Dr Konrad Kowalski

The Glutathione Index As A Functional Biomarker For Oxidative Stress

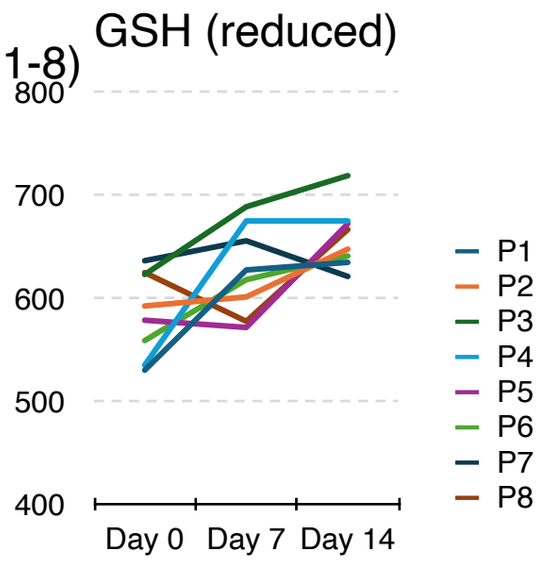
ALZHEIMER'S PREVENTION: NEW FRONTIERS

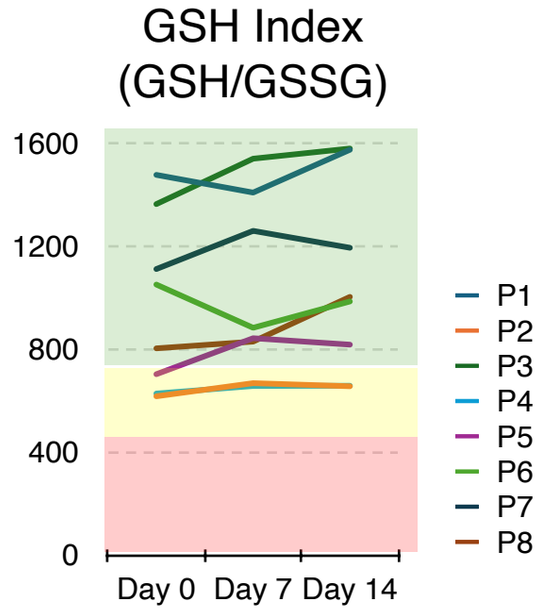
28 APRIL 2026 · ONLINE

ISOM FOOD FOR THE BRAIN

NAC experiment
14 day supplementation with 8 patients (P1-8)

N-acetylcysteine (NAC) - 500mg/day
Lipoic acid – 200 mg/day
Silybum marianum extract - 125 mg/day
Vitamin C - 80mg/day

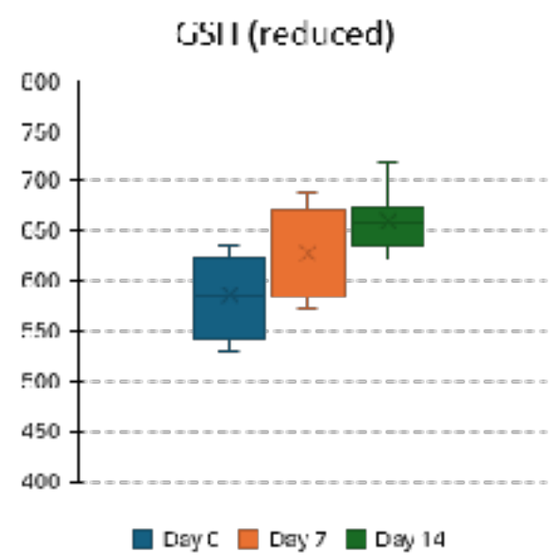


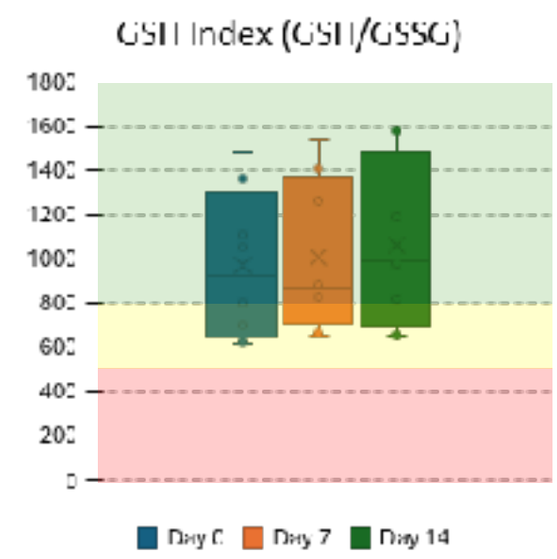


Conclusion:

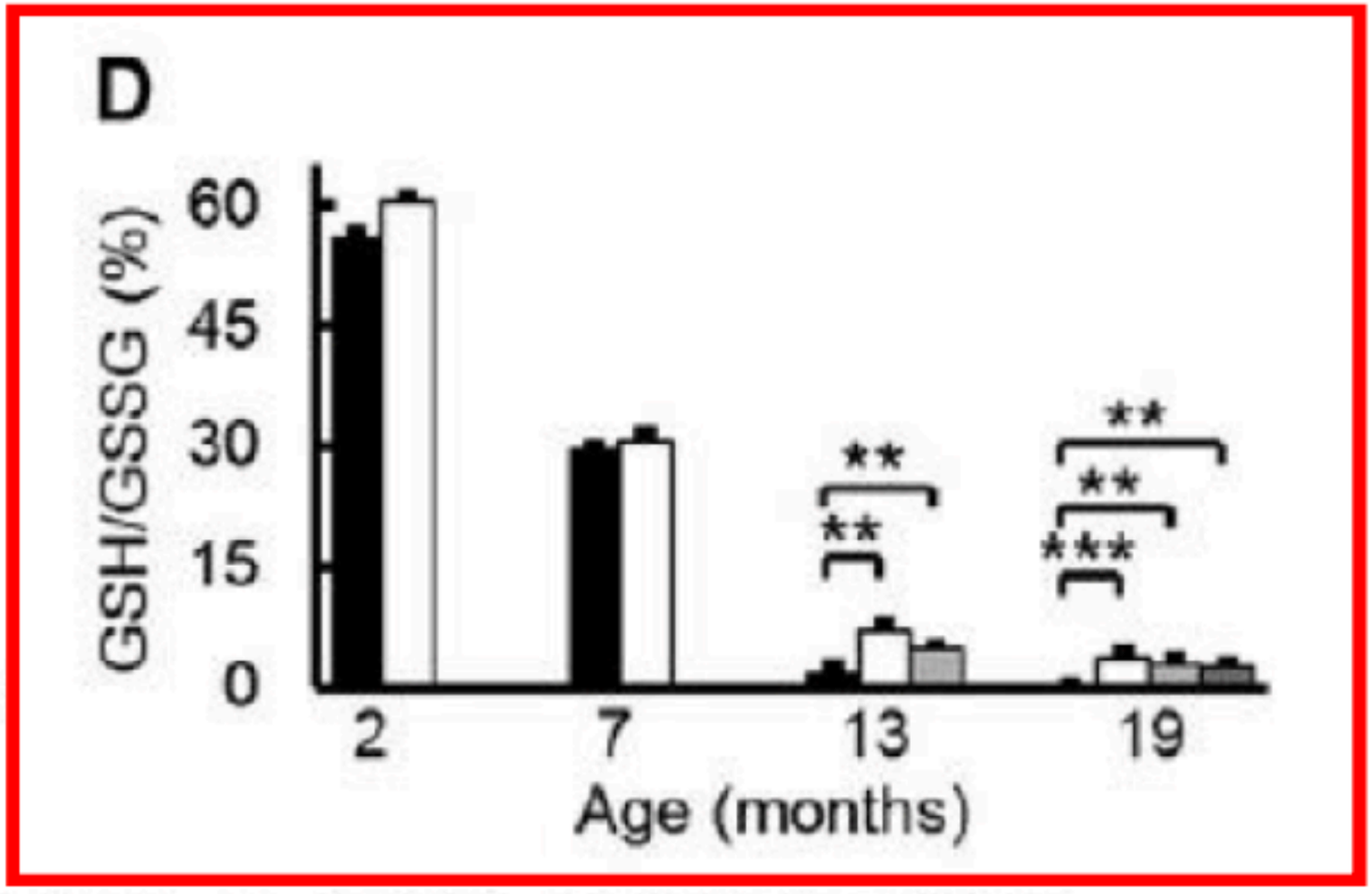
In a preliminary experiment, supplementation with a product containing NAC resulted in a positive effect on reduced GSH concentration, suggesting an increased synthesis of this compound. However, it was observed that higher GSH synthesis was not necessarily associated with a significant increase in the glutathione index.

This observation suggests that an absolute increase in GSH concentration does not necessarily equate to effective GSH ←→ GSSG recycling.





Ubiquinol supplementation ameliorates the reduced GSH/GSSG ratio in liver during aging in SAMP1 mice

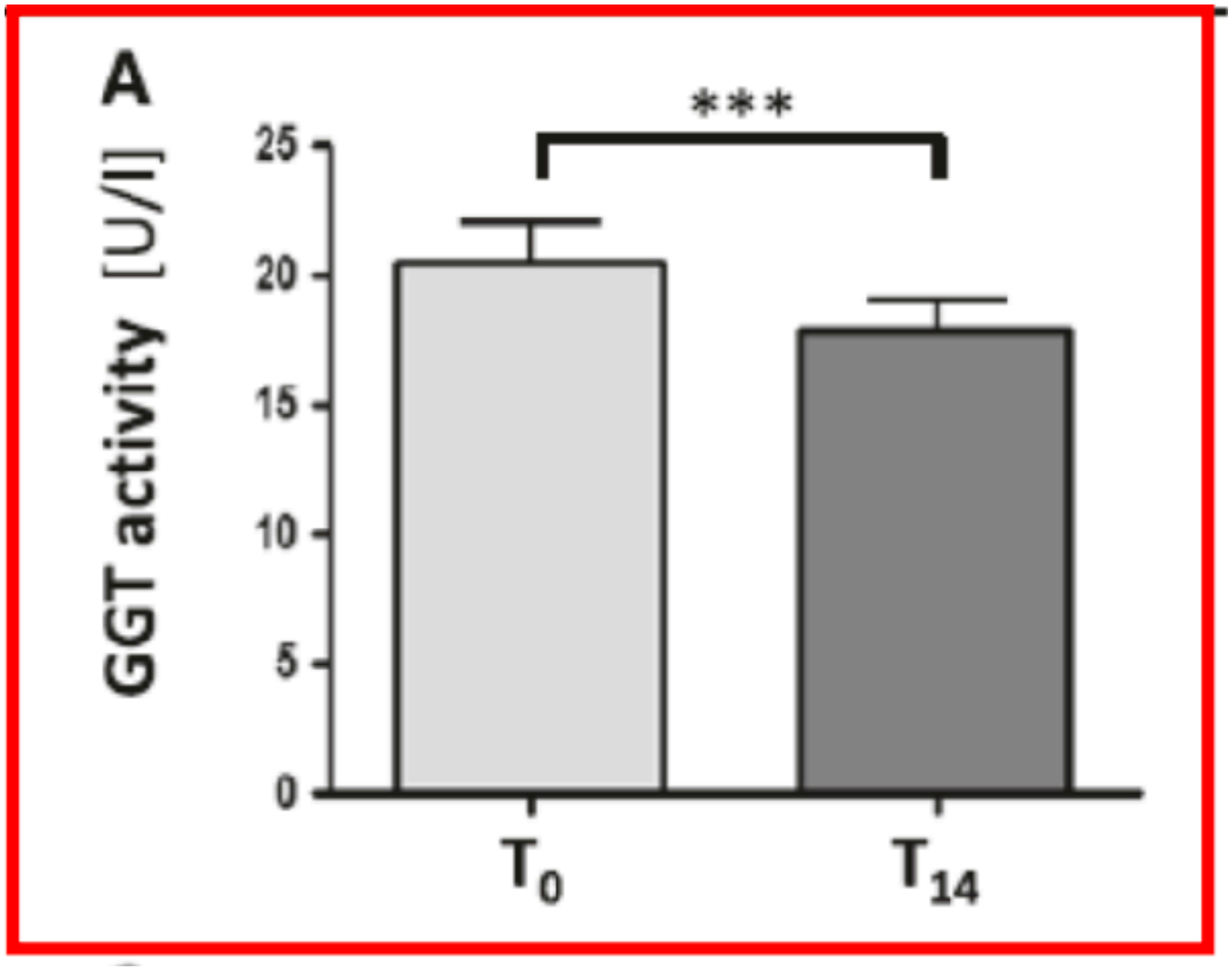


(Tian G et al, Antioxid Redox Signal . 2014 ;20(16):2606-20.)

FIG. 1. Ubiquinol-10 decelerated the increase in oxidative stress associated with aging in SAMP1 mice. (A, B) Western blot analysis of oxidative damage to lipids (malondialdehyde) (A) and proteins (protein carbonyls) (B) in livers from 2-, 7-, 13-, and 19-month-old SAMP1 mice fed a control or ubiquinol-10-supplemented diet beginning in young, middle, or old age ($n=3$–5). (C) Oxidative damage to DNA (AP sites) was measured in livers from 2-, 7-, 13-, and 19-month-old SAMP1 mice fed a control or ubiquinol-10-supplemented diet beginning during young, middle, or old age ($n=3$–5). (D) Ratios of liver GSH:GSSG were measured ($n=3$–5). $^{*}p<0.05$; $^{**}p<0.01$; $^{***}p<0.001$. AP, apurinic/apyrimidiric; GSH, reduced glutathione; GSSG, oxidized glutathione; SAMP1, senescence-accelerated mouse prone 1.

Ubiquinol supplementation reduces gamma glutamyltransferase (GGT) in humans

(Onur S et al, BMC Res Notes. 2014 Jul 4:7:427.)



Fifty three healthy male volunteers between 21 and 48 years of age received 150 mg/day of ubiquinol for 14 days.

GGT initiates the degradation of extracellular GSH by hydrolyzing the γ-glutamyl-cysteine bond in GSH [Hanigan MH et al, Extracellular glutathione is a source of cysteine for cells that express gamma-glutamyl transpeptidase. Biochemistry 1993,32(24):6302–6306.16].

Table 3 Metabolic profiles, biomarkers of inflammation and oxidative stress at baseline and 8 weeks after the intervention in patients with MetS

	Placebo group ($n = 30$)			Coenzyme Q10 group ($n = 30$)			P^a
	Baseline	End of trial	Change	Baseline	End of trial	Change	
FPG (mg/dL)	132.3 ± 47.5	132.0 ± 56.2	−0.3 ± 30.3	125.0 ± 40.5	120.7 ± 41.4	−4.4 ± 20.3	0.54
Insulin (μIU/mL)	11.9 ± 7.2	16.0 ± 9.9*	4.1 ± 7.8	11.8 ± 8.6	9.7 ± 4.5	−2.1 ± 7.1	0.002
HOMA-IR	4.1 ± 3.2	5.1 ± 3.8*	1.0 ± 2.0	3.8 ± 3.2	3.1 ± 2.2	−0.7 ± 2.1	0.002
HOMA-B	31.5 ± 21.7	47.3 ± 41.4*	15.9 ± 34.0	31.9 ± 27.5	26.0 ± 14.4	−5.9 ± 22.2	0.005
QUICKI	0.32 ± 0.03	0.31 ± 0.04	−0.01 ± 0.03	0.33 ± 0.04	0.33 ± 0.03	0.007 ± 0.02	0.13
Triglycerides (mg/dL)	149.7 ± 74.2	155.1 ± 78.2	5.4 ± 34.1	136.9 ± 64.1	126.9 ± 46.3	−10.0 ± 35.9	0.09
VLDL cholesterol (mg/dL)	29.9 ± 14.8	31.0 ± 15.6	1.1 ± 6.8	27.4 ± 12.8	25.4 ± 9.3	−2.0 ± 7.2	0.09
Total cholesterol (mg/dL)	150.6 ± 30.2	149.9 ± 30.5	−0.7 ± 17.3	153.5 ± 35.7	143.5 ± 29.5	−10.0 ± 29.1	0.14
LDL cholesterol (mg/dL)	72.8 ± 25.6	69.8 ± 22.3	−3.0 ± 18.0	78.2 ± 27.0	71.0 ± 23.6	−7.2 ± 22.3	0.42
HDL cholesterol (mg/dL)	47.8 ± 7.2	49.1 ± 8.5	1.2 ± 6.1	47.8 ± 6.5	47.1 ± 7.3	−0.7 ± 4.9	0.16
hs-CRP (ng/mL)	2912.5 ± 3050.4	2630.8 ± 2572.2	−281.7 ± 1842.4	1506.1 ± 1572.2	1402.3 ± 1527.4	−103.8 ± 911.5	0.63
NO (μmol/L)	43.3 ± 10.7	38.8 ± 11.0*	−4.5 ± 8.1	51.3 ± 10.8	45.9 ± 11.1*	−5.4 ± 11.4	0.70
TAC (mmol/L)	1156.5 ± 333.9	994.3 ± 196.3*	−162.2 ± 361.8	834.0 ± 156.4	860.1 ± 190.8	26.0 ± 105.0	0.008
GSH (μmol/L)	516.5 ± 120.1	488.8 ± 159.3	−27.7 ± 143.3	377.3 ± 104.3	405.8 ± 92.3	28.5 ± 81.1	0.06
MDA (μmol/L)	5.3 ± 1.9	5.1 ± 1.7	−0.2 ± 1.1	5.3 ± 1.4	4.5 ± 1.2*	−0.8 ± 1.3	0.08

