

Supplement: Plantinga *et al.*, Fluid Cognition among Individuals with Systemic Lupus Erythematosus

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Table S1. Percentage agreement and kappa for potential cognitive impairment for individual subdomains vs. overall fluid cognition impairment^a

Potential impairment in:	Percent agreement (kappa)					
	Overall fluid cognition	Episodic memory	Working memory	Attention & inhibitory control	Processing speed	Cognitive flexibility
Overall fluid cognition	—	—	—	—	—	—
Episodic memory	74.9% (0.15)	—	—	—	—	—
Working memory	77.9% (0.40)	79.9% (0.14)	—	—	—	—
Attention & inhibitory control	82.9% (0.60)	67.8% (0.08)	70.9% (0.28)	—	—	—
Processing speed	85.4% (0.60)	79.4% (0.10)	73.4% (0.18)	77.4% (0.44)	—	—
Cognitive flexibility	81.4% (0.43)	86.4% (0.07)	75.4% (0.09)	68.8% (0.17)	81.9% (0.32)	—

^aPotential impairment as >1.5 SD below the mean (age-corrected standard score < 77.5).

Table S2. Comparison of characteristics of participants included vs. excluded in this study, as well as of characteristics participants in the parent study (GOAL)

Characteristic	Study Participants			P ^a	GOAL Study Participants ^b
	Overall	Included	Excluded		
N	451	199	252	—	987
Dates of visits/surveys	10/8/19-5/12/22	10/8/19-3/10/20; 7/20/21-5/12/22	10/6/20-3/9/22	—	3/30/20-8/31/21
Sociodemographics					
Mean (SD) age	46.2 (11.8)	46.1 (12.4)	46.2 (11.4)	>0.9	49.1 (13.8)
Age category, n (%)				0.7	
18-34	92 (20.4%)	44 (21.1%)	48 (19.1%)		186 (18.8%)
35-49	174 (38.6%)	74 (37.2%)	100 (39.7%)		334 (33.8%)
≥50	185 (41.0%)	81 (40.7%)	104 (41.3%)		467 (47.3%)
Sex, ^c n (%)				0.003	
Female	414 (91.8%)	174 (87.4%)	240 (95.2%)		922 (93.4%)
Male	37 (8.2%)	25 (12.6%)	12 (4.8%)		65 (6.6%)
Race, n (%)				0.06	
Black	372 (82.5%)	172 (86.4%)	200 (79.4%)		789 (79.9%)
Other	27 (6.0%)	12 (6.0%)	15 (5.9%)		25 (2.5%)
White	52 (11.5%)	15 (7.6%)	37 (14.7%)		173 (17.5%)
Ethnicity, n (%)				0.7	
Hispanic	25 (5.6%)	10 (5.0%)	15 (6.0%)		58 (5.9%)
Not Hispanic	425 (94.4%)	196 (95.0%)	229 (94.0%)		921 (94.1%)
Highest level of education completed, n (%)				0.1	
High school degree or lower	103 (23.1%)	54 (27.1%)	49 (19.4%)		272 (28.2%)
Some college/associates degree	169 (37.9%)	70 (35.2%)	103 (40.9%)		320 (33.1%)
College graduate or higher	174 (39.0%)	75 (37.7%)	100 (39.7%)		374 (38.7%)
Currently employed, n (%)				0.2	
Yes	207 (47.2%)	84 (44.0%)	123 (49.6%)		367 (40.0%)
No	232 (52.9%)	107 (56.0%)	125 (50.4%)		551 (60.0%)
Clinical					
Median (IQR) disease duration, years	14.8 (9.3-22.3)	14.7 (8.3-23.0)	14.9 (10.0-21.8)	0.3	15.9 (9.1-23.7)

Characteristic	Study Participants			P ^a	GOAL Study Participants ^b
	Overall	Included	Excluded		
Median (IQR) SLAQ score	11.0 (6.0-16.0)	11.0 (7.0-16.0)	10.0 (6.0-15.0)	0.09	13.0 (7.0-20.0)
Median (IQR) BILD scores	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	0.6	2.0 (1.0-4.0)
Mean (SD) BMI, kg/m ²	30.1 (8.2)	30.8 (8.9)	29.6 (7.6)	0.1	29.3 (7.8)
Mean (SD) depression T-score ^d	48.0 (9.2)	48.5 (9.1)	47.7 (9.2)	0.3	49.9 (9.9)
Mean (SD) perceived stress score ^e	15.2 (7.1)	15.2 (7.3)	15.2 (7.0)	>0.9	16.7 (7.6)
Currently taking steroids, n (%)	192 (42.7%)	76 (38.4%)	116 (46.0%)	0.1	443 (46.1%)

APPEAL, Approaches to Positive, Patient-Centered Experiences of Aging in Lupus; BILD, Brief Index of Lupus Damage (range, 0-46; 46 is maximum damage); BMI, body mass index; GOAL, Georgians Organized Against Lupus (parent study); IQR, interquartile range (25th-75th percentile); SLAQ, Systemic Lupus Activity Questionnaire (range, 0-47; 47 is maximum activity).

^aFor in-person vs. remote APPEAL participants, by *t* or chi-squared test, as appropriate.

^bFrom GOAL Wave 7; includes *n*=250 participants who also participated in APPEAL.

^cRepresents sex at birth.

^dFrom the Patient Reported Outcomes Measurement Information System (PROMIS) Depression Short Form-8a.

^eFrom Cohen's 10-item Perceived Stress Scale (range, 0-40; higher scores representing greater perceived stress).

Table S3. Summary of NIH Toolbox Fluid Cognition assessment scores among individuals with SLE, comparing age-corrected standard scores with uncorrected standard scores and fully adjusted T-scores and associated percentiles

Score	Composite	Fluid Cognition Assessment				
		Episodic memory	Working memory	Attention & inhibitory control	Processing speed	Cognitive flexibility
Age-corrected standard score^a						
Mean (SD)	87.2 (15.6)	96.2 (12.5)	91.4 (16.9)	82.0 (12.3)	93.4 (18.8)	94.7 (15.6)
Median (IQR)	88 (76-97)	95 (87-104)	89 (79-106)	82 (74-89)	95 (81-105)	95 (84-104)
Uncorrected standard score^b						
Mean (SD)	92.8 (12.5)	95.9 (12.2)	94.5 (15.0)	92.9 (9.2)	95.8 (16.6)	99.5 (10.6)
Median (IQR)	93 (84-102)	94 (87-103)	94 (86-105)	94 (89-99)	97 (84-107)	101 (95-107)
Fully adjusted T-score^c						
Mean (SD)	45.3 (11.2)	49.3 (8.9)	46.8 (11.8)	41.2 (8.1)	49.8 (13.3)	48.0 (11.9)
Median (IQR)	45 (38-54)	49 (43-54)	47 (38-56)	41 (36-46)	51 (41-59)	48 (39-56)
Median percentile associated with T-score (IQR)	32 (12-66)	45 (25-66)	39 (12-73)	19 (8-34)	55 (19-82)	42 (14-73)
Interpretation of median percentile ^d	Borderline	Average	Low average	Inferior	Average	Low Average

IQR, interquartile range (25th-75th percentile).

