

Does sunshine improve the mental and cognitive health of older adults?

David Lee

Arthritis Research UK Epidemiology Unit

Sunlight effects on the brain...

- Seasonality
 - Light/Dark cycle
 - Circadian rhythm
 - Melatonin
 - Serotonin

Seasonal Affective Disorder

- Diagnostic & Statistical Manual of Mental Disorders (DSM-IV-TR)
- SAD – considered a subtype of another mood disorder diagnosis
- Recognised as a recurrent depressive disorder with a seasonal pattern

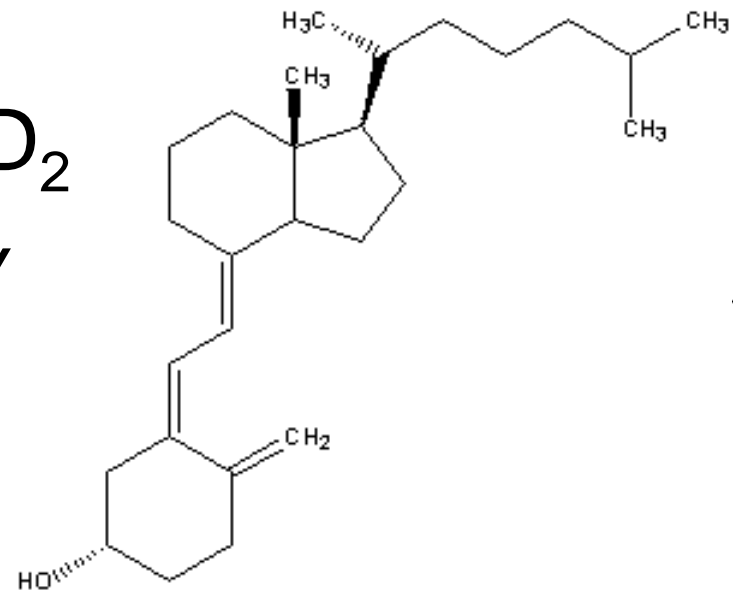
SUNLIGHT EXPOSURE?



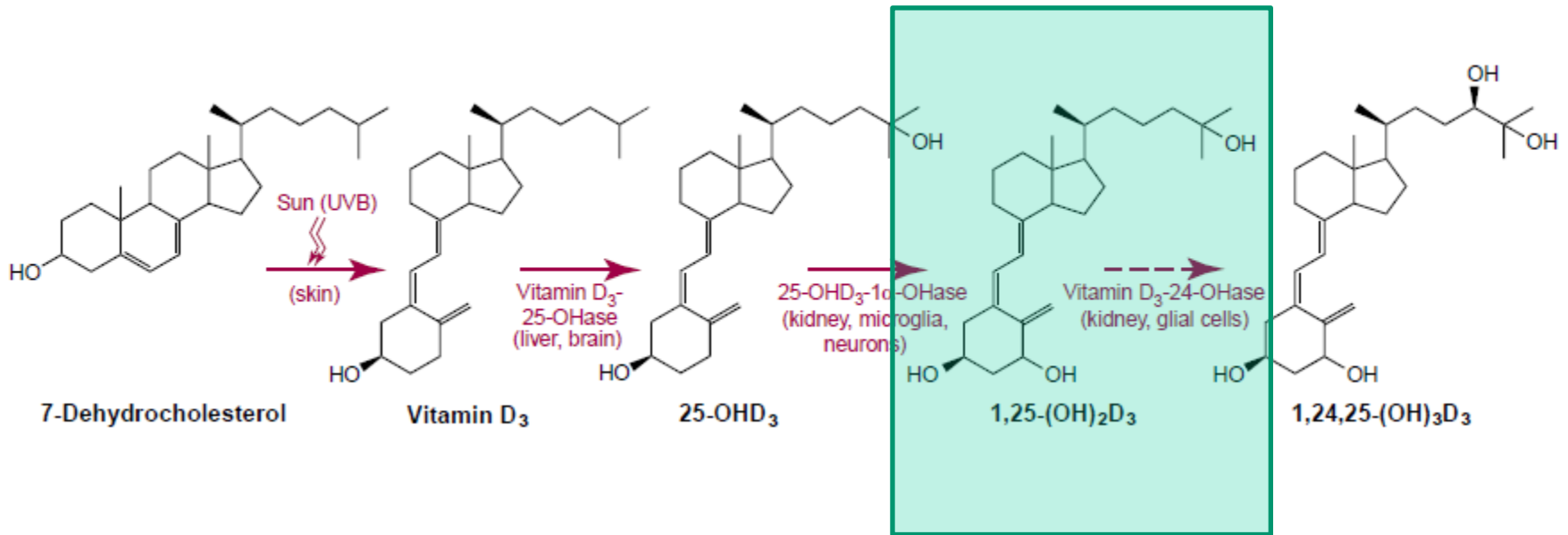
Synthesis of vitamin D...

Vitamin D

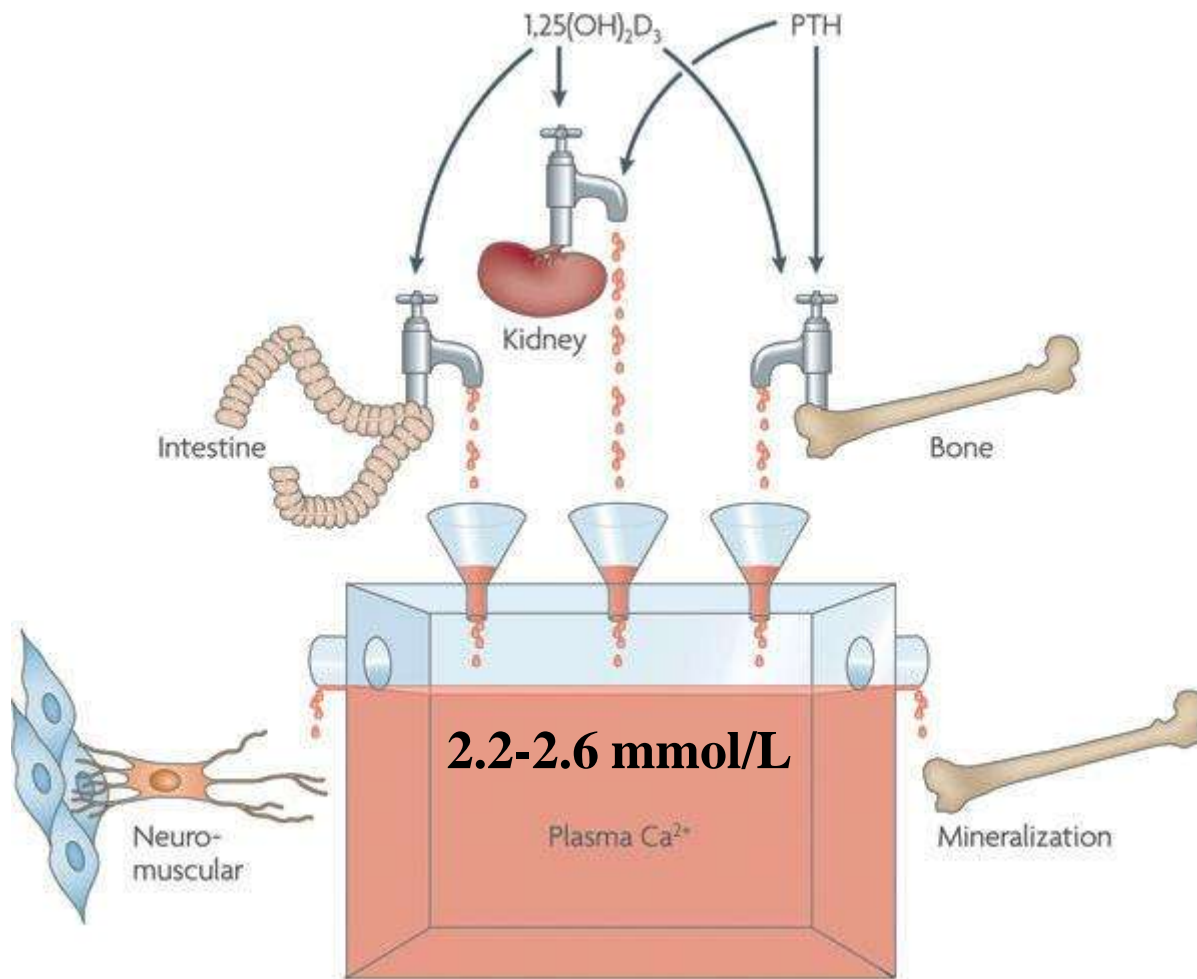
- Secosteroid
- Analogues: vitamin D₃ / D₂
- In this form – *biologically inert*



