Establishing Age-Specific Normative Data for the NIH Toolbox among Urban-Dwelling American Indian and Alaska Native Elders in the URBANE Study

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Abstract

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Epidemiology

This study presents group norms for fluid, crystallized, and total cognition scores on the NIH Toolbox among urban-dwelling American Indian and Alaska Native (AI/AN) Elders. From 2021 to 2024, the URBan Native Elders study recruited 1007 (n = 994) Elders to elucidate risk and protective factors for Alzheimer's Disease and related dementias (ADRD). Volunteers self-identified as AI/AN, were aged 55 years and older, and lived in or commuted to urban areas in the United States defined by Rural Urban Commuter Area codes. Participants underwent extensive medical interview and neurocognitive assessment. When comparing total participants assigned female at birth to total participants assigned male at birth, the former had higher overall uncorrected standard scores across fluid (mean 88.0, SD 11.1 vs mean 83.6, SD 13.0), crystallized (mean 105, SD 10.3 vs mean 104, SD 10.0), and total (mean 95.4, SD 10.3 vs mean 92.8, SD 11.9) domains than the latter. Potential influential factors for differences in composite scores include a high burden of traumatic brain injury (34.9%) and 66.2% attending at least one year of college. Findings from this data will inform clinical and public health decisions while forming the foundation of future longitudinal research on ADRD in AI/AN people.

Background and Significance

Alzheimer's disease and related dementias (ADRD) and mild cognitive impairment (MCI) are a growing public health concern for American Indian and Alaska Native (AI/AN) peoples. MCI is defined as performance that is lower than expected on cognitive function tests relative to age, or as a clinically significant decline in performance that does not substantially interfere with activities of daily life.[1] Individuals with MCI may or may not go on to experience dementia.[2] The cognitive variables of executive functioning and short- and long-delay memory recall predict the largest proportion of the variance in the progression of MCI to ADRD.[3] "Dementia" is an umbrella term used to signify a deterioration of global intellectual ability that interferes with occupational and social functioning and with independence in everyday activities.[1] The brain pathologies of ADRD include progressive accumulation of amyloid beta-protein fragments and twisted strands of the tau protein, both of which lead to neuronal damage and death. Neurodegeneration in ADRD is thought to begin years before clinical dementia, which is divided into 3 phases: 1) preclinical, 2) mild cognitive impairment (MCI), and 3) clinical dementia.[1]

The primary risk factor for ADRD is age where older age is associated with higher prevalence of ADRD. Using data from 28,027,071 Medicare Fee-for-Service beneficiaries 65 years old and older in 2014, a study in 2019 estimated the prevalence of ADRD to be 11.5% in the study and 1.6% in the US population with age-group disparities. The prevalence of ADRD ranged from 3.6% among those 65 to 75 years old, to 13.6% for those aged 75 to 84 years, and the highest at 34.6% for those older than 85 years.[4] So, the age distribution of the enrolled cohort will affect the prevalence of probable ADRD in the sample. An emerging genetic factor is the apolipoprotein E ε4 (ApoE) genotype.[5] Among clinical risk factors, advancing age presents the strongest risk,[6] with possible modifying effects from biological sex or gender-based life experience.[7,8] Low socioeconomic status and limited social or mental engagement also predict higher risk.[9–12] Race and ethnicity may be additional risk factors that are more likely to be explained by disparities in related demographic factors, especially education.[13,14] Many vascular comorbidities are also associated with ADRD, including smoking,[15,16] diabetes,[17,18] hypertension,[19–21] and high cholesterol.[22] A history of traumatic brain injury (TBI) also elevates risk.[23] Injuries to the head and neck can trigger vascular brain injuries (VBI) such as stroke. The only prospective cohort study in Indian Country found that 33% of its sample demonstrated evidence of VBI.[24] Outcomes of MCI and dementia related to VBI result from disruption of blood supplying oxygen and glucose to downstream tissues through blockage (ischemic) or bleeds (hemorrhagic).[25] Protective factors include physical activity and diets low in saturated fats and rich in vegetables and fruits.[26–29] Additionally, bilingual fluency is associated with better executive function,[30–32] and some[30,31] but not all[32] studies have argued that the ability to speak a second language protects against cognitive decline and dementia.

AI/AN peoples bear high burdens of many ADRD risk factors, including hypertension, type 2 diabetes, TBI, VBI, and stroke,[33,34] but are profoundly underrepresented in ADRD research. As the population grows older, more and more people are likely to experience effects of MCI and ADRD. Further, the limited available data about AI/AN communities and their burden of ADRD indicates that AI/AN are more likely to die of ADRD compared to their rural counterparts (21 vs 17/100,000).[34]

Settler colonialism has displaced and continues to displace many AI/AN people from their homelands into urban spaces. Settler colonialism is a structure, not an event, that systematically eliminates AI/AN peoples and nations for non-AI/AN people to inherit lands.[35] This structure is codified into Federal Indian Law and Policy such as the Termination Act and Relocation Act that "legally" facilitate these displacements to increasingly urban areas.[36] The result is urban-dwelling AI/AN people make up 72% of the 5.2 million AI/AN people in the US. The urban proportion of AI/AN Elders aged 65 years and older exceeds 80%.[37] Most work done to address MCI among AI/AN communities focused on rural or reservation settings. While

important, this work is not generalizable to a majority of AI/AN people who are domicile to urban areas.[38]

Specific aims

The aim of this project was to establish age-specific normative values for performance on the National Institutes of Health (NIH) Toolbox V2 (version 1.27.7219)[39] for cognition among urban-dwelling AI/AN Elders in the URBAn Native Elders (URBANE): Risk and Protective Factors for Alzheimer's Disease and Related Dementias study. This was the first large epidemiologic study of health among urban-dwelling AI/AN Elders. The goal of the URBANE study as to better understand baseline prevalence of risk and protective factors in domains of cognitive impairment, ADRD, and associations with clinical, genetic, neuroimaging, behavioral, and lifestyle factors. Findings from this data will inform clinical and public health decisions while forming the foundation of future longitudinal research on ADRD in AI/AN people.

