SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara

"Il ruolo della Vit. D nell'anziano"

Dr. Amedeo Zurlo
U.O. Geriatria
Azienda Ospedaliera Universitaria di Ferrara

Convegno "La vitamina D nel soggetto sano e malato" Ferrara 21/5/2016

“ …Una vitamina è una sostanza che rende malati se non la si assume …… Le scoperte consistono nel vedere ciò che tutti hanno visto e nel pensare ciò che nessuno ha pensato…”

Albert Szent-Gyorgyi

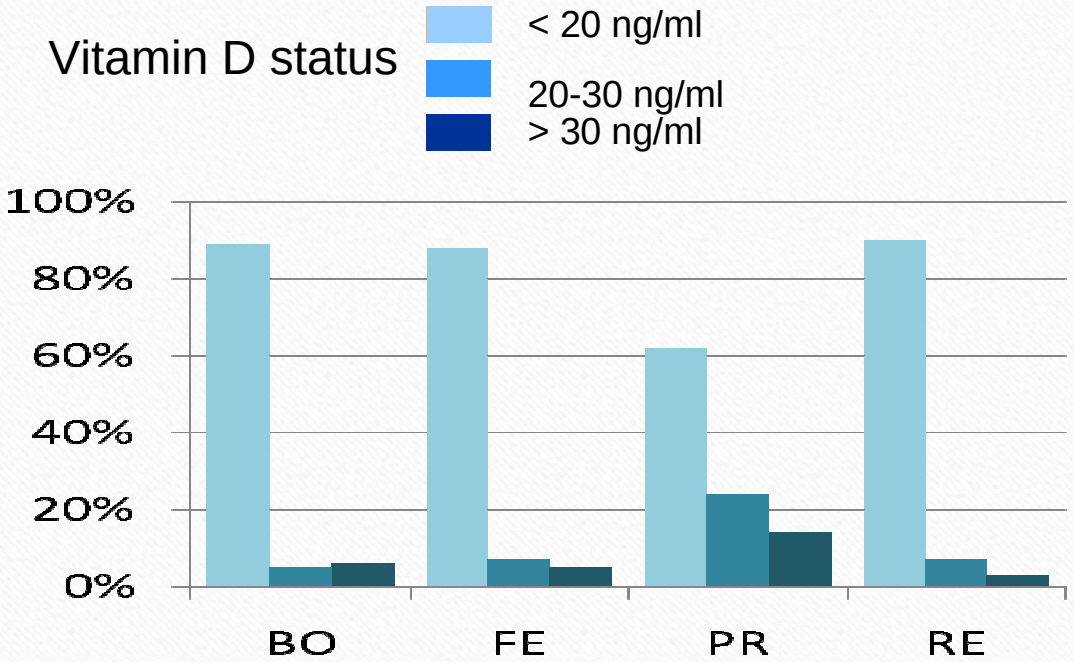
(premio Nobel 1937 per la scoperta della vitamina C)

RegioneEmilia-Romagna

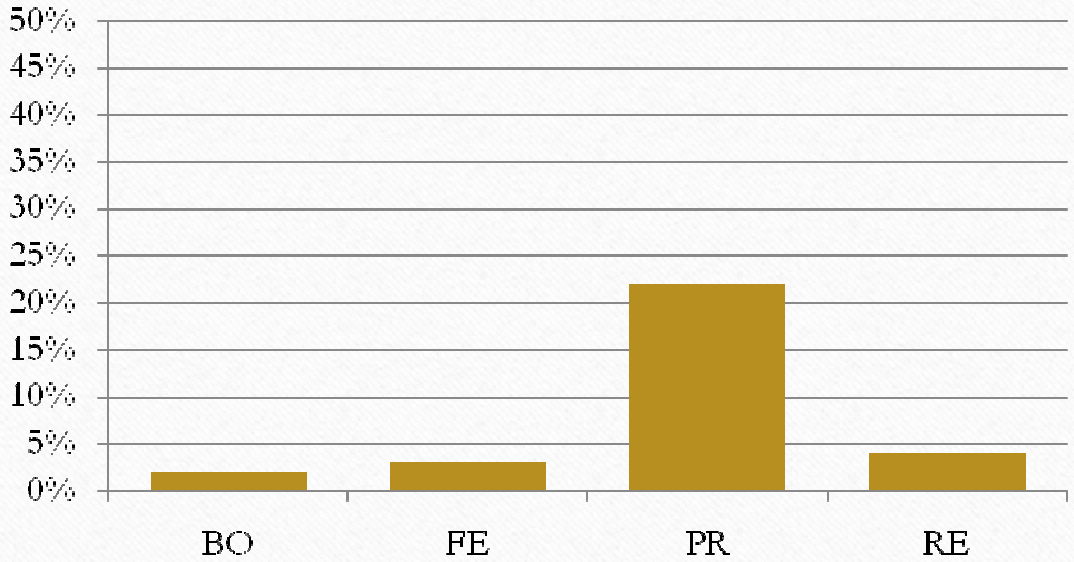
Vitamina D e anziani con frattura di femor

	 BO	 FE	 PR	 RE	ALL (**974 cases, age 85,8 ± 5.6**)	p
25-OH2-(ng/ml)	13,0 ± 8,5	**10,4 ± 9,2**	19,1 ± 9,43	8,7 ± 7,9	**12,2 ± 9,4**	,000
PTH (pg/ml)	94,6 ± 61,2	**94,7 ± 68,24**	80,4 ± 31,0	144 ± 108	**106 ± 80**	,000
Hyper-PTH (%)	52%	**51%**	60%	75%	**60%**	

