.49 (1.13, 1.95) | 1.90 (1.34, 2.70) | 1.38 (0.83, 2.32) | 1.20 (0.85, 1.71) | 1.61 (1.19, 2.19) |
| Diabetes (Yes vs No) | 1.44 (0.94, 2.19) | 1.15 (0.88, 1.50) | 1.67 (0.89, 3.13) | 1.22 (0.83, 1.80) | 1.08 (0.64, 1.83) | 1.18 (0.85, 1.64) |
| Hyperlipidemia (Yes vs No) | 1.33 (1.04, 1.71) | 0.97 (0.74, 1.26) | 1.35 (0.95, 1.92) | 1.14 (0.77, 1.70) | 1.29 (0.96, 1.75) | 0.93 (0.67, 1.30) |
| History of coronary heart disease (Yes vs No) | 0.81 (0.36, 1.85) | 1.01 (0.70, 1.46) | † | 0.92 (0.49, 1.73) | 1.29 (0.57, 2.94) | 1.03 (0.66, 1.61) |

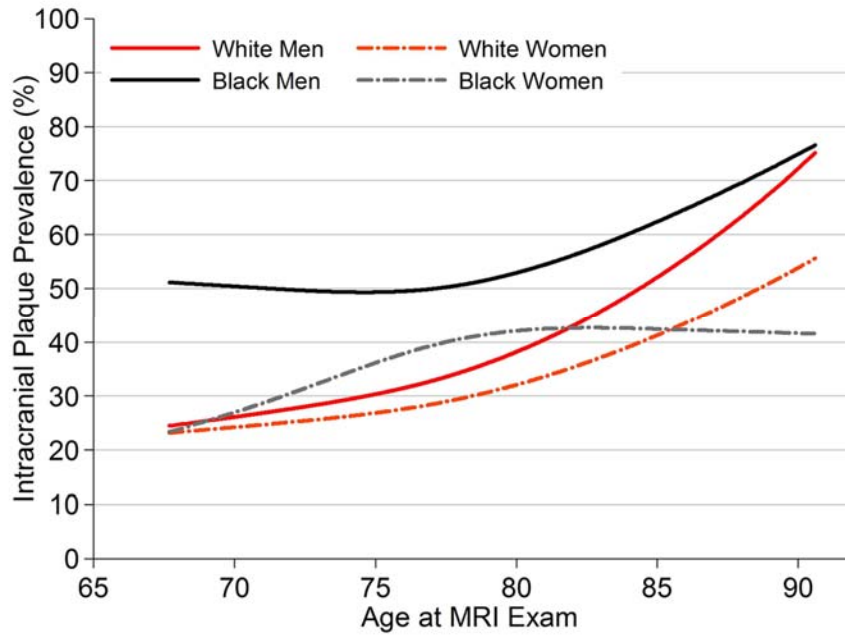
Includes risk factors from both visits in negative binomial models. Age is based on the time of the Visit 5 MRI exam. Bold indicates strongest associations. *, significant difference between blacks and whites including all main terms and interactions between race and each risk factor. †, dropped from the model (only 3 blacks with history of coronary heart disease). ††, dropped from the model. CVD, cardiovascular disease; ICAD, intracranial atherosclerotic disease.

eTable3. Average Differences with 95% Confidence Intervals in Maximum Normalized Wall Index Adjusted for CVD Risk Factors

| | Overall | | Black | | White | |
|---|-----------------------------|---------------------|-----------------------------|---------------------|-----------------------------|---------------------|
| | Vsit-1 & Visit-5 factors | | Vsit-1 & Visit-5 factors | | Vsit-1 & Visit-5 factors | |
| Age (5-year increments) | 0.79 (0.41, 1.18) | | 0.28 (-0.40, 0.96) | | 0.88 (0.44, 1.33) | |
| Gender (men vs women) | -1.29 (-2.13, -0.45) | | -1.56 (-3.01, -0.11) | | -1.33 (-2.31, -0.35) | |
| Race (blacks vs whites) | 1.02 (0.17, 1.86) | | - | | - | |
| Smoking status | Visit-1 | Visit-5 | Visit-1 | Visit-5 | Visit-1 | Visit-5 |
| Current vs Never | -0.69 (-2.51, 1.13) | 0.49 (-1.91, 2.89) | 0.47 (-2.47, 3.41)* | 0.03 (-3.55, 3.61) | -1.14 (-3.29, 1.01)* | 0.95 (-1.94, 3.84) |
| Former vs Never | 0.68 (-0.99, 2.35) | -0.28 (-1.88, 1.33) | 0.52 (-2.03, 3.08) | -0.78 (-3.24, 1.69) | 0.73 (-1.27, 2.73) | -0.11 (-2.05, 1.82) |
| Hypertension (Yes vs No) | 1.11(0.21, 2.01) | -0.25 (-1.21, 0.72) | 1.32 (-0.07, 2.71) | -1.04 (-3.30, 1.22) | 0.80 (-0.46, 2.05) | -0.04 (-1.09, 1.01) |
| Diabetes (Yes vs No) | -0.57 (-2.63, 1.50) | -0.00 (-0.92, 0.92) | 1.79 (-1.32, 4.89)* | 0.65 (-0.71, 2.01) | -1.15 (-3.51, 1.20)* | -0.16 (-1.33, 1.01) |
| Hyperlipidemia (Yes vs No) | 0.41 (-0.48, 1.29) | -0.34 (-1.23, 0.54) | 1.29 (-0.22, 2.79) | -0.12 (-1.60, 1.36) | 0.08 (-0.97, 1.14) | -0.45 (-1.51, 0.61) |
| History of coronary heart disease (Yes vs No) | 2.50 -1.62, 6.63) | -0.05 (-1.92, 1.82) | † | -2.13 (-4.27, 0.02) | 3.30 (-1.28, 7.87) | 0.41 (-1.66, 2.47) |

Based on multivariable linear regression adjusted for CVD risk factors and race. Age is based on the time of the Visit 5 MRI exam. Bold indicates strongest associations. *, significant difference between blacks and whites including all main terms and interactions between race and each risk factor. †, dropped from the model (only 3 blacks with history of coronary heart disease). CVD, cardiovascular disease; ICAD, intracranial atherosclerotic disease; CI, confidence interval.

eFigure 1. Racial differences in ICAD prevalence by age.



eFigure 2. Associations of ICAD prevalence with continuous CVD risk factors from Visit 5 using Poisson regression models adjusting for prevalence of hypertension, diabetes, cardiovascular disease, and hyperlipidemia at Visit 1

