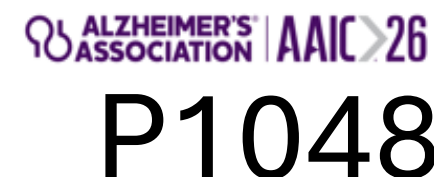
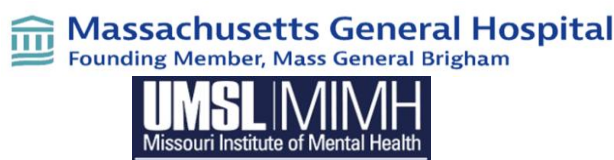


Known and Unique Modifiable Risk Factors of Brain Health and Dementia Biomarkers in an African Cohort



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Hearing loss, heavy alcohol use, and low SES are associated with worse global cognition in a cohort of older adults in Uganda (mean age 60) living with well-treated HIV and without HIV.

Background

- The 2024 Lancet Commission identified 14 potentially modifiable dementia risk factors, using mainly data from the Global North.^{1,2}
- Problem:** The greatest dementia burden is in Global South, particularly in sub-Saharan Africa (sSA), where data are limited.³
- Purpose:** Evaluate known and unique potentially modifiable risk factors in a population-representative cohort in sSA to inform local prevention efforts.



Methods

- Study Design:** Prospective longitudinal cohort
- Predictors:** (A) 13 Known and (B) 6 Unique potentially modifiable dementia risk factors
- Outcomes:** Global cognition (composite Z-score) and plasma biomarkers (natural log-transformed)
 - NfL and GFAP (Quanterix, n=564)
 - p-tau217, Aβ42/40, and p-tau217/Aβ42 (Lumipulse, n=227)
- Statistical Analysis:** Linear and logistic multivariate regressions

Table 1. Characteristics in the Uganda Aging and Dementia Cohort

Characteristic	Total Cohort (n=564)
Age in years, mean (SD; range)	60.3 (6.4; 48-90)
Female, n (%)	284 (50%)
Education, n (%)	
No schooling	83 (15%)
Some primary school	204 (36%)
Completed primary education	130 (23%)
Some secondary school	81 (14%)
Secondary school or higher	66 (12%)
Literacy (ability to read & write), n (%)	
No	89 (16%)
Yes	475 (84%)
Urbanicity, n (%)	
Semi-urban (Mbarara)	233 (41%)
Rural (Kabwohe)	331 (59%)
HIV Positive, n (%)	275 (49%)

Results

- High LDL, vision loss, urbanicity, low SES, & hypertension demonstrated high sample prevalence & effect size (**Fig. 1**).
- TBI and diabetes are associated with elevated NfL, and current smoking is associated with decreased GFAP. Urbanicity is associated with decreased NfL and GFAP. No significant associations were identified with p-tau217, Aβ42/40, and p-tau217/Aβ42 (**Table 2**).