All values are means ± SDs

FPG fasting plasma glucose, *GSH* total glutathione, *HOMA-IR* homeostasis model of assessment-insulin resistance, *HOMA-B* homeostasis model of assessment-estimated b cell function, *hs-CRP* high-sensitivity C-reactive protein, *MetS* metabolic syndrome, *MDA* malondialdehyde, *NO* nitric oxide, *QUICKI* quantitative insulin sensitivity check index, *TAC* total antioxidant capacity

* Differed significantly from baseline

[a] *P* values represent the time × group interaction (computed by analysis of the two-way repeated-measures ANOVA)

In CoQ10 group, compared with the placebo group, a significant positive trends in plasma glutathione levels (P = 0.06)

foodforthebrain.org/the-science-behind-our-glutathione-index/

Protect your brain. ... | Buy Patrick Holford ... | PubMed Home | Page not found - Fo... | Holford Natural Heli... | Apple TV+ (UK) | Home - Dropbox | Dashboard ‹ Holfor... | Google

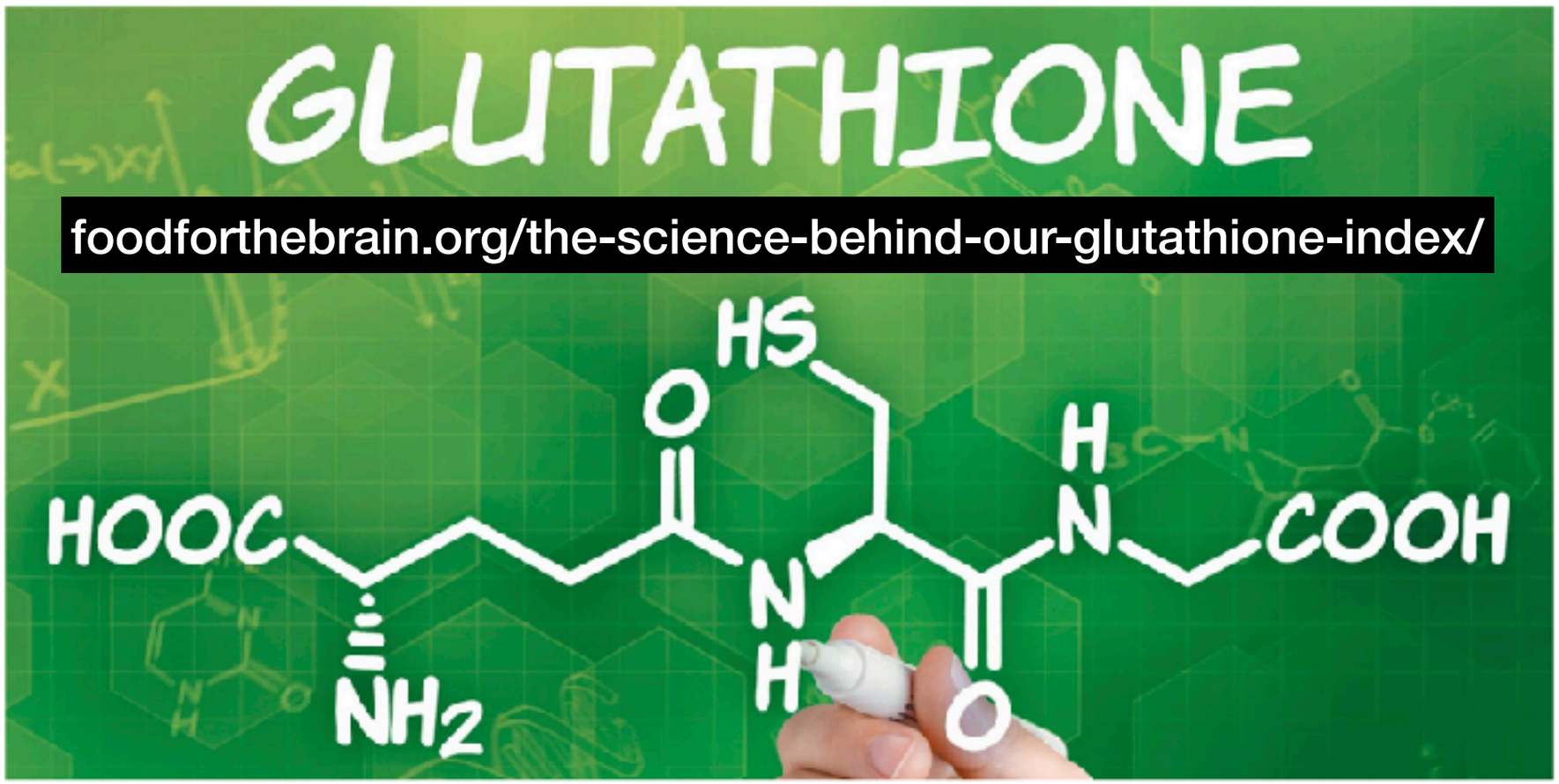
FOOD FOR THE BRAIN FOUNDATION

because prevention is better than cure.

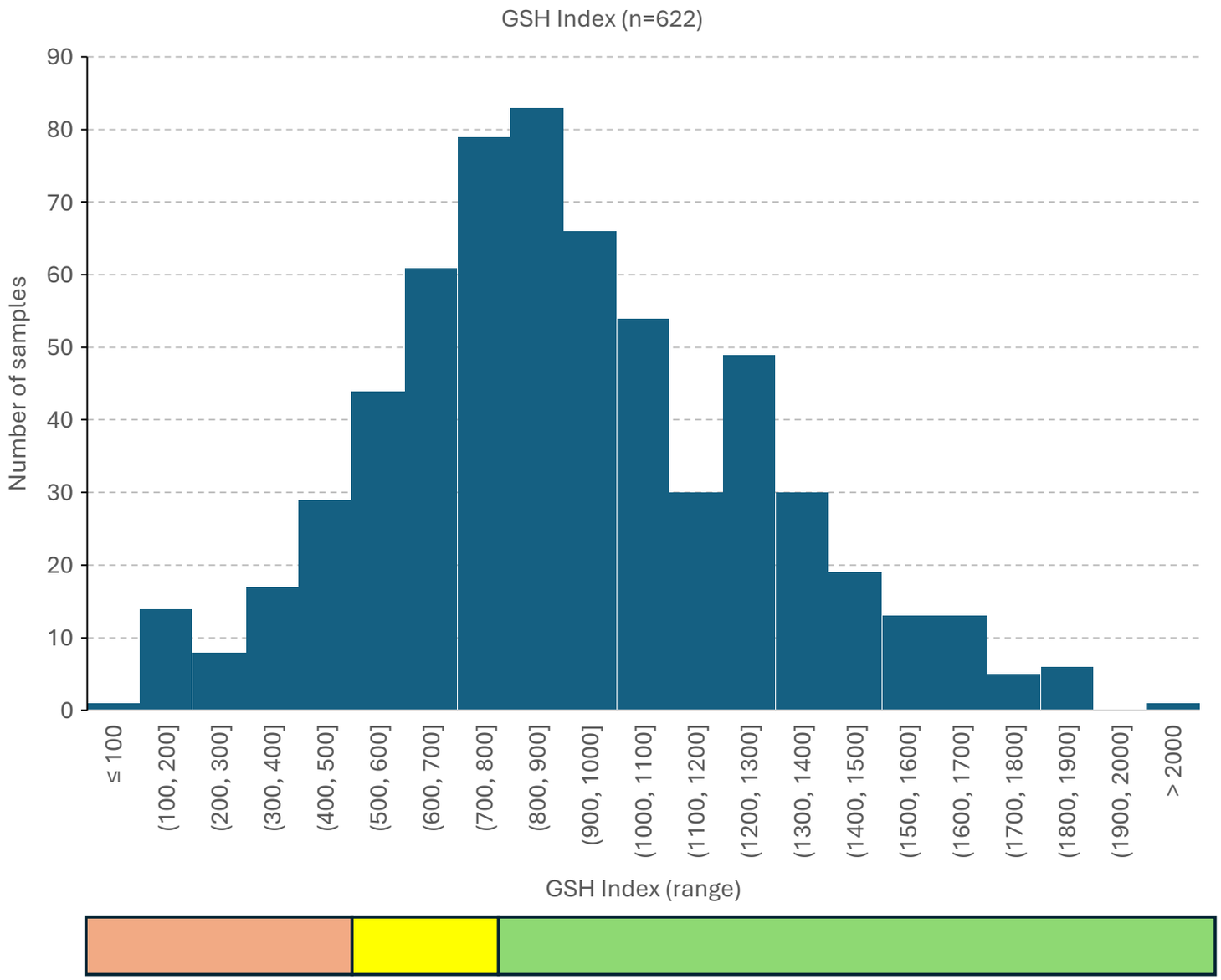
Dashboard | Cognitive Function Test | Become a FRIEND | Donate | 0

About | Our Work | Articles and Pods | Blood Tests and Books | Events | Get involved

Your Glutathione Index Defines How Your Cells Are Ageing



Nutritional therapists have been measuring red cell glutathione and supplementing glutathione or its precursor N-Acetyl-Cysteine (NAC) for decades. But it's really hard, and expensive, to measure accurately. Until now.


GSH Index (n=622)
Number of samples
90
80
70
60
50
40
30
20
10
0
≤ 100
(100, 200]
(200, 300]
(300, 400]
(400, 500]
(500, 600]
(600, 700]
(700, 800]
(800, 900]
(900, 1000]
(1000, 1100]
(1100, 1200]
(1200, 1300]
(1300, 1400]
(1400, 1500]
(1500, 1600]
(1600, 1700]
(1700, 1800]
(1800, 1900]
(1900, 2000]
> 2000
GSH Index (range)

Patrick Holford

Nutritional Biomarkers For Cognition – The DRIfT Index

ALZHEIMER'S PREVENTION: NEW FRONTIERS

28 APRIL 2026 · ONLINE

ISOM FOOD FOR THE BRAIN

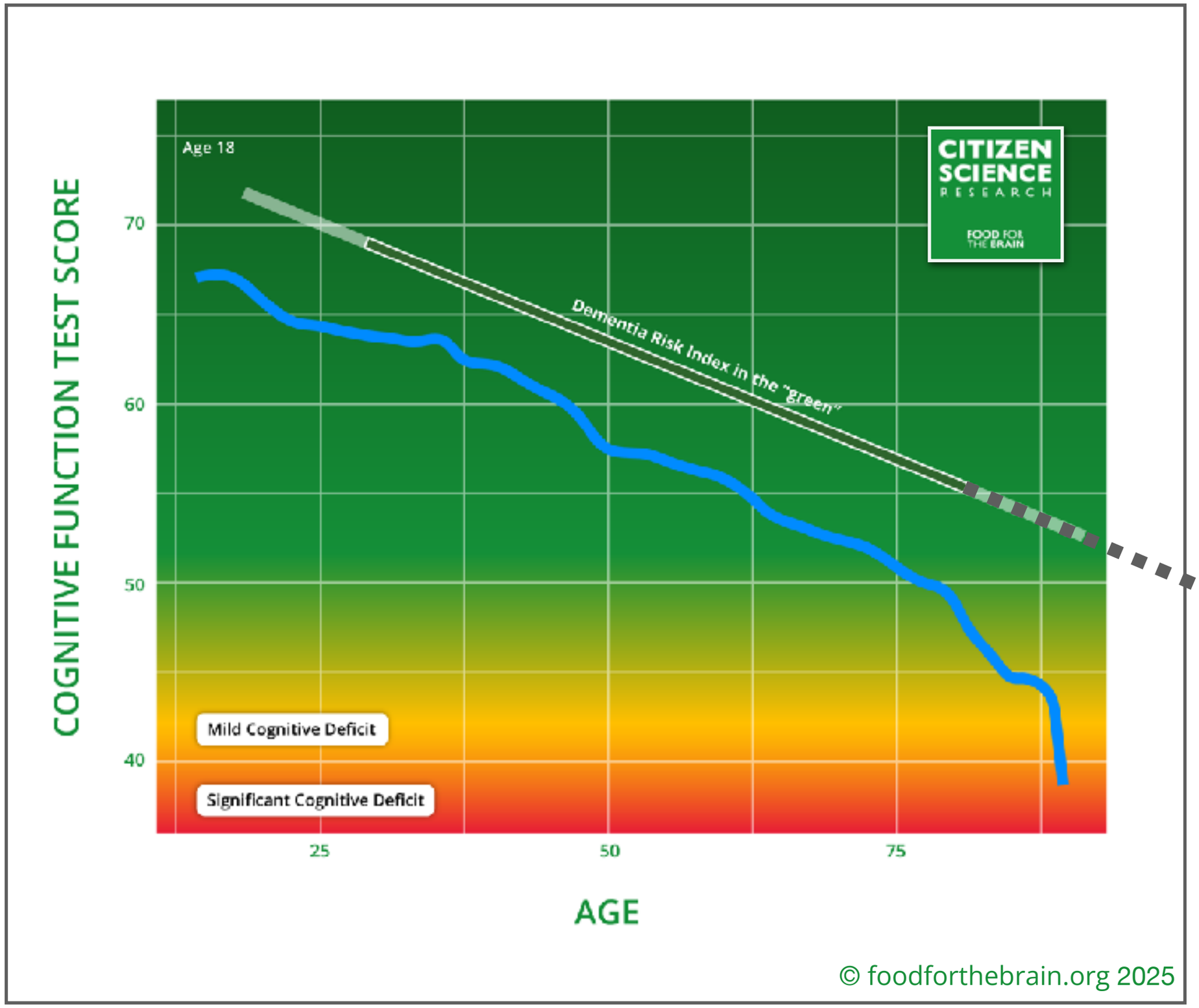
YOUR COGNITIVE FUNCTION SCORE

Your Cognitive Function Test result showed that you performed at or above the norm for your age. This suggests that you are not showing the early cognitive function problems that that can be a symptom of future cognitive impairment and Alzheimers disease. To find out more about what your score means see Interpreting Your Cognitive Function Test Results and Frequently Asked Questions.

YOUR DEMENTIA RISK INDEX

You are aiming for a Dementia Risk Index (DRI) score of 0% which means you have no risk and are doing all the right things to reduce your future risk of cognitive decline. The cogs show your weakest and strongest domains. Your aim is to get all domains into the green.