Methods and Positionality

Theoretical orientations that inform my work include relational accountability and standing with and speaking as faith. Relational accountability is a guiding principle to my approach because knowledge is relational.[40] Because knowledge exists in the collective, my analysis and critique are influenced by and constructed through the many Indigenous scholars' and community members' work I pull from. Wilson asserts, "Indigenous research methodology means talking about relational accountability. As a researcher you are answering to all your relations when you are doing research" (2001, p. 177).[40] Tuhiwai-Smith is concerned "not so much with the actual technique of selecting a method but much more with the context in which research problems are conceptualized and designed, and with the implications of research for its participants and their communities" (2012, p. ix).[41] I am to conduct this research such that I refuse the insider/outsider dynamic and notions of "giving back" to instead turn toward "Standing With and Speaking As Faith."[42] I seek to inquire in concert with AI/AN communities on shared conceptual ground and shared stakes with those among whom knowledge is built. This approach is appropriate due to my standpoint as an Indigenous person and researcher whose communities are directly impacted by the results of the work. I cannot separate myself from the "subject," and instead co-construct knowledge with the investigators and participants who share their experiences in the research process.

Study Design/Study Population

The URBANE study is a cross-sectional study of 1007 participants aged 55 years and older from AI/AN communities and tribes in five geographically diverse metropolitan areas with large Native populations: Anchorage, AK; Oklahoma City, OK; Phoenix, AZ; San Bernardino, CA; and Seattle, WA. Of note, this study began during the COVID-19 SARS-CoV-2 virus pandemic with data collection spanning from 2021-2024. Stay-at-home orders, higher risk for severe infection and impacts[43] posed recruitment challenges. To be eligible for URBANE, participants self-identified as AI/AN, be 55 and older, and lived in, or regularly commuted to a large city or town, not on a reservation. Multi-racial participants were eligible to participate. Among many AI/AN people, barriers such as time to travel back to Tribal headquarters, record mismanagement, sealed adoption records, Blood Quantum rules, and more contribute to difficulty getting federally recognized "proof" of tribal affiliation. Further, some AI/AN communities are ineligible or federal recognition. As such, the study did not require Certificate Degree of Indian Blood (CDIB) for eligibility. Urbanicity is defined through 2010 Rural Urban Commuter Area (RUCA) code scoring via zip code.[44] People were excluded if they did not meet the inclusion criteria and if they participated in the Cerebrovascular Disease and Its Consequences in American Indians[24] study or the Strong Heart Stroke Study[2,45] due to protocol overlap. The study recruited through a variety of methods such as fliers, radio station announcements, outreach at Urban Indian Health Organizations, community outreach events

(e.g., tabling at powwows), word of mouth referral, and social media marketing through the BuildClinical[46] platform on Facebook, Instagram, and YouTube.

Data Collection

Participants underwent extensive medical interview, clinical examination, neurocognitive testing, anthropometric measurement, physical function evaluation, and provided blood and urine specimens. Participants completed the computer-administered NIH Toolbox assessments when they are most alert (e.g., in the morning or within four hours of waking) with a certified study staff member. Tasks within the NIH Toolbox assess attention and inhibitory control, episodic memory, working memory, language functioning, and speed of mental processing. Study staff administered structured interviews covering demographics, health behaviors, and medical history. Eligible participants completed a cranial MRI and a neuroradiologist reviewed all participant scans for interpretation of findings.

Data Quality Assurance and Quality Control

The study implemented quality assurance and quality control protocols to ensure that the interviews, cognitive examinations, and clinical measurements were conducted accurately and consistently throughout the project. Quality assurances were conducted during the initial examinations and then on a regular basis. An essential part of quality assurance for work in Indian Country includes the incorporation of staff with knowledge of and experience working with AI/AN communities in the research enterprise. While not always available in applicant pool, preference for hiring personnel with knowledge of and experience working with AI/AN communities was given based on cultural competence considerations such as familiarity with norms for interactions with Elders. Standardized training to certify new staff on study procedures was conducted by study investigators using a “train the trainer” method and every staff member responsible for administering the cognitive assessment was certified by the lead clinical neuropsychologist. The coordinating center team conducted internal audits, double entered data to ensure data integrity and accuracy, flagged erroneous data, and re-trained site staff as needed. Five percent of the sample had their measurements or lab samples taken twice to evaluate accuracy and consistency.

Variables of Interest

Primary outcome of interest: NIH Toolbox: The NIH Toolbox software generates composite scores for fluid cognition, crystallized cognition, and total cognition for participants who completed the practice and live items in each test. For fluid cognition that assesses processing of new information and learning, the tasks include the Dimensional Change Card Sort, Flanker Inhibitory Control and Attention, List Sorting Working Memory, Pattern Comparison Processing Speed, and Picture Sequence Memory tests. If the Picture Sequence Memory test is incomplete, a fluid cognition score is not generated. The Oral Reading Recognition and Picture Vocabulary tests are used to generate the crystallized cognition composite that is influenced by past learning experiences, such as education. Then, the total cognition composite score uses the fluid and crystalized cognition scores to calculate the overall score for performance, equivalent to a Full-Scale Intelligence Quotient. If a fluid cognition score is unavailable, a total cognition composite score is not calculated for that participant.