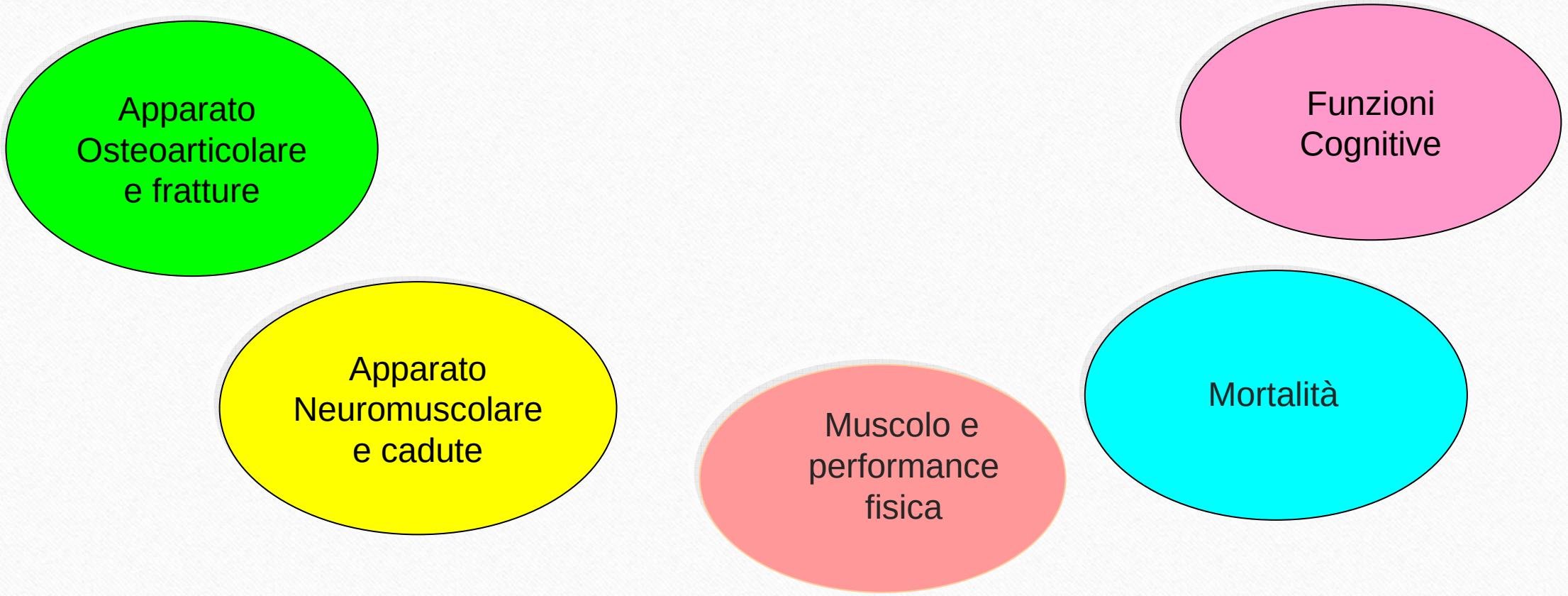
Vitamin D status



Vitamin D supplementation



La Vitamina D nell'anziano



La Vit. D e la prevenzione delle fratture nell'anziano

L'apparato osteoarticolare

Vitamin D and vitamin D analogues for preventing fractures in post-menopausal women and older men (Review)

Avenell A, Mak JCS, O'Connell D

THE COCHRANE COLLABORATION®

here is high quality evidence that vitamin D alone, in the formats and doses tested, is unlikely to be effective in preventing hip fracture
1 trials, 27,693 participants; risk ratio (RR) 1.12, 95% confidence intervals (CI) 0.98 to 1.29) or any new fracture (15 trials, 28,271
rticipants; RR 1.03, 95% CI 0.96 to 1.11).
here is high quality evidence that vitamin D plus calcium results in a small reduction in hip fracture risk (nine trials, 49,853 participants;
R 0.84, 95% confidence interval (CI) 0.74 to 0.96; P value 0.01). In low-risk populations (residents in the community: with an
timated eight hip fractures per 1000 per year), this equates to one fewer hip fracture per 1000 older adults per year (95% CI 0 to 2).
high risk populations (residents in institutions: with an estimated 54 hip fractures per 1000 per year), this equates to nine fewer hip
ctures per 1000 older adults per year (95% CI 2 to 14).
here is high quality evidence that vitamin D plus calcium is associated with a statistically significant reduction in incidence of new
on-vertebral fractures. However, there is only moderate quality evidence of an absence of a statistically significant preventive effect on
inical vertebral fractures. There is high quality evidence that vitamin D plus calcium reduces the risk of any type of fracture (10 trials,
,976 participants; RR 0.95, 95% CI 0.90 to 0.99).

uthors' conclusions

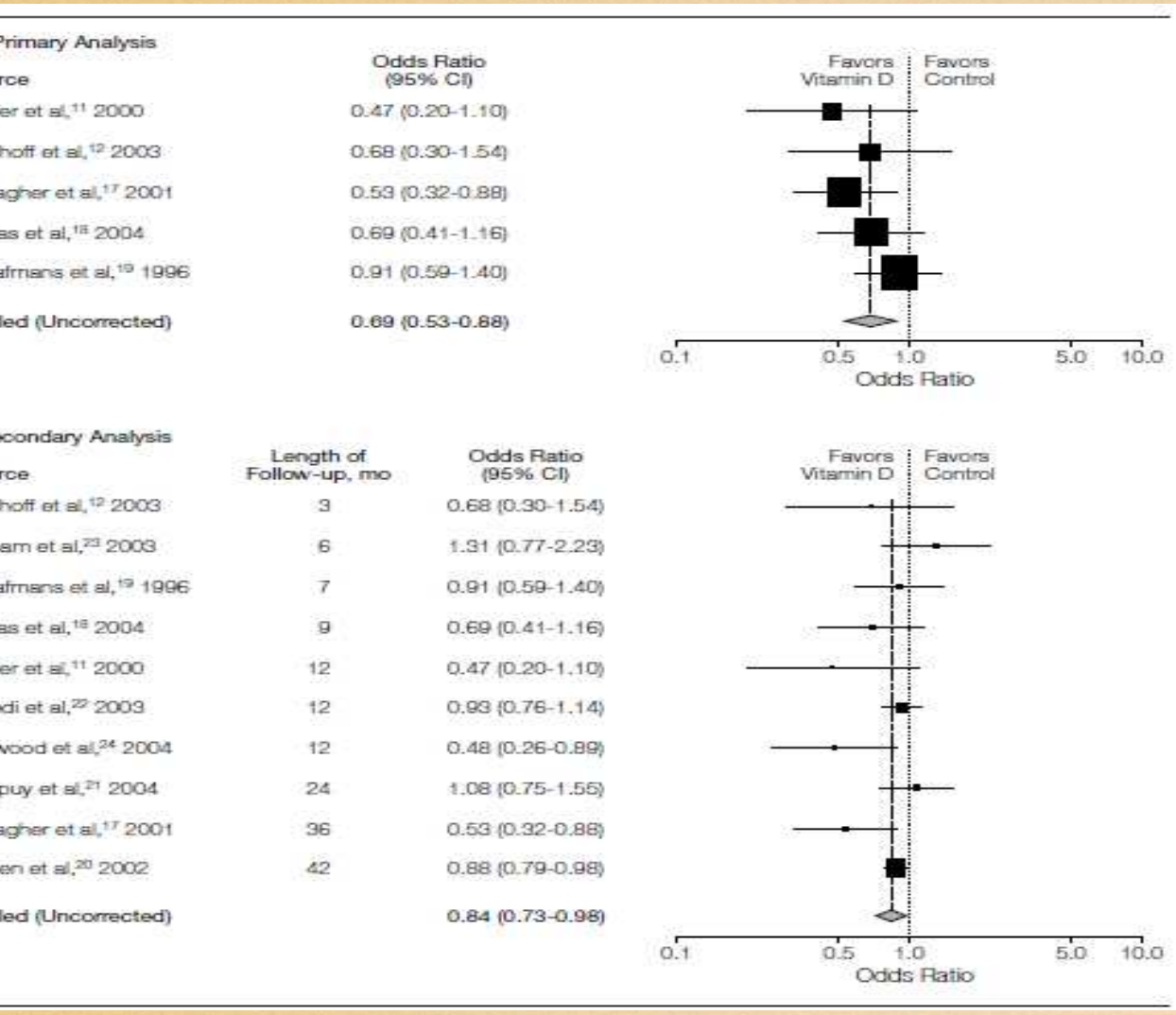
itamin D alone is unlikely to prevent fractures in the doses and formulations tested so far in older people. Supplements of vitamin D
nd calcium may prevent hip or any type of fracture. There was a small but significant increase in gastrointestinal symptoms and renal
isease associated with vitamin D and calcium. This review found that there was no increased risk of death from taking calcium and
itamin D.