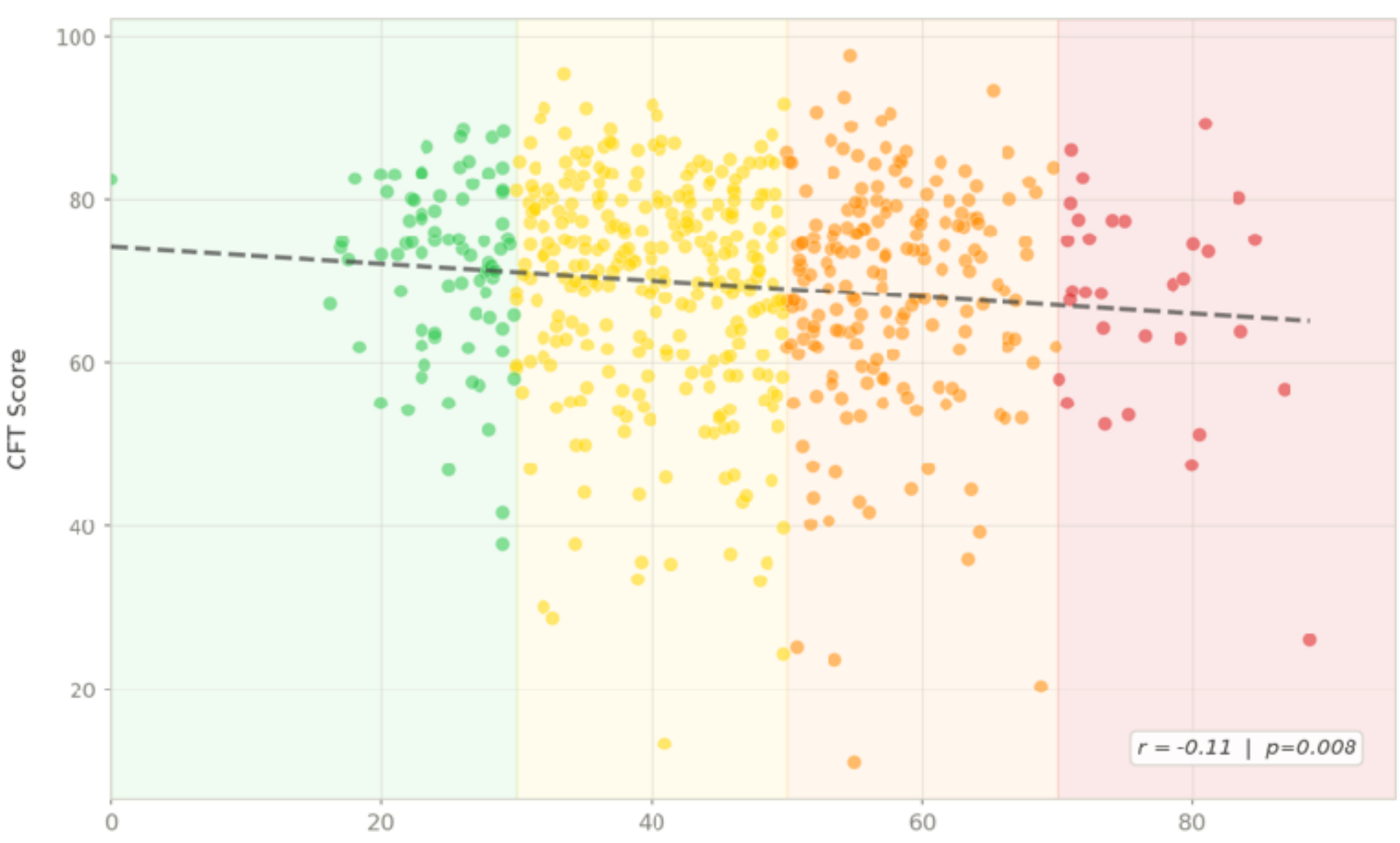
YOUR RISK FACTORS



COGNITION® BIOBANK

FOOD FOR THE BRAIN

Dementia Risk Index *vs* Cognitive Function Test



DRI Scoring

< 30%
Protective habits lower risk

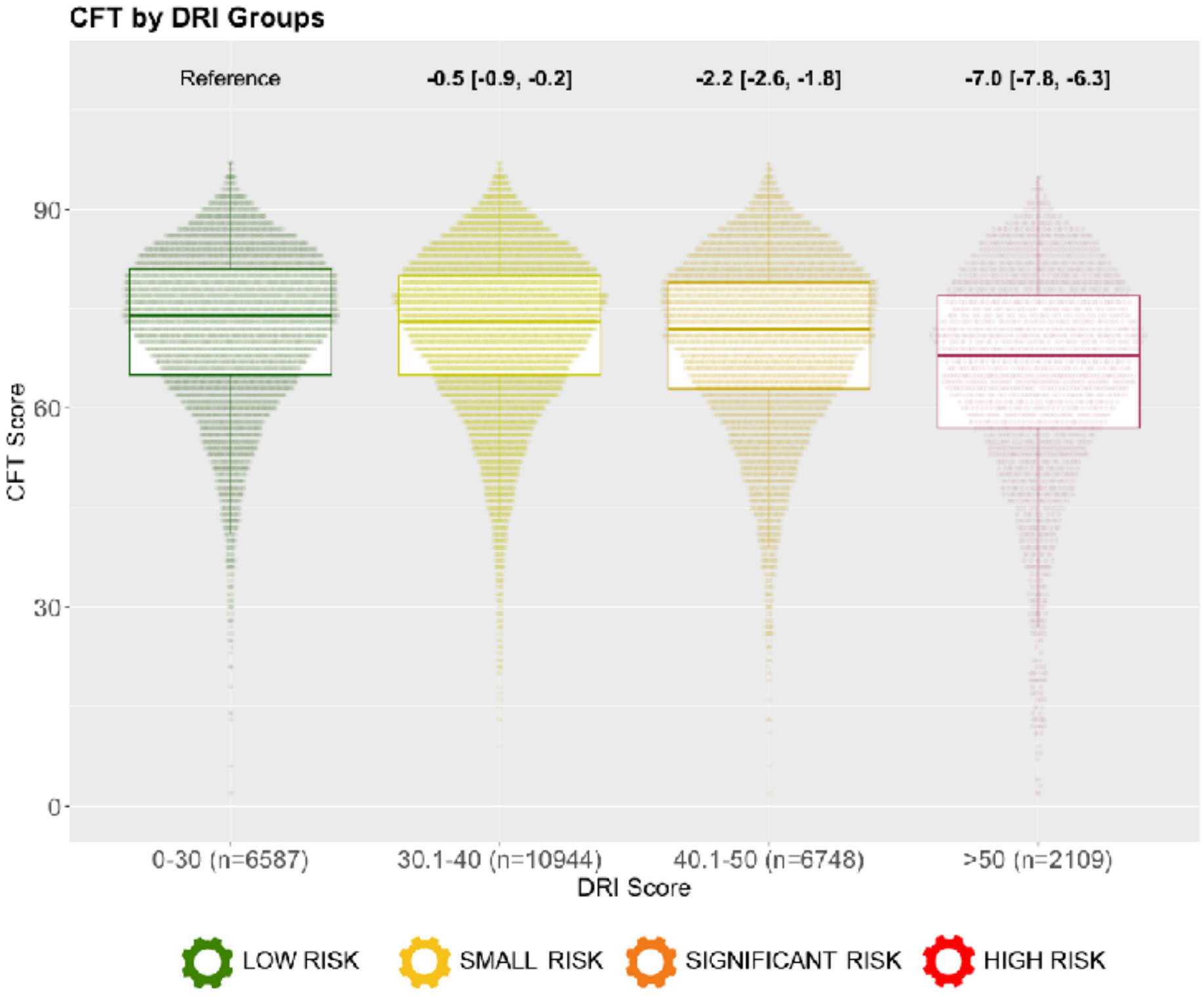
30-50%
Areas for improvement

50-70%
Habits increasing risk

> 70%
Significantly increased risk

LOW RISK SMALL RISK SIGNIFICANT RISK HIGH RISK

Source: COGNITICN Biobank, Food for the Brain Foundation | n=587 | April 2026



CFT decreases by -0.01 points per year (95% CI -0.03, -0.00; p=0.026) from 25-65 and then by -0.78 points per year (95% CI -0.81, -0.74; p<0.001) from 65+.

OMEGA-3 INDEX

VITAMIN D

HOMOCYSTEINE

HBAIC

GLUTATHIONE INDEX


Hb
A1C
H
D
FOOD FOR THE BRAIN
DRIfT®
5-in-1 Test
Your comprehensive
brain health blood test kit
DRIfT & COGNITION

DRI functional TEST (DRIfT) PROGESS REPORT

This is your Dementia Risk Index based on five functional tests - HBA1c for sugar control; omega-3 index and vitamin D for brain fats; homocysteine for B vitamins; glutathione index for antioxidants.

DRIfT

LOW RISK SMALL SIGNIFICANT HIGH RISK

64

SIGNIFICANT

>7
7-10.9
11-14.9
>15

Homocysteine

SMALL

>8%
6-8%
4-6%
<4%

Omega-3

SMALL

>100
75-100
50-74
<30

Vitamin D

HIGH RISK

<41
42-52
43-74
>75

HbA1c

SIGNIFICANT

>499
400-499
300-399
<300

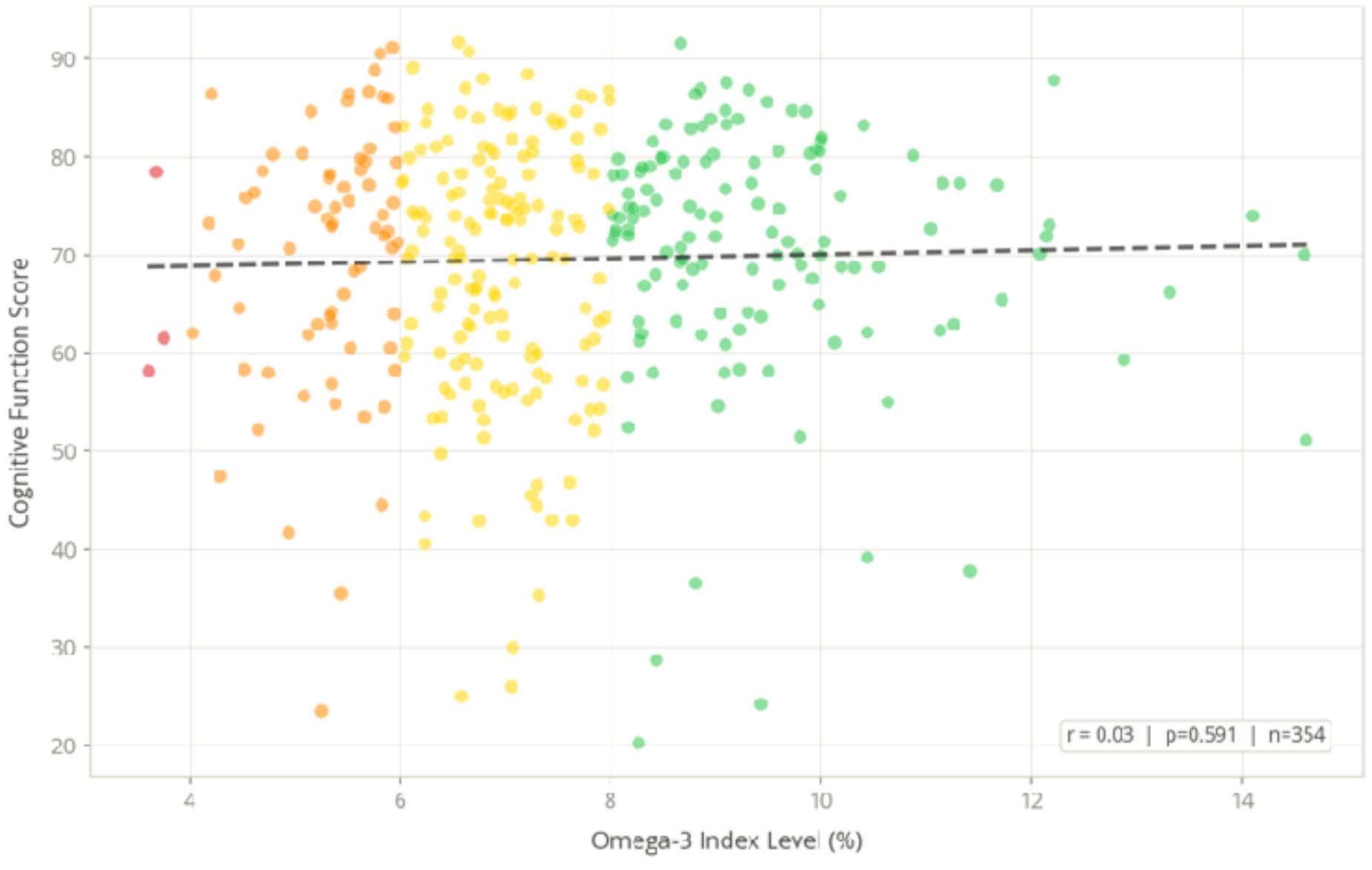
Glutathione

Omega-3 Index Level vs Cognitive Function

Each dot represents one person | Omega-3 Index Level & Cognitive Function Test within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN



≥ 8%
Optimal

6–8%
Below optimal

4–6%
Low

< 4%
High risk

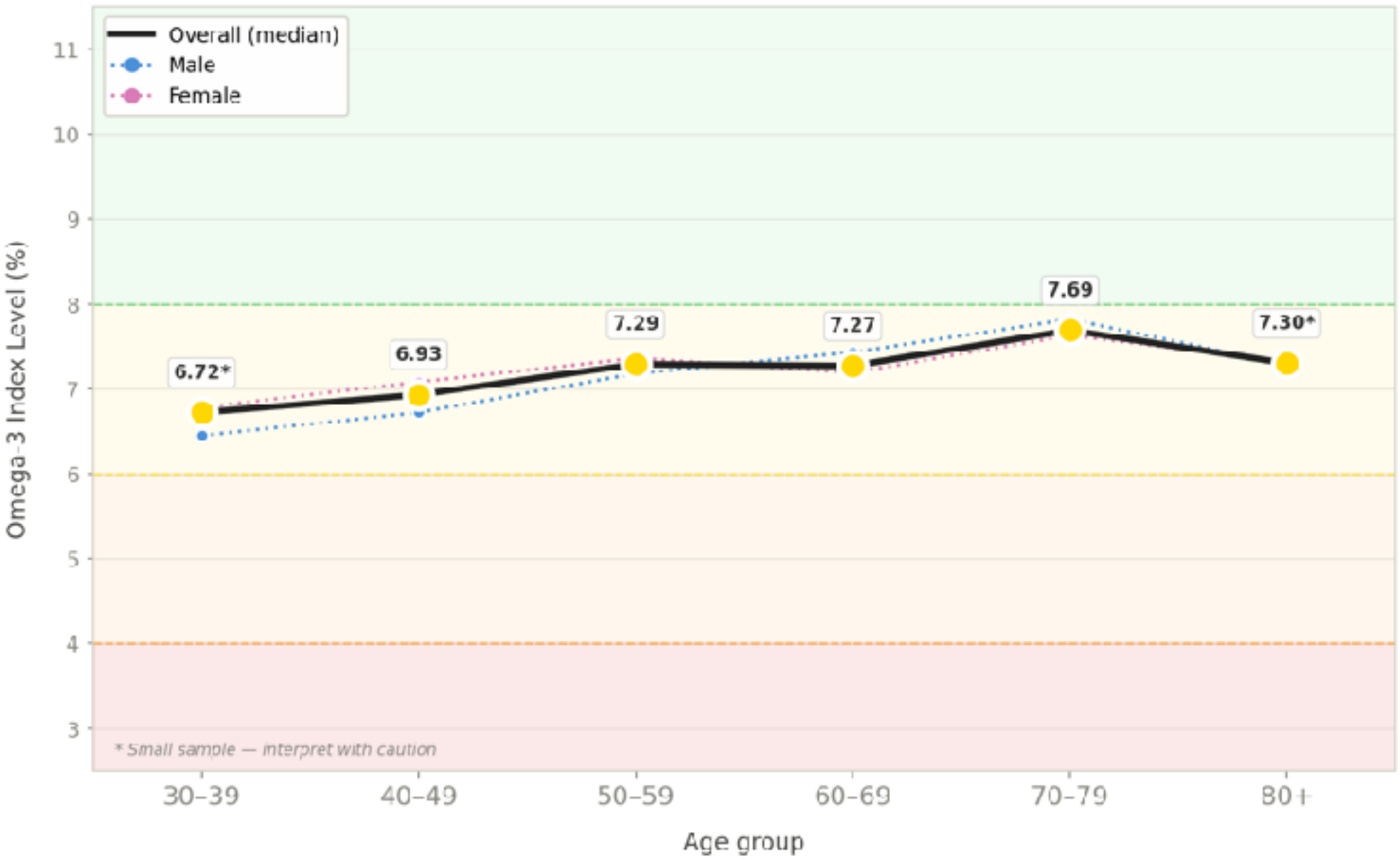
Source: COGNITION Biobank, Food for the Brain Foundation | n=354 | April 2026