Primary exposures of interest: Exposures of interest include age at time of assessment, race (monoracial AI/AN and another race in addition to AI/AN), sex assigned at birth, education attainment, urbanicity defined by RUCA score, and annual income reported during the staff-administered interview.

Covariates of interest: Self-report neurological history of TBI, stroke, transient ischemic attack (TIA), and any diagnosis of Alzheimer’s disease or dementia during the interview. Specifically, history of TBI was assessed by endorsement on questions about injuries to the

head or neck in their lifetime from crashes, falls, sports injuries, violence, gunshots, and military service that resulted in loss of consciousness or post-traumatic amnesia.

Data Analysis

All data were analyzed in the statistical software R.[48] Descriptive statistics and measures of central tendency in our exposures and covariates are presented by eight five-year age groups. Means and standard deviations were be calculated for fluid, crystalized, and total composite scores in the whole sample, then stratified by age and sex assigned at birth. Finally, z-scores were be calculated for NIH Toolbox performance stratified by five age categories. Due to small cell sizes, age groups of participants older than 75 years were truncated to five groups in the calculation of stratified means and z-scores.

Results

After accounting for participants who had withdrawn, asked for their data to be excluded from analysis, or their data marked as missing, the final analyzable sample comprised of 994 Elders aged 55 and older. Descriptive statistics are presented in Table 1. Among these 994 Elders, 84% (835) identified mono-racially as AI/AN and 873 (87.8%) identified as not Hispanic or Latino. The age (in years) of participants ranged from 55 to over 85 (mean 63.8, SD 6.95) with the majority (323/994, 32.5%) being 55 to 59 years old. Education attainment varied among the 994 Elders with 416 (41.9%) having attended college while 171 (17.2%) did not have a high school diploma.

Table 1. Characteristics of American Indian and Alaska Native Elders in the URBANE Study

	Total (N=994)	55 to 59 (N=323)	60 to 64 (N=272)	65 to 69 (N=214)	70 to 74 (N=101)	75 to 79 (N=50)	80 to 84 (N=24)	85+ (N=10)
Sex Assigned at Birth								
Female	723 (72.7%)	231 (71.5%)	185 (68.0%)	172 (80.4%)	76 (75.2%)	35 (70.0%)	18 (75.0%)	6 (60.0%)
Male	271 (27.3%)	92 (28.5%)	87 (32.0%)	42 (19.6%)	25 (24.8%)	15 (30.0%)	6 (25.0%)	4 (40.0%)
Age (years)								
Mean (SD)	63.8 (6.95)	56.9 (1.44)	62.0 (1.39)	66.8 (1.43)	71.6 (1.42)	76.9 (1.35)	81.5 (1.38)	87.2 (1.81)
Median [Min, Max]	63.0 [55.0, 90.0]	57.0 [55.0, 59.0]	62.0 [60.0, 64.0]	66.0 [65.0, 69.0]	71.0 [70.0, 74.0]	77.0 [75.0, 79.0]	81.0 [80.0, 84.0]	86.5 [85.0, 90.0]
Race								
AI/AN & Another Race	159 (16.0%)	53 (16.4%)	43 (15.8%)	34 (15.9%)	16 (15.8%)	7 (14.0%)	6 (25.0%)	0 (0%)
AI/AN Only	835 (84.0%)	270 (83.6%)	229 (84.2%)	180 (84.1%)	85 (84.2%)	43 (86.0%)	18 (75.0%)	10 (100%)
Ethnicity								
Hispanic or Latino	121 (12.2%)	43 (13.3%)	39 (14.3%)	26 (12.1%)	6 (5.9%)	6 (12.0%)	1 (4.2%)	0 (0%)
Not Hispanic or Latino	873 (87.8%)	280 (86.7%)	233 (85.7%)	188 (87.9%)	95 (94.1%)	44 (88.0%)	23 (95.8%)	10 (100%)
RUCA Code[a]								
Urban	974 (98.0%)	318 (98.5%)	263 (96.7%)	209 (97.7%)	100 (99.0%)	50 (100%)	24 (100%)	10 (100%)
Large Rural City or Town	19 (1.9%)	5 (1.5%)	8 (2.9%)	5 (2.3%)	1 (1.0%)	0 (0%)	0 (0%)	0 (0%)
Missing	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