Biosynthetic pathway



Calcium homeostasis



Vitamin D - Deficiency

Rickets in childhood
Osteomalacia in adults

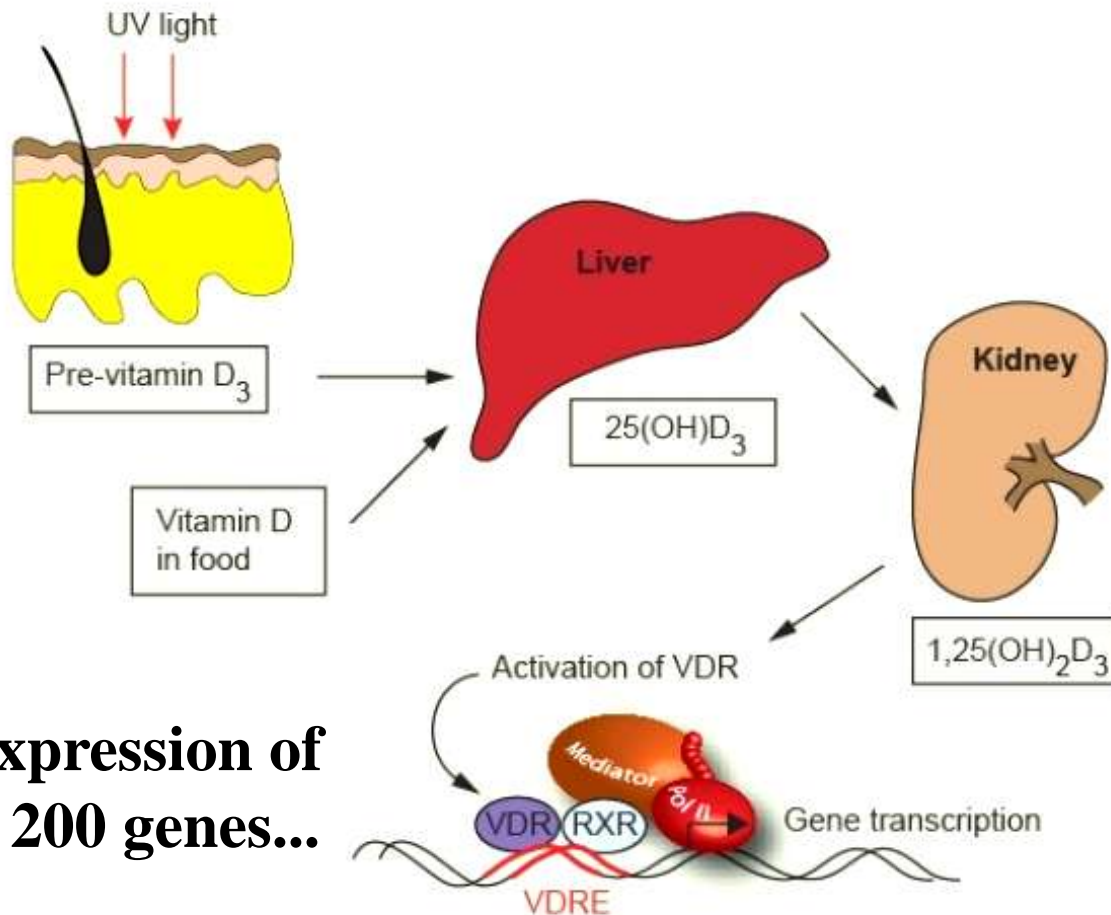
**Emerging evidence of
non-skeletal effects...**



Vitamin D - Assessment

- 25-hydroxyvitamin D \Rightarrow *vitamin D status*
- Levels < 25 nmol/L \Rightarrow 'deficiency'
- Vitamin D > 25 nmol/l \Rightarrow *adverse outcomes*

Broader biological function?



Controls expression of more than 200 genes...

Non-skeletal effects?

- Biological plausibility – vitamin D receptor (VDR) widely distributed [>50 tissues]
- The VDR and 1α -hydroxylase are usually co-localised
- VDR knockout mouse – autoimmune inflammatory diseases, sarcopaenia, cardiovascular diseases, behavioural abnormalities

Vitamin D and the brain

- VDR widely distributed in the brain – *cortex, cerebellum and limbic system*
- Neurotrophic and neuroprotective properties, retards hippocampal ageing
- Vitamin D inadequacy – effects on cognitive and behavioural endpoints?
- *Current epidemiological evidence?*

Observational studies

Cognitive function

- Deficiency associated with poorer working memory

ZENIT

Comprehensive adjustment for confounding factors?

- No relationship with serum 25(OH)D levels
NHANES III (2007)

Depression

- Lower 25(OH)D levels associated with

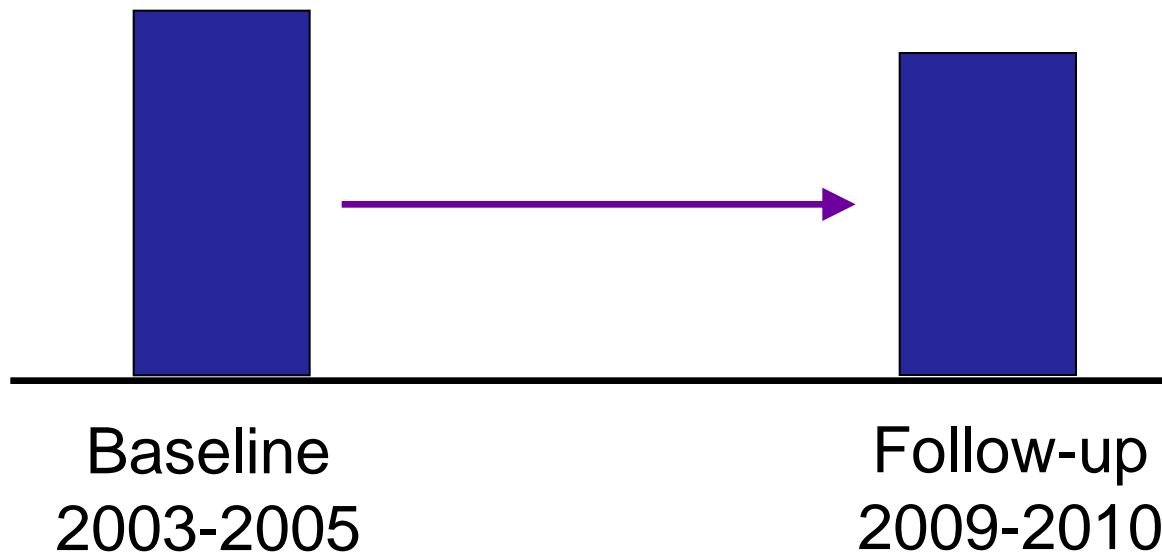
- Deficiency associated with low mood
ADRC (2006)

Unresolved questions...

- What is the relationship between serum vitamin D levels and psychological health among community-dwelling older adults?
- Is there any evidence of a dose-dependent relationship?
- Are any associations explained by adverse health and lifestyle factors?

European Male Ageing Study

- Prospective, multi-centre study
- 3,369 men aged 40-79 years





Baseline assessment

Questionnaire

- Cognitive Function
- Depression (BDI-II)
- Physical activity (PASE)
- Morbidities – *CVD*
Diabetes
- Lifestyle - *Alcohol*
Smoking

Measurement

- Height & weight

Fasting Blood

- Vitamin D
 - 25(OH)D
 - 1,25(OH)₂D
- Parathyroid hormone

Subject characteristics ($n = 3,131$)

	Mean (SD)
Age (years)	59.9 (10.9)
Body mass index (kg/m ²)	27.7 (4.1)
25(OH)D (nmol/L)	62.5 (31.4)
Heart condition	16%
Diabetes	8%
Current smoker	21%
Alcohol (\geq once/week)	58%
Depression*	15%

*BDI \geq 14 and/or using antidepressants

Vitamin D and adverse health factors

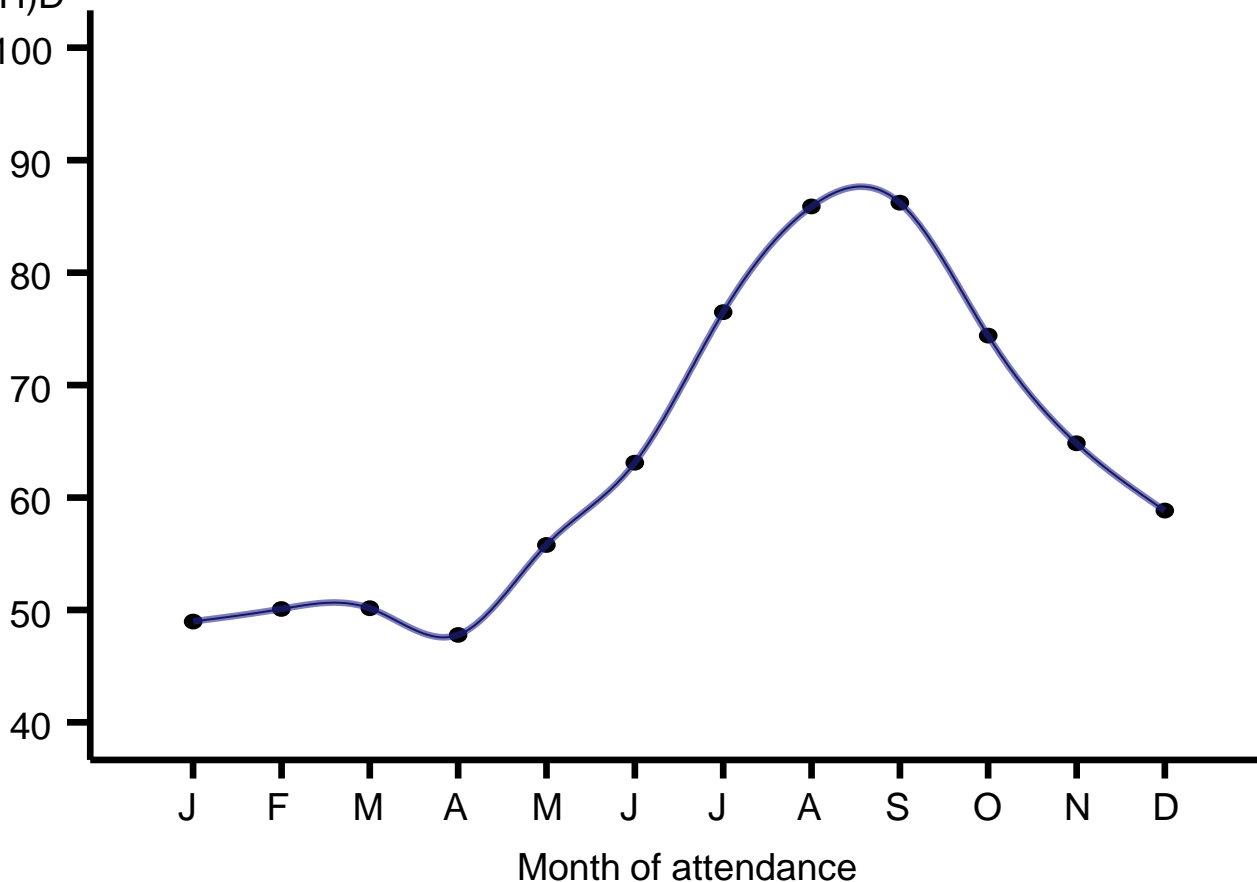
Variable	β coefficient
Body mass index (kg/m ²)	-0.83
Physical activity (PASE)	0.04
† ...adjustment for ‡ confounding factors...	
Current smoker	-11.7
Alcohol (\geq once/week)	9.21
Depression	-8.96