^aAge-corrected standard scores compare the scores to those in the NIH Toolbox nationally representative normative sample at the same age, where a score of 100 indicates performance that was at the national average for the test-taking participant's age (SD =15, such that a score of 85 is 1 SD below the mean for the test-taker's age).

^bUncorrected standard scores compare the score of the test-taker to those in the entire NIH Toolbox nationally representative normative sample, regardless of age or any other variable (*i.e.*, overall performance when compared with the general U.S. population). A standard score of 100 indicates performance that was at the national average for the general U.S. population (SD =15, such that a score of 85 is 1 SD below the mean for the general population).

^cT-scores adjusted for age, sex, race, ethnicity, and education, with a score of 50 representing the population mean and a score of 40 representing a score 1 SD below the mean for the population of the same age, sex, race, ethnicity, and education level.

^dPercentiles represent the following levels of performance: very superior ($\geq 70^{\text{th}}$ percentile), superior (63^{rd} to $< 70^{\text{th}}$ percentile), high average ($> 56^{\text{th}}$ percentile to $< 63^{\text{rd}}$ percentile), average (43^{rd} to 56^{th} percentile), low average ($> 36^{\text{th}}$ to $< 43^{\text{rd}}$ percentile), borderline (30^{th} to 36^{th} percentile), inferior ($< 30^{\text{th}}$ percentile).

Table S4. Adjusted^a associations of alternate definitions of overall fluid cognition impairment and score with selected characteristics

Characteristic	Primary analysis ^b		Impairment defined by:						
	Primary analysis ^b	OR (95% CI)	Primary analysis ^b excluding those aged ≥ 65	Age-corrected standard score >1 SD below mean (OR 95% CI)	Age-corrected standard score >1 SD below mean	Fully adjusted ^c T-score >1.5 SD below mean	Fully adjusted ^c T-score >1 SD below mean	T-score- associated percentiles ^d OR (95% CI)	
					OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	β (95% CI)
Age, per +10 years	0.84 (0.64-1.09)	0.95 (0.71-1.26)		0.87 (0.69-1.11)	0.88 (0.65-1.20)	0.87 (0.68-1.12)	0.92 (0.71-1.19)		1.19 (-0.54,2.92)
Age category									
18-34 vs. ≥ 50	1.00 (0.12-8.68)	2.46 (0.25-24.5)		2.21 (0.31-15.9)	3.51 (0.25-49.9)	2.60 (0.33-20.8)	1.06 (0.13-8.94)		-9.08 (-23.5,5.38)
35-49 vs. ≥ 50	0.93 (0.24-3.62)	1.39 (0.35-5.60)		1.40 (0.41-4.77)	2.81 (0.54-14.7)	1.52 (0.42-5.50)	0.93 (0.25-3.46)		-3.09 (-12.0,5.78)
Male vs. female	0.77 (0.29-2.10)	0.88 (0.32-2.45)		0.84 (0.35-2.03)	1.28 (0.44-3.71)	0.82 (0.32-2.09)	1.01 (0.40-2.58)		0.34 (-6.04,6.71)
Race									
Other vs. Black	0.39 (0.08-1.88)	0.39 (0.08-1.88)		0.20 (0.04-0.96)	0.38 (0.05-3.11)	0.64 (0.16-2.50)	0.79 (0.20-3.08)		8.63 (-0.34,17.6)
White vs. Black	—	—		0.18 (0.01-0.81)	0.33 (0.04-2.64)	0.80 (0.24-2.64)	0.64 (0.17-2.38)		14.8 (6.78,22.8)
Highest level of education completed									
≤High school graduate vs. \geq college graduate	3.82 (1.67-8.75)	3.97 (1.72-9.18)		3.02 (1.40-6.52)	1.98 (0.78-5.04)	2.44 (1.12-5.28)	1.81 (0.83-3.96)		-9.93 (-15.3,-4.60)
Some college vs. \geq college graduate	1.27 (0.55-2.94)	1.32 (0.57-3.07)		1.06 (0.53-2.15)	0.89 (0.34-2.37)	0.90 (0.41-1.95)	0.79 (0.37-1.80)		-4.02 (-8.87,0.83)
Currently working vs. not	0.30 (0.14-0.64)	0.30 (0.14-0.63)		0.32 (0.17-0.63)	0.26 (0.10-0.67)	0.37 (0.19-0.75)	0.27 (0.13-0.58)		10.3 (5.96,14.7)
Disease duration, per +10 years	1.48 (1.00-2.18)	1.46 (0.98-2.18)		1.32 (0.93-1.87)	1.65 (1.04-2.62)	1.26 (0.87-1.82)	1.41 (0.96-2.09)		-0.76 (-3.30,1.78)
SLAQ score, per 1 SD	1.05 (0.76-1.47)	1.05 (0.75-1.46)		1.21 (0.89-1.64)	1.00 (0.68-1.47)	1.11 (0.81-1.51)	1.13 (0.82-1.56)		-1.57 (-3.77,0.63)
BILD score, per 1 SD	0.98 (0.70-1.37)	1.01 (0.72-1.42)		1.17 (0.86-1.59)	1.06 (0.72-1.55)	1.12 (0.82-1.52)	1.11 (0.80-1.52)		-1.93 (-4.13,0.28)
Self-reported moderate/severe forgetfulness, vs. mild/none	0.89 (0.42-1.88)	0.87 (0.41-1.87)		1.12 (0.58-2.19)	0.92 (0.38-2.24)	0.77 (0.38-1.58)	1.11 (0.54-2.28)		-1.84 (-6.75,3.06)
Neuropsychiatric damage vs. not	1.77 (0.80-3.93)	1.69 (0.75-3.77)		1.00 (0.47-2.15)	1.06 (0.40-2.82)	1.70 (0.79-3.66)	1.31 (0.59-2.91)		-3.17 (-8.79,2.44)
Currently taking steroids vs. not	1.47 (0.74-2.91)	1.46 (0.74-2.91)		1.44 (0.77-2.68)	1.51 (0.68-3.32)	1.53 (0.80-2.92)	1.54 (0.79-3.00)		-2.44 (-7.00,2.12)
BMI, per 1 SD	0.75 (0.53-1.07)	0.74 (0.52-1.06)		0.77 (0.56-1.05)	0.86 (0.57-1.30)	0.83 (0.59-1.16)	0.85 (0.61-1.21)		1.25 (-1.02,3.52)
Depressive symptoms T-score, per 1 SD	1.26 (0.88-1.81)	1.26 (0.88-1.81)		1.10 (0.79-1.52)	1.39 (0.90-2.15)	1.32 (0.93-1.86)	1.25 (0.87-1.78)		-2.07 (-4.43,0.30)