La Vit. D e la prevenzione delle cadute nell'anziano

L'efficienza neuromuscolare

Effect of Vitamin D on F
A Meta-analysis

Heike A. Bischoff-Ferrari



Conclusions Vitamin D supplementation appears to reduce the risk of fa ambulatory or institutionalized older individuals with stable health by more t

Further studies examining the effect of alternative types of vitamin D and th the role of calcium supplementation, and effects in men should be conside

pril 28, 2004—Vol 291, No. 16

NICE National Institute for Health and Care Excellence

Falls in older people: assessing risk and prevention

NICE guideline

Vitamin D. There is evidence[1] that vitamin D deficiency and insufficiency are common among older people and that, when present, they impair muscle strength and possibly neuromuscular function, via CNS-mediated pathways. In addition, the use of combined calcium and vitamin D3 supplementation has been found to reduce fracture rates in older people in residential/nursing homes and sheltered accommodation. Although there is emerging evidence[1] that correction of vitamin D deficiency or insufficiency may reduce the propensity for falling, there is uncertainty about the relative contribution to fracture reduction via this mechanism (as opposed to bone mass) and about the dose and route of administration required. No firm recommendation can therefore currently be made on its use for this indication.[2] **[2004, amended 2013]**

nical guideline
olished: 12 June 2013
e.org.uk/guidance/cg161

American Geriatrics Society Consensus Statement:
tamin D for Prevention of Falls and their Consequences in Older Adults 20

- Vitamin D supplements of at least 800 IU per day should be provided to older persons with proven vitamin D deficiency. [A]
- Vitamin D supplements of at least 800 IU per day should be considered for people with suspected vitamin D deficiency or who are otherwise at increased risk for falls. [B]

AGS | THE AMERICAN GERIATRICS SOCIETY
Geriatrics Health Professionals.
Leading change. Improving care for older adults.

La Vit. D e la performance fisica nell'anziano

Il muscolo

ngitudinal Aging Study Amsterdam
Studio prospettico 3 anni
3107 soggetti 55-85 anni

Vitamin D Status Predicts Physical Performance and I Decline in Older Persons

***J Clin Endocrinol Metab* 92: 2058–2065, 2007**

Ilse S. Wich

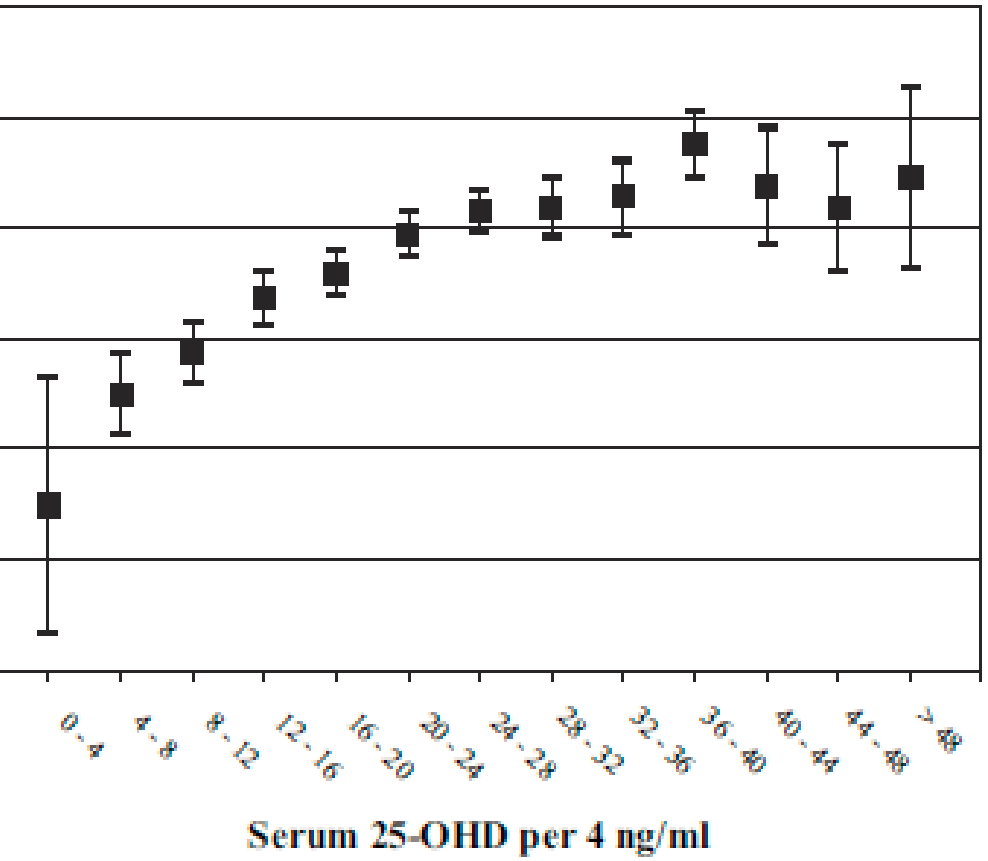


TABLE 3. Results of logistic regression analyses: OR for decline in physical performance after 3 yr according to baseline categories of baseline serum 25-OHD (n = 979)

25-OHD category	Decline in physical performance
<10 ng/ml (n = 89)	2.21 [1.00–4.87]^a
10–20 ng/ml (n = 347)	2.01 [1.06–3.81]^a
20–30 ng/ml (n = 348)	1.56 [0.82–2.97]
≥30 ng/ml (n = 195)	1.0 (reference group)

- **Conclusions:** Serum 25-OH concentrations below 20 ng/ml associated with poorer physical performan and a greater decline in physical performan in older men and women. Because almo 50% of the population had serum 25-OH below 20 ng/ml, public health strateg should be aimed at this group.

