ROMA 16-18 SETTEMBRE 2021

HOTEL SHERATON PARCO DE' MEDICI

UNIVERSITA' DI VERONA

U.O.C. REUMATOLOGIA

Prof. Davide Gatti

SOCIETÀ ITALIANA G.U.I.D.A.
PER LA GESTIONE UNIFICATA E INTERDISCIPLINARE DEL DOLORE MUSCOLO-SCHELETRICO E DELL'ALGODISTROFIA

III CONGRESSO NAZIONALE

Vitamina D e dolore da osteoporosi

AMGEN

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MSD-ITALIA

ORGANON

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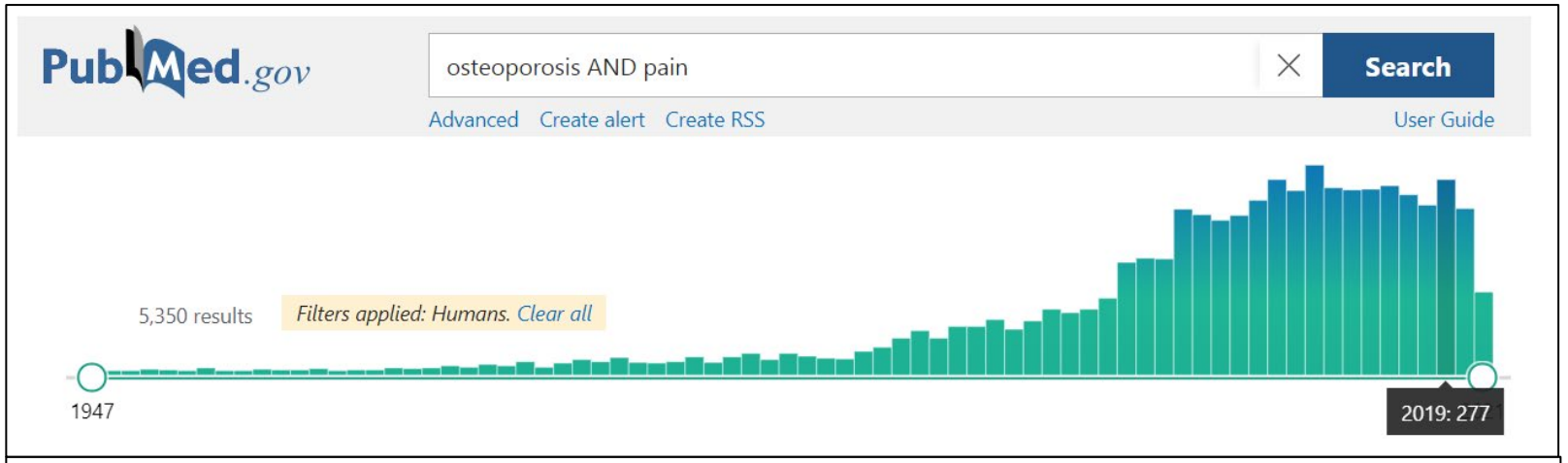
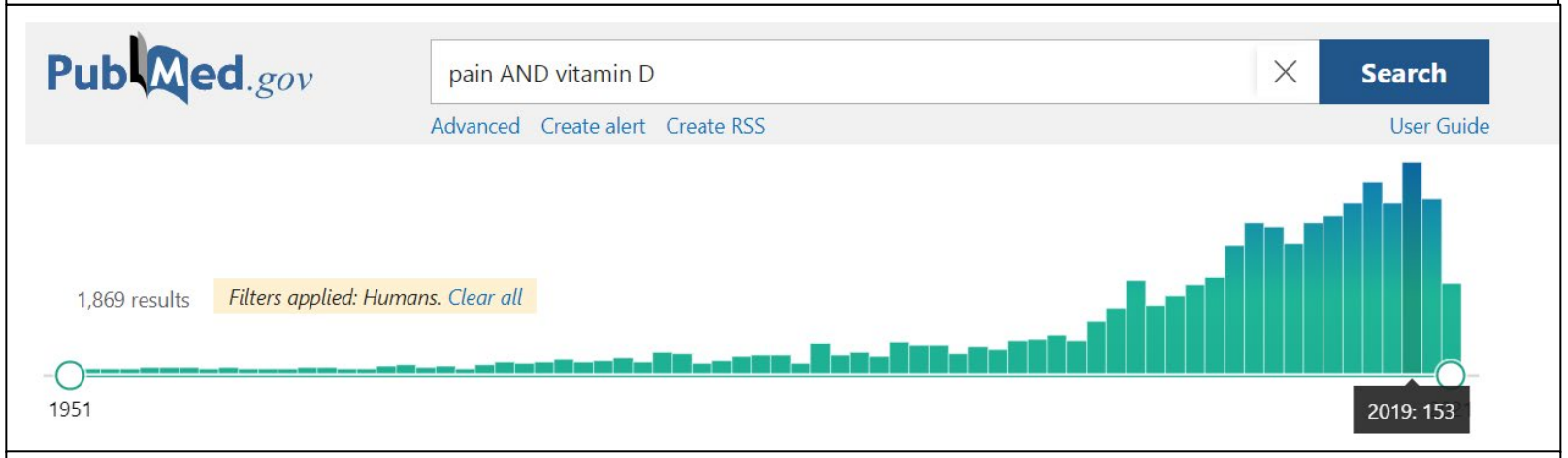
ANNI 2019- 2020-2021