Characteristic	Primary analysis ^b		Age-corrected standard score >1 SD below mean (OR 95% CI)	Impairment defined by:				Continuous age-corrected standard score β (95% CI)
	Primary analysis ^b OR (95% CI)	Primary analysis ^b excluding those aged ≥ 65 OR (95% CI)		Fully adjusted ^c T-score >1.5 SD below mean OR (95% CI)	Fully adjusted ^c T-score >1 SD below mean OR (95% CI)	T-score-associated percentiles ^d OR (95% CI)		
Perceived stress score, per 1 SD	0.99 (0.71-1.39)	0.97 (0.70-1.36)	0.93 (0.69-1.27)	0.96 (0.64-1.42)	1.07 (0.78-1.48)	1.08 (0.78-1.50)	-1.21 (-3.41,0.99)	
Self-reported physical functioning, per 1 SD	0.46 (0.28-0.75)	0.46 (0.28-0.76)	0.47 (0.30-0.73)	0.59 (0.34-1.01)	0.50 (0.32-0.79)	0.54 (0.34-0.86)	5.13 (2.47,7.78)	
Overall SPPB score, per 1 unit	0.72 (0.59-0.87)	0.69 (0.56-0.85)	0.72 (0.59-0.87)	0.71 (0.58-0.86)	0.75 (0.63-0.89)	0.69 (0.57-0.84)	2.72 (1.66,3.77)	

—, no variation in outcome.

^aAdjusted for age, sex, and race.

^bImpairment defined as age-corrected standard scores for overall fluid cognition >1.5 SD below the mean.

^cAdjusted for age, sex, race, ethnicity, and education.

^dImpairment defined as ≥ 2 NIH Toolbox fully adjusted fluid cognition individual domain scores <9th percentile, ≥ 3 domain scores <16th percentile, or ≥ 4 domain scores <25th percentile.

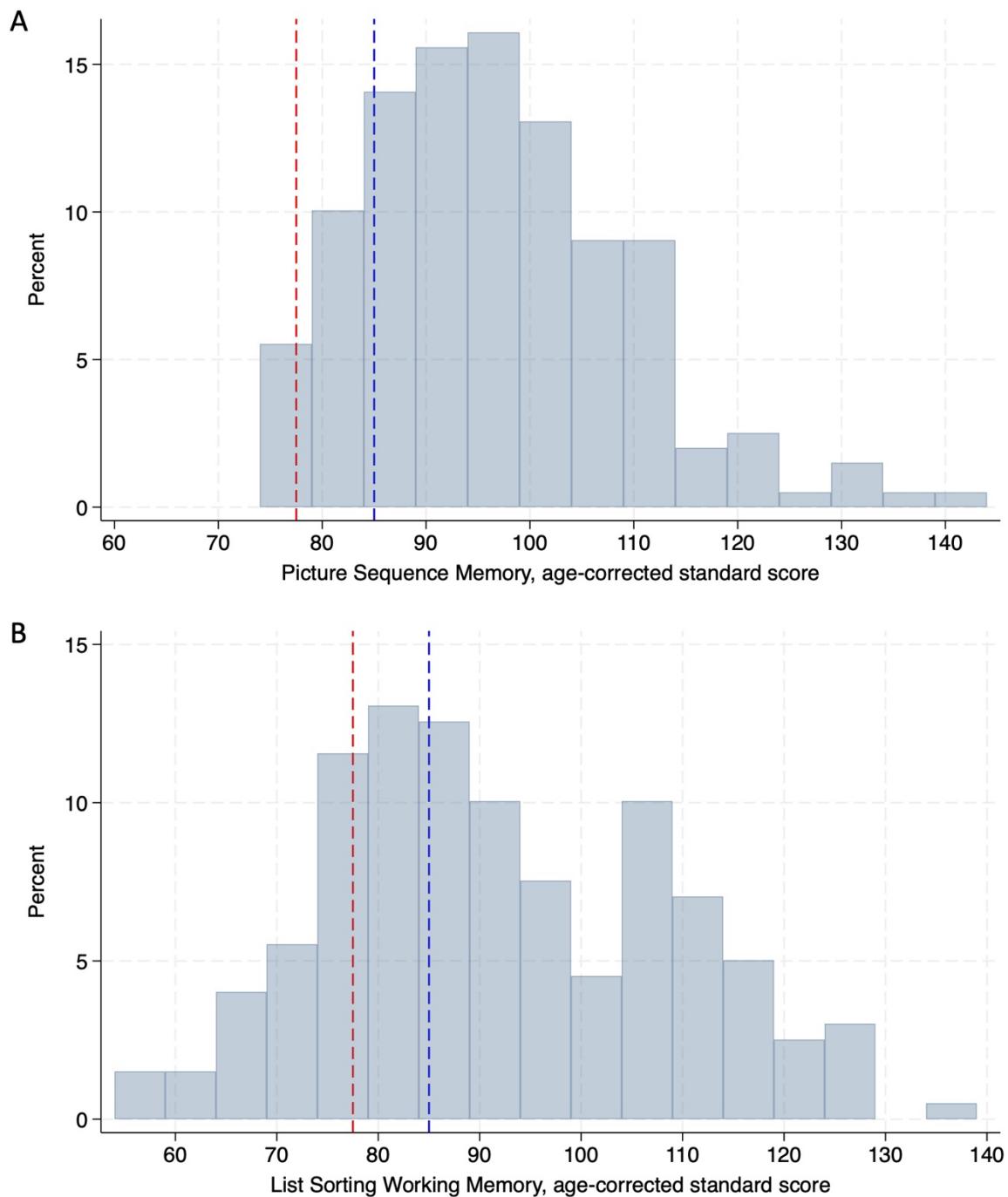
Table S5. Adjusted^a associations of potential impairment in individual fluid cognition domains with selected patient characteristics