Performance fisica derivata dalla somma di 3 test

- walking test
- chair stands
- tandem stand

ew Article

min D: A Review on Its Effects on Muscle Strength, Risk of Fall, and Frailty

Matthieu Halfon, Olivier Phan, and Daniel Teta

BioMed Research International
Volume 2015, Article ID 95324

1,25 vitamin D

10. Conclusion

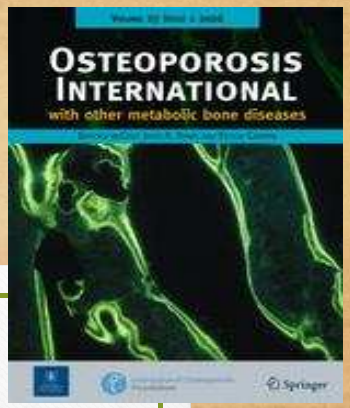
Consistent **relationships exist between vitamin D status and muscle function**, especially in the elderly frail patient.There is evidence that **hypovitaminosis D is associated with a decline in muscle function**. **Vitamin D supplementation has beneficial effects on muscle strength, balance, and gait** in diverse settings including adolescents, the elderly, and CKD patients. However, the effects of vitamin D on the prevention of falls are still a matter of debate due to conflicting interpretation of data…….A low vitamin D status is consistently associated with frailty. Considering that vitamin D supplementation is safe and inexpensive, it is **worthy to recommend vitaminD supplementation in patients at risk for falls, such as elderly patients, nursing home residents, frail patients with gait and balance and visual impairments, and patients with chronic diseases.**These patients are most likely to have low levels of vitamin D and muscle loss/dysfunction, thus **justifying supplementation independent of a putative effect on the prevention of falls.**

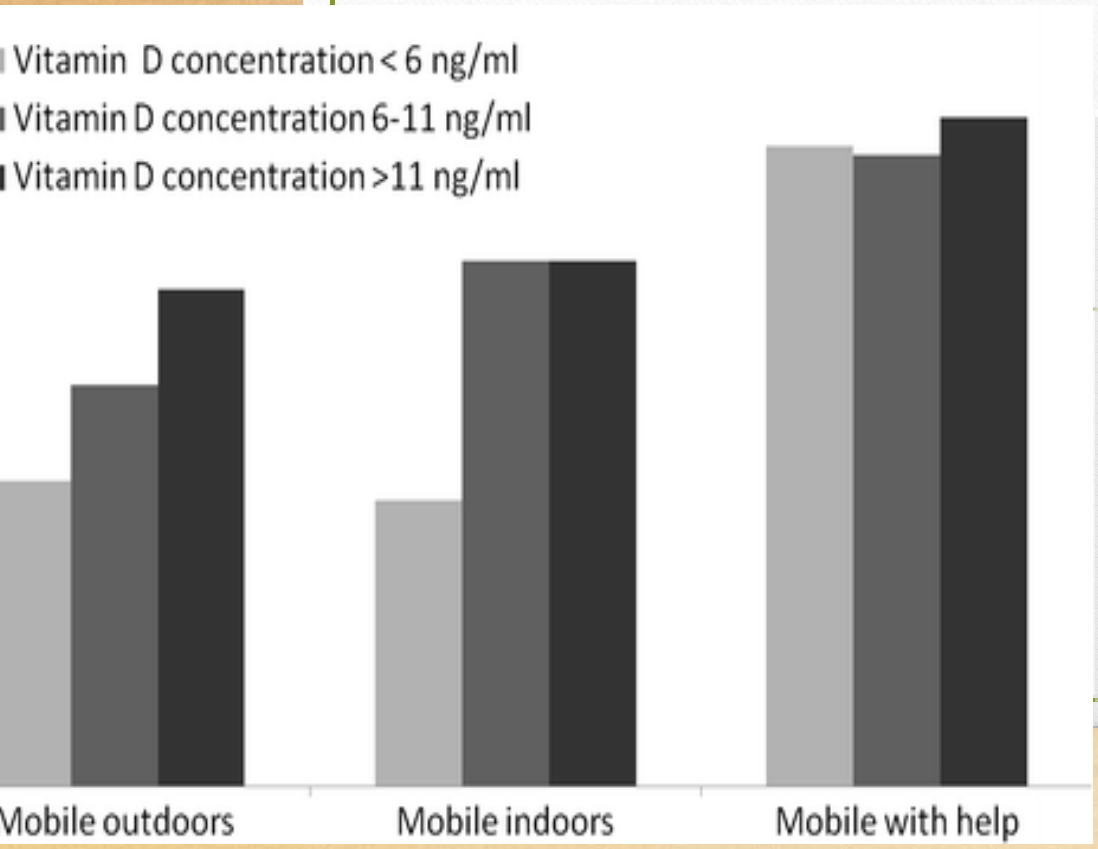
Osteoporos Int
DOI 10.1007/s00198-016-3485-y

ORIGINAL ARTICLE

Modifiable and non-modifiable risk factors affecting walking recovery after hip fracture

G. Pioli[1] · F. Lauretani[2] · F. Pellicciotti[1] · P. Pignedoli[3] · C. Bendini[1] · M. L. Davoli[1] · E. Martini[4] · A. Zagatti[5] · A. Giordano[2] · A. Nardelli[2] · A. Zurlo[5] · D. Bianchini[6] · E. Sabetta[3] · A. Ferrari[1] · C. Tedeschi[6] · M. L. Lunardelli[4]





Walking recovery at sixth month according to the pre-fracture mobility and 25-hydroxyvitamin D tertiles

…. However, patients with 25-hydroxyvitamin D levels hig than 11 ng/ml had a higher probability to recover prefract walking ability. These findings are in accordance with other studies that found 25-hydroxyvitamin D levels at the time of fracture higher than 9 ng/ml were associated w better lower extremity task performance and a reduced likelihood of falling during the year following a hip fracture 25-hydroxyvitamin D deficiency appears to be an importa modifiable component of the global assessment that influe walking recovery, especially in patients with higher pre-frac performance.