	Total (N=994)	55 to 59 (N=323)	60 to 64 (N=272)	65 to 69 (N=214)	70 to 74 (N=101)	75 to 79 (N=50)	80 to 84 (N=24)	85+ (N=10)
Education Attainment								
No HS Diploma	171 (17.2%)	63 (19.5%)	46 (16.9%)	38 (17.8%)	12 (11.9%)	8 (16.0%)	3 (12.5%)	1 (10.0%)
HS Diploma or GED	165 (16.6%)	63 (19.5%)	46 (16.9%)	27 (12.6%)	16 (15.8%)	6 (12.0%)	3 (12.5%)	4 (40.0%)
Attended College	416 (41.9%)	135 (41.8%)	122 (44.9%)	83 (38.8%)	45 (44.6%)	24 (48.0%)	5 (20.8%)	2 (20.0%)
Four-Year Degree	141 (14.2%)	36 (11.1%)	35 (12.9%)	40 (18.7%)	13 (12.9%)	7 (14.0%)	9 (37.5%)	1 (10.0%)
Advanced Degree	101 (10.2%)	26 (8.0%)	23 (8.5%)	26 (12.1%)	15 (14.9%)	5 (10.0%)	4 (16.7%)	2 (20.0%)
Annual Household Income (USD)								
≤ $15K	234 (23.5%)	95 (29.4%)	61 (22.4%)	49 (22.9%)	15 (14.9%)	8 (16.0%)	4 (16.7%)	2 (20.0%)
> $15K ≤ $25K	99 (10.0%)	26 (8.0%)	26 (9.6%)	23 (10.7%)	15 (14.9%)	6 (12.0%)	1 (4.2%)	2 (20.0%)
> $25K ≤ $35K	109 (11.0%)	26 (8.0%)	29 (10.7%)	27 (12.6%)	14 (13.9%)	6 (12.0%)	3 (12.5%)	4 (40.0%)
> $35K ≤ $50K	132 (13.3%)	36 (11.1%)	45 (16.5%)	29 (13.6%)	12 (11.9%)	7 (14.0%)	3 (12.5%)	0 (0%)
> $50K ≤ $70K	123 (12.4%)	32 (9.9%)	35 (12.9%)	28 (13.1%)	14 (13.9%)	7 (14.0%)	6 (25.0%)	1 (10.0%)
> $70K	204 (20.5%)	80 (24.8%)	54 (19.9%)	34 (15.9%)	21 (20.8%)	9 (18.0%)	5 (20.8%)	1 (10.0%)
Refused	87 (8.8%)	25 (7.7%)	22 (8.1%)	23 (10.7%)	8 (7.9%)	7 (14.0%)	2 (8.3%)	0 (0%)
Missing	6 (0.6%)	3 (0.9%)	0 (0%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Neurological Disorder[b]								
No	937 (94.3%)	303 (93.8%)	252 (92.6%)	206 (96.3%)	96 (95.0%)	46 (92.0%)	24 (100%)	10 (100%)
Yes	49 (4.9%)	17 (5.3%)	18 (6.6%)	7 (3.3%)	3 (3.0%)	4 (8.0%)	0 (0%)	0 (0%)
Missing	8 (0.8%)	3 (0.9%)	2 (0.7%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Alzheimer's Disease[b]								
No	975 (98.1%)	316 (97.8%)	267 (98.2%)	212 (99.1%)	98 (97.0%)	48 (96.0%)	24 (100%)	10 (100%)
Yes	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)
Missing	18 (1.8%)	7 (2.2%)	5 (1.8%)	2 (0.9%)	3 (3.0%)	1 (2.0%)	0 (0%)	0 (0%)
Dementia[b]								
No	975 (98.1%)	316 (97.8%)	267 (98.2%)	212 (99.1%)	98 (97.0%)	48 (96.0%)	24 (100%)	10 (100%)
Yes	1 (0.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (2.0%)	0 (0%)	0 (0%)
Missing	18 (1.8%)	7 (2.2%)	5 (1.8%)	2 (0.9%)	3 (3.0%)	1 (2.0%)	0 (0%)	0 (0%)
Stroke								
No	925 (93.1%)	303 (93.8%)	261 (96.0%)	196 (91.6%)	94 (93.1%)	42 (84.0%)	21 (87.5%)	8 (80.0%)
Yes	63 (6.3%)	17 (5.3%)	11 (4.0%)	17 (7.9%)	5 (5.0%)	8 (16.0%)	3 (12.5%)	2 (20.0%)
Missing	6 (0.6%)	3 (0.9%)	0 (0%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)

	Total (N=994)	55 to 59 (N=323)	60 to 64 (N=272)	65 to 69 (N=214)	70 to 74 (N=101)	75 to 79 (N=50)	80 to 84 (N=24)	85+ (N=10)
Transient Ischemic Attack								
No	916 (92.2%)	302 (93.5%)	261 (96.0%)	189 (88.3%)	89 (88.1%)	45 (90.0%)	21 (87.5%)	9 (90.0%)
Yes	72 (7.2%)	18 (5.6%)	11 (4.0%)	24 (11.2%)	10 (9.9%)	5 (10.0%)	3 (12.5%)	1 (10.0%)
Missing	6 (0.6%)	3 (0.9%)	0 (0%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Traumatic Brain Injury[c]								
No	623 (62.7%)	177 (54.8%)	183 (67.3%)	134 (62.6%)	68 (67.3%)	35 (70.0%)	18 (75.0%)	8 (80.0%)
Yes	347 (34.9%)	136 (42.1%)	84 (30.9%)	74 (34.6%)	30 (29.7%)	15 (30.0%)	6 (25.0%)	2 (20.0%)
Don't Know	3 (0.3%)	1 (0.3%)	1 (0.4%)	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Applicable	3 (0.3%)	1 (0.3%)	1 (0.4%)	1 (0.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	18 (1.8%)	8 (2.5%)	3 (1.1%)	4 (1.9%)	3 (3.0%)	0 (0%)	0 (0%)	0 (0%)
Treated in ER After Injury[d]								
No	634 (63.8%)	188 (58.2%)	179 (65.8%)	134 (62.6%)	70 (69.3%)	34 (68.0%)	21 (87.5%)	8 (80.0%)
Yes	353 (35.5%)	132 (40.9%)	92 (33.8%)	79 (36.9%)	29 (28.7%)	16 (32.0%)	3 (12.5%)	2 (20.0%)
Don't Know	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	6 (0.6%)	3 (0.9%)	0 (0%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Vehicular Accident								
No	637 (64.1%)	193 (59.8%)	180 (66.2%)	130 (60.7%)	67 (66.3%)	39 (78.0%)	19 (79.2%)	9 (90.0%)
Yes	348 (35.0%)	126 (39.0%)	91 (33.5%)	83 (38.8%)	31 (30.7%)	11 (22.0%)	5 (20.8%)	1 (10.0%)
Don't Know	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	8 (0.8%)	4 (1.2%)	0 (0%)	1 (0.5%)	3 (3.0%)	0 (0%)	0 (0%)	0 (0%)
Fallen or Hit by Object								
No	581 (58.5%)	164 (50.8%)	158 (58.1%)	135 (63.1%)	69 (68.3%)	32 (64.0%)	15 (62.5%)	8 (80.0%)
Yes	405 (40.7%)	156 (48.3%)	112 (41.2%)	78 (36.4%)	30 (29.7%)	18 (36.0%)	9 (37.5%)	2 (20.0%)
Don't Know	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	7 (0.7%)	3 (0.9%)	1 (0.4%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Shaken Violently or Shot in Head								
No	735 (73.9%)	213 (65.9%)	199 (73.2%)	159 (74.3%)	86 (85.1%)	47 (94.0%)	22 (91.7%)	9 (90.0%)
Yes	252 (25.4%)	107 (33.1%)	72 (26.5%)	54 (25.2%)	13 (12.9%)	3 (6.0%)	2 (8.3%)	1 (10.0%)
Don't Know	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	6 (0.6%)	3 (0.9%)	0 (0%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)