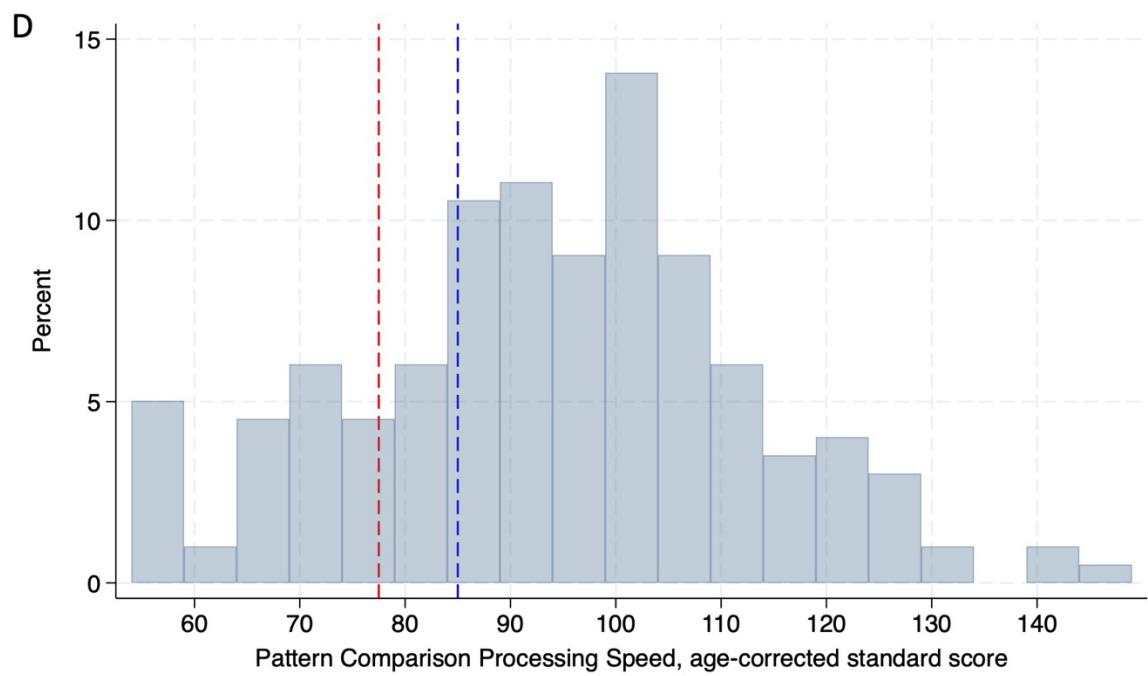
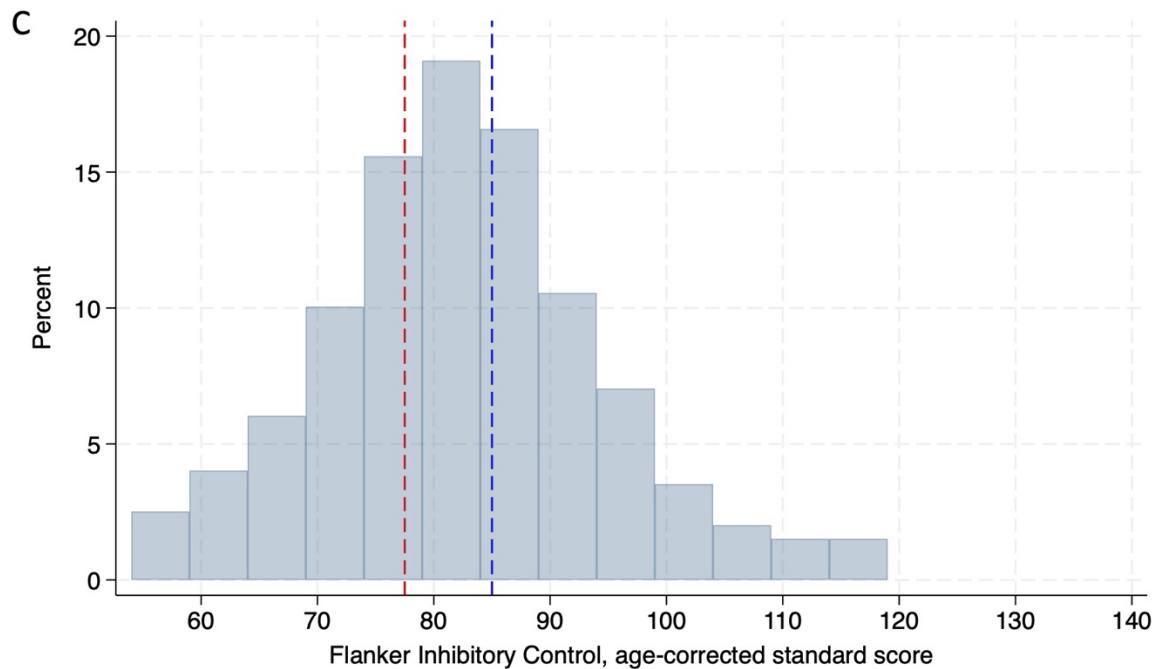
Characteristic	Potential impairment ^b in:					
	Overall fluid cognition	Episodic memory	Working memory	Attention & inhibitory control	Processing speed	Cognitive flexibility
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age, per +10 years	0.84 (0.64-1.09)	3.10 (1.26-7.63)	0.90 (0.66-1.23)	0.68 (0.50-0.91)	1.06 (0.77-1.46)	0.89 (0.62-1.28)
Age category						
18-34 vs. \geq 50	1.00 (0.12-8.68)	—	36.0 (2.06-630)	0.21 (0.02-2.59)	1.35 (0.10-18.8)	4.11 (0.17-100)
35-49 vs. \geq 50	0.93 (0.24-3.62)	14.6 (0.41-517)	5.85 (0.95-35.8)	0.42 (0.10-1.90)	0.59 (0.11-3.16)	4.23 (0.59-30.4)
Male vs. female	0.77 (0.29-2.10)	—	0.98 (0.31-3.12)	0.66 (0.21-2.07)	1.06 (0.33-3.35)	1.55 (0.48-5.04)
Race						
Other vs. Black	0.39 (0.08-1.08)	—	0.88 (0.18-4.29)	0.56 (0.11-2.79)	—	1.43 (0.28-7.22)
White vs. Black	—	—	—	1.05 (0.27-4.04)	0.78 (0.17-3.65)	0.56 (0.07-4.48)
Highest level of education completed						
\leq High school graduate vs. \geq college graduate	3.82 (1.67-8.75)	1.74 (0.22-13.9)	3.82 (1.25-11.7)	2.57 (1.04-6.33)	1.31 (0.51-3.39)	1.00 (0.35-2.84)
Some college vs. \geq college graduate	1.27 (0.55-2.94)	1.43 (0.22-9.54)	3.34 (1.12-9.96)	1.16 (0.47-2.87)	0.55 (0.20-1.50)	0.49 (0.16-1.55))
Currently working vs. not	0.30 (0.14-0.64)	—	0.29 (0.11-0.76)	0.31 (0.13-0.72)	0.33 (0.12-0.88)	0.40 (0.14-1.18)
Disease duration, per +10 years	1.48 (1.00-2.18)	0.71 (0.31-1.58)	1.36 (0.86-2.16)	1.06 (0.68-1.67)	1.28 (0.81-2.03)	1.70 (0.99-2.91)
SLAQ score, per 1 SD	1.05 (0.76-1.47)	0.92 (0.36-2.31)	1.02 (0.69-1.51)	1.35 (0.95-1.92)	1.10 (0.74-1.64)	0.94 (0.59-1.50)
BILD score, per 1 SD	0.98 (0.70-1.37)	1.21 (0.65-2.25)	1.30 (0.91-1.87)	1.33 (0.93-1.89)	1.24 (0.86-1.79)	1.28 (0.85-1.92)
Self-reported moderate-severe forgetfulness, any vs. none	0.89 (0.42-1.88)	0.82 (0.14-4.62)	1.78 (0.77-4.12)	1.21 (0.54-2.71)	1.18 (0.49-2.81)	0.60 (0.19-1.87)
Neuropsychiatric damage vs. not	1.77 (0.80-3.93)	3.99 (0.76-20.8)	1.12 (0.42-3.00)	2.30 (0.99-5.35)	2.89 (1.20-6.97)	1.91 (0.69-5.33)
Currently taking steroids vs. not	1.47 (0.74-2.91)	0.65 (0.07-6.21)	1.11 (0.49-2.53)	1.36 (0.65-2.84)	1.33 (0.58-3.05)	0.91 (0.36-2.30)
BMI, per 1 SD	0.75 (0.53-1.07)	0.98 (0.43-2.24)	0.92 (0.61-1.39)	0.89 (0.60-1.30)	1.07 (0.72-1.60)	0.75 (0.45-1.27)
Depressive symptoms T-score, per 1 SD	1.26 (0.88-1.81)	0.89 (0.31-2.54)	1.09 (0.71-1.67)	1.22 (0.82-1.82)	0.94 (0.60-1.47)	0.92 (0.56-1.53)
Perceived stress score, per 1 SD	0.99 (0.71-1.39)	0.77 (0.30-1.98)	0.95 (0.63-1.41)	1.04 (0.71-1.52)	0.84 (0.55-1.27)	0.56 (0.35-0.90)
Self-reported physical functioning, per 1 SD	0.46 (0.28-0.75)	0.90 (0.28-2.89)	0.98 (0.60-1.60)	0.49 (0.29-0.83)	0.47 (0.26-0.87)	0.71 (0.39-1.29)
Overall SPPB score, per 1 unit	0.72 (0.59-0.87)	0.88 (0.66-1.18)	0.91 (0.76-1.09)	0.66 (0.54-0.82)	0.77 (0.64-0.93)	0.79 (0.65-0.96)