Vit. D, iperparatitoidismo secondario e mortalità

ım Parathyroid Hormone Is Associated with eased Mortality Independent of 25-Hydroxy Vitamin atus, Bone Mass, and Renal Function in the Frail Very Old: A Cohort Study

P. N. SAMBROOK,

J Clin Endocrinol Metab 89:5477–5481, 200

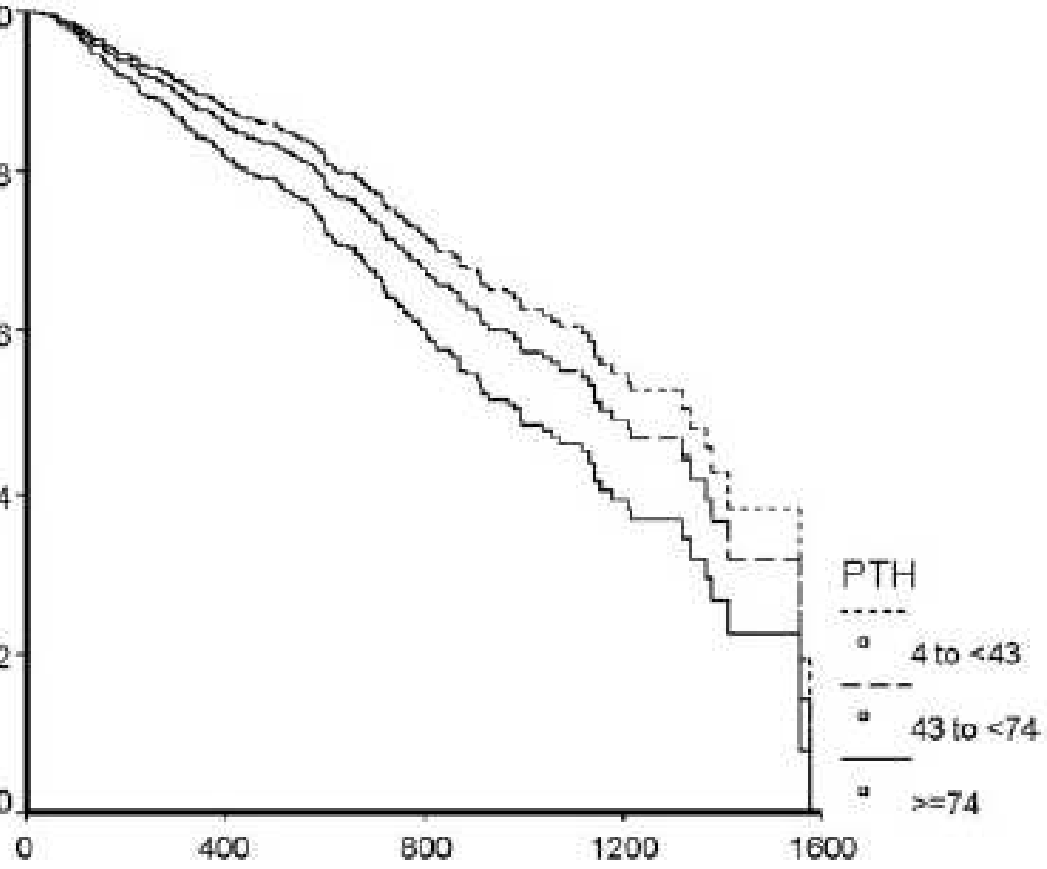


FIG. 1. Survival curve by tertiles of PTH.

862 soggetti etaà media 81,9 anni
FU medio 31 mesi Esclusi pz con IRC

Our findings support the hypothesis that like some rep
in primary hyperparathyroidism, secondary hyperparat
roidism is associated with increased mortality, especi
cardiovascular mortality. Because this effect appears ir
pendent of vitamin D status, renal function, bone mass,
comorbidities, its mechanisms require further investigat