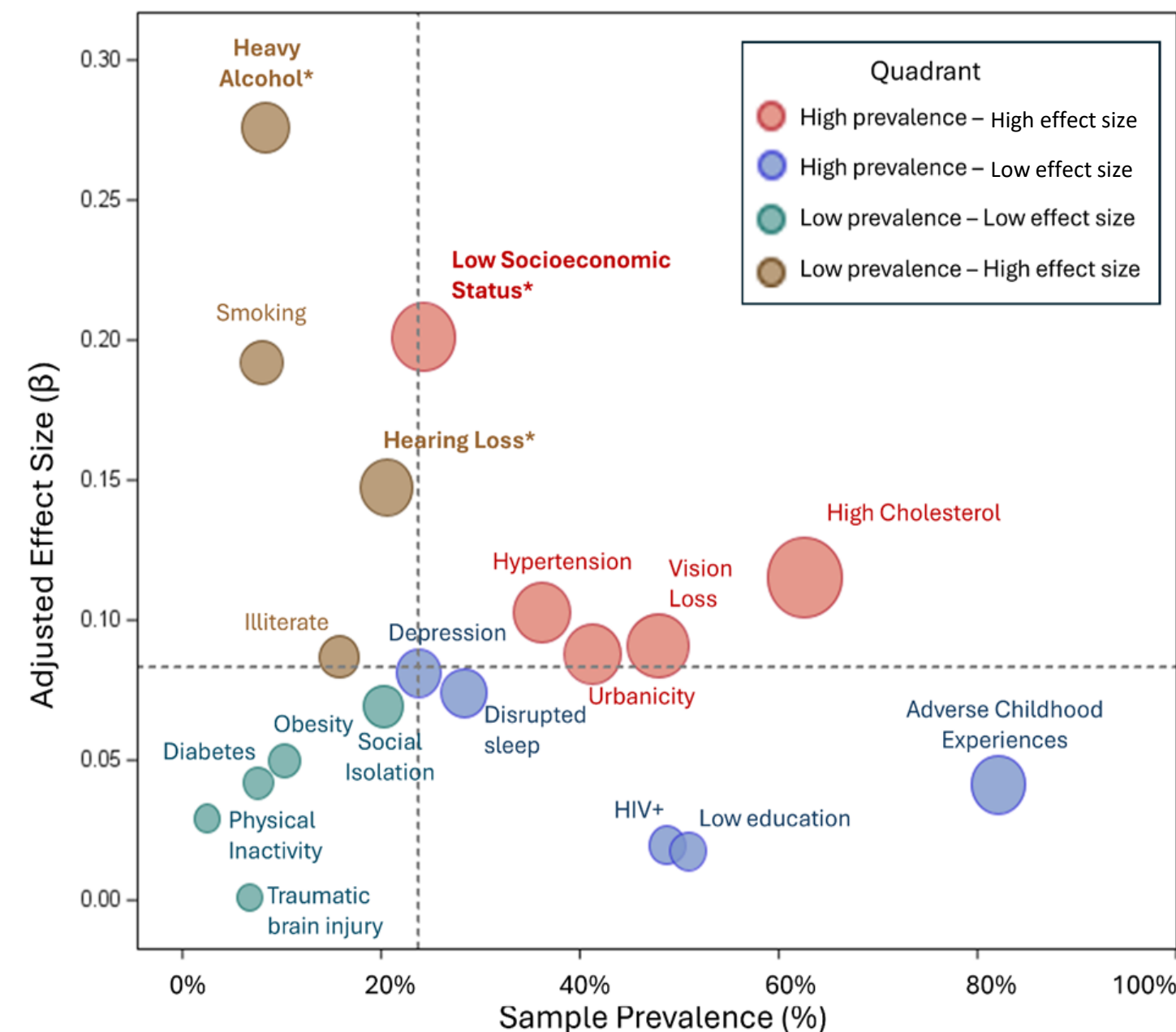


Figure 1. Bubble plot of potentially modifiable risk factors of global cognitive performance in the Uganda Aging and Dementia Cohort ¹

¹ = Bubble size reflects sample prevalence and sample effect size, where larger size reflects higher prevalence and/ or effect size. Effect sizes are based on linear regressions with adjustment for age, sex, education, and site, as appropriate. Median sample prevalence and effect size are used to demarcate the four quadrants.
* = Statistically significant association with cognition, p-value < 0.05.