^aAdjusted for age, sex, and race. For episodic memory, sex and race were dropped due to collinearity/perfect prediction of failure.^bImpairment defined as an age-corrected standard score >1.5 SD below the mean (<77.5).

Figure S1. Distributions of NIH Toolbox age-corrected standard scores for fluid cognition in our cohort

Blue lines, standard score=85 (1 SD below mean); red lines, standard score=77.5 (1.5 SD below mean).





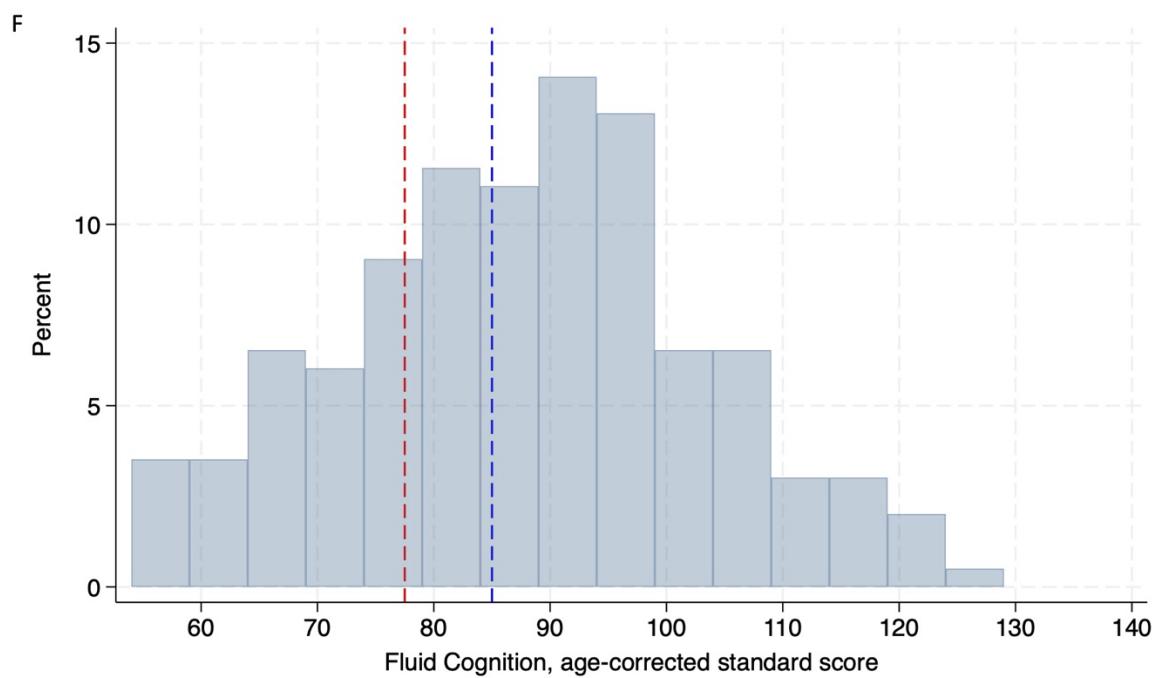
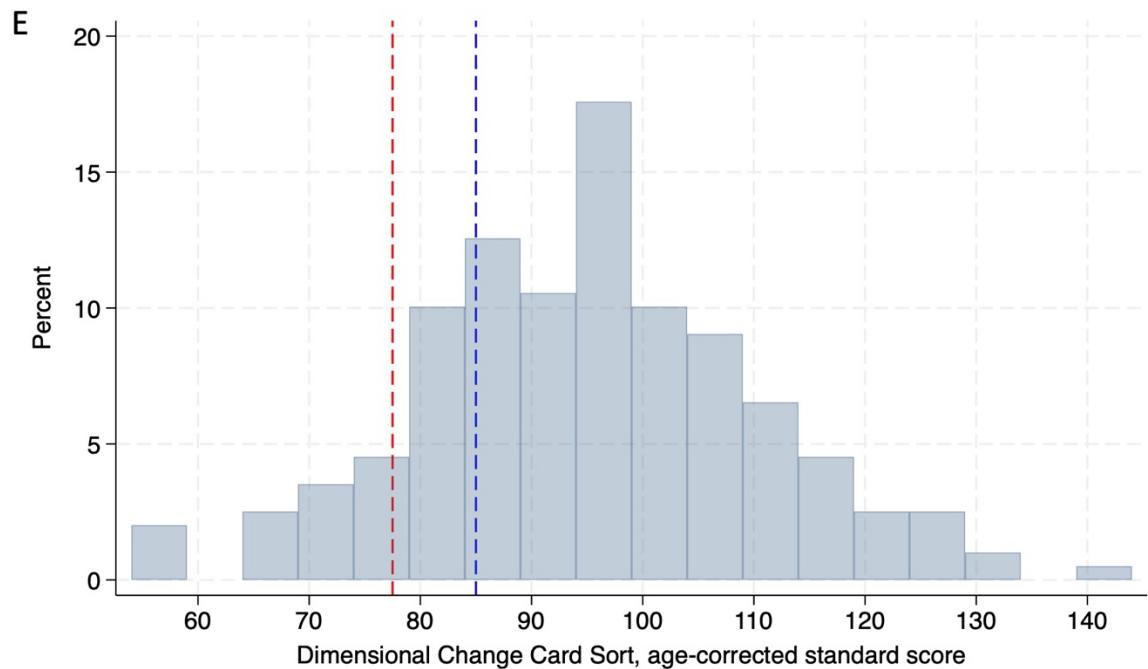


Figure S2. Correlations between age-corrected standard scores for individual fluid cognition domains and overall NIH Toolbox Fluid Cognition age-corrected standard scores