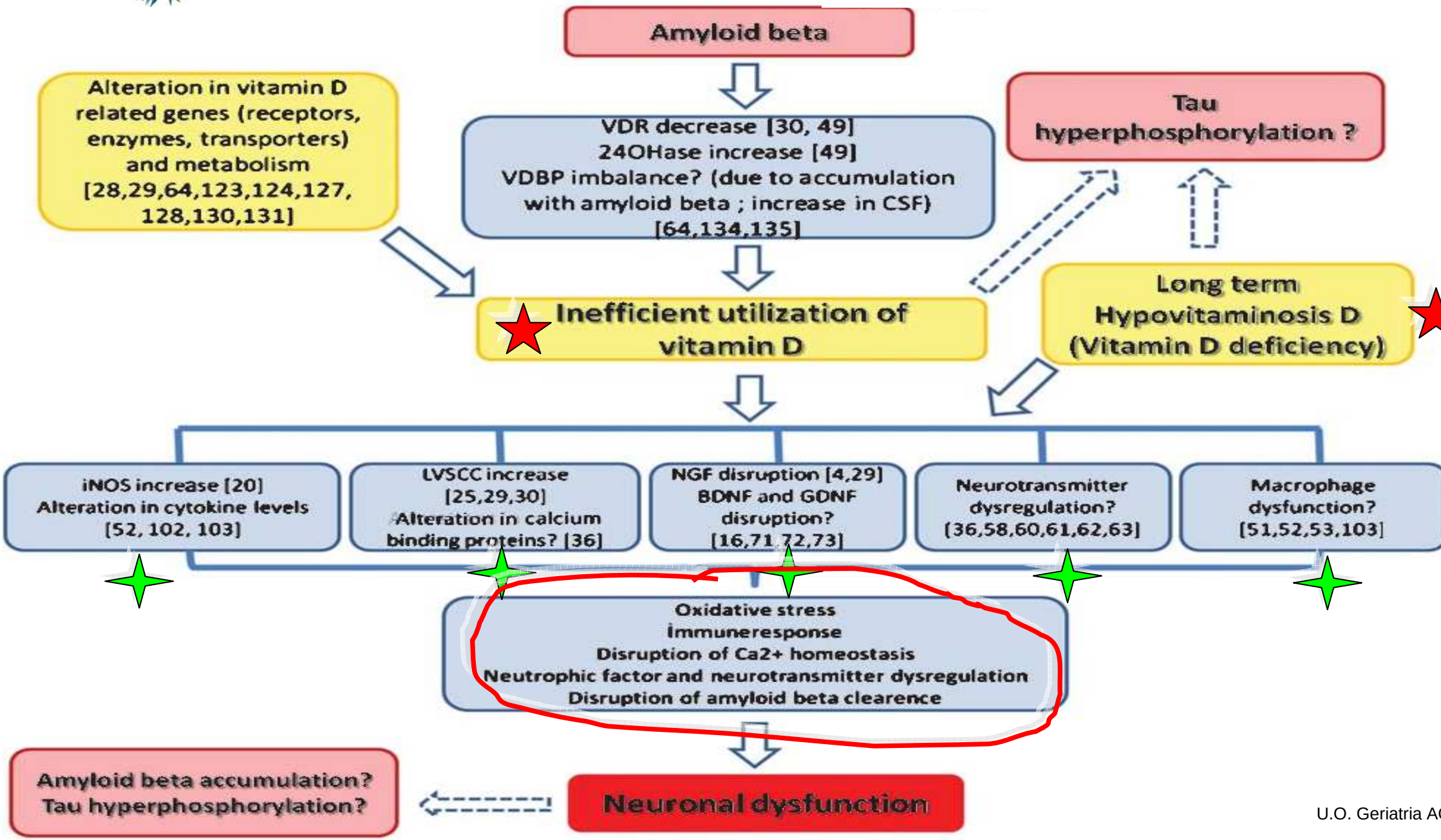
Vitamina D e processi cognitivi

Una D-menza ?

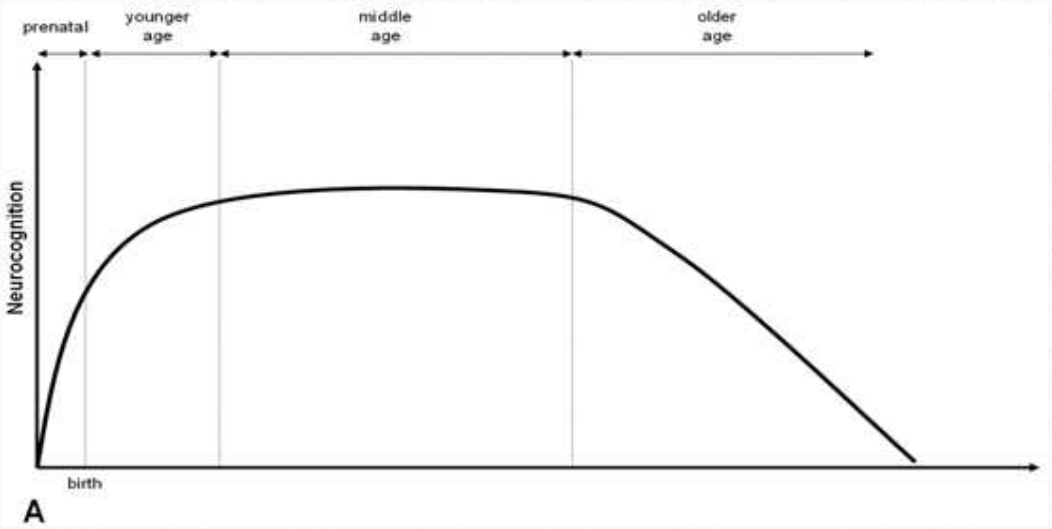
Le evidenze neurobiologiche

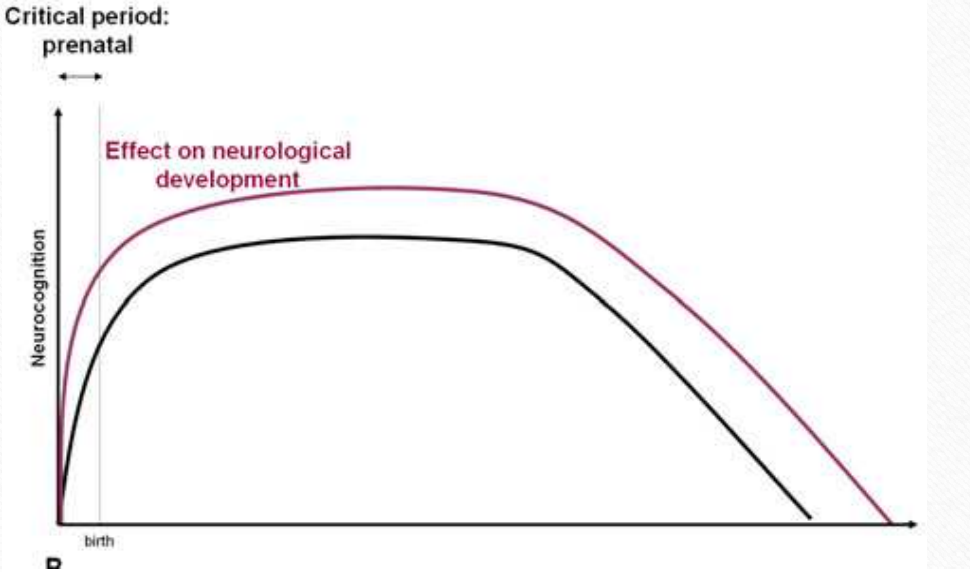
VITAMINA D → ORMONE NEUROSTEROIDE

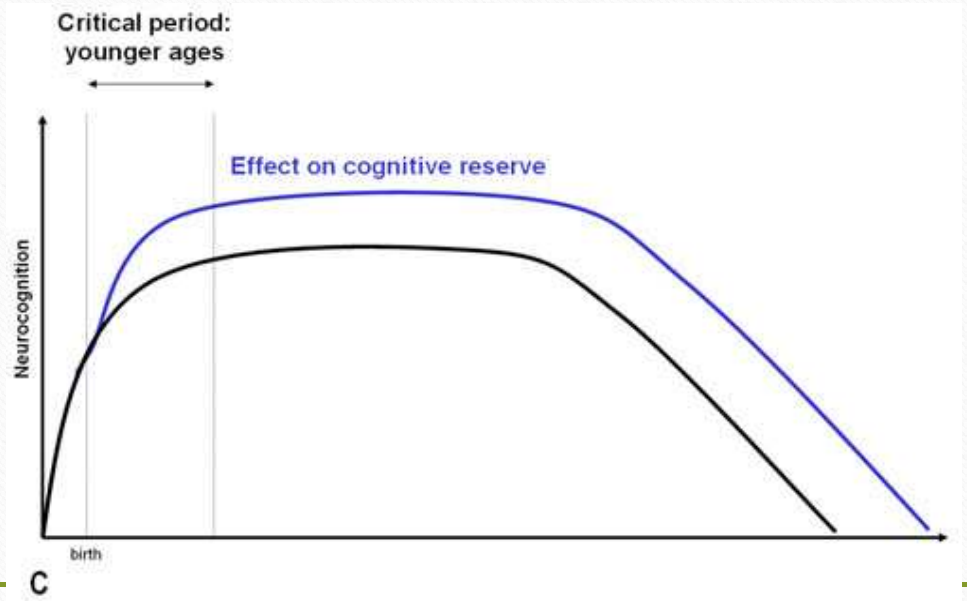
Sviluppo sinaptico, migrazione e crescita neurale	Segnale intraneuronale del calcio
Neurotrasmissione, eccitatoria e inibitoria	Attività antiossidante
Prevezione eccessiva proliferazione cellulare	Controllo espressione di geni coinvolti nella struttura e metabolismo cellulare
Induzione differenziazione cellulare, specie cellule immunologiche	Regolazione del glutatione
Espressione del NGF	Protezione tossicità glutamatergica
Regolazione citochine infiammatorie	Stimolazione fagocitosi beta-amiloide da macrofagi