Adjusted for age & centre: all $p < 0.05$

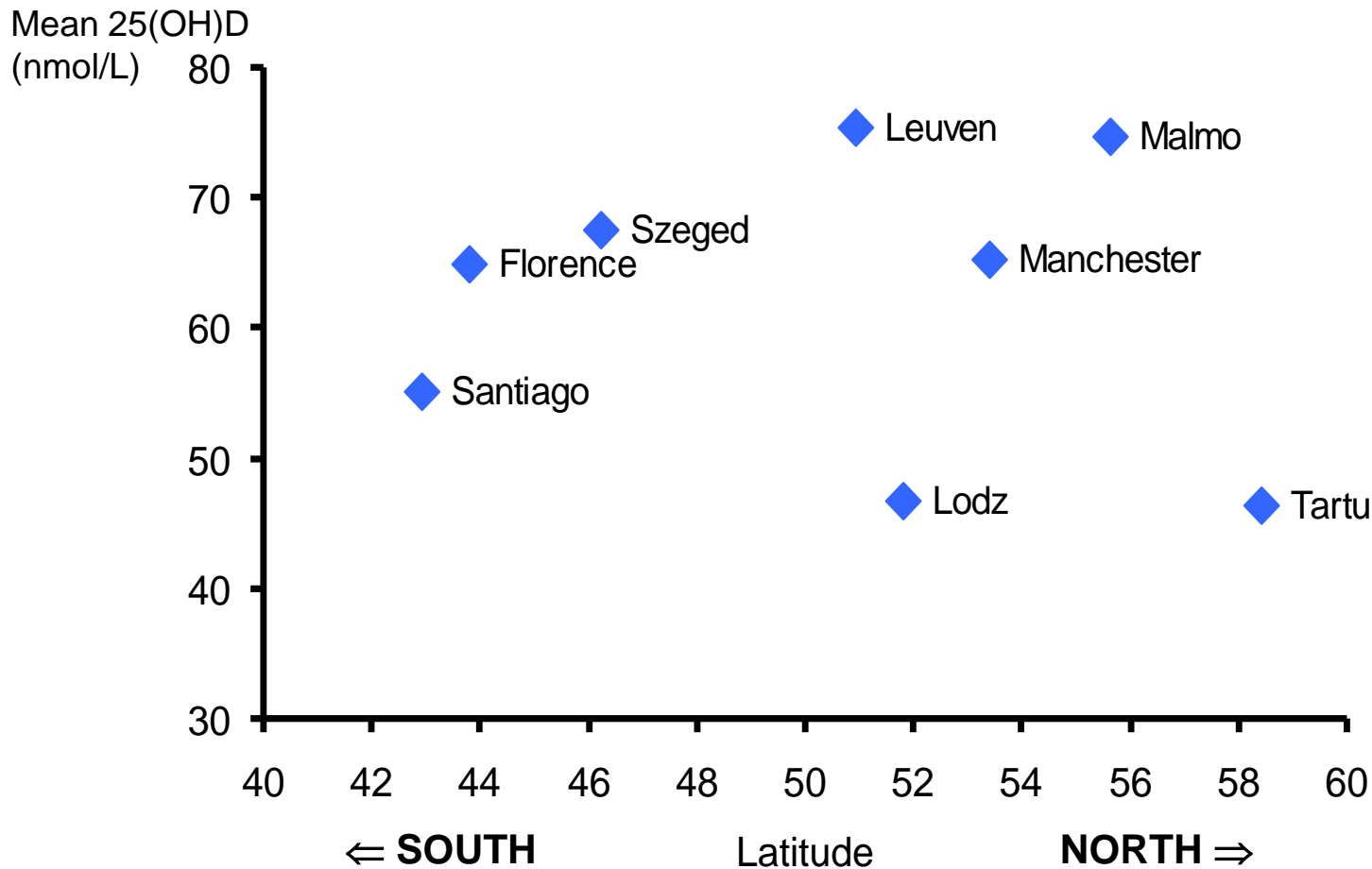
*Self-report and/or using anti-diabetic drugs

Influence of Season

Mean 25(OH)D
(nmol/L)