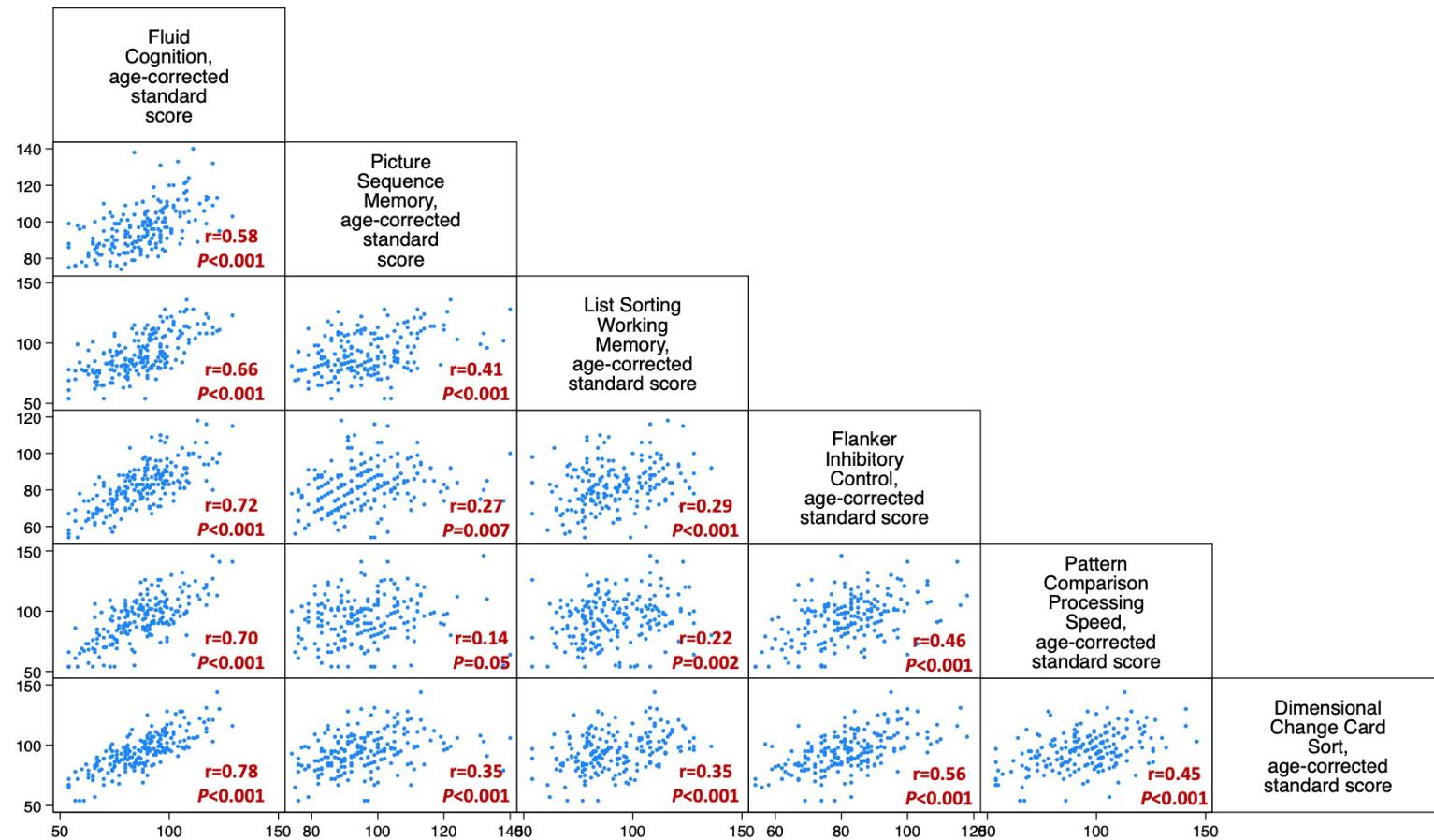


Figure S3. UpSet plot of potential individual domain impairment among those with fluid cognition impairment

Figure shows all combinations of potential impairment across the five individual assessments that were observed among our participants with fluid cognition impairment and the percentages of participants with those respective patterns. For example, 20.0% of those with potential overall fluid cognition impairment demonstrated potential impairment in attention and inhibitory control and processing speed (first bar on left). Individual domain impairment was defined by age-corrected standard scores < 77.5 (> 1.5 SD below mean).