	Total (N=994)	55 to 59 (N=323)	60 to 64 (N=272)	65 to 69 (N=214)	70 to 74 (N=101)	75 to 79 (N=50)	80 to 84 (N=24)	85+ (N=10)
Nearby Blast								
No	897 (90.2%)	285 (88.2%)	244 (89.7%)	196 (91.6%)	95 (94.1%)	44 (88.0%)	23 (95.8%)	10 (100%)
Yes	90 (9.1%)	35 (10.8%)	27 (9.9%)	17 (7.9%)	4 (4.0%)	6 (12.0%)	1 (4.2%)	0 (0%)
Don't Know	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	6 (0.6%)	3 (0.9%)	0 (0%)	1 (0.5%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Repeated Impacts to Head[e]								
No	794 (79.9%)	241 (74.6%)	213 (78.3%)	172 (80.4%)	88 (87.1%)	49 (98.0%)	21 (87.5%)	10 (100%)
Yes	186 (18.7%)	76 (23.5%)	57 (21.0%)	38 (17.8%)	11 (10.9%)	1 (2.0%)	3 (12.5%)	0 (0%)
Don't Know	1 (0.1%)	0 (0%)	1 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Missing	13 (1.3%)	6 (1.9%)	1 (0.4%)	4 (1.9%)	2 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Fluid Composite								
Mean (SD)	87.0 (11.7)							
Median [Min, Max]	88.0 [44.0, 122]							
Missing	11 (1.1%)							
Crystallized Composite								
Mean (SD)	105 (9.91)							
Median [Min, Max]	106 [58.0, 132]							
Total Composite Score								
Mean (SD)	94.7 (10.8)							
Median [Min, Max]	95.0 [53.0, 122]							
Missing	11 (1.1%)							

[a] Rural Urban Commuter Area Code
[b] Ever told by doctor or medical professional they had condition
[c] Resulting in loss of consciousness or post-traumatic amnesia
[d] Emergency Room
[e] History of abuse, contact sports, or military duty

Within the sample, one participant (1/994, 0.1%) reported having been told by a doctor that they had AD and dementia. Many participants stated they experienced a head or neck injury with a fall being the most common cause (405/994, 40.7%; Figure 1) and being nearby during and explosion or blast being the least common (90/994, 9.1%). Just under 35% (347/994) experienced a loss of consciousness or post-traumatic amnesia, constituting a TBI (Figure 2).

Performance on the NIH Toolbox by the overall sample of 994 is presented in Table 1. All participants received scores for the crystallized composite. However, 11 participants were unable to complete the Picture Sequence Memory test, lowering the total number of fluid cognition and total cognition scores by 11. Overall mean performance scores on the cognition domains are as follows: fluid (mean 87, SD 11.7), crystallized (mean 105, SD 9.91), and total (mean 94.7, SD 10.8).

After stratifying by sex assigned at birth, the age groups of 75 to 79, 80 to 84, and 85 or older had small cell sizes. Once the three groups were truncated into one, there were at least 25 participants in each grouping. As a result, the mean uncorrected standard scores presented in Table 2 and Figure 3 reflect five age groups instead of eight as in Table 1. When comparing total participants assigned female at birth to total participants assigned male at birth, the former had higher overall uncorrected standard scores across fluid (mean 88.0, SD 11.1 vs mean 83.6, SD 13.0), crystallized (mean 105, SD 10.3 vs mean 104, SD 10.0), and total (mean 95.4, SD 10.3 vs mean 92.8, SD 11.9) cognition domains than the latter, respectively.