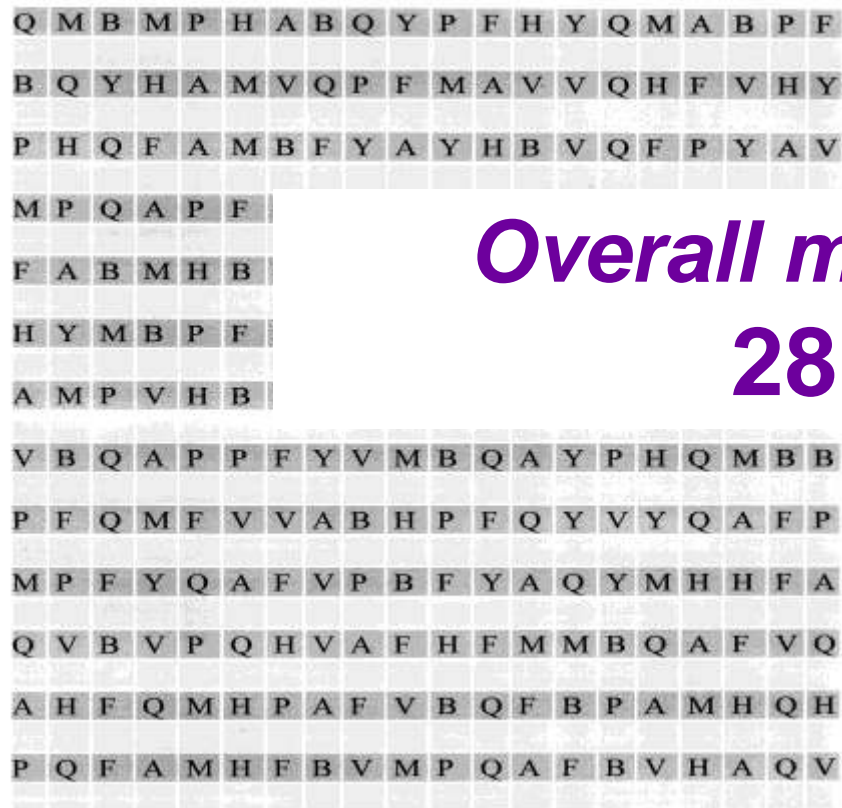


Influence of Geography



Vitamin D and Cognitive Function

H	Y	Q	A	M	B	V	P	F
3	6	2	9	4	1	7	5	8



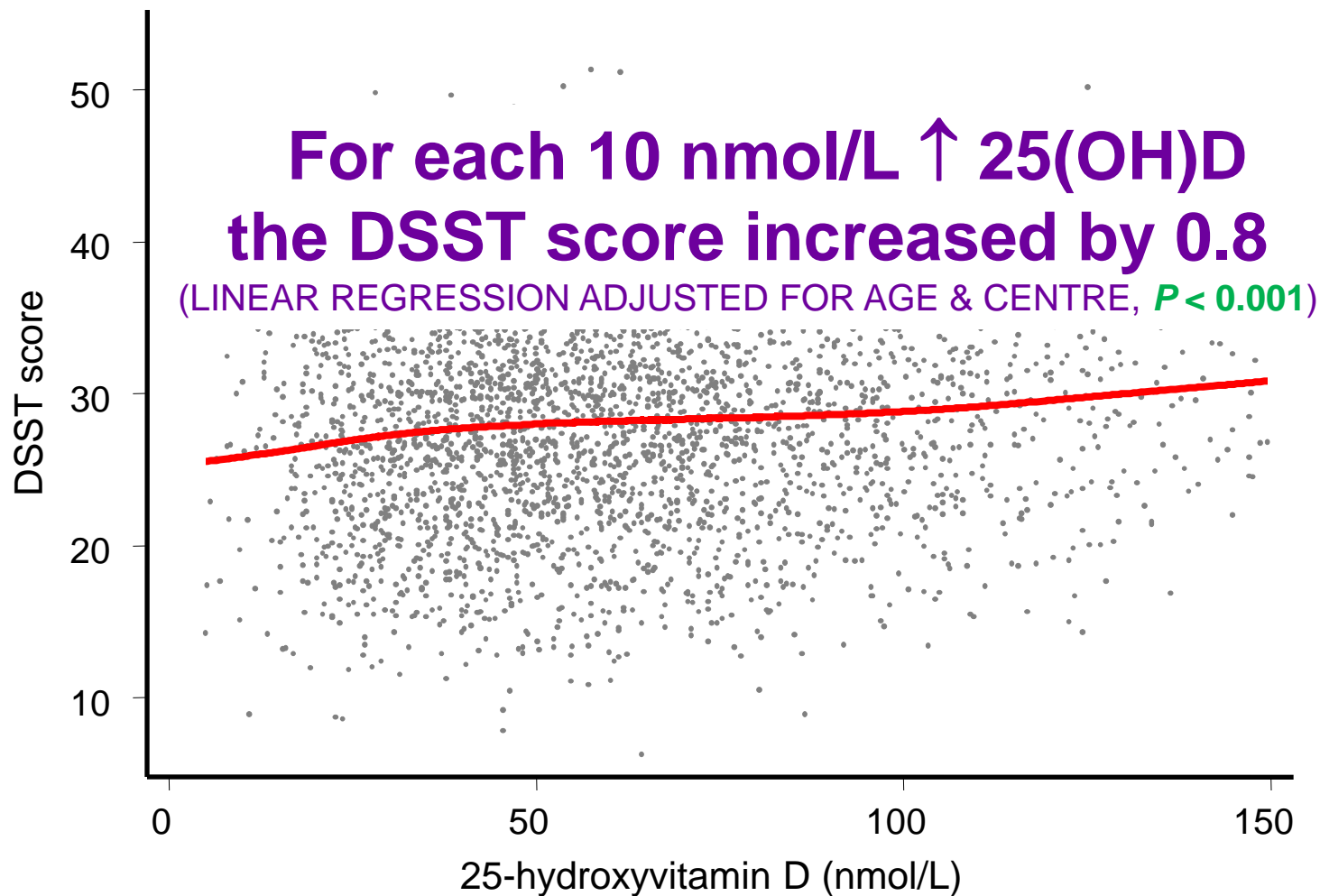
Overall mean score

28 ± 9

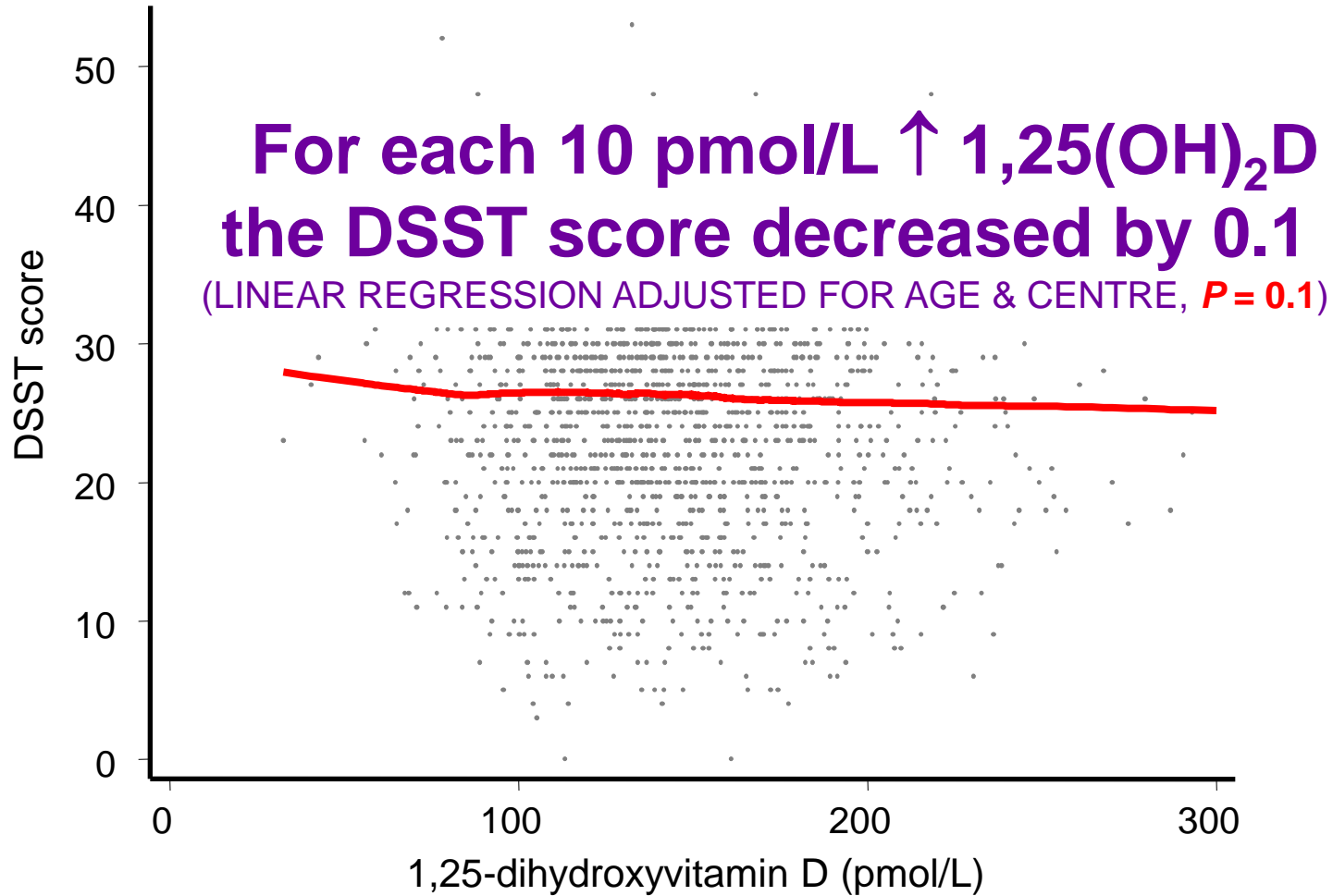
- Digit Symbol Substitution Test

- No ceiling effect
- perceptual speed, visual scanning and memory

Vitamin D and Processing Speed



1,25(OH)₂D and Processing Speed

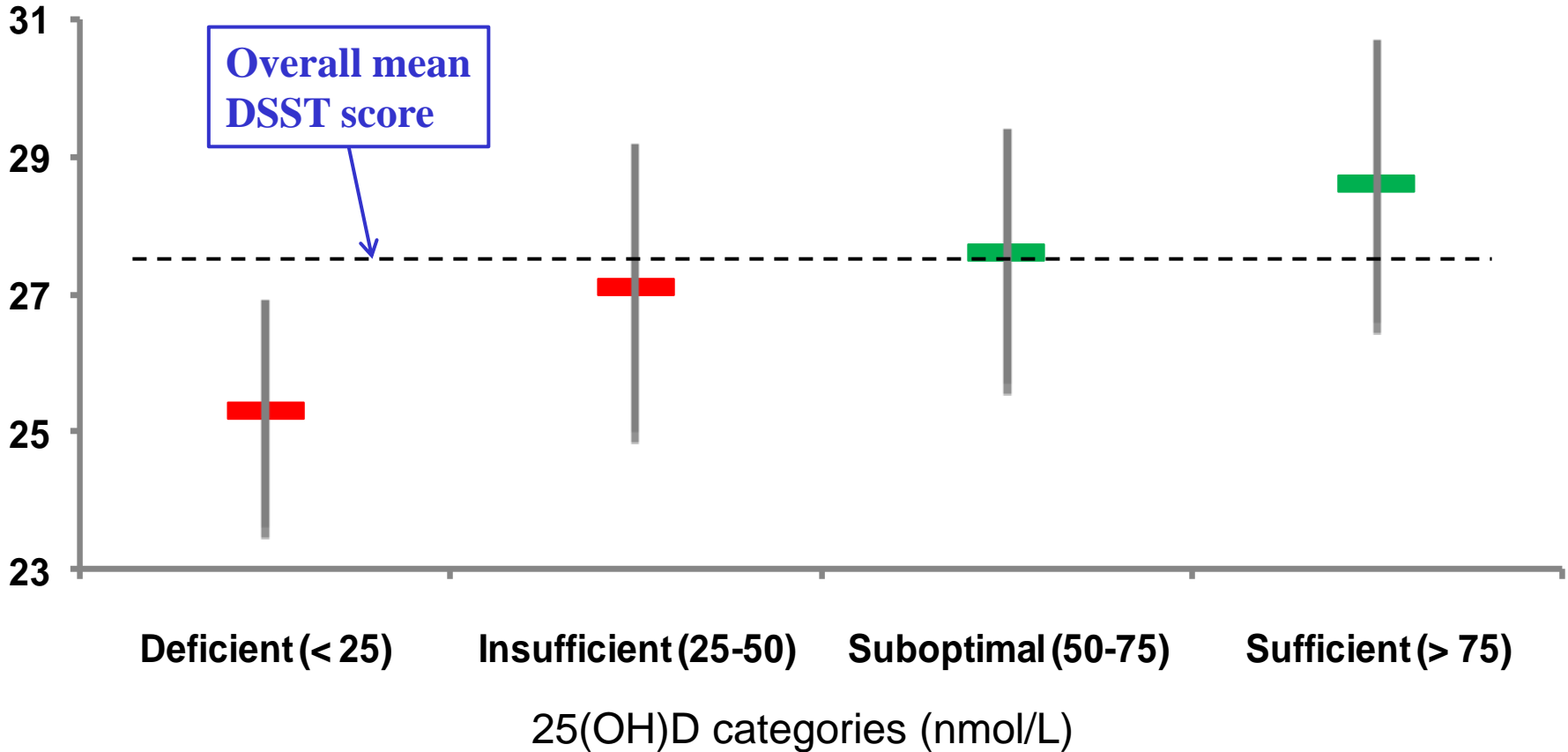


Vitamin D categories ($n = 3,131$)

25(OH)D	Number	(%)	Category
< 25 nmol/L	247	(8)	<i>Deficient</i>
25-49 nmol/L	1028	(33)	<i>Insufficient</i>
50-74 nmol/L	956	(30)	<i>Suboptimal</i>
≥ 75 nmol/L	900	(29)	<i>Sufficient</i>