Vitamina D e dolore da osteoporosi

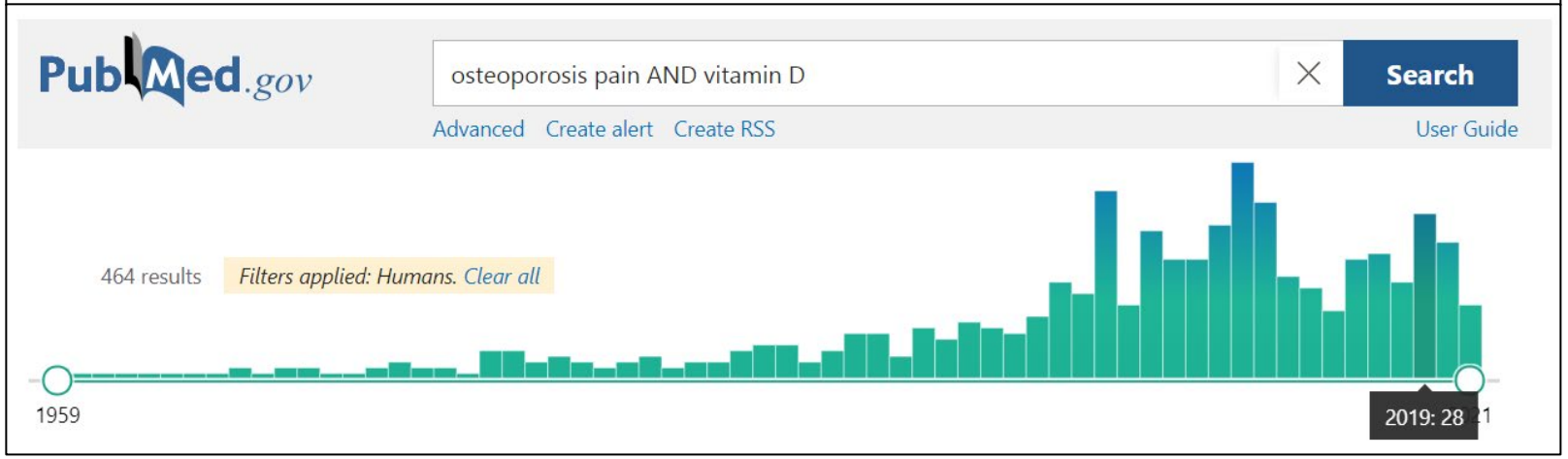
Vitamina D	Osteoporosi	Dolore
Dolore	Vitamina D	Osteoporosi
Osteoporosi	Dolore	Vitamina D



Dolore
Osteoporosi



Dolore
Vitamina D



Vitamina D
Dolore
Osteoporosi

SIOMMMS

STORIA DI UNA LADRA DI OSSA

Vuole rubarti la qualità della vita: fermala!

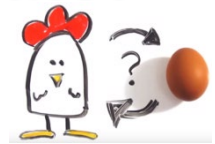
Vitamina D e DOLORE OP

Liangming Zhang*
Chuncheung Chan*
Yang Yang
Bin Liu
Yeqing Zhu
Ruiqiang Chen
Limin Rong

MEDICAL SCIENCE MONITOR 25 years

Published: 2019.11.03

Vitamin D Deficiency/Insufficiency Is Associated with Risk of Osteoporotic Thoracolumbar Junction Vertebral Fractures