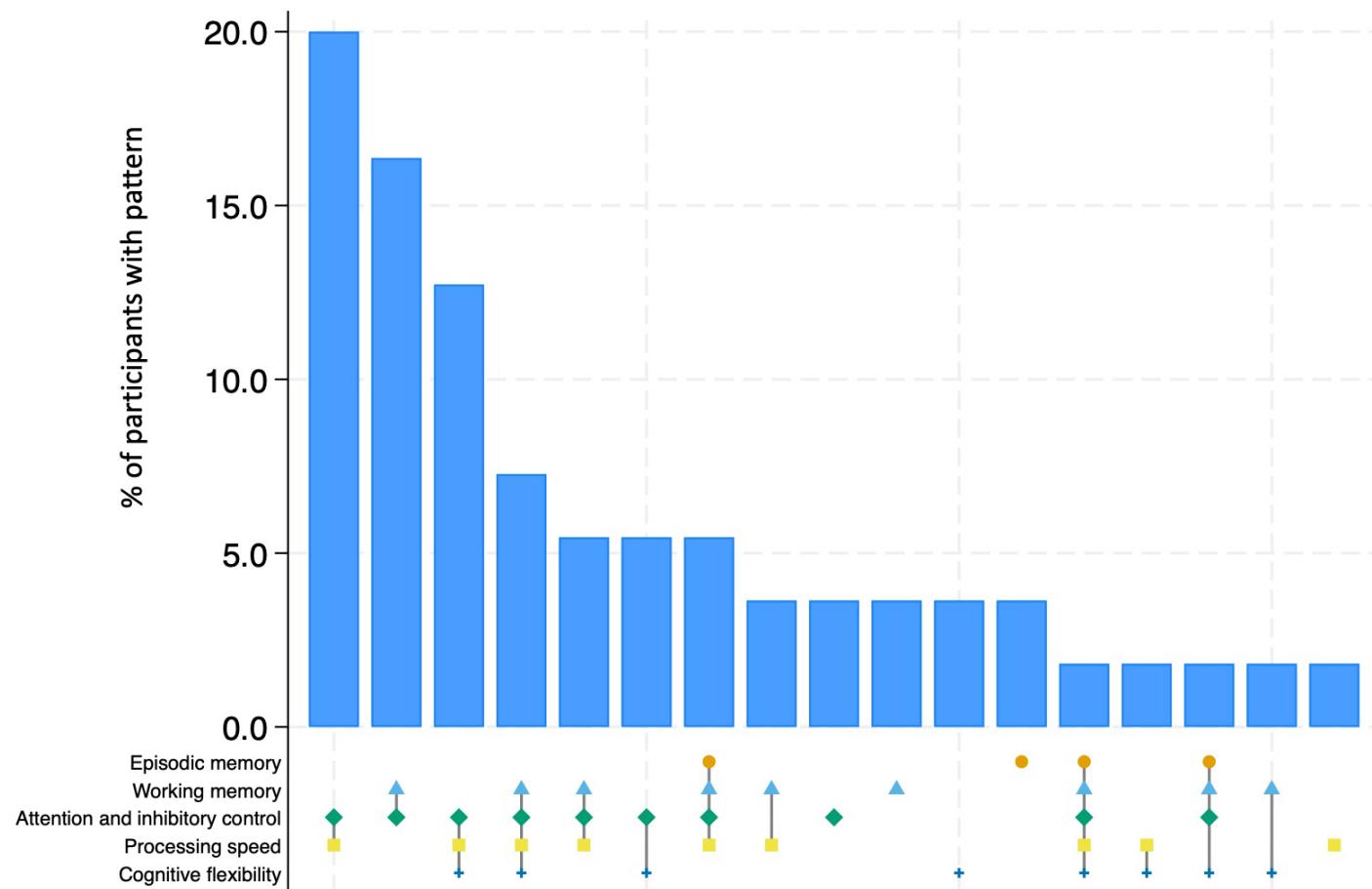
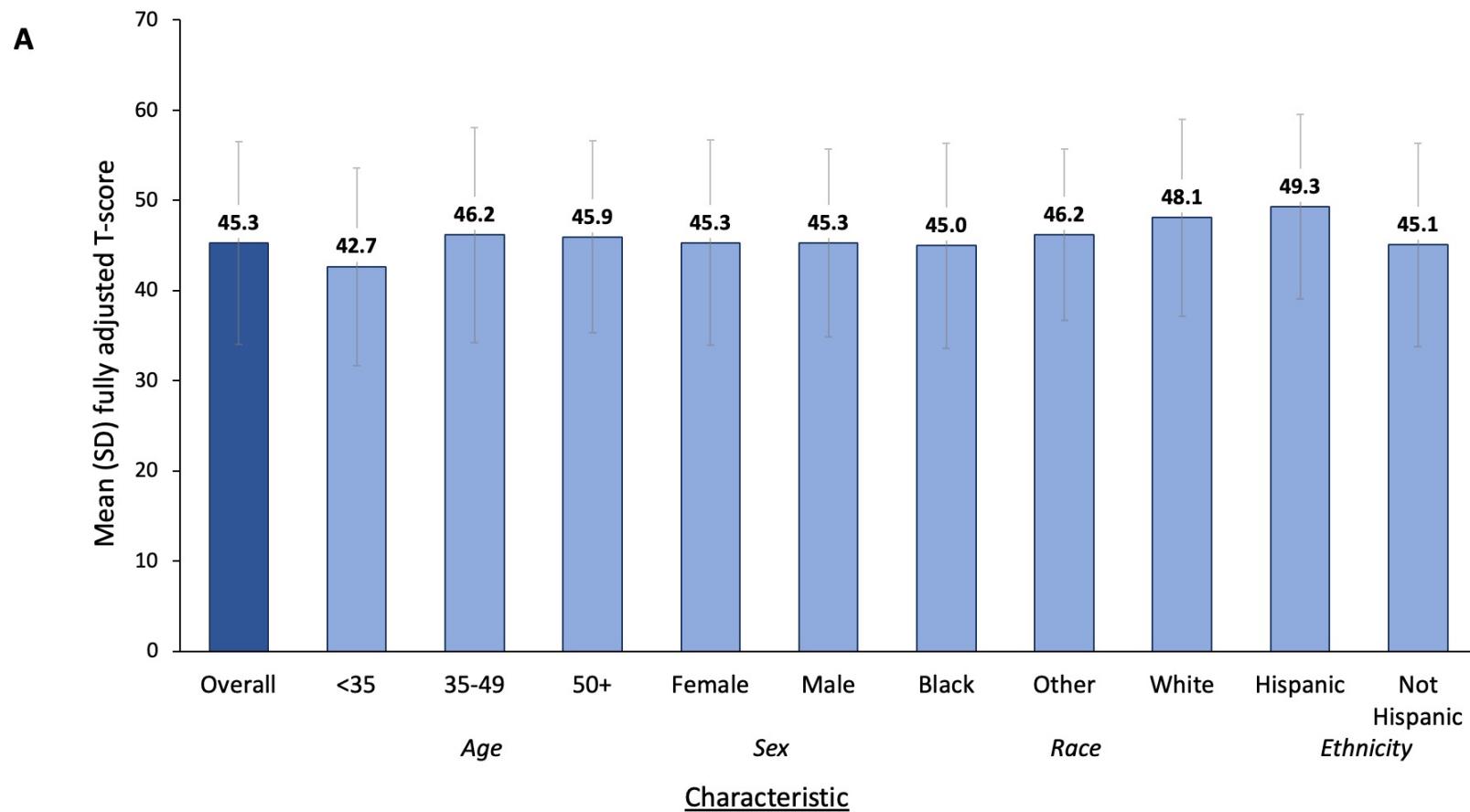


Figure S4. Fully adjusted fluid cognition T-scores (A) and percentage with potentially impaired fluid cognition (B), by selected demographics

Error bars, SD. Fully adjusted T-scores adjusted for age, sex, race, ethnicity, and education. Impairment defined as ≥ 2 NIH Toolbox fully adjusted fluid cognition individual domain scores $< 9^{\text{th}}$ percentile, ≥ 3 domain scores $< 16^{\text{th}}$ percentile, or ≥ 4 domain scores $< 25^{\text{th}}$ percentile. $P > 0.05$ for all comparisons.