Vitamin D and Processing Speed

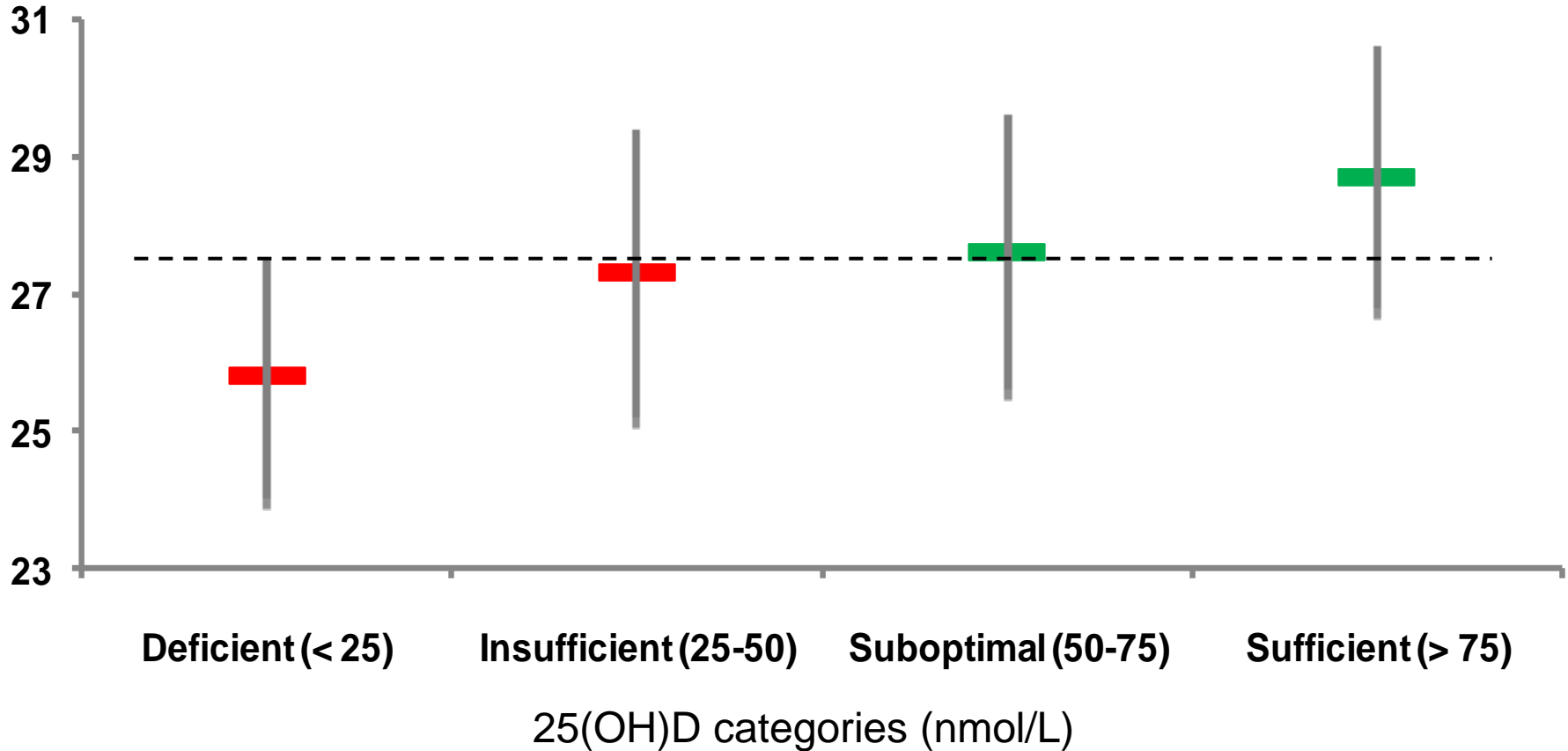
Adjusted mean DSST
score (95% CI)



Adjusted for age & centre

Vitamin D and Processing Speed

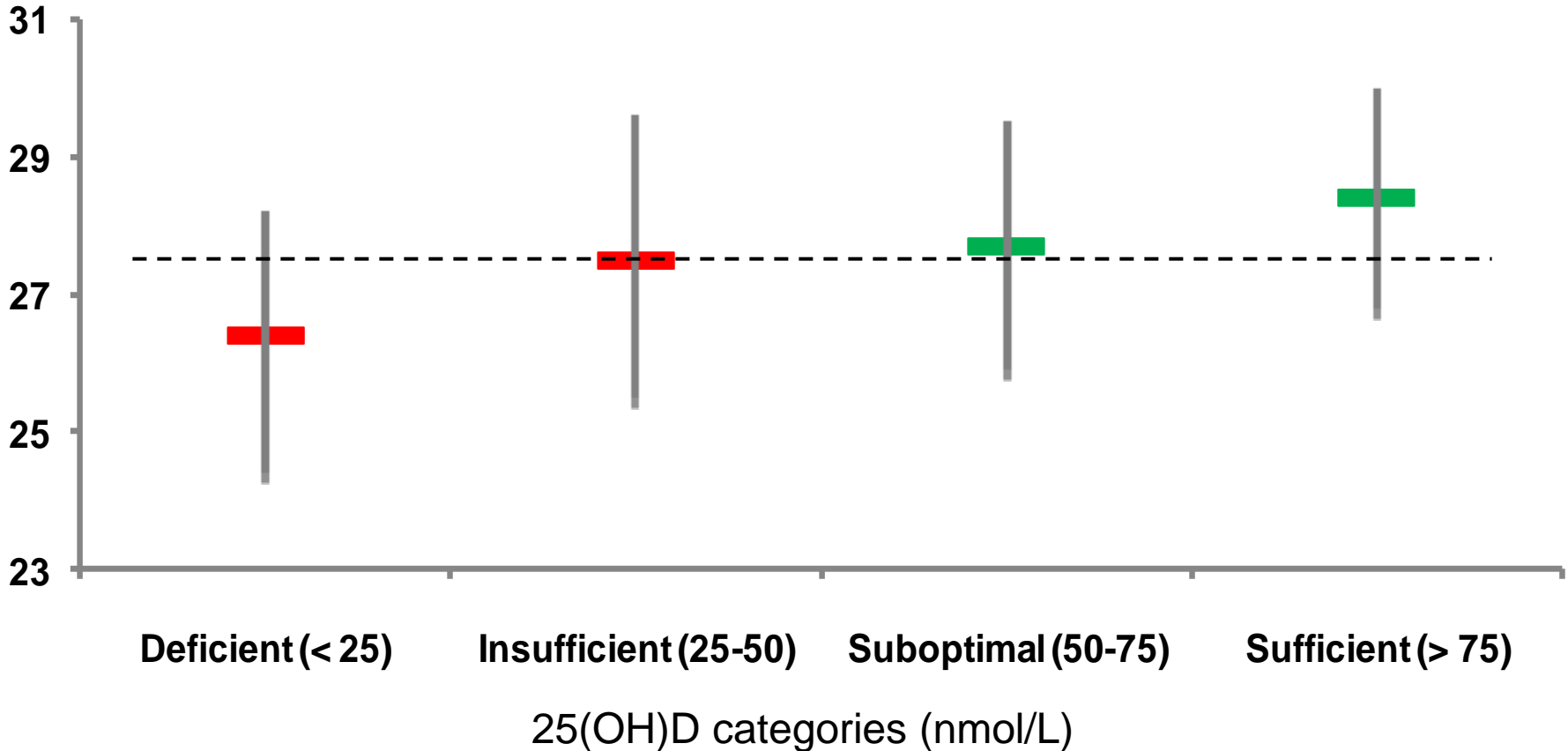
Adjusted mean DSST
score (95% CI)



Adjusted for age, centre, education, depression

Vitamin D and Processing Speed

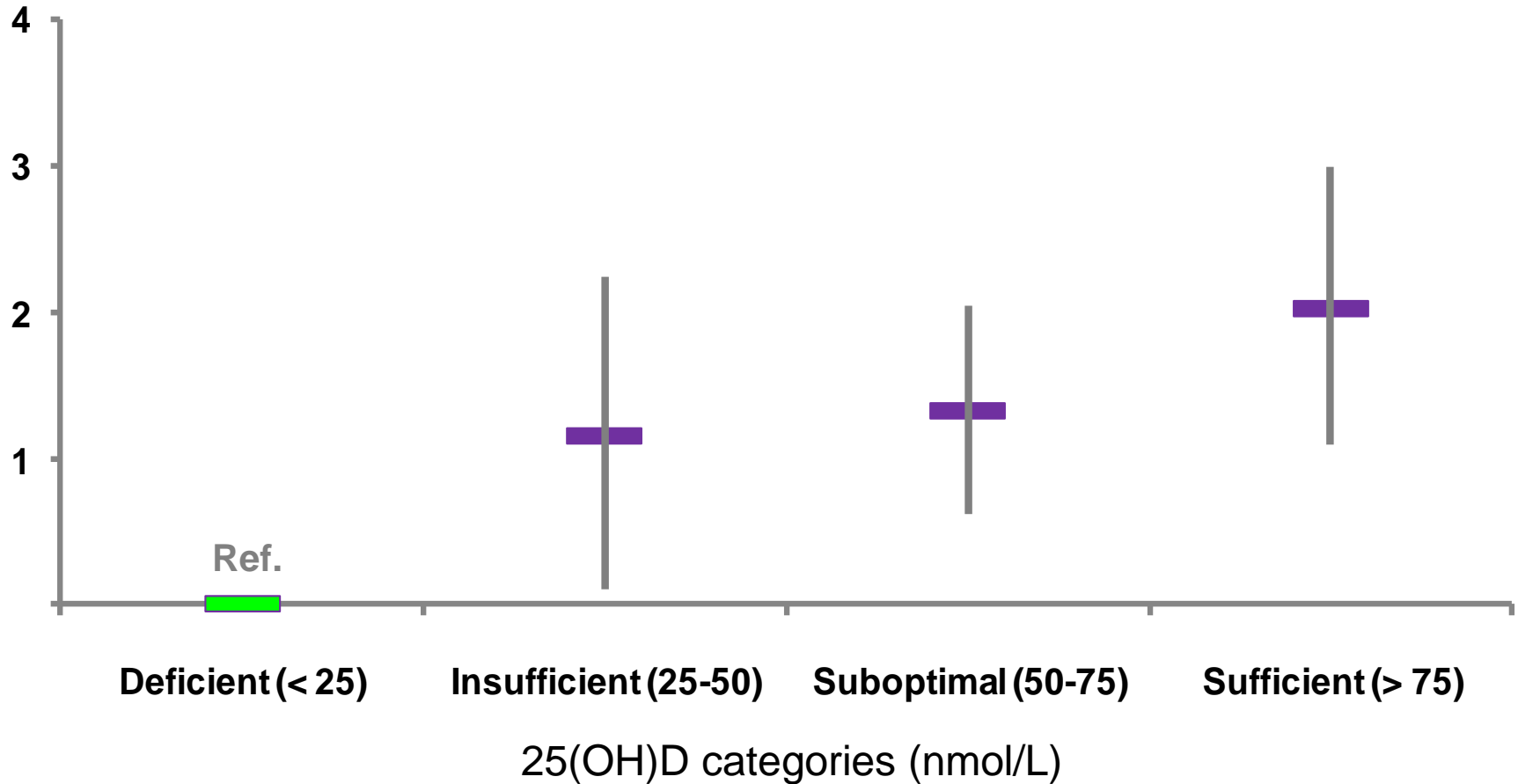
Adjusted mean DSST
score (95% CI)