Omega-3 Index vs Age and Gender

Median Omega-3 Index level (%) by age group | overall, male and female

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≥ 8%
Optimal

6–8%
Below optimal

4–6%
Low

< 4%
High risk

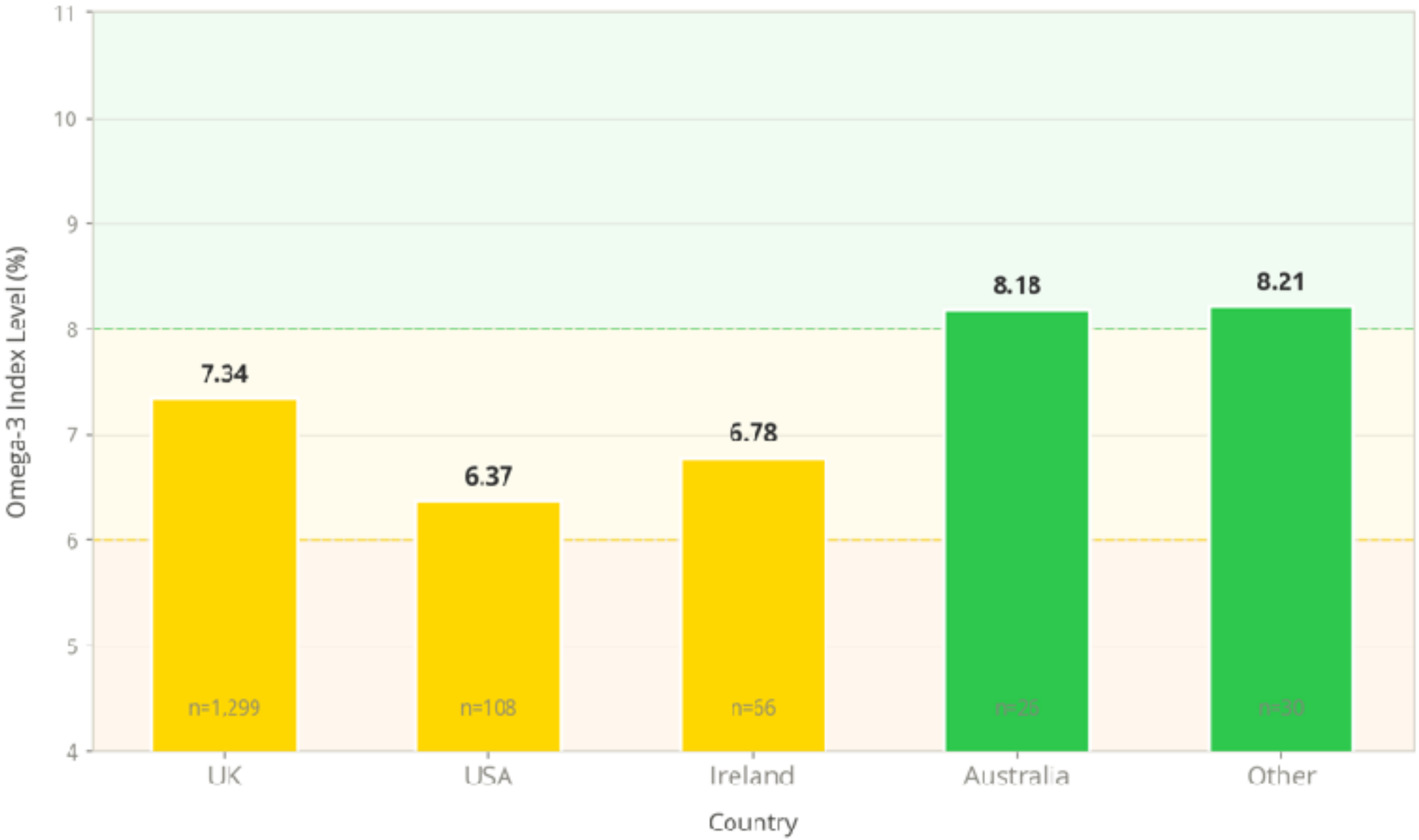
Source: COGNITION Biobank, Food for the Brain Foundation | n=1,739 (ages 30+) | April 2026

Omega-3 Index Level vs Country

Median Omega-3 Index level (%) by country

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



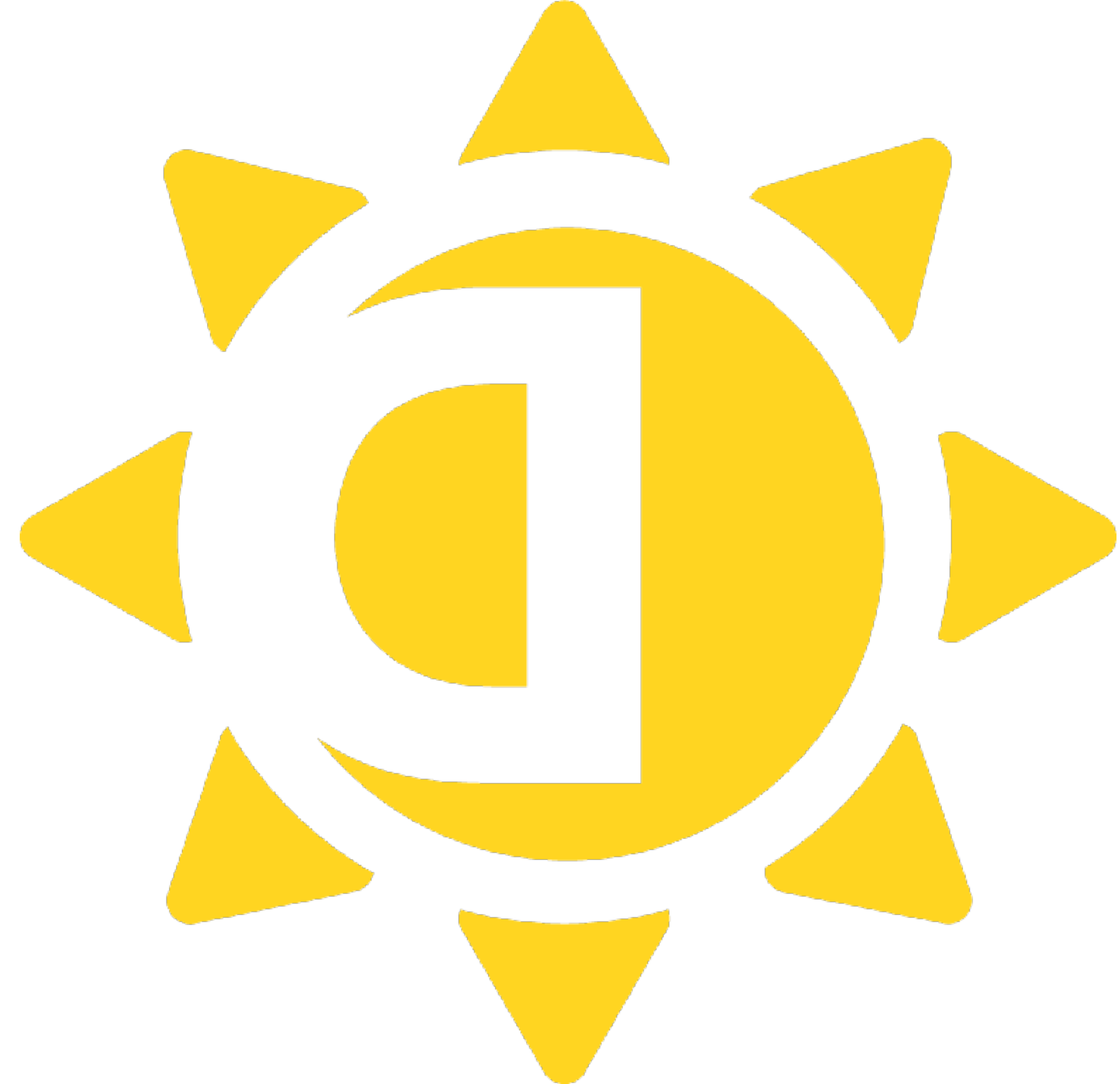
≥ 8%
Optimal

6–8%
Below optimal

4–6%
Low

< 4%
High risk

Source: COGNITION Biobank, Food for the Brain Foundation | n=1,522 | April 2026

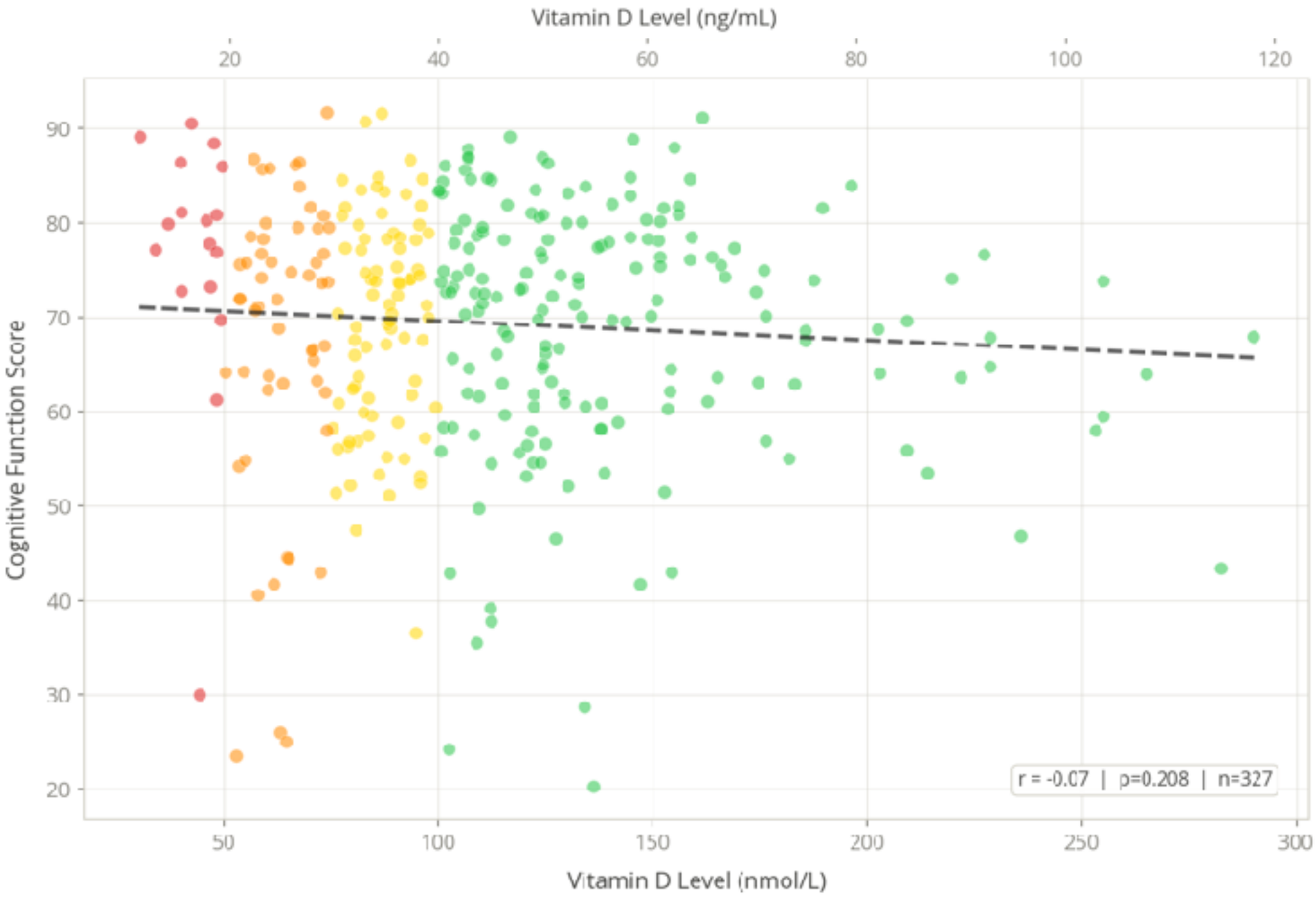


Vitamin D Level vs Cognitive Function

Each dot represents one test | Vitamin D Level & Cognitive Function Test within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



> 39.9 ng/mL

> 99.8 nmol/L

Optimal

30.0–39.9 ng/mL

75.0–99.8 nmol/L

Below optimal

20.0–29.9 ng/mL

50.0–74.9 nmol/L

Low

< 20.0 ng/mL

< 50.0 nmol/L

High risk

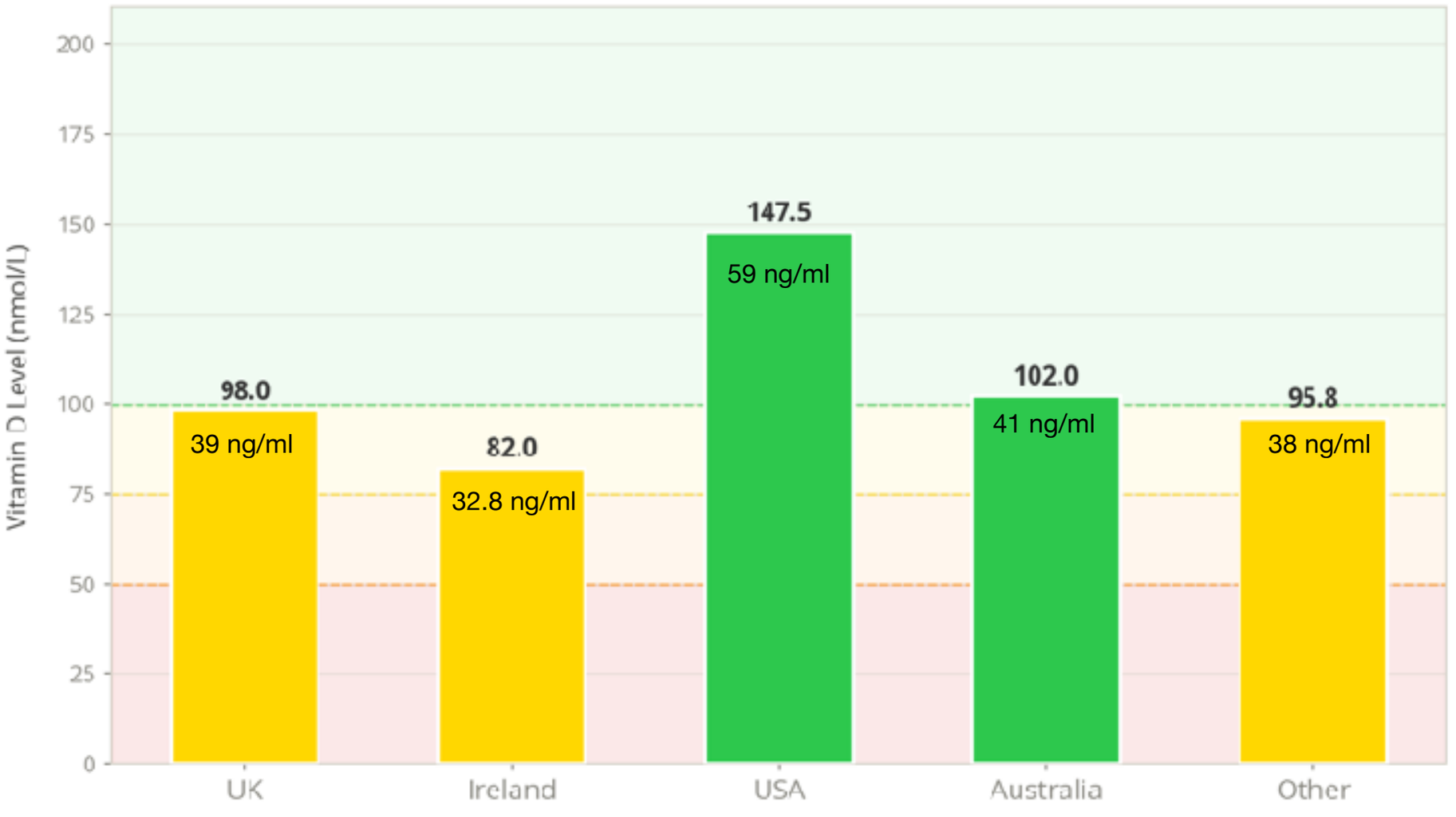
Source: COGNITION Biobank, Food for the Brain Foundation | n=327 | April 2026