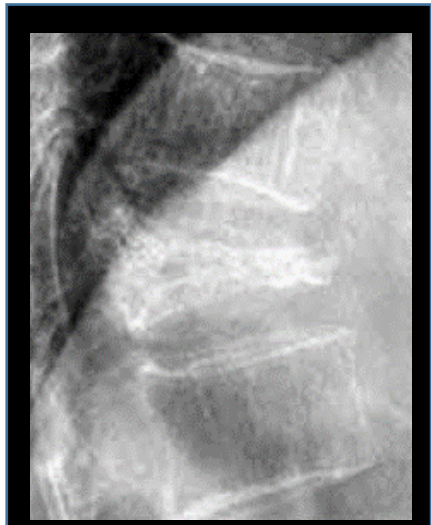


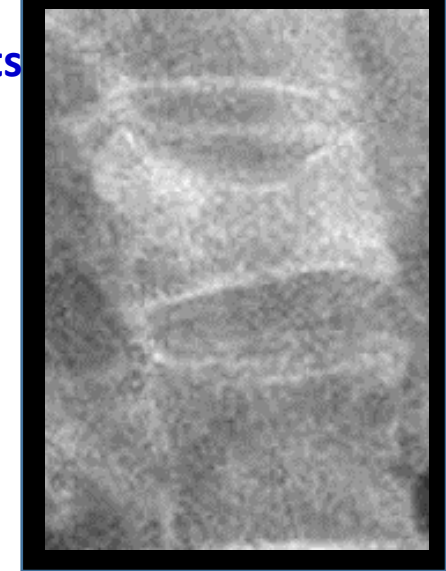
		Female				Male			
		VFx (n, %)	Control (n, %)	*P*-value	*P*-adjusted*	VFx (n, %)	Control (n, %)	*P*-value	*P*-adjusted*
25(OH)D (nmol/L)	<30	61 (14.3)	40 (9.2)	0.004	0.029	17 (15.7)	8 (5.9)	0.019	0.055
	30–49.9	162 (38.0)	142 (32.7)			38 (35.2)	42 (31.1)		
	≥50	203 (47.7)	252 (58.1)			53 (49.1)	85 (63.0)		

VFx – vertebral fracture. *P*-adjusted – adjusted by age and BMI.

Variables	25(OH)D level (nmol/L)			*P*-value	*P*-adjusted[a]
	<30	30–49.9	≥50		
Grade of VFx (n, %)[b]					
Normal	48 (8.4)	184 (32.3)	337 (59.3)		
Grade 1	17 (14.5)	45 (38.5)	55 (47.0)		
Grade 2	23 (15.1)	67 (44.1)	62 (40.8)		
Grade 3	38 (14.3)	88 (33.2)	139 (52.5)	0.001	0.024
Number of VFx (n, %)					
0	48 (8.4)	184 (32.3)	337 (59.2)		
1	52 (15.1)	133 (38.7)	159 (46.2)		
≥2	26 (13.7)	67 (35.3)	97 (51.1)	0.001	0.038

534 patients with primary osteoporotic thoracolumbar junction VFx (T10–L2)
and
569 elderly orthopedic patients with back pain (without osteoporotic VFx) as controls.





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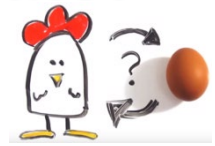
Vitamina D e DOLORE OP

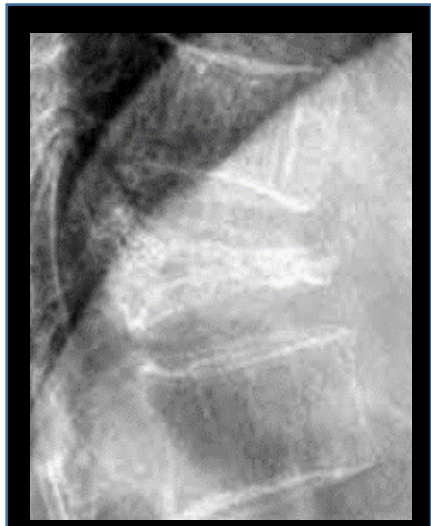
Vitamin D Deficiency/Insufficiency Is Associated with Risk of Osteoporotic Thoracolumbar Junction Vertebral Fractures