Adjusted for age, centre, education, depression, smoking, alcohol, morbidities, body mass index, physical activity, season

Vitamin D and Processing Speed

Mean difference in
DSST score (95% CI)

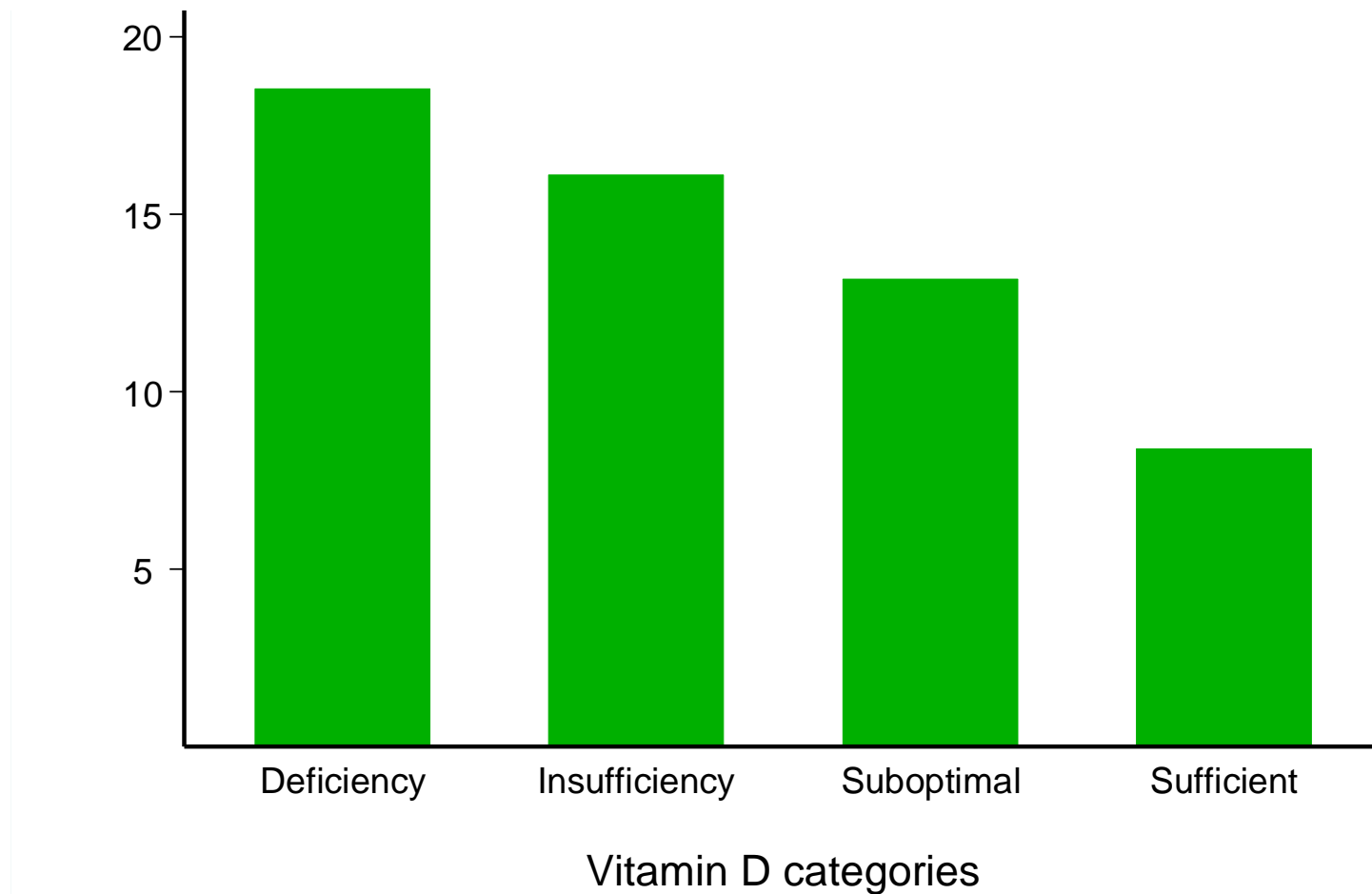


Adjusted for age, centre, education, depression, smoking, alcohol, morbidities, body mass index, physical activity, season

Vitamin D and Depression

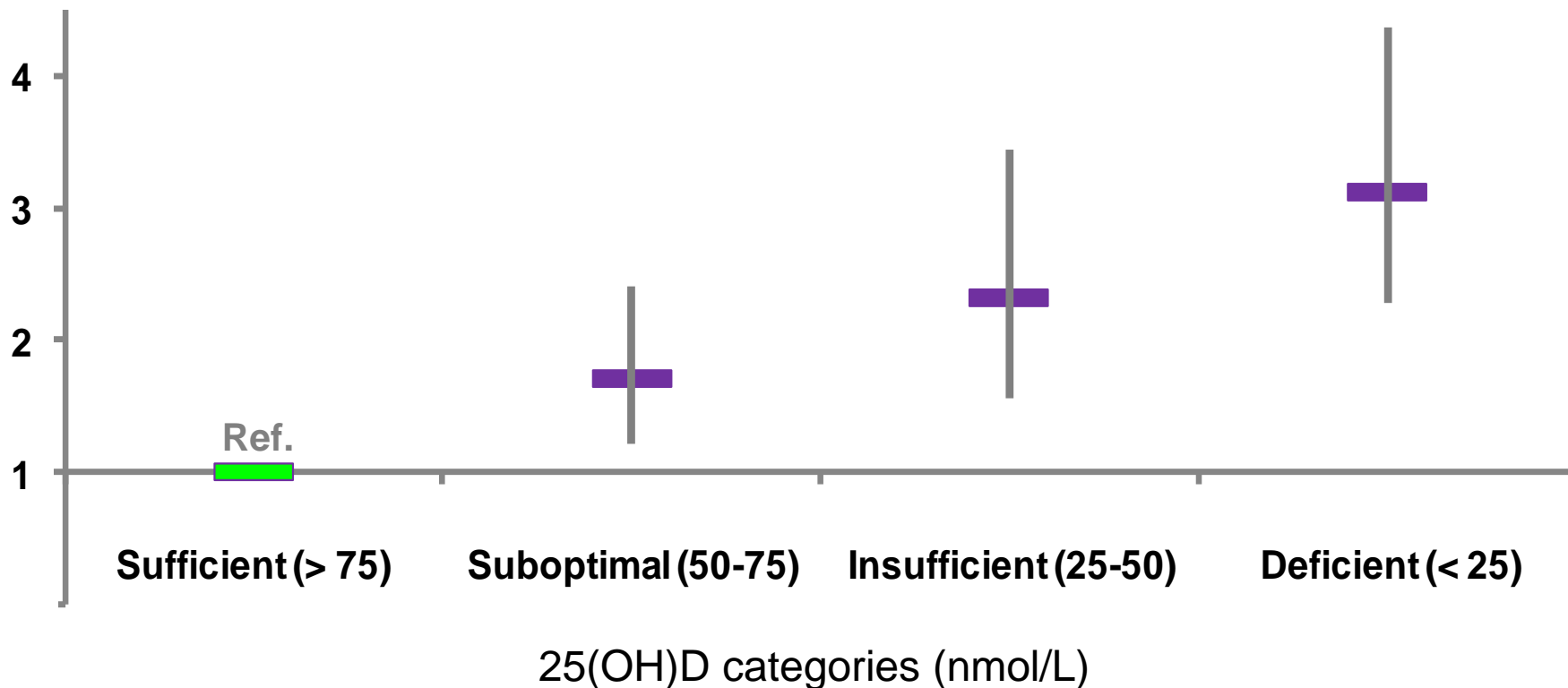
- Beck's Depression Inventory-II (BDI-II)
- Commonly used as a community screening instrument
- Score range of 0-63, higher scores indicate more severe depression
- Cut-off points: 0-13 '*no depression*', 14-63 '*mild to severe depression*'

Vitamin D and Depression



Vitamin D and Depression

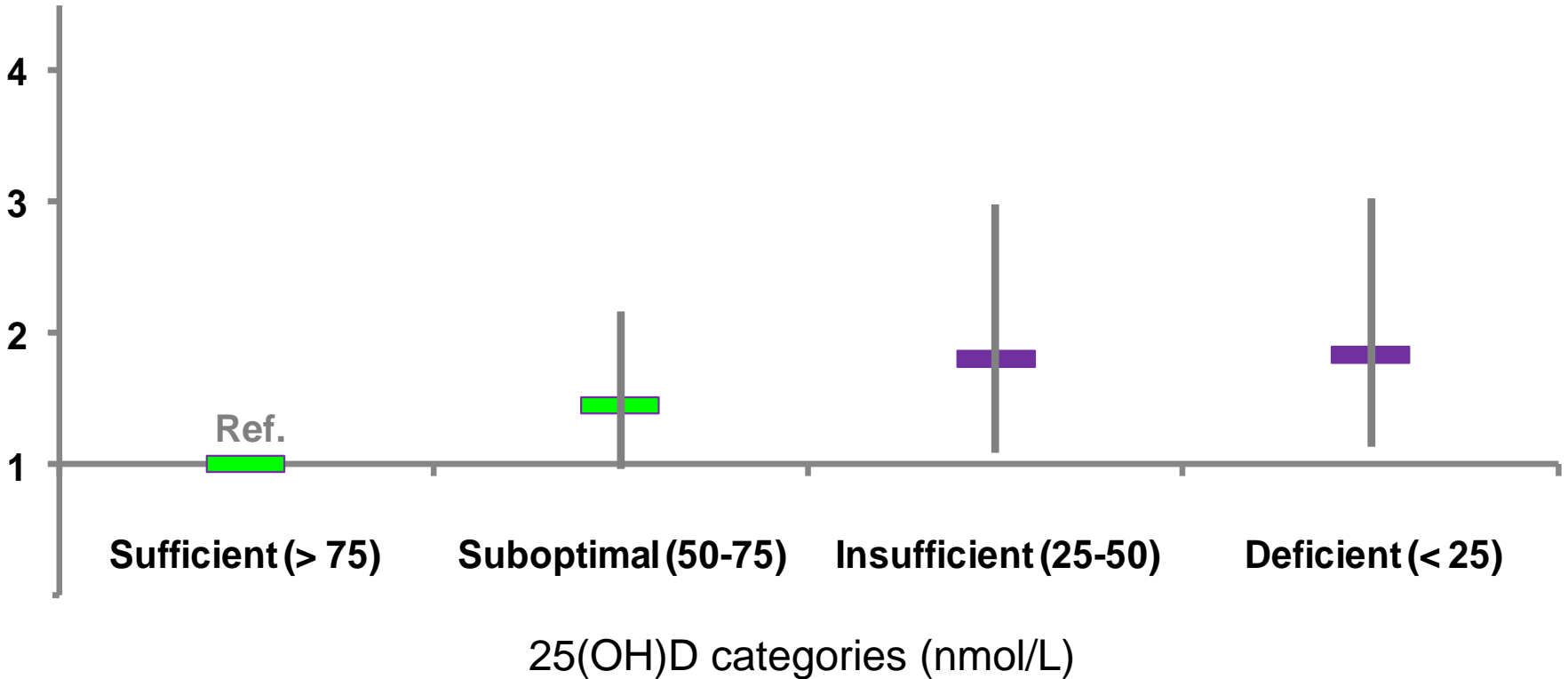
Odds ratio of
depression (95% CI)