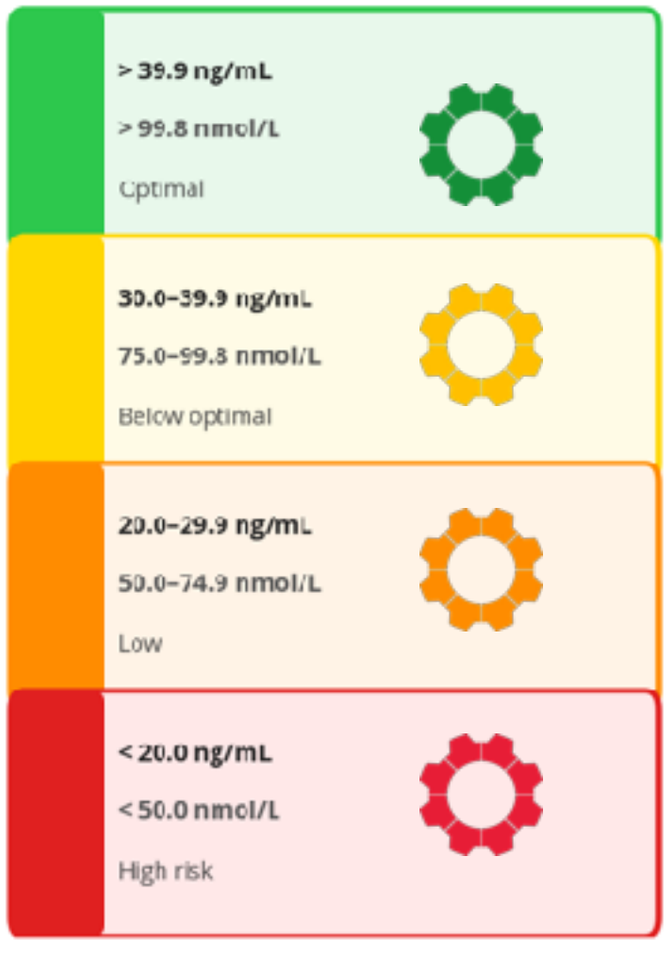
Vitamin D by Country

Median Vitamin D level (nmol/L) by country

COGNITION® BIOBANK

FOOD FOR THE BRAIN





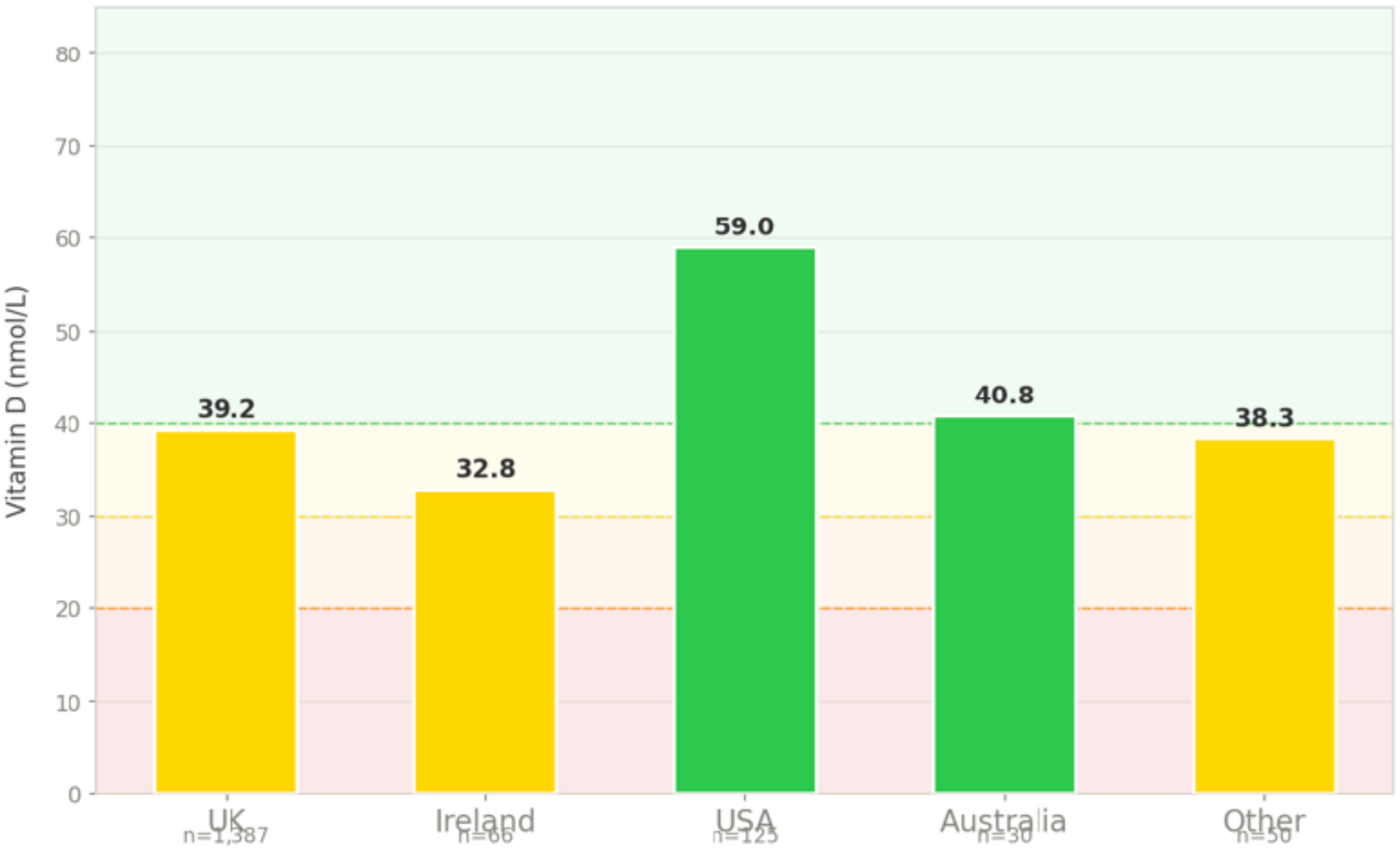
Source: COGNITION Biobank, Food for the Brain Foundation | n=1,658 | April 2025

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION

Vitamin D by Country

Median Vitamin D (nmol/L) by country



FFB Scoring

Green
≥ 40 nmol/L

Yellow
30-40 nmol/L

Amber
20-30 nmol/L

Red
< 20 nmol/L

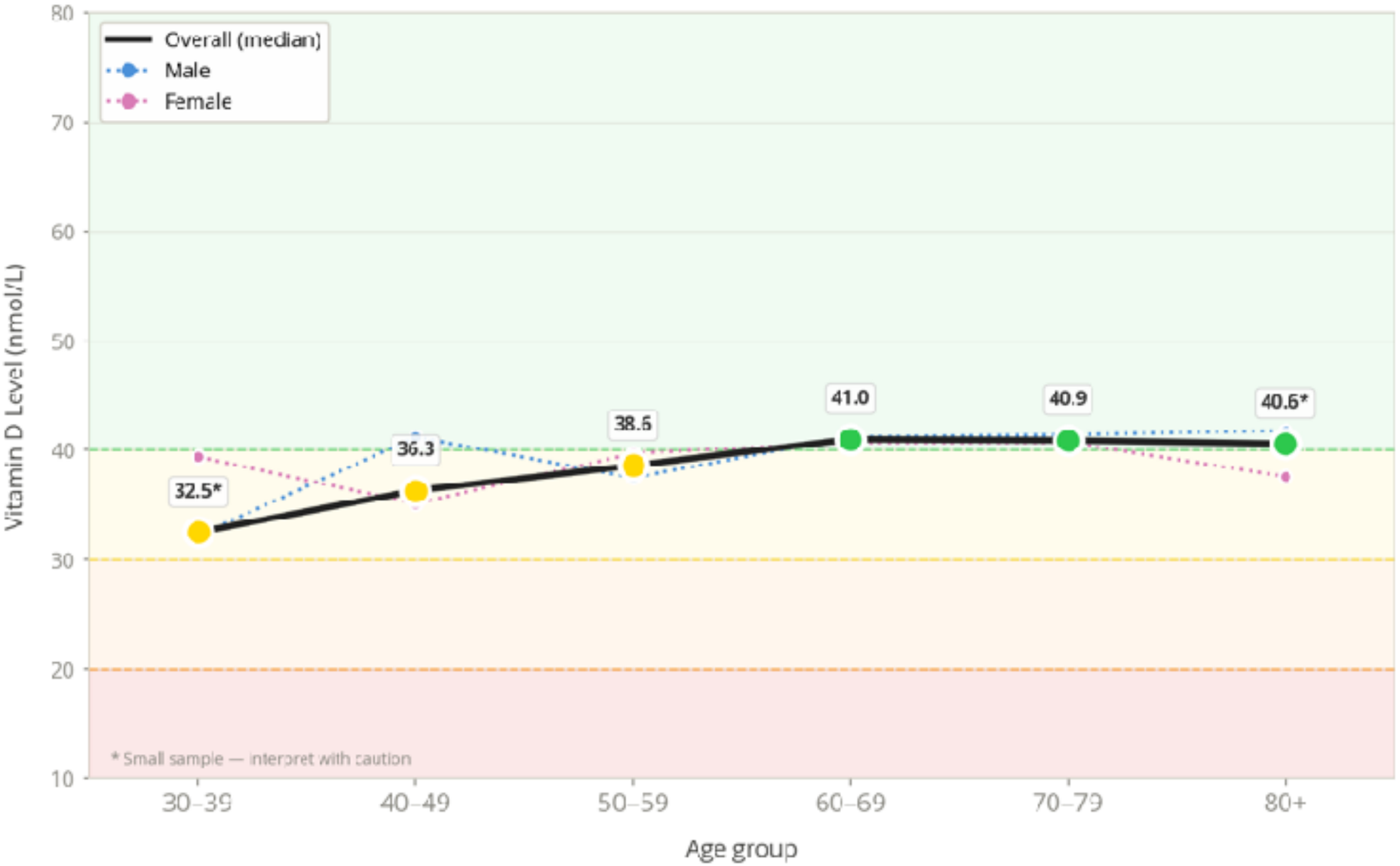
Source: COGNITION Biobank, Food for the Brain Fourdation | n=1,658 | April 2026

Vitamin D vs Age and Gender

Median Vitamin D level (nmol/L) by age group | overall, male and female

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≥ 40 nmol/L
Optimal

30–40 nmol/L
Below optimal

20–30 nmol/L
Low

< 20 nmol/L
High risk

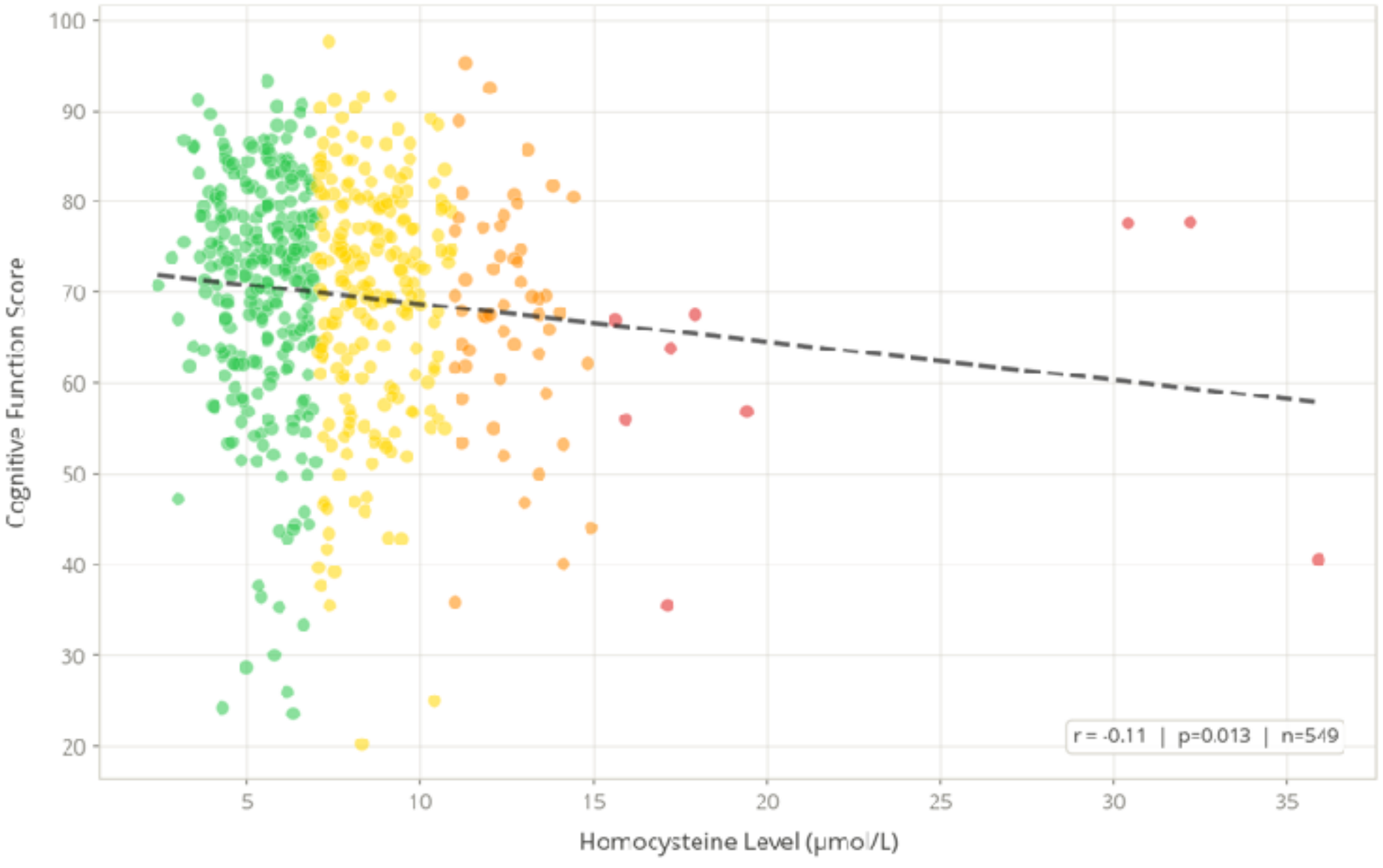
Source: COGNITION Biobank, Food for the Brain Foundation | n=1,574 (ages 30+) | April 2026

Homocysteine Level vs Cognitive Function

Each dot represents one person | Homocysteine Level & Cognitive Function Test within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≤ 7 µmol/L
Optimal

7–11 µmol/L
Below optimal

11–15 µmol/L
Elevated

> 15 µmol/L
High risk

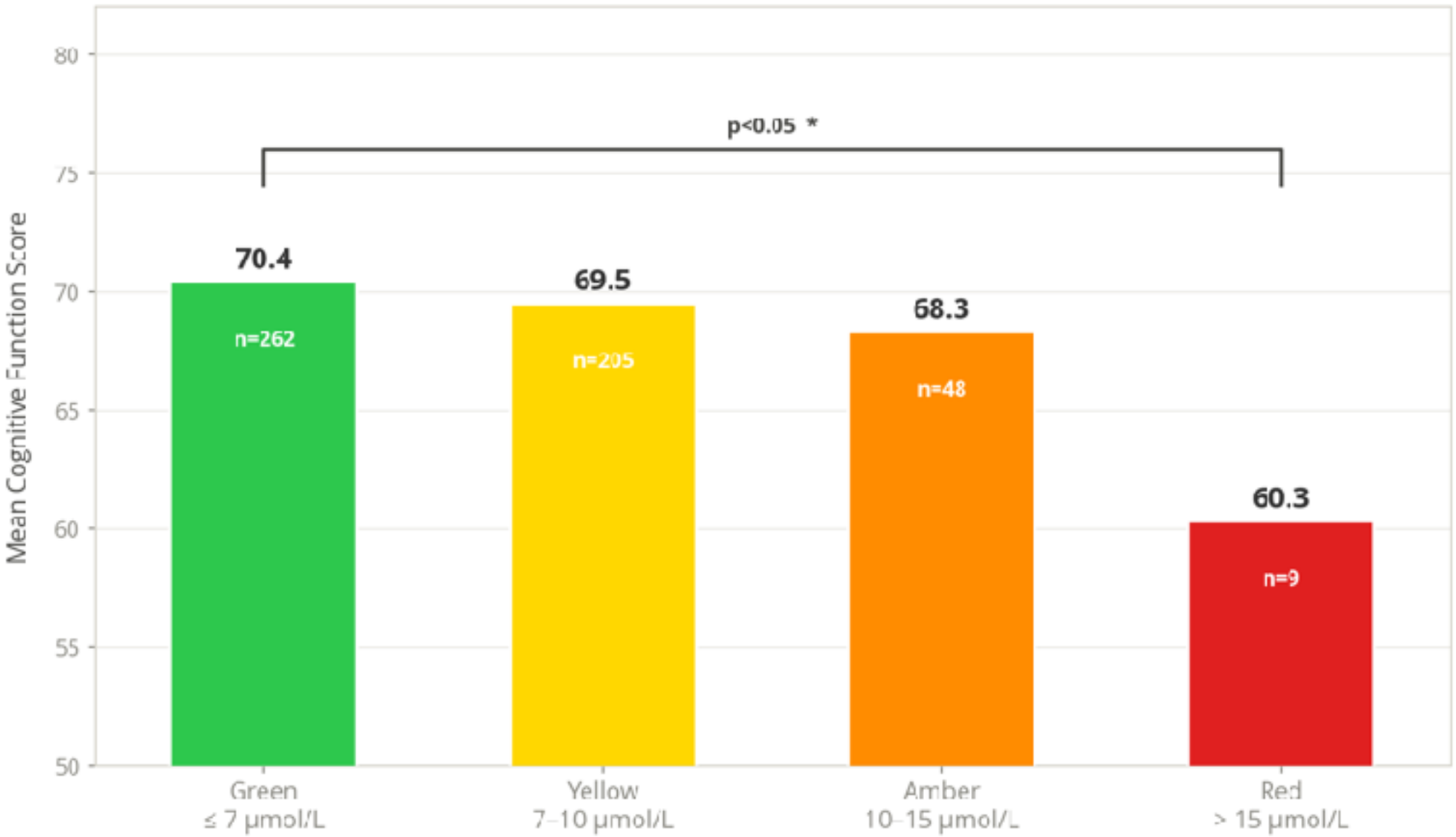
Source: COGNITION Biobank, Food for the Brain Foundation | n=549 | April 2026

Homocysteine Level vs Cognitive Function

Mean Cognitive Function Score by homocysteine level | paired within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≤ 7 µmol/L
Optimal