Figure 1. Causes and Effects of Head and Neck Injury in Lifetime

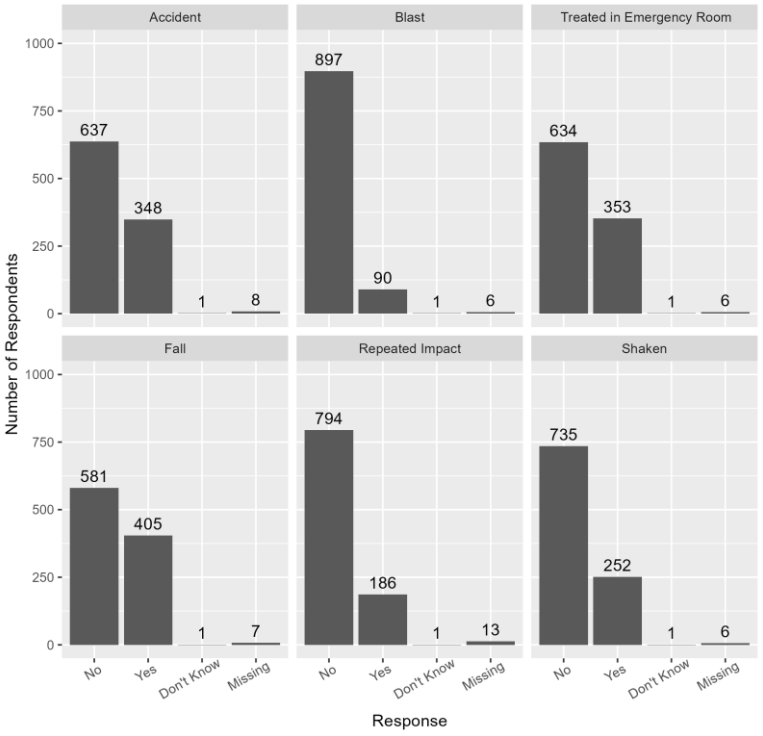

Figure 2. Traumatic Brain Injury in Lifetime After Loss of Consciousness or Post-Traumatic Amnesia

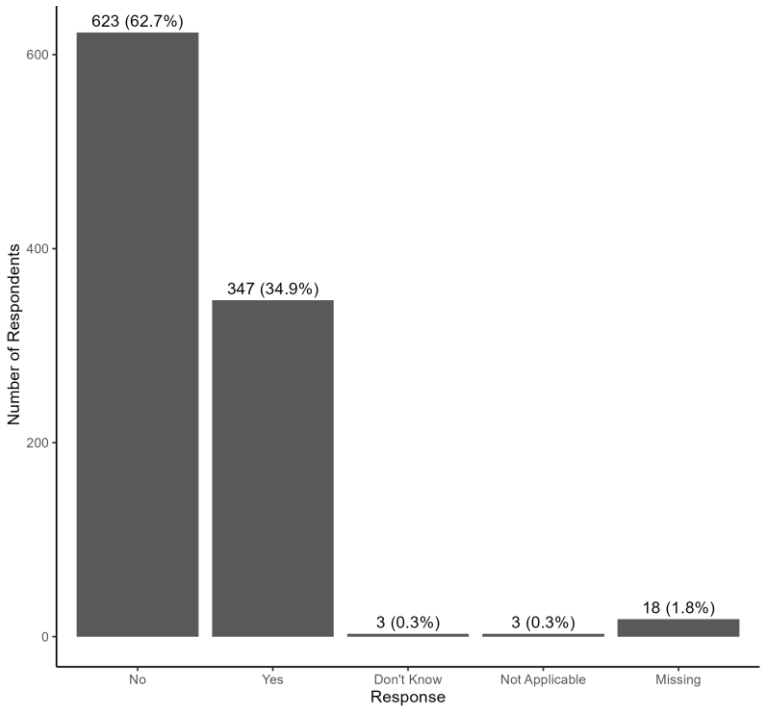

Table 2. Cognition Uncorrected Standard Scores Stratified by Sex Assigned at Birth and Age Group[a]

Male	Total (N=271)	55 to 59 (N=92)	60 to 64 (N=87)	65 to 69 (N=42)	70 to 74 (N=25)	75+ (N=25)
Fluid Composite						
Mean (SD)	84.6 (13.0)	89.1 (12.2)	85.0 (11.5)	80.4 (14.2)	78.3 (14.7)	79.4 (10.4)
Median [Min, Max]	85.0 [48.0, 118]	89.0 [63.0, 118]	87.0 [51.0, 107]	81.5 [52.0, 117]	86.0 [48.0, 97.0]	84.0 [56.0, 95.0]
Missing	4 (1.5%)	1 (1.1%)	1 (1.1%)	0 (0%)	0 (0%)	2 (8.0%)
Crystallized Composite						
Mean (SD)	104 (10.0)	103 (8.77)	104 (10.5)	104 (10.7)	107 (13.2)	106 (8.13)
Median [Min, Max]	105 [73.0, 129]	104 [83.0, 124]	105 [80.0, 124]	103 [78.0, 125]	109 [73.0, 125]	105 [94.0, 129]
Total Composite Score						
Mean (SD)	92.8 (11.9)	95.0 (10.7)	92.9 (11.6)	90.2 (13.2)	90.6 (15.7)	90.8 (9.04)
Median [Min, Max]	93.0 [53.0, 121]	95.0 [74.0, 121]	93.5 [60.0, 116]	91.0 [58.0, 121]	97.0 [53.0, 108]	92.0 [70.0, 107]
Missing	4 (1.5%)	1 (1.1%)	1 (1.1%)	0 (0%)	0 (0%)	2 (8.0%)
Female	Total (N=723)	55 to 59 (N=231)	60 to 64 (N=185)	65 to 69 (N=172)	70 to 74 (N=76)	75+ (N=59)
Fluid Composite						
Mean (SD)	88.0 (11.1)	92.1 (11.2)	88.2 (9.69)	86.8 (9.53)	83.9 (11.2)	79.5 (11.6)
Median [Min, Max]	89.0 [44.0, 122]	93.0 [53.0, 122]	89.0 [63.0, 112]	86.0 [61.0, 111]	85.0 [50.0, 111]	82.0 [44.0, 100]
Missing	7 (1.0%)	1 (0.4%)	2 (1.1%)	3 (1.7%)	0 (0%)	1 (1.7%)
Crystallized Composite						
Mean (SD)	105 (9.86)	104 (9.53)	105 (9.38)	106 (9.59)	108 (9.66)	105 (12.9)
Median [Min, Max]	106 [58.0, 132]	105 [77.0, 128]	106 [80.0, 132]	107 [77.0, 131]	109 [72.0, 125]	107 [58.0, 126]
Total Composite Score						
Mean (SD)	95.4 (10.3)	97.0 (10.6)	95.6 (9.41)	95.0 (9.30)	94.4 (11.2)	90.6 (12.0)
Median [Min, Max]	96.0 [55.0, 122]	98.0 [59.0, 122]	96.0 [72.0, 117]	96.0 [66.0, 116]	95.0 [59.0, 114]	92.0 [55.0, 112]
Missing	7 (1.0%)	1 (0.4%)	2 (1.1%)	3 (1.7%)	0 (0%)	1 (1.7%)