Hearing Loss = Speech-frequency pure tone hearing loss average ≥ 25 dB in the better ear; Vision Loss = Self-reported vision trouble, including with glasses (if applicable);

High LDL cholesterol = LDL ≥ 100 mg/dL; Depression = Center for Epidemiologic Studies Depression Scale mean composite score ≥ 1.75; TBI = Any loss of consciousness > 30 minutes; Physical inactivity = Low activity per International Physical Activity Scale (adapted to a Ugandan context); Diabetes = A1c ≥ 6.5%; Hypertension = Systolic blood pressure > 130 mmHg; Obesity = BMI ≥ 30 kg/m²; Excessive Alcohol = AUDIT-C composite score ≥ 5; Social Isolation = UCLA Loneliness scale composite ≥ 5; Urbanicity = Participants with testing at semi-urban site (Mbarara); Disrupted sleep = Nightly hours spent asleep < 6 hours; Adverse childhood experiences = ACE Questionnaire composite score ≥ 1; Low local socioeconomic status = 1st quartile score based on modified Filmer & Pritchett scale

Table 2. Prevalence and adjusted effect sizes for potentially modifiable risk factors of cognition, including significant plasma biomarkers

	Sample Prevalence n (%)	Global Cognitive Composite ¹ β (SE), p	Plasma NfL ² β (SE), p	Plasma GFAP ² β (SE), p
Lancet Commission Potentially Modifiable Risk Factors				
Low Education (less than primary school)	287 (51%)	0.02 (0.06), 0.76	-0.02 (0.04), 0.64	-0.01 (0.04), 0.88
Hearing Loss	116 (21%)	-0.15 (0.07), 0.04	-0.01 (0.05), 0.85	0.01 (0.05), 0.81
Vision Loss	269 (48%)	-0.09 (0.06), 0.11	0.03 (0.04), 0.47	0.01 (0.04), 0.80
High LDL Cholesterol	327 (63%)	0.12 (0.06), 0.07	0.00 (0.04), 0.95	0.06 (0.04), 0.13
Depression	134 (24%)	-0.08 (0.07), 0.24	0.00 (0.05), 0.98	0.02 (0.05), 0.61
TBI (moderate or severe)	38 (7%)	0.00 (0.11), 0.99	0.16 (0.08), 0.049	0.09 (0.08), 0.25
Physical Inactivity	14 (2.5%)	0.03 (0.18), 0.87	0.15 (0.12), 0.23	0.18 (0.12), 0.14
Diabetes	43 (8%)	0.04 (0.11), 0.69	0.26 (0.08), <.001	-0.09 (0.07), 0.24
Current Smoking	45 (8%)	-0.19 (0.11), 0.07	-0.02 (0.07), 0.74	-0.16 (0.07), 0.03
Hypertension	204 (36%)	0.10 (0.06), 0.08	0.07 (0.04), 0.10	0.07 (0.04), 0.10
Obesity	58 (10%)	-0.05 (0.10), 0.61	-0.09 (0.07), 0.18	-0.08 (0.07), 0.23
Excessive Alcohol	47 (8%)	-0.28 (0.11), <.01	0.08 (0.07), 0.27	-0.04 (0.07), 0.56
Social Isolation	114 (20%)	-0.07 (0.07), 0.33	-0.05 (0.05), 0.34	0.00 (0.05), 0.97
Unique Potentially Modifiable Risk Factors				
HIV Positive (well-treated)	275 (49%)	0.02 (0.06), 0.73	-0.02 (0.04), 0.62	0.05 (0.04), 0.26
Illiteracy	89 (16%)	0.09 (0.09), 0.33	0.01 (0.06), 0.82	0.02 (0.06), 0.67
Urbanicity	233 (41%)	0.09 (0.06), 0.12	-0.12 (0.04), 0.004	-0.14 (0.04), 0.0005
Disrupted Sleep	160 (28%)	0.07 (0.06), 0.24	0.02 (0.05), 0.73	0.06 (0.04), 0.18
Adverse Childhood Experiences	450 (82%)	-0.04 (0.07), 0.58	0.04 (0.05), 0.44	0.04 (0.05), 0.39
Low Local Socioeconomic Status	137 (24%)	-0.20 (0.07), <.01	-0.01 (0.05), 0.76	0.01 (0.04), 0.79

¹ = Model adjusted for age, sex, education, and site, as appropriate.
² = Model adjusted for age, sex, and renal function.

Conclusions

- Brain health initiatives in Uganda should prioritize these factors.

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