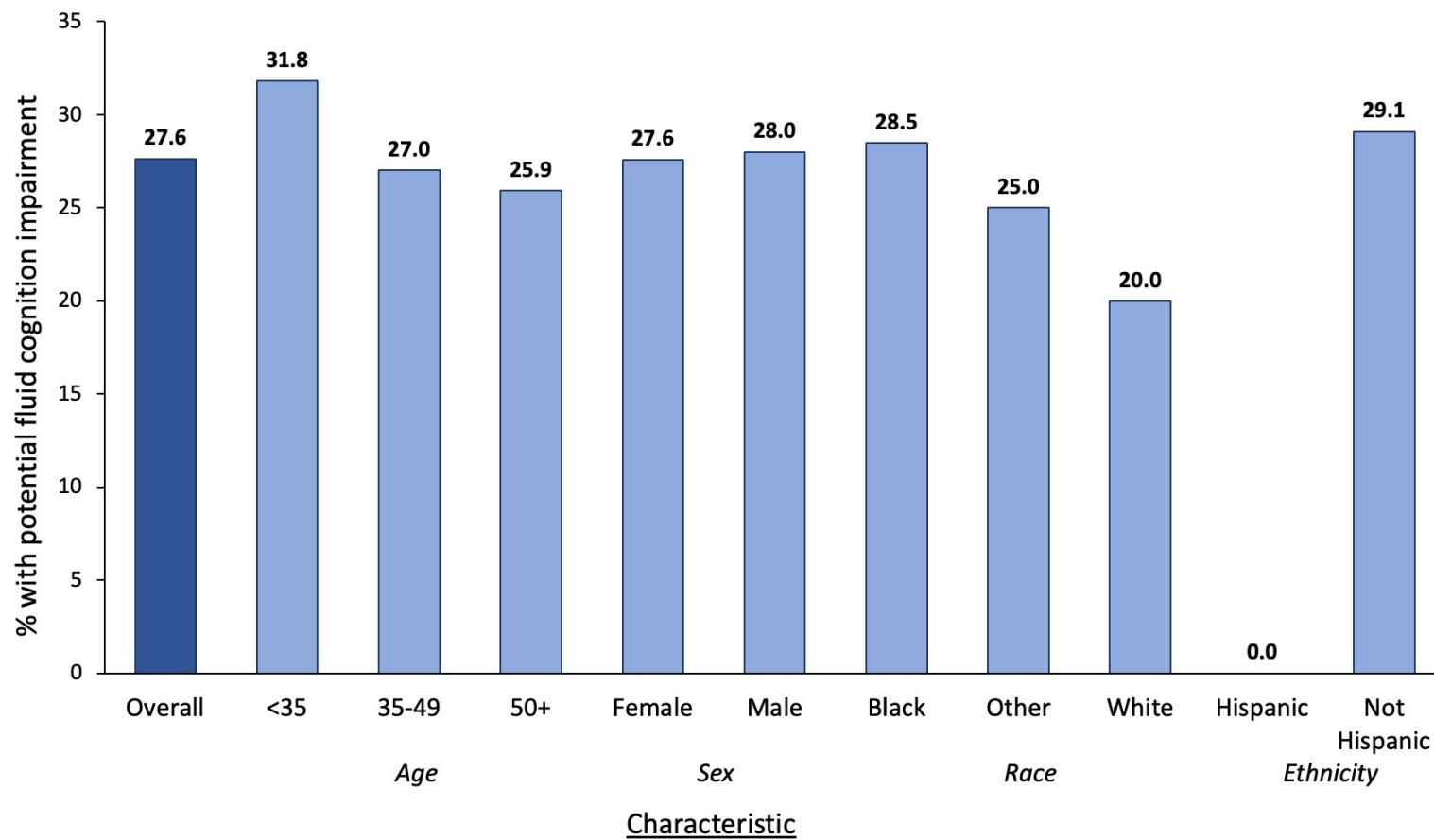
B

Figure S5. Spaghetti plot of change in age-corrected standard scores for fluid cognition over time, among the $n=28$ participants who completed a pilot assessment

Red line, overall average trajectory.

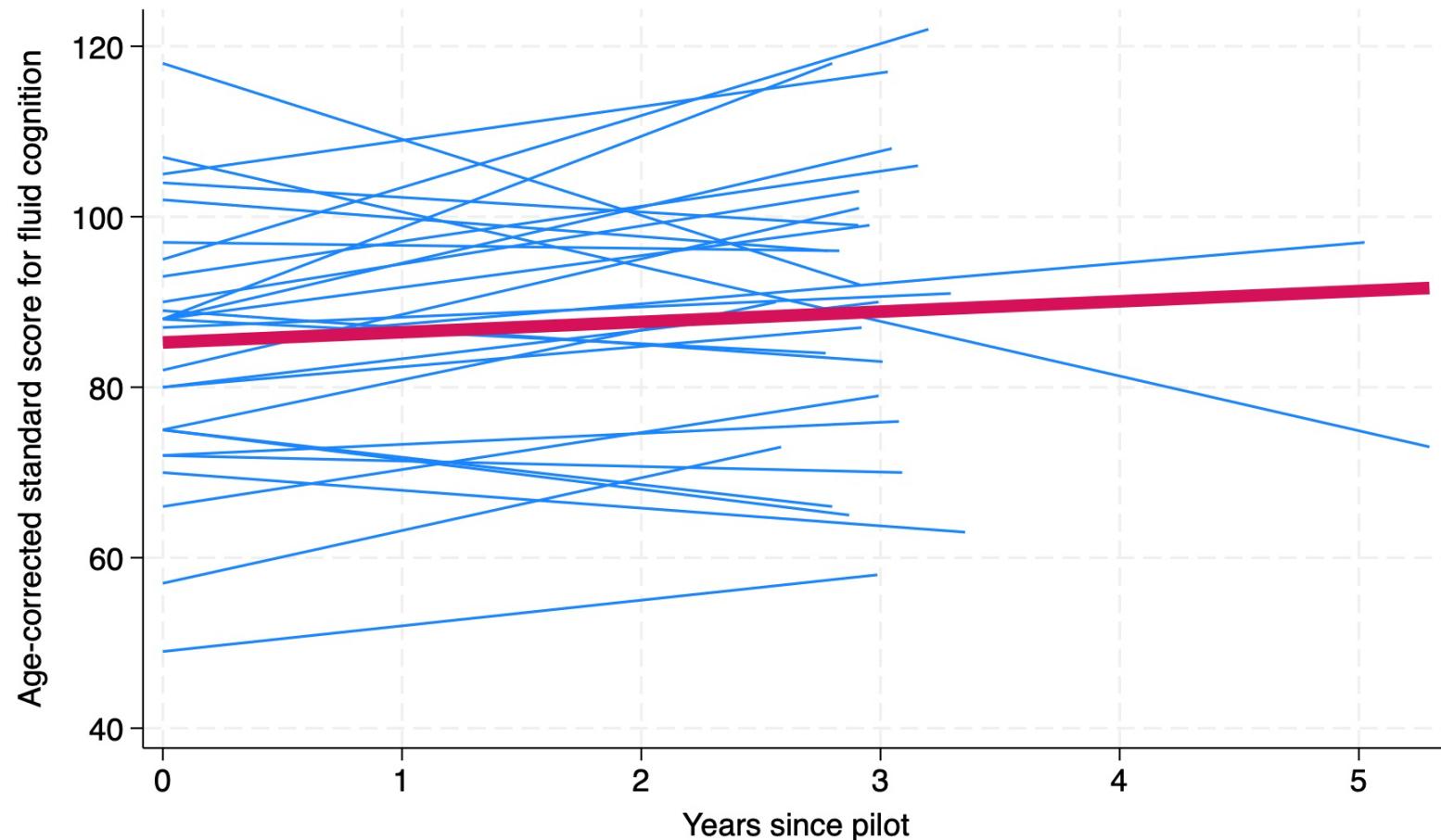


Figure S6. Percentage of individuals with SLE with potentially impaired fluid cognition, by definition, overall and by domain
Impairment was defined as fully adjusted T-scores > 1 SD below the mean (T-scores < 40), fully adjusted T-scores > 1.5 SD below the mean (T-scores < 35), fully adjusted T-scores corresponding with < 5th percentile, and age-corrected standard scores > 1.5 SD below the mean. For the composite score only, impairment was additionally defined across multiple subdomains (≥ 2 NIH Toolbox fluid cognition individual domain scores < 9th percentile, ≥ 3 domain scores < 16th percentile, or ≥ 4 domain scores < 25th percentile).