Adjusted for age & centre

Vitamin D and Depression

Odds ratio of
depression (95% CI)



Adjusted for age, centre, smoking, alcohol, physical activity, physical function, BMI, morbidities, adverse life events, psychotropic drugs

Methodological limitations

- Measurement of association...
- No information on directionality of relationships...
- Caucasian men...
- Confounding...

Longitudinal data

- Currently very limited...
- InCHIANTI population-based study (858 adults, 65 years and older)
- Assessed cognitive change over 6 years
- Subjects with deficient levels of 25(OH)D were at increased risk of cognitive decline

Randomised clinical trials

- Small numbers; cognition minor outcome
- **VITamin D and OmegA-3 Trial (VITAL)**
- Recruiting 20,000 men and women (60+) – 2,000 IU vitamin D₃ per day for 5 years
- Main outcomes \Rightarrow *incident cancer and cardiovascular disease*
- Information on memory loss & depression

Summary

- Positive association between vitamin D and psychomotor processing speed
- Negative association between vitamin D and likelihood of depression
- Associations remained after adjustment for adverse health & lifestyle factors

Conclusions

- Increasing levels of vitamin D associated with improved psychological health
- Magnitude of effect modest, though may be important at the population level
- Need to investigate vitamin D relationship ‘biological link’ vs. ‘marker of poor health’

Principal Investigators

G Bartfai (Szeged)

F Casanueva (Santiago de Compostela)

G Forti (Florence)

A Giwercman (Malmö)

I Huhtaniemi (Turku)

K Kula (Lodz)

M Punab (Tartu)

F Wu, A Silman (Manchester)

D Vanderscheuren (Leuven)

Expert Advisors

S Boonen (Leuven)

M Lean, J Lara, T Han (Glasgow)

D O'Connor (Leeds)

N Pendleton, G McFarlane, J Adams, E Riley (Manchester)

J McKinlay (Boston)

Co-ordination

J Finn, C Moseley, P Steer (Manchester)

Data Analysis

G Dunn

M Lunt

T O'Neill

A Tajar

S Pye

D Lee

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Vitamin D may be a gain for the brain

Eating fish – long considered ‘brain food’ – may really be good for the old grey matter, as is a healthy dose of sunshine, new research suggests.

University of Manchester scientists, in collaboration with colleagues from other European centres, have shown that higher levels of vitamin D – primarily synthesised in the skin following sun exposure but also found in certain foods such as oily fish – are associated with improved cognitive function in middle-aged and older men.

The study, published in the *Journal of Neurology, Neurosurgery and Psychiatry*, compared the cognitive performance of more than 3,000 men aged 40 to 79 years at eight test centres across Europe.

The researchers found that men with higher levels of vitamin D performed consistently better in a simple and sensitive neuropsychological test that assesses an individual’s short-term memory, attention and speed of information processing.



“Previous studies exploring the relationship between vitamin D and cognitive performance in adults have produced inconsistent findings but we observed a significant, independent association between a slower information processing speed and lower levels of vitamin D,” said lead author Dr David Lee, in Manchester’s School of Translational Medicine.

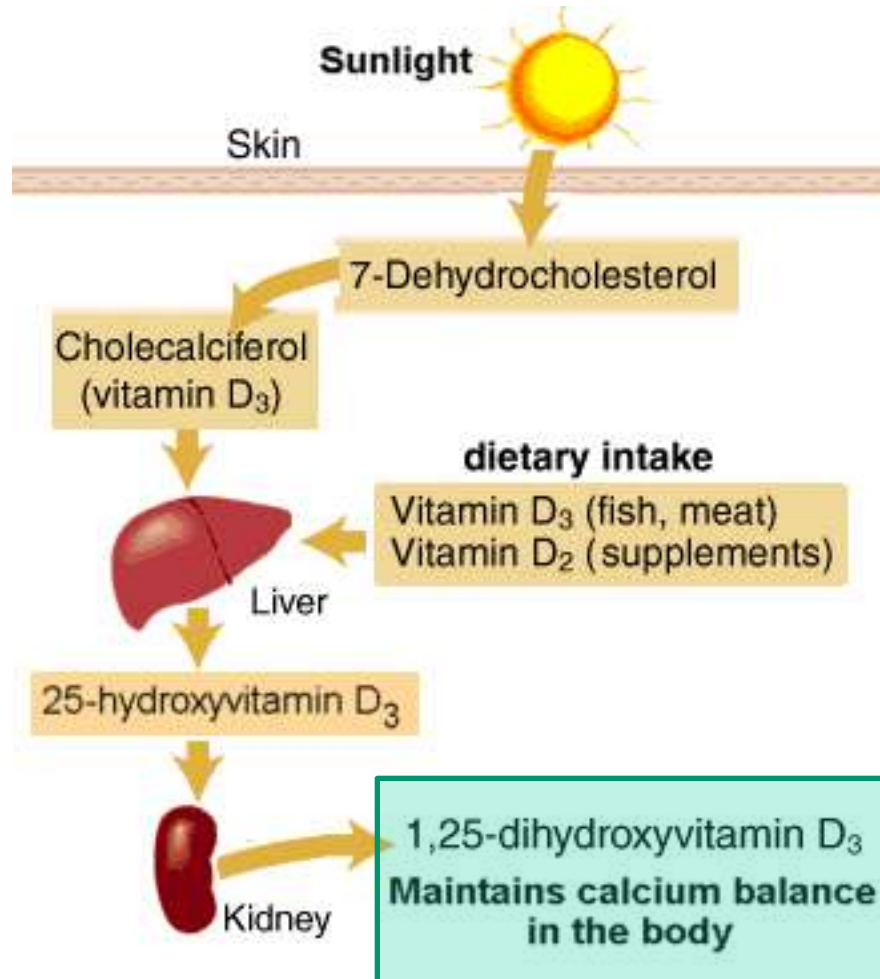
“The main strengths of our study are that it is based on a large population sample and took into account potential interfering

factors, such as depression, season and levels of physical activity.

“Interestingly, the association between increased vitamin D and faster information processing was more significant in men aged over 60 years, although the biological reasons for this remain unclear”.

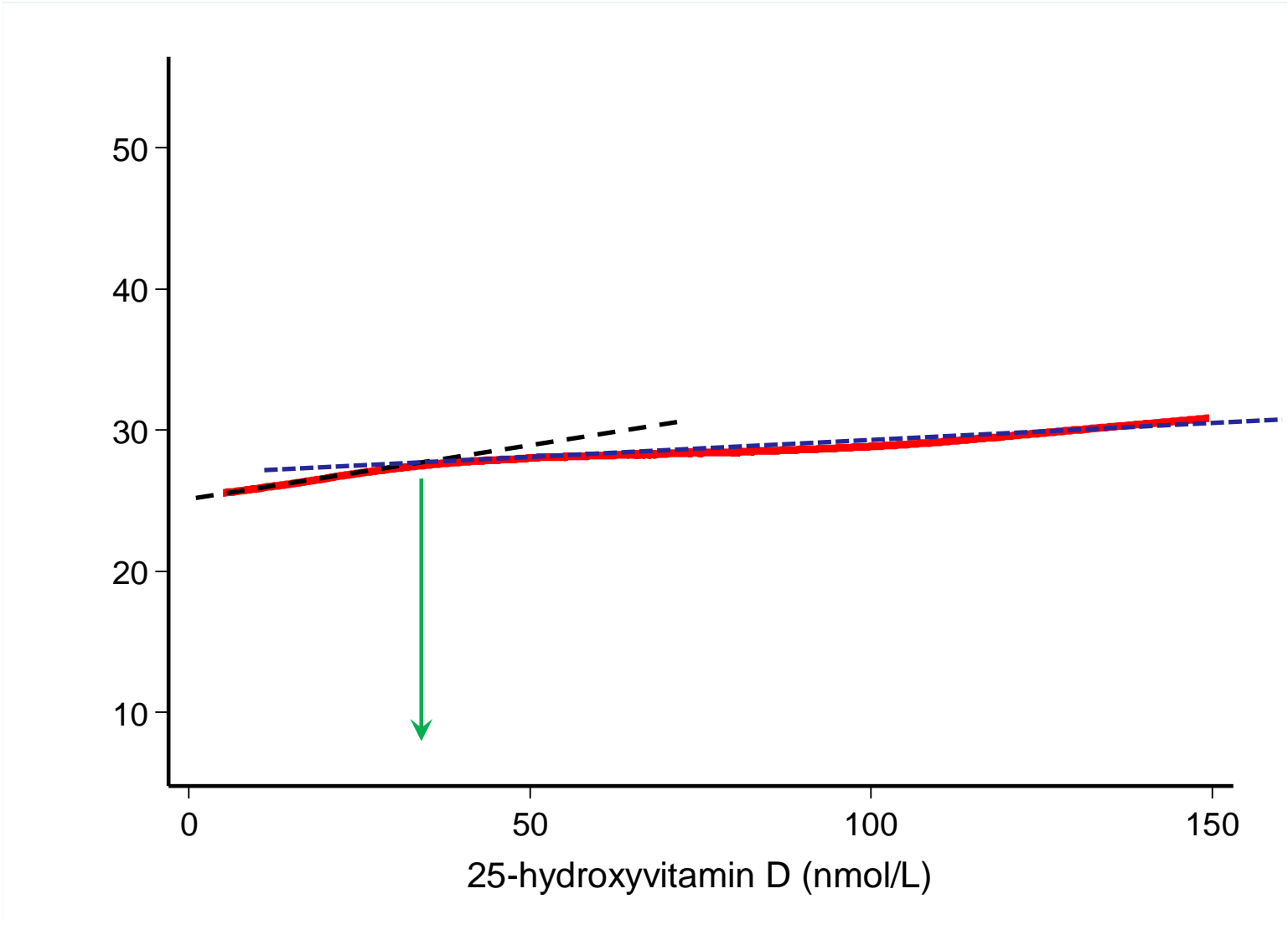
“The positive effects vitamin D appears to have on the brain need to be explored further but certainly raise questions about its potential benefit for minimising ageing-related declines in cognitive performance.”