7–10 µmol/L
Below optimal

10–15 µmol/L
Elevated

> 15 µmol/L
High risk

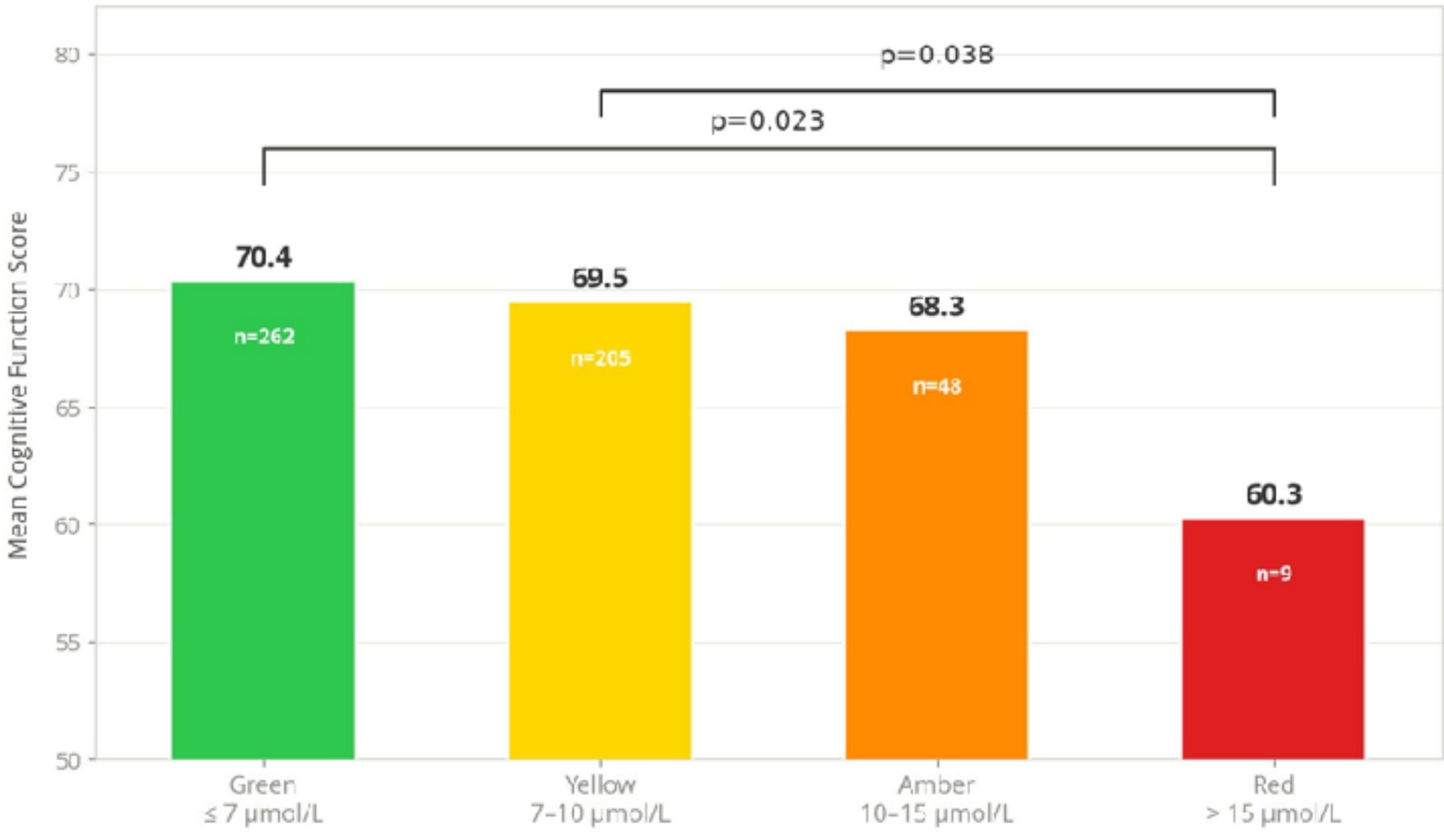
Source: COGNITION Biobank, Food for the Brain Foundation | n=524 | April 2026

Homocysteine Level vs Cognitive Function

Mean Cognitive Function Score by homocysteine level | paired within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≤ 7 µmol/L
Optimal

7–10 µmol/L
Below optimal

10–15 µmol/L
Elevated

> 15 µmol/L
High risk

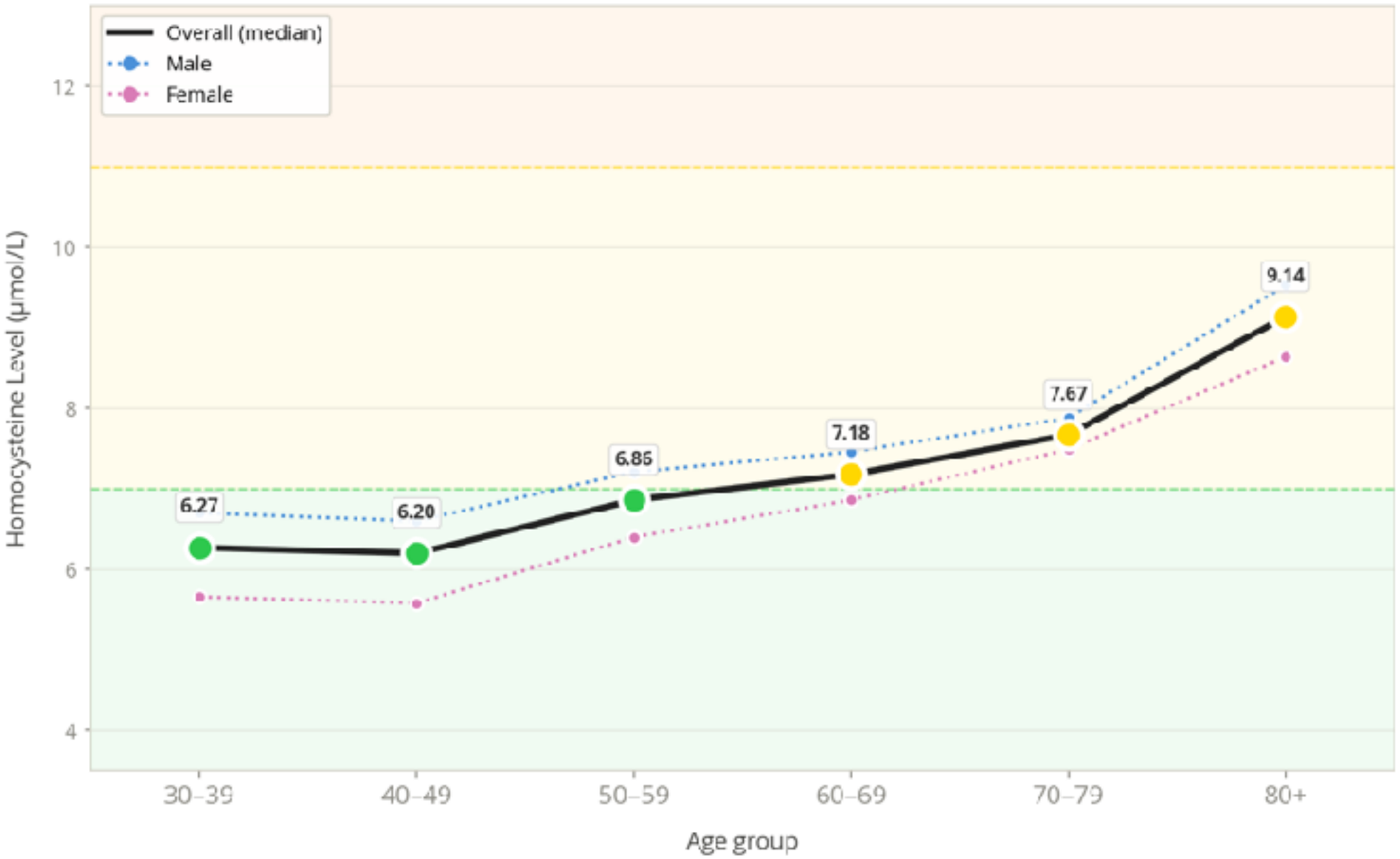
Source: COGNITION Biobank, Food for the Brain Foundation | n=524 | April 2026

Homocysteine vs Age and Gender

Median homocysteine level (µmol/L) by age group | overall, male and female

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≤ 7 µmol/L
Optimal

7–11 µmol/L
Below optimal

11–15 µmol/L
Elevated

> 15 µmol/L
High risk

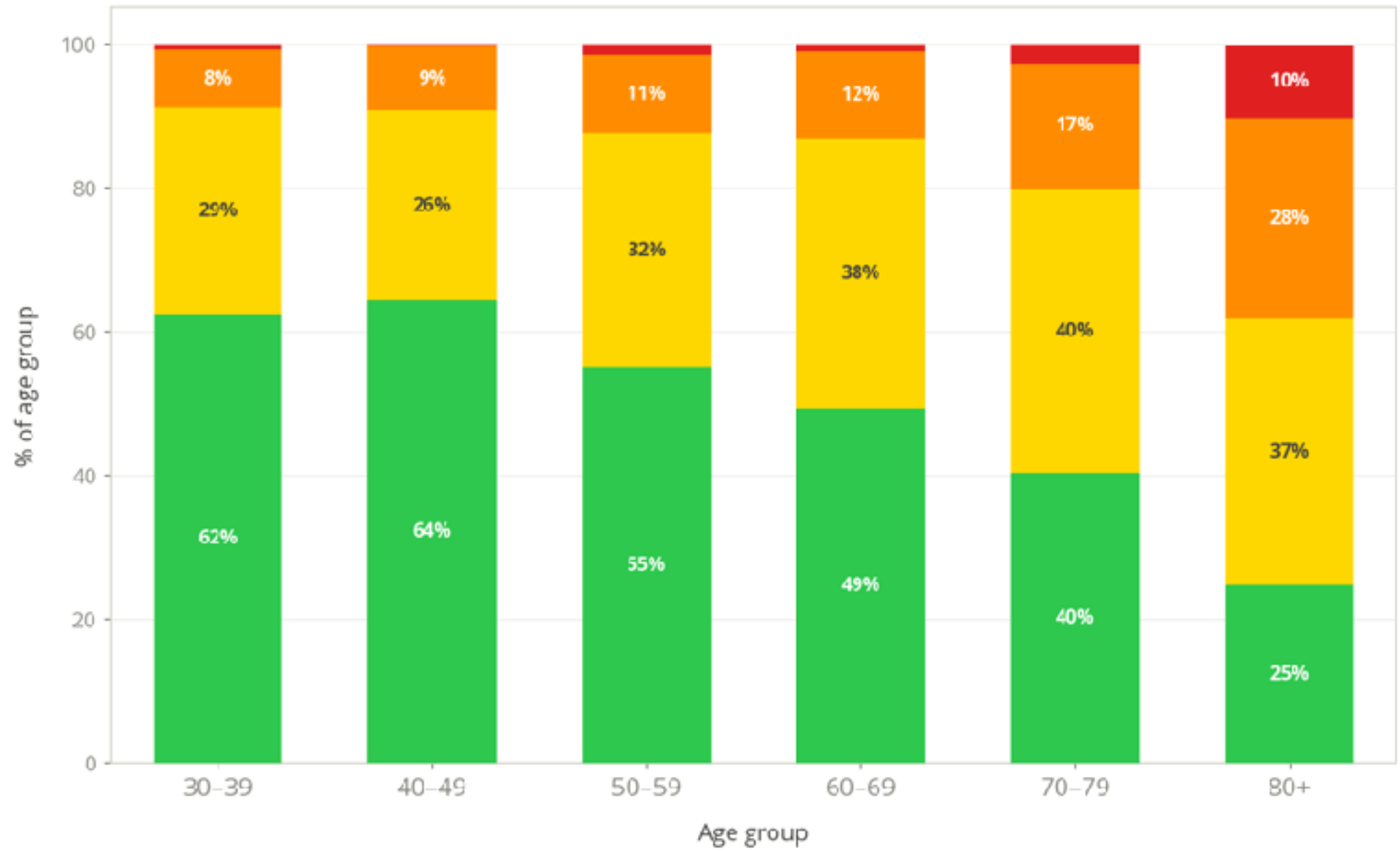
Source: COGNITION Biobank, Food for the Brain Foundation | n=3,135 (ages 30+) | April 2026

Homocysteine Level vs Age

% of people in each homocysteine level by age group | n=2,633 (ages 30+)

COGNITION® BIOBANK

FOOD FOR THE BRAIN



≤ 7 µmol/L
Optimal

7–10 µmol/L
Below optimal

10–15 µmol/L
Elevated

> 15 µmol/L
High risk

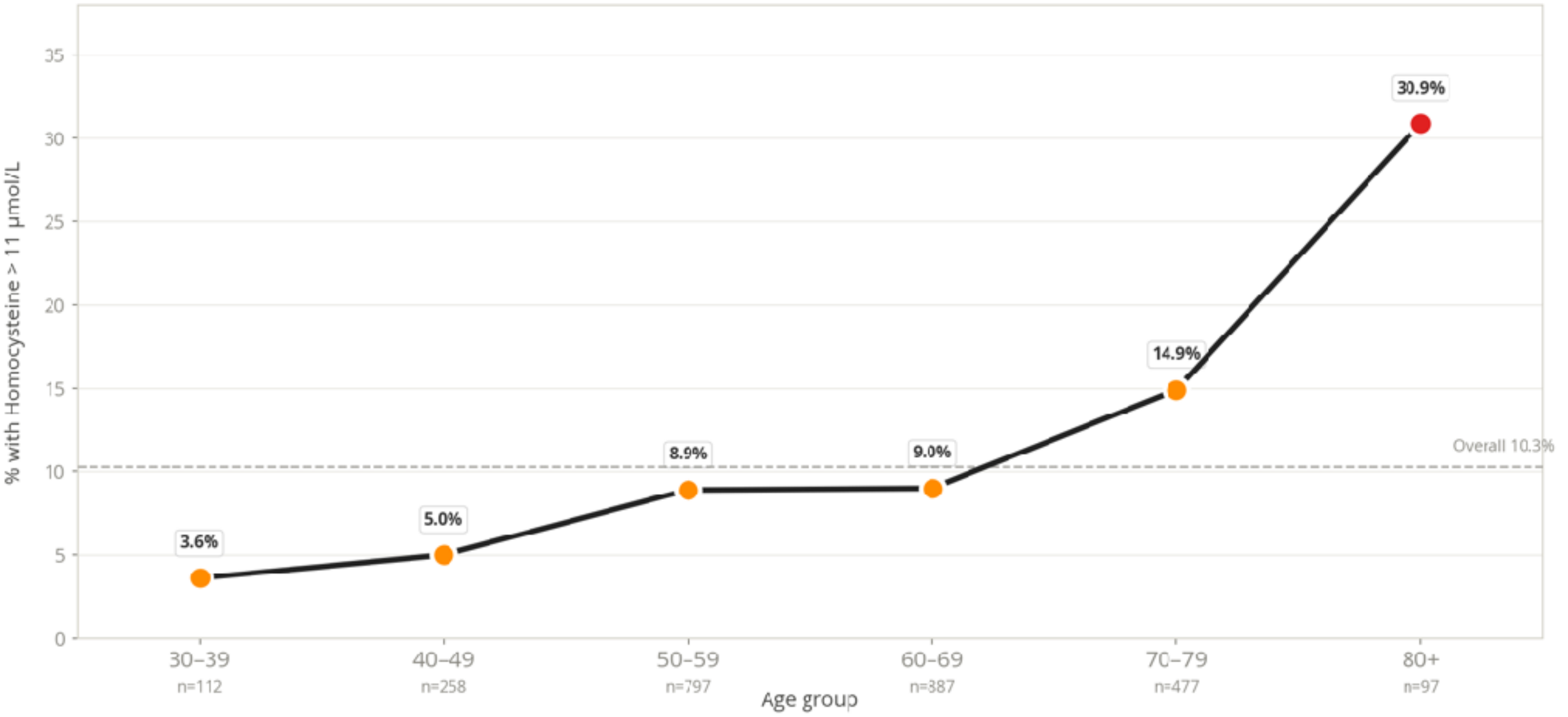
Source: COGNITION Biobank, Food for the Brain Foundation | April 2026

Homocysteine Level > 11 µmol/L vs Age

% of people with homocysteine > 11 µmol/L (brain shrinkage threshold) by age group

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



Source: COGNITION Biobank, Food for the Brain Foundation | n=2,633 (ages 30+) | April 2026

Homocysteine levels in 60+ year olds

Pfeiffer C, Clin Chem. 2008; R. Xu, Nature Scientific Reports 2022; Vogiatzlou A, Neurology, 2008 ++