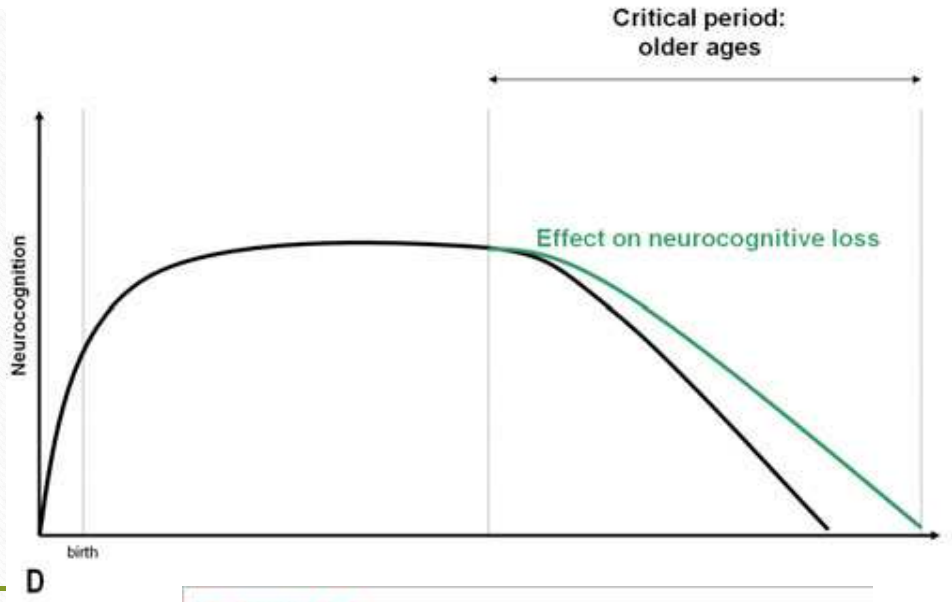

Amyloid beta
Alteration in vitamin D related genes (receptors, enzymes, transporters) and metabolism [28,29,64,123,124,127, 128,130,131]
VDR decrease [30, 49]
24OHase increase [49]
VDBP imbalance? (due to accumulation with amyloid beta ; increase in CSF) [64,134,135]
Tau hyperphosphorylation ?
Inefficient utilization of vitamin D
Long term Hypovitaminosis D (Vitamin D deficiency)
iNOS increase [20]
Alteration in cytokine levels [52, 102, 103]
LVSCC increase [25,29,30]
Alteration in calcium binding proteins? [36]
NGF disruption [4,29]
BDNF and GDNF disruption? [16,71,72,73]
Neurotransmitter dysregulation? [36,58,60,61,62,63]
Macrophage dysfunction? [51,52,53,103]
Oxidative stress
Immuneresponse
Disruption of Ca2+ homeostasis
Neutrophic factor and neurotransmitter dysregulation
Disruption of amyloid beta clearence
Amyloid beta accumulation?
Tau hyperphosphorylation?
Neuronal dysfunction

VIT. D E SVILUPPO/DEGRADO DEI SISTEMI COGNITIVI: L'IPOTESI DEL "PERIODO CRITICO"









Vitamina D e processi cognitivi

I dati osservazionali e le linee di indirizzo

LE EVIDENZE: GLI STUDI DI POPOLAZIONE 1

ore	Casistica	Titolo	Anno	Fonte
uell et	Cross-sectional 1.080	Vitamin D Is Associated With Cognitive Function in Elders Receiving Home Health Services	2009	The Journals of gerontology series a
Lee	Coess-sectional 3.369	Association between 25-hydroxyvitamin D levels and cognitive performance in middle-aged and older European men	2009	Journal of NEUROLOGY, NEUROSURGERY & PSYCHIATRY
ellyn	Population-based study 7.998	Serum 25-Hydroxyvitamin D Concentration and Cognitive Impairment	2009	Journal of Geriatric Psychiatry and Neurology
linin	Cross-sectional 1.604	25-Hydroxyvitamin D levels and cognitive performance and decline in elderly men	2010	AMERICAN ACADEM NEUROLO
weiler	Cross-sectional 5.596	Dietary intake of vitamin D and cognition in older women	2010	AMERICAN ACADEMY NEUROLOG
uell et	Cross-sectional 318	25-Hydroxyvitamin D, dementia, and cerebrovascular pathology in elders receiving home services	2010	AMERICAN ACADEM NEUROLOG