Vitamin D synthesis



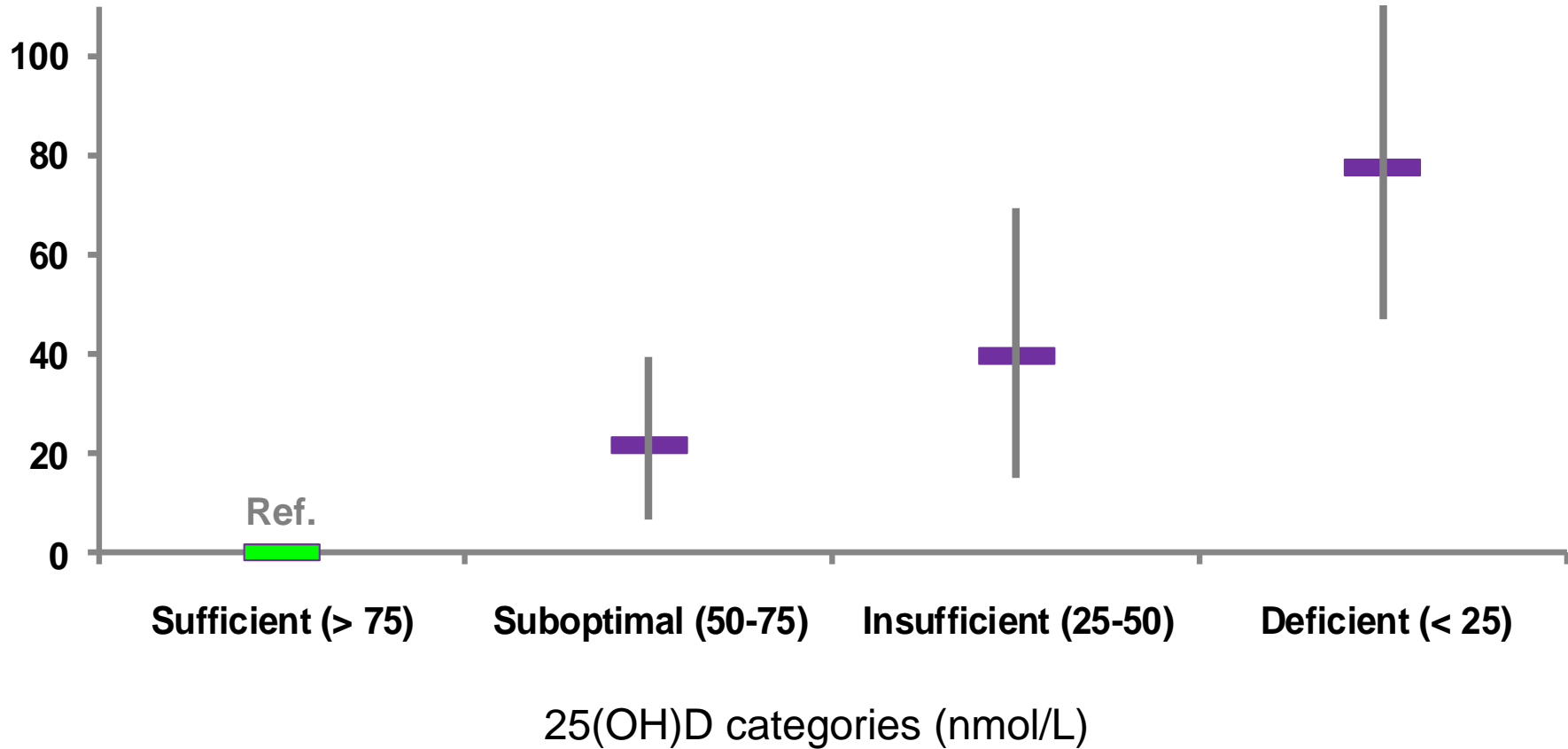
Vitamin D

- Solar UV-B exposure 7-dehydrocholesterol → Vitamin D₃
- Dietary sources of vitamin D are limited
- Vitamin D₃ $\xrightarrow{\text{Vitamin D-25-hydroxylase}}$ 25(OH)D in the liver
- 25(OH)D $\xrightarrow{1\alpha\text{-hydroxylase (CYP27B1)}}$ 1,25(OH)₂D primarily in the kidneys



Vitamin D and Depression

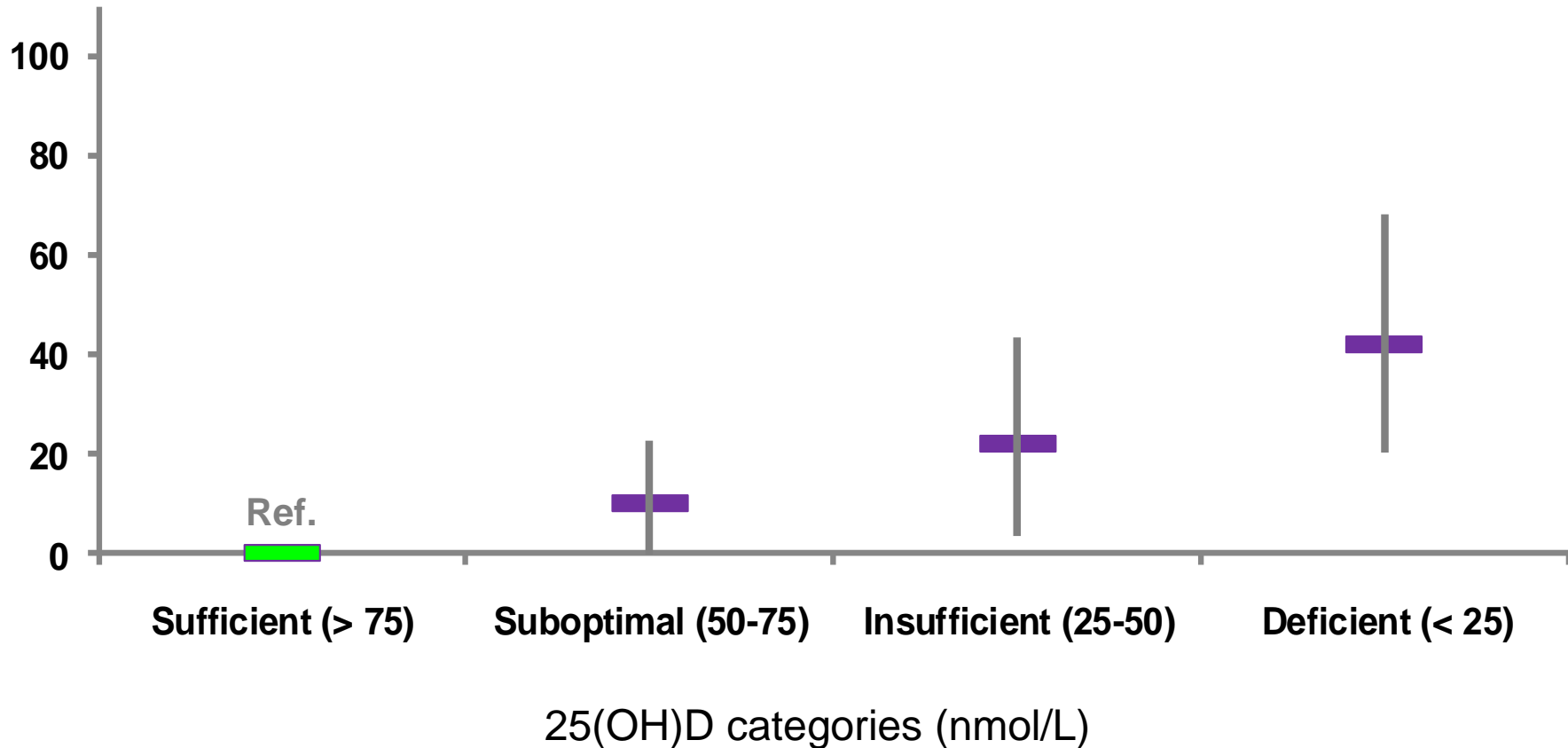
Percentage change in
BDI-II score (95% CI)



Adjusted for age & centre

Vitamin D and Depression

Percentage change in
BDI-II score (95% CI)



Adjusted for age, centre, smoking, alcohol, physical activity, physical function, morbidities, adverse life events, psychotropic drugs