US - 40% over 60 have homocysteine above 11µmol/l

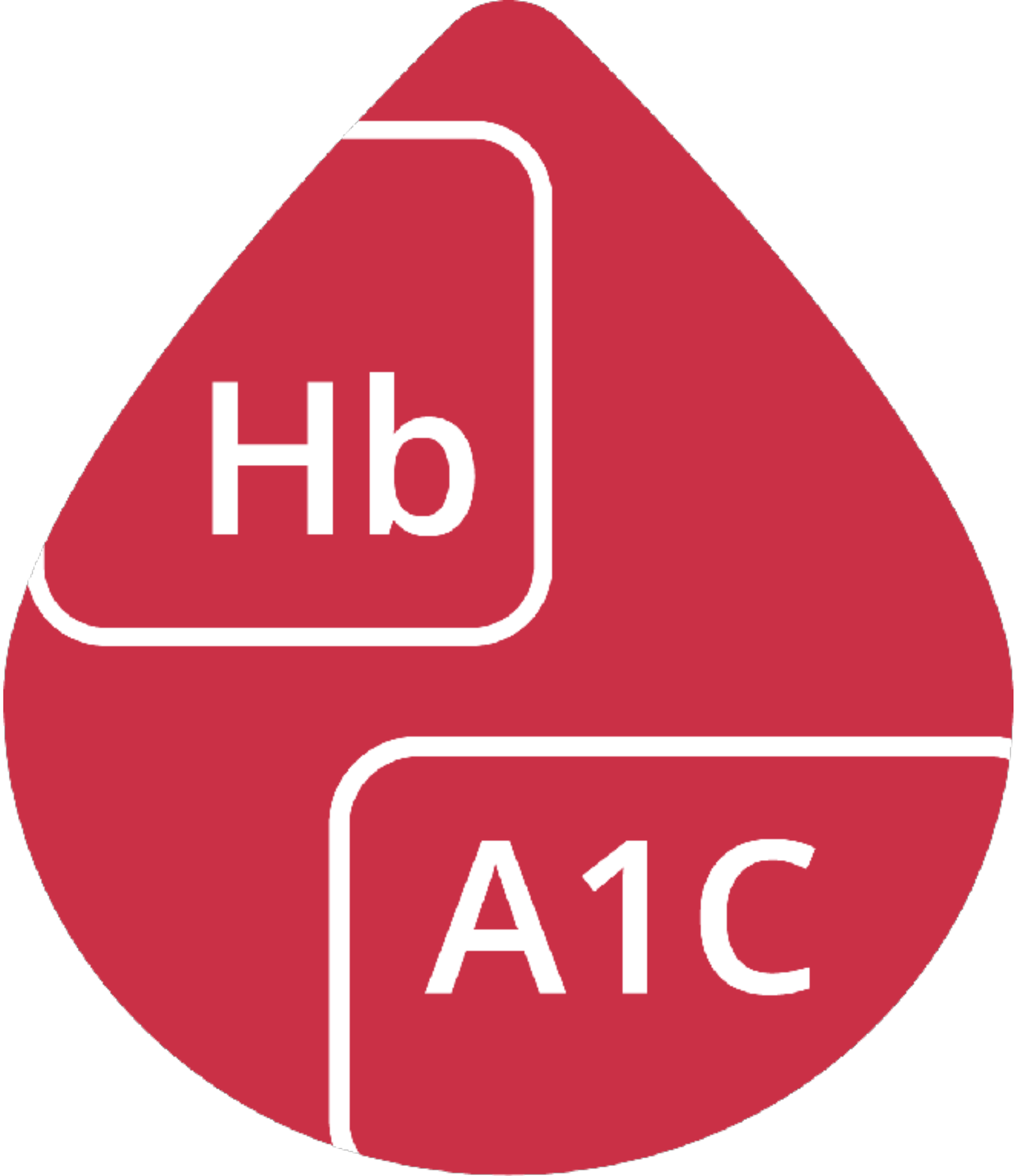
China - .In a study of almost 8,000 people in 2020, the average level in men was 12.5 and in women was 9.1.

S. Korea - 40% of men over age 18 40% had a homocysteine level over 11.

UK - 2 in 5 over 61 have insufficient plasma B12 to prevent accelerated brain shrinkage.

Ireland - 3 in 5 over 50 have have insufficient B12 to prevent accelerated brain shrinkage.

Above 10 mcmol/l needs treatment with B12 500mcg, B6 20mg, folate >400mcg

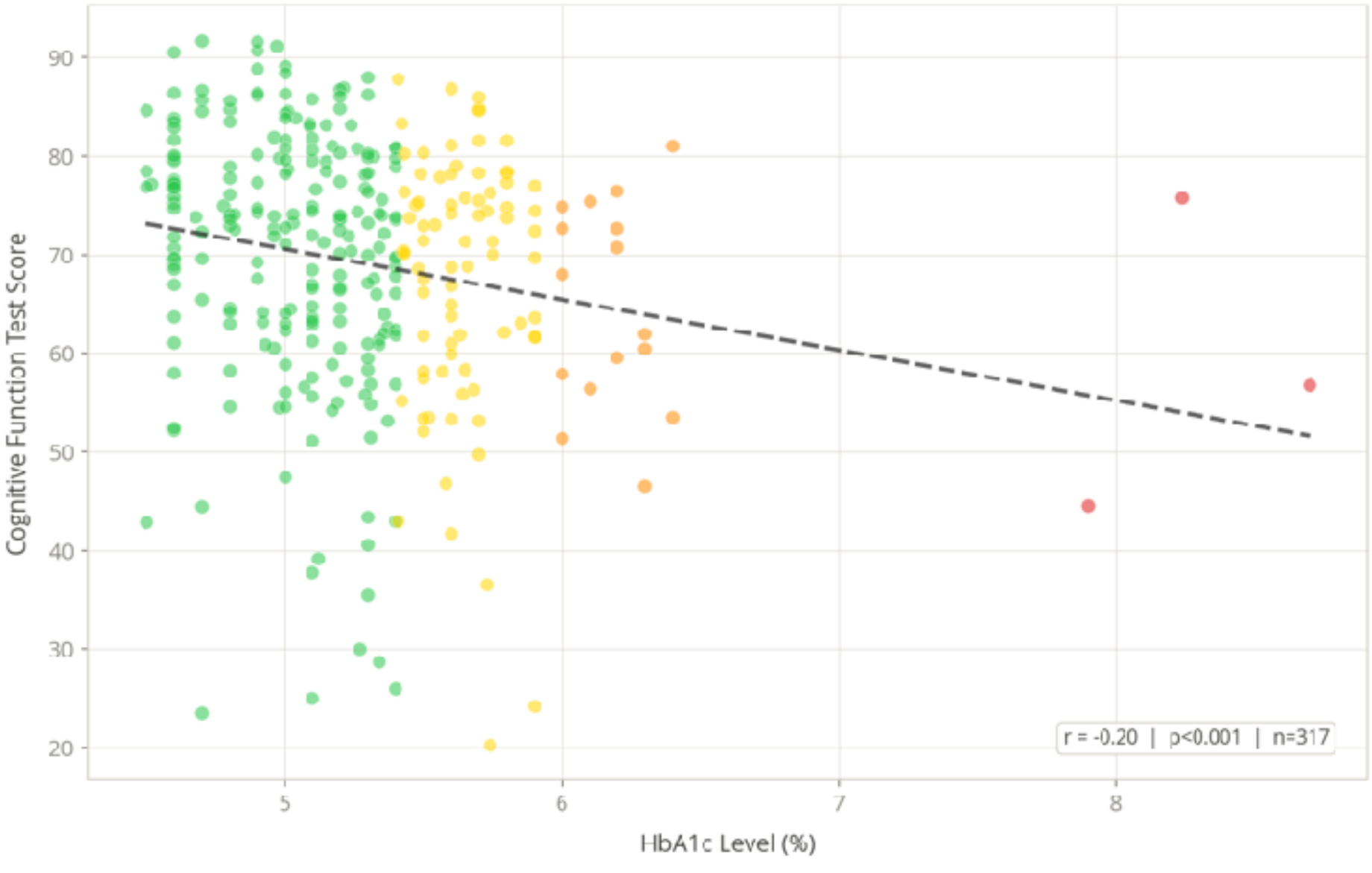

Hb
A1C

HbA1c vs Cognitive Function Test

Each dot represents one person | HbA1c & Cognitive Function Test within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≤ 5.4%
Optimal

5.4–6.0%
Below optimal

6.0–7.4%
Elevated

> 7.4%
High risk

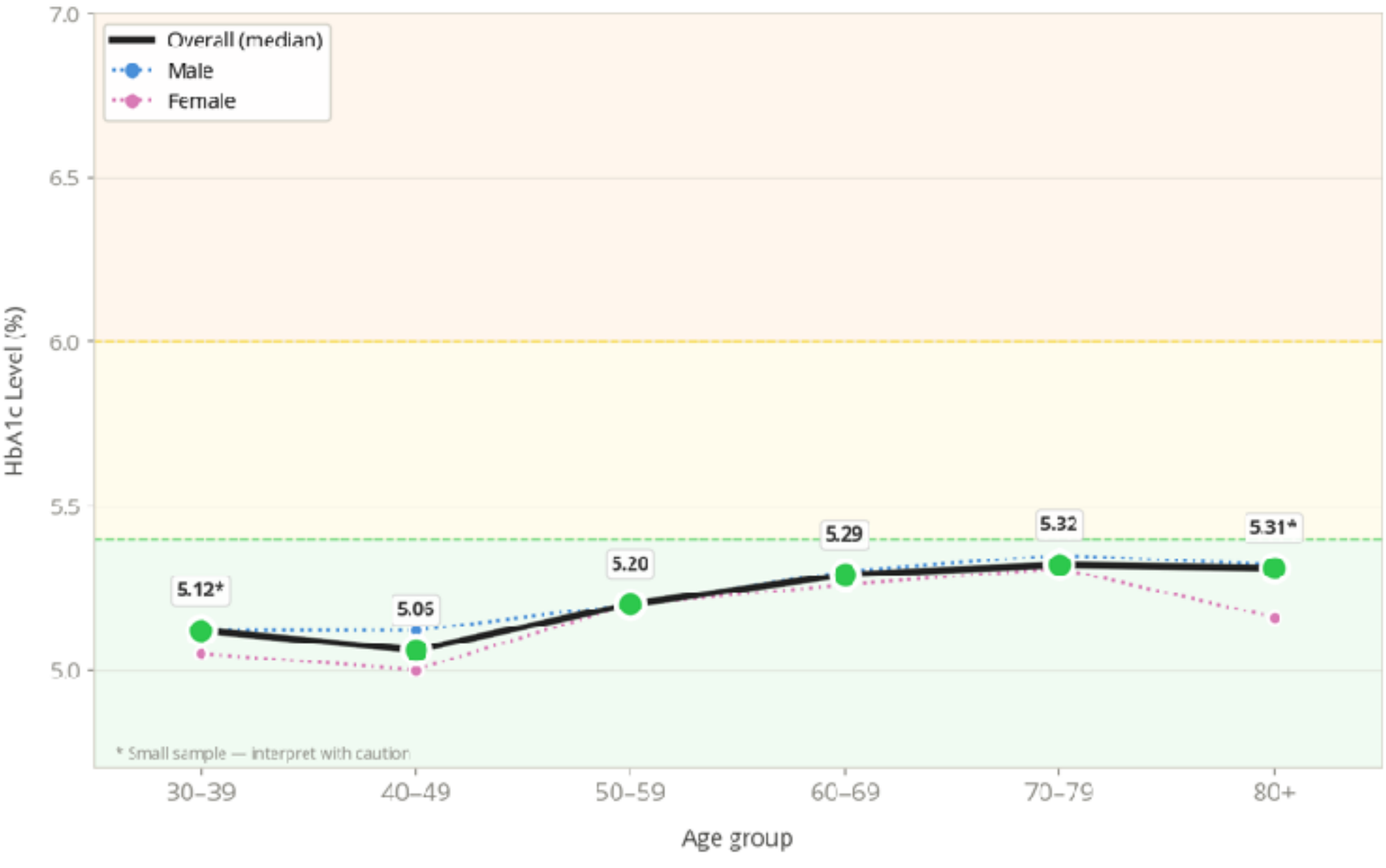
Source: COGNITION Biobank, Food for the Brain Foundation | n=317 | April 2026

HbA1c vs Age and Gender

Median HbA1c level (%) by age group | overall, male and female

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



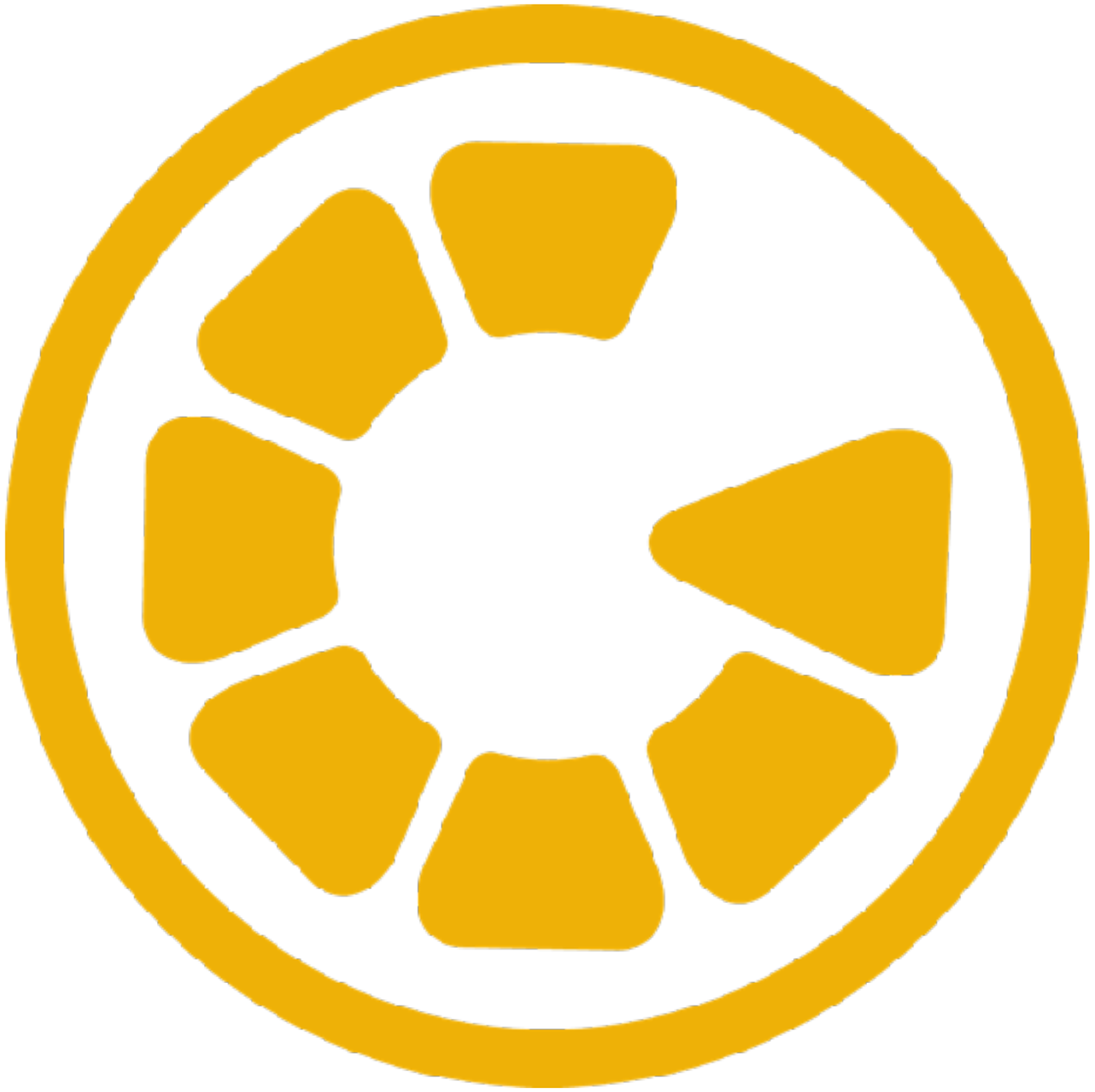
< 5.4%
Optimal

5.4–6.0%
Below optimal

6.0–7.4%
Elevated

> 7.4%
High risk

Source: COGNITION Biobank, Food for the Brain Foundation | n=1,546 (ages 30+) | April 2026