LE EVIDENZE: GLI STUDI DI POPOLAZIONE 2

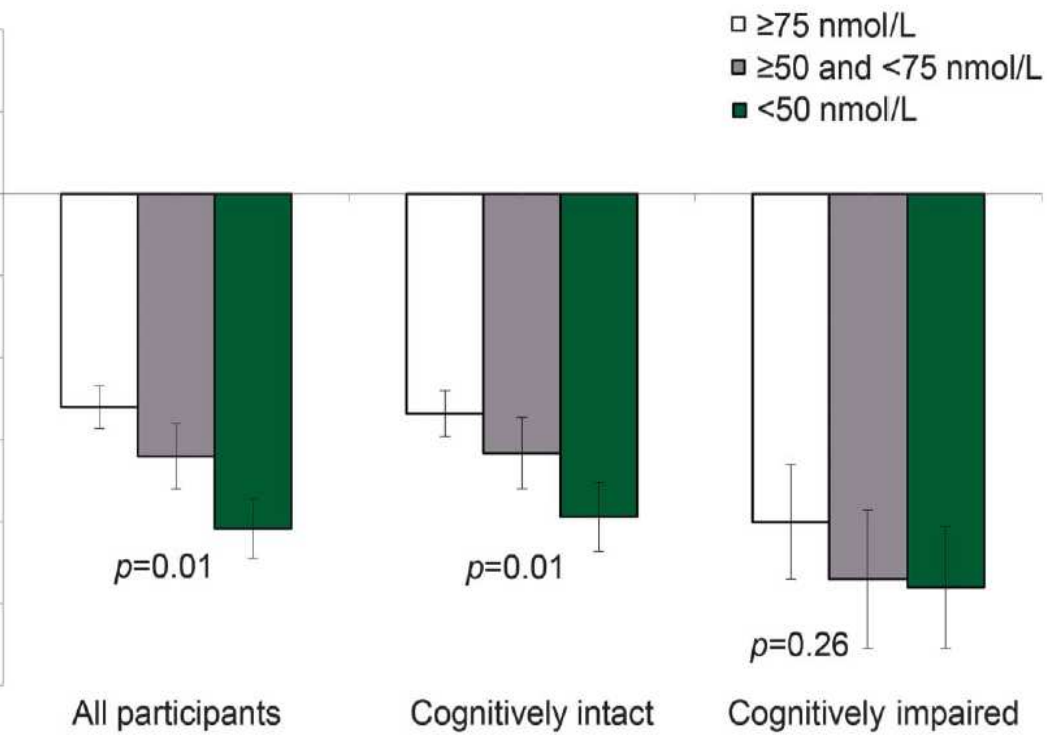
utore	Casistica	Titolo	Anno	Fonte
. ewellyn	Prospective population based study **858 pt.**	**Vitamin D and Risk of Cognitive Decline in Elderly Persons**	2010	ARCHIVES OF INTERNAL MEDIC
nnweiler	Cross-sectional **752**	**Association of vitamin D deficiency with cognitive impairment in older women**	2010	AMERICAN ACADE NEUROLO
Balion	Meta-analysis **> 50.000**	**Vitamin D, cognition, and dementia**	2012	AMERICAN ACADE NEUROLO
Slinin	Cross-sectional **6.257**	**Association Between Serum 25(OH) Vitamin D and the Risk of Cognitive Decline in Older Women**	2012	the Journals of gerontology
J. ttlejohns	Proscpective population-based study **1.658**	**Vitamin D and the risk of dementia and Alzheimer disease**	2014	AMERICAN ACADEM NEUROLO
Knekt	Proscpective population-based study **5010**	**Serum 25-Hydroxyvitamin D Concentration and Risk of Dementia**	Nov. 2014	EPIDEMIOLOGY

Vitamin D deficiency predicts cognitive decline in older men and women

The Pro.V.A. Study

Toffanello E.D., Crepaldi G., Manzato E., Sergi G. et al.

Changes in MMSE scores over the follow-up according to 25OHD levels



Objective: To test the hypothesis that hypovitaminosis D is associated with a higher risk nitive decline over a 4.4-year follow-up in a large sample of older adults.

Methods: This research was part of the *Progetto Veneto Anziani* (Pro.V.A.), an Italian pop based cohort study of 1,927 elderly subjects. Serum 25-hydroxyvitamin D (25OHD) lev measured at the baseline. Global cognitive function was measured with the Mini-Ment Examination (MMSE); scores lower than 24 were indicative of cognitive dysfunction, and a of 3 or more points on the MMSE over the follow-up was considered as clinically sig Analyses were adjusted for relevant confounders, including health and performance sta

Results: Participants with 25OHD deficiency (<50 nmol/L) or insufficiency (50–75 nmo more likely to have declining MMSE scores during the follow-up than those who were sufficient (≥75 nmol/L). Among participants cognitively intact (baseline MMSE scores ≥ without diagnosis of dementia), the multivariate adjusted relative risk (95% confidence [CI]) of the onset of cognitive dysfunction was 1.36 (95% CI: 1.04–1.80; $p = 0.02$) for th vitamin D deficiency and 1.29 (95% CI: 1.00–1.76; $p = 0.05$) for those with vitamin D ciency by comparison with individuals with normal 25OHD levels.

Conclusion: The results of our study support an independent association between low levels and cognitive decline in elderly individuals. In cognitively intact elderly subjects, levels below 75 nmol/L are already predictive of global cognitive dysfunction at 4.

Neurology® 2014;83:2292-2298

AMERICAN ACADEMY OF NEUROLOGY®

Vitamin D and the risk of dementia and Alzheimer disease T.J. Littlejohns et al. *Neurology August 2014; 83:1-9*

" …Conclusioni: I risultati confermano che

la carenza di vit.D è associata a un rischio sostanzialmente aumentato di demenza per tutte le cause e per AD.

Ciò si aggiunge al dibattito in corso

circa il ruolo della vit. D in alterazioni organiche non scheletriche…"

Take Home Messages

- Una situazione di **carenza** di livelli di vit: D (< 20 nmol/l) nell'anziano è particolarmente frequente, specie oltre gli 80 aa. e in condizioni di fragilità o disabilità (> 80%).
- La supplementazione di vitamina D in associazione al calcio nei soggetti carenti è correlata ad una **riduzione del rischio di frattura** nell'anziano (prevenzione primaria)
- La supplementazione di Calcio e Vitamina D (insieme alla terapia antiriassorbitiva/anabolica) è indicata in tutti i casi di **prevenzione secondaria** delle fratture da fragilità nell'anziano
- La **performance fisica** nell'anziano in termini di efficienza muscolare appare in stretta relazione con i livelli corporei di vitamina D
- Esistono dati contrastanti in merito all'effetto della carenza di Vit. D di incrementare in assoluto (di per se) **il rischio di caduta** nell'anziano; probabilmente tale effetto è più consistente nelle **popolazioni di anziani a rischio** (pazienti più anziani, soggetti con instabilità posturale, soggetti sarcopenici, pazienti istituzionalizzati, pazienti affetti da patologie croniche) in cui la supplementazione di vitamina D appare raccomandabile
- Esistono evidenze osservazionali che mettono **in relazione la riduzione delle performances cognitive nei pazienti anziani con una situazione di deficit dei livelli di vitamina D; c**iò depone a **favore di una condotta nutrizionale o terapeutica che prevenga tale situazione di carenza** nei pazienti anziani con iniziali sintomi di una diminuita efficienza delle funzioni cognitive