[a] Due to small cell sizes in higher age categories, the age groups for those 75 years and older were truncated.

URBANE participants assigned female at birth had higher mean uncorrected standard scores across all age groups and composite scores with exception of the 75 and older age group in crystallized and total composite scores. The mean crystallized composite score for those assigned male at birth aged 75 years was higher by one at 105 (SD 8.13) compared to 105 (SD 12.9) for those of the same age assigned female at birth. A mean total composite score of 90.8 (SD 9.04) was 0.2 higher for participants assigned male compared to a mean of 90.6 (SD 12.0) for participants assigned female (see Table 2 and Figure 3).

Group norms were calculated for the fluid, crystallized, and total composite scores for each sex assigned at birth and the five age groups using the means and standard deviations to create z-distributions. Table 3, Table 4, and Table 5 present the uncorrected standard score needed to correspond with a z-score on a z-distribution from +2 to -2 at intervals of 0.5.

Figure 3. NIH Toolbox Composite Scores Stratified by Sex Assigned at Birth and Age Group

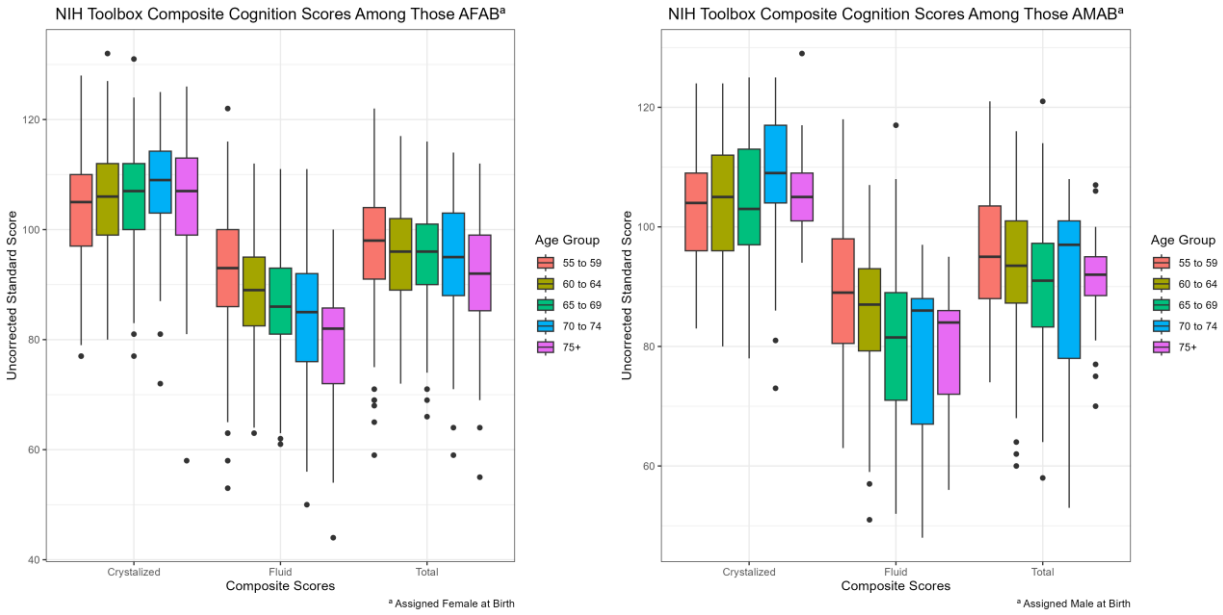

Table 3. Fluid Cognition z-Scores Stratified by Sex Assigned at Birth and Age Group[a]

		Age Group and Uncorrected Standard Score				
Male	z-score	55 to 59	60 to 64	65 to 69	70 to 74	75+
	2.0	117	108	109	108	100
	1.5	111	102	102	100	95
	1.0	106	97	95	93	90
	0.5	100	91	87	86	85
	0.0	95	85	80	78	80
	- 0.5	90	79	73	71	74
	-1.0	84	73	66	64	69
	- 1.5	79	68	59	56	64
	- 2.0	73	62	52	49	59
		Age Group and Uncorrected Standard Score				
Female	z-score	55 to 59	60 to 64	65 to 69	70 to 74	75+
	2.0	115	108	106	107	103
	1.5	109	103	101	101	97
	1.0	103	98	96	96	91
	0.5	98	93	92	90	85
	0.0	92	88	87	84	79
	- 0.5	86	83	82	78	73
	-1.0	81	79	77	73	68
	- 1.5	75	74	72	67	62
	- 2.0	70	69	68	61	56