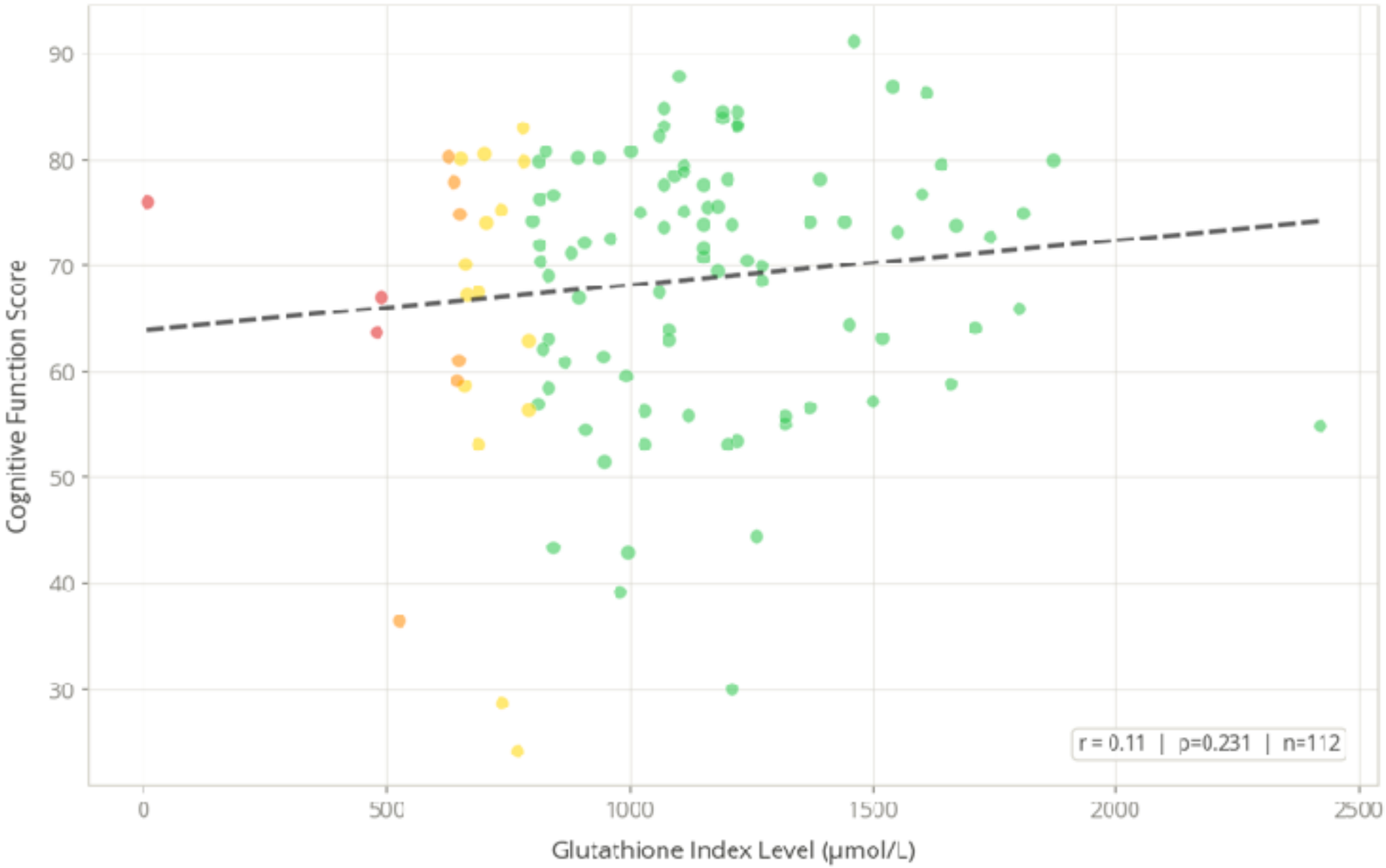


Glutathione Index Level vs Cognitive Function

Each dot represents one person | Glutathione Index Level & Cognitive Function Test within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≥ 800 µmol/L
Optimal

650–799 µmol/L
Below optimal

500–649 µmol/L
Low

< 500 µmol/L
High risk

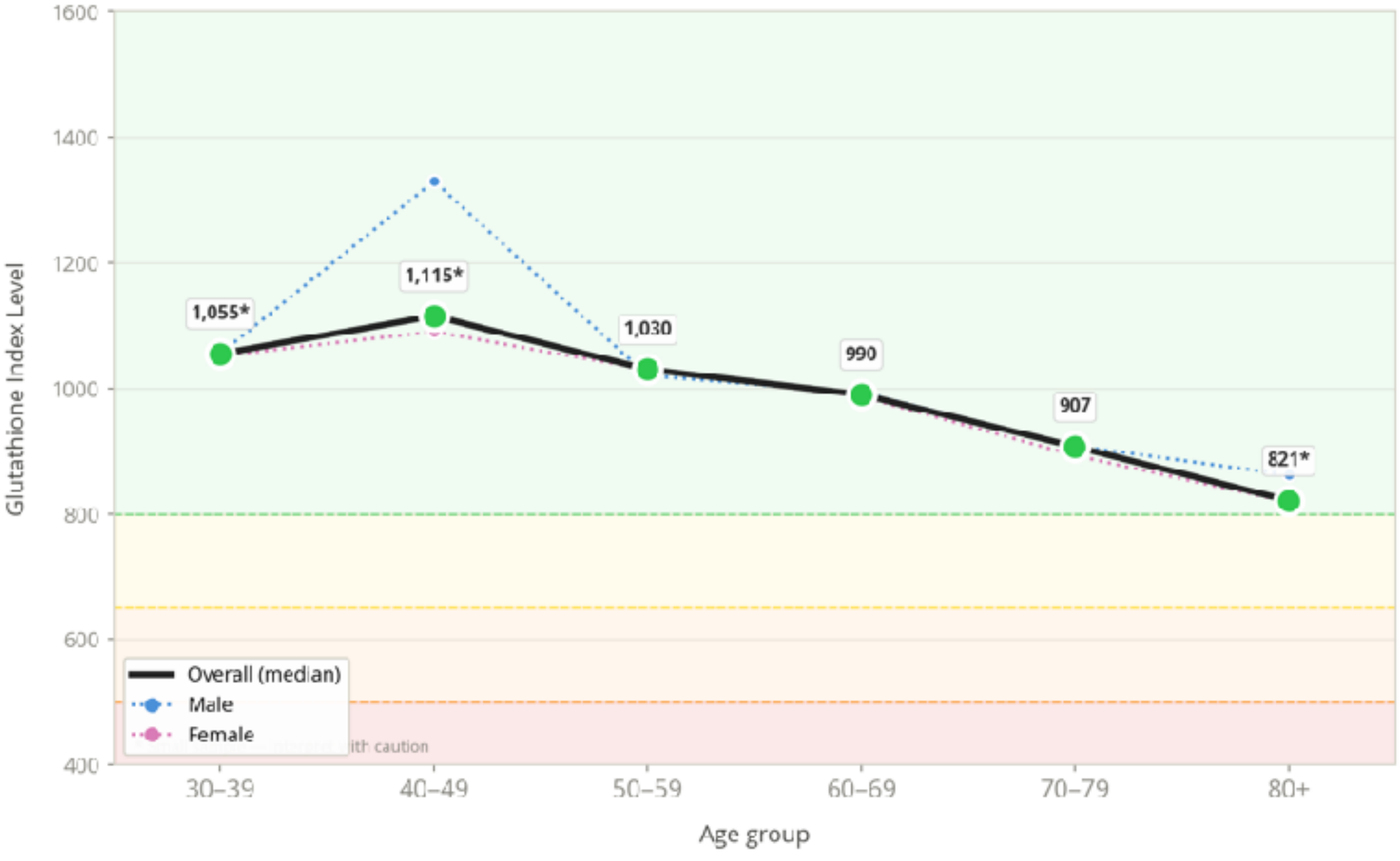
Source: COGNITION Biobank, Food for the Brain Foundation | n=112 | April 2026

Glutathione Index vs Age and Gender

Median Glutathione Index level by age group | overall, male and female

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



≥ 800
Optimal

650–799
Below optimal

500–649
Low

< 500
High risk

Source: COGNITION Biobank, Food for the Brain Foundation | n=748 (ages 30+) | April 2026

DRIfT®

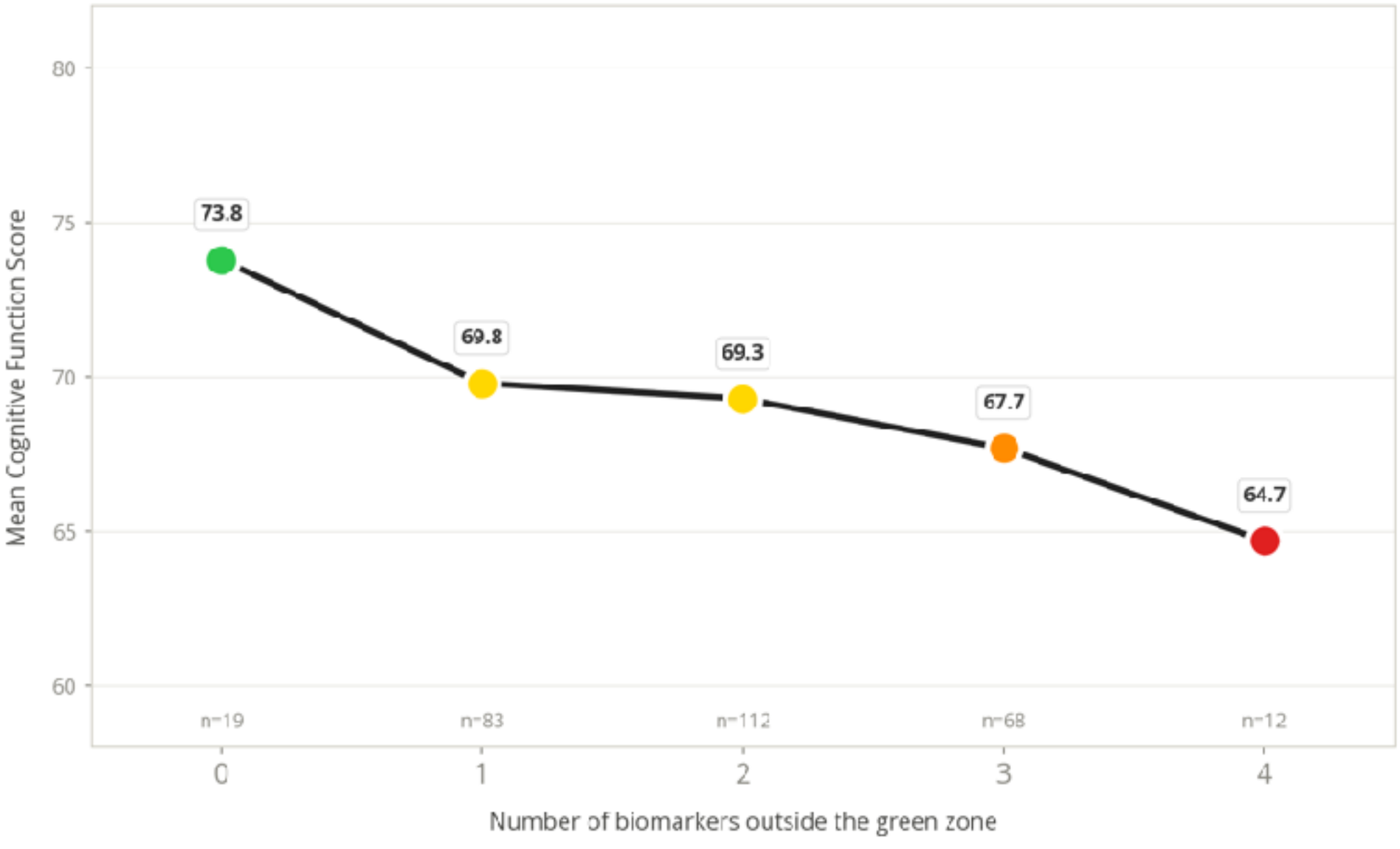
HbA1C (*sugar*) | OMEGA-3 INDEX | VITAMIN D (*brain fats*) | HOMOCYSTEINE (*B vitamins*) | GLUTATHIONE INDEX (*antioxidants*)

Increasing Biomarker Risk vs Cognitive Function

Mean Cognitive Function Score by number of biomarkers outside the green zone | DRIfT kit users within 30 days

COGNITION® BIOBANK

FOOD FOR THE BRAIN FOUNDATION



Source: COGNITION Biobank, Food for the Brain Foundation | n=295 | April 2026

Biomarkers tested:

Homocysteine
Omega-3 Index
Vitamin D
HbA1c
Glutathione Index

Green zone = optimal for each biomarker

0 = all biomarkers in green zone

4 = four biomarkers outside green zone

LOW RISK SMALL RISK SIGNIFICANT RISK HIGH RISK

ELSEVIER

Alzheimer's & Dementia: Translational Research & Clinical Interventions 5 (2019) 953-963

Alzheimer's & Dementia

Featured Article

A blood-based nutritional risk index explains cognitive enhancement and decline in the multidomain Alzheimer prevention trial

Gene L. Bowman[a,b,c,l,*], Hiroko H. Dodge[b,d], Sophie Guyonnet[e,f], Nina Zhou[g], Juliana Donohue[a], Aline Bichsel[a], Jeroen Schmitt[h], Claudie Hooper[e], Tamas Bartfai[i], Sandrine Andrieu[f,j], Bruno Vellas[e,f], the MAPT/DSA Study Group

Being low in omega-3, vitamin D and homocysteine increased risk of cognitive decline.

"While n-3 PUFA and HCy were not independently associated with cognitive decline but when combined acceleration in cognitive decline ensued"

Abstract

Introduction: Multinutrient approaches may produce more robust effects on brain health through interactive qualities. We hypothesized that a blood-based nutritional risk index (NRI) including three biomarkers of diet quality can explain cognitive trajectories in the multidomain Alzheimer prevention trial (MAPT) over 3-years.

Methods: The NRI included erythrocyte n-3 polyunsaturated fatty acids (n-3 PUFA 22:6n-3 and 20:5n-3), serum 25-hydroxyvitamin D, and plasma homocysteine. The NRI scores reflect the number of nutritional risk factors (0–3). The primary outcome in MAPT was a cognitive composite *Z* score within each participant that was fit with linear mixed-effects models.

Results: Eighty percent had at lease one nutritional risk factor for cognitive decline (NRI $\geq$1: 573 of 712). Participants presenting without nutritional risk factors (NRI=0) exhibited cognitive enhancement (β = 0.03 standard units [SU]/y), whereas each NRI point increase corresponded to an incremental acceleration in rates of cognitive decline (NRI-1: β = −0.04 SU/y, P = .03; NRI-2: β = −0.08 SU/y, P < .0001; and NRI-3: β = −0.11 SU/y, P = .0008).

Discussion: Identifying and addressing these well-established nutritional risk factors may reduce age-related cognitive decline in older adults; an observation that warrants further study.

DOI: 10.1002/alz.13884

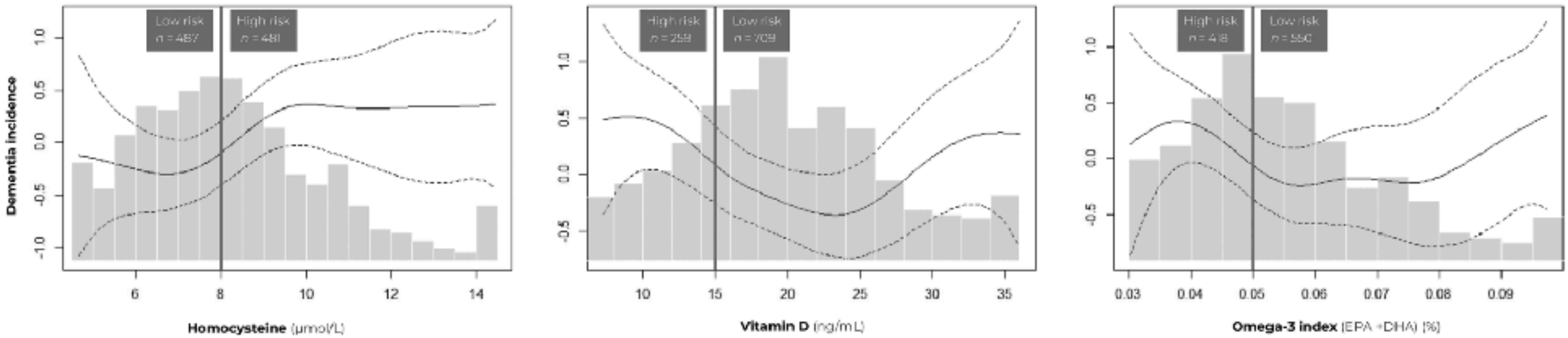
RESEARCH ARTICLE

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

Concurrent nutrient deficiencies are associated with dementia incidence

Annick P. M. van Soest[1] | Lisette C. P. G. M. de Groot[1] | Renger F. Witkamp[1] | Debora Melo van Lent[2,3,4] | Sudha Seshadri[2,3,4] | Ondine van de Rest[1]

4.6 times increased risk for dementia



Hcy >8 VitD <45 Omega3Index <5%

FIGURE 1 Dose-response relationships between nutrient status of homocysteine, vitamin D, and omega-3 polyunsaturated fatty acids and dementia risk, used to set cut-offs for optimal (low risk) and suboptimal (high risk) status to construct the nutrient status index. EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

DRIfT® research project

funding required

CITIZEN SCIENCE RESEARCH

FOOD FOR THE BRAIN

- **Aims & Approach:** The proposed study investigates how blood biomarkers relate to cognitive function by comparing results from two tools developed by Food for the Brain:

- The **DRIfT test**, measuring five key blood biomarkers: Homocysteine, HbA1c, Vitamin D, Omega-3 Index, and Glutathione Index.

- The **Cognitive Function Test** , a validated, self-administered digital tool assessing executive function, episodic memory, recognition memory, and processing speed.

- **Impact Statement:** This research marks a shift in dementia prevention from late diagnosis to early action, identifying modifiable factors that build brain resilience and preserve cognitive function, thus reducing risk of developing dementia later in life.

-