Table 4. Crystallized Cognition z-Scores Stratified by Sex Assigned at Birth and Age Group[a]

		Age Group and Uncorrected Standard Score				
Male	z-score	55 to 59	60 to 64	65 to 69	70 to 74	75+
	2.0	121	125	126	133	122
	1.5	117	120	120	127	118
	1.0	112	115	115	120	114
	0.5	108	109	110	113	110
	0.0	104	104	104	107	106
	- 0.5	99	99	99	100	102
	-1.0	95	94	94	94	98
	- 1.5	91	88	88	87	94
	- 2.0	86	83	83	80	90
		Age Group and Uncorrected Standard Score				
Female	z-score	55 to 59	60 to 64	65 to 69	70 to 74	75+
	2.0	123	124	125	127	131
	1.5	118	119	120	112	124
	1.0	114	115	115	117	118
	0.5	109	110	111	113	111
	0.0	104	105	106	108	105
	- 0.5	99	100	101	103	98
	-1.0	95	96	96	98	92
	- 1.5	90	91	91	93	86
	- 2.0	85	86	87	88	79

Table 5. Total Cognition z-Scores Stratified by Sex Assigned at Birth and Age Group[a]

		Age Group and Uncorrected Standard Score				
Male	z-score	55 to 59	60 to 64	65 to 69	70 to 74	75+
	2.0	116	116	117	122	109
	1.5	111	110	110	114	104
	1.0	106	105	103	106	100
	0.5	100	99	97	99	95
	0.0	95	93	90	91	91
	- 0.5	90	87	84	83	86
	-1.0	84	81	77	75	82
	- 1.5	79	76	70	67	77
	- 2.0	74	70	64	59	73
		Age Group and Uncorrected Standard Score				
Female	z-score	55 to 59	60 to 64	65 to 69	70 to 74	75+
	2.0	118	114	114	117	115
	1.5	113	110	109	111	109
	1.0	108	105	104	106	103
	0.5	102	100	100	100	97
	0.0	97	96	95	94	91
	- 0.5	92	91	90	89	84
	-1.0	86	86	86	83	78
	- 1.5	81	82	81	78	72
	- 2.0	76	77	76	72	67

Discussion

This project reports normative data for performance on the NIH Toolbox assessment by age group and sex assigned at birth for AI/AN Elders aged 55 and older who live in urban areas. Calculation of these norms begin to address the dearth of research on aging and cognitive resilience among this population. Fluid cognition scores were lower overall as well as when stratified by age group and sex assigned at birth. Our findings are consistent with literature that describes how the burden of chronic disease such as cardiovascular disease[47] and lifetime TBI[48,49] can negatively impact working and episodic memory measured by the fluid cognition domain in the NIH Toolbox. Of the 994 participants in our sample, 34.9% (347/994) reported TBI, 12% higher than the proportion from a US Army Brigade Combat Team (22.8%).[50] Lower performance on the fluid domain also impacts calculation of the total composite score for each participant and contributes to larger standard deviations for fluid and composite scores in this study. Figure 3 shows the interquartile range of each domain appears larger for the 70 to 74 years old category compared to the 75 or older category. Survival bias may be affecting our estimates, especially among those assigned male at birth. In contrast to the fluid and total composite scores, the crystallized cognition scores overall and within stratification were slightly above average. In another study of AI/AN Elders,[51] those deemed cognitively intact had 13.6 mean years of education. Of the 994 elders sampled, 41.9% (416) attended college, 14.2% (141) graduated with a four-year degree, and 10.2% (101) held an advanced degree. This high proportion of formal education could contribute to the mean crystallized cognition scores for our sample. Future analysis for this study could incorporate investigation of education attainment, burden of chronic diseases such as diabetes, and their associations with cognitive performance.

Limitations

To accurately describe the experience of a wide range of urban-dwelling AI/AN Elders, the URBANE study sampled five urban centers in multiple geographic regions. Challenges in recruitment and retention due to the pandemic and the use of cognitive tests which do not have appropriate norms affect our ability to interpret the study results. Increased infection and severity of illness due to COVID-19 SARS-CoV-2 infection in the AI/AN community affected research sites' ability to start and continue data collection. Stay-at-home orders and important shifts in organizations' resources toward supporting the direct health care needs reduced the availability of person-power for research indirectly related to pandemic response.[52] Meeting these challenges, research sites worked to build networks of trust with the community and local organizations to help identify interested and eligible residents, much like other studies in the literature.[53,54] Additionally, the cognitive tests used to diagnose cognitive dysfunction lack normative data in marginalized populations and cultural considerations (e.g., language, lifestyle factors). Using state-of-the-art measurement such as the NIH Toolbox based on item-response theory helped the efficiency and accuracy of our assessments of cognition.[55,56]

Conclusion

The URBANE study recruited a diverse sample of urban-dwelling AI/AN Elders with the goal of better understanding the risk and protective factors associated with ADRD. This project sought to establish age-specific normative data for the fluid, crystallized, and total composite domains of the NIH Toolbox that are appropriate for interpreting AI/AN Elders' performance on the assessment. This analysis also contributes to the growing foundation of research on ADRD in AI/AN people. With these more representative norms in hand, decisions about urban AI/AN Elder's aging processes, and health care can be better informed.

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