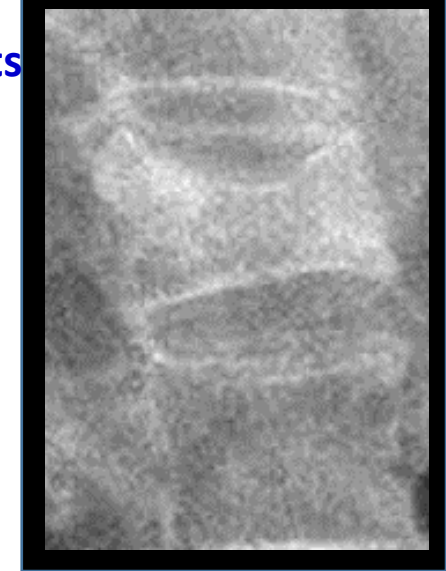


Variables	25(OH)D (nmol/L)	VFx (n, Q%)	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]
Per SD increase in 25(OH)D			0.72 (0.62–0.83)[f]	0.80 (0.68–0.93)[e]	0.79 (0.67–0.94)[e]	0.79 (0.67–0.94)[e]
Q1	29.67±6.18	168 (31.5%)	Referent	Referent	Referent	Referent
Q2	45.40±3.95	135 (25.3%)	0.62 (0.44–0.87)[e]	0.66 (0.44–0.98)[e]	0.70 (0.46–1.07)	0.70 (0.46–1.07)
Q3	60.91±5.12	121 (22.7%)	0.56 (0.40–0.78)[f]	0.59 (0.40–0.88)[e]	0.58 (0.38–0.89)[e]	0.58 (0.38–0.89)[e]
Q4	103.3±44.21	110 (20.6%)	0.44 (0.31–0.62)[f]	0.56 (0.38–0.83)[e]	0.54 (0.36–0.83)[e]	0.54 (0.36–0.83)[e]
P for trend			<0.001	0.017	0.021	0.021
Q2, Q3, Q4			Referent	Referent	Referent	Referent
Q1			1.87 (1.42–2.45)f	1.66 (1.20–2.30)e	1.65 (1.17–2.32)e	1.65 (1.17–2.32)e

OR – odd ratio. CI – confidence interval. Q – quartile of serum 25(OH)D. [a] Model 1 basic model without adjustment; [b] Model 2 adjusted for sex, age, BMI and comorbidities. [c] Model 3 adjusted for sex, age, BMI, comorbidities and lumbar spine BMD. [d] Model 4 adjusted for sex, age, BMI, comorbidities, lumbar spine BMD and season. [e] $P<0.01$; [f] $P<0.001$.

534 patients with primary osteoporotic thoracolumbar junction VFx (T10–L2)
and
569 elderly orthopedic patients with back pain (without osteoporotic VFx) as controls.





RESEARCH ARTICLE Lee et al. Journal of Orthopaedic Surgery and Research (2020) 15:328 Open Access

Vitamina D e DOLORE OP

Low vitamin D levels in post-menopausal women are associated with complex regional pain syndrome type I in surgically treated distal radius fractures

Sang-Uk Lee[1], Ki-Tae Na[1], Yoon-Min Lee[2], Jong Hwa Park[1] and Sun Young Joo[1*]

Association analysis between vitamin D level and CRPSI

25(OH)D_3	N (%)	Group 1 *N* (%)	Group 2 *N* (%)	OR (95% CIs)
Sufficiency	13 (100)	1 (8)	12 (92)	0.301 (0.036-2.536)
Insufficiency	34 (100)	5 (15)	29 (85)	0.623 (0.201-1.931)
Deficiency	60 (100)	13 (22)	47 (78)	1

32 ng/ml

20 ng/ml

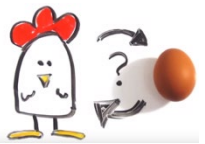
68%

53%

Mean comparison analysis between two groups

Variable	Mean values (mean ± SE)			*p* value
	Total	DRF with CRPS I (group 1)	DRF without CRPS I (group 2)	
N	107	19	88	
Age (years)	67.3 ± 0.9	62.7 ± 2.0	68.3 ± 1.0	0.023
25(OH)D_3 (ng/ml)	19.6 ± 0.9	15.2 ± 1.7	20.5 ± 1.0	0.027
Osteocalcin (ng/ml)	23.4 ± 2.3	21.1 ± 1.9	24.0 ± 2.8	0.628
ALP (U/l)	93.6 ± 3.7	91.2 ± 10.6	94.1 ± 3.9	0.458
BMI (kg/m^2)	24.1 ± 0.3	23.9 ± 0.8	24.1 ± 0.3	0.758
BMD (femur)	−1.9 ± 0.1	−1.6 ± 0.2	−1.9 ± 0.1	0.301
BMD (spine)	−2.4 ± 0.1	−2.6 ± 0.3	−0.6 ± 1.2	0.645

SE standard error, *DRF* distal radius fracture, *CRPS I* complex regional pain syndrome type I, *25(OH) D_3* 25-hydroxyvitamin D_3, *ALP* alkaline phosphatase, *BMI* body mass index, *BMD* bone mineral density



Vitamina D e dolore da osteoporosi

LA IPOVITAMONOSI D SI CONFERMA IL PRINCIPALE FATTORE DI RISCHIO DI FRATTURA IN SOGGETTI CHE ASSUMONO BISFOSFONATI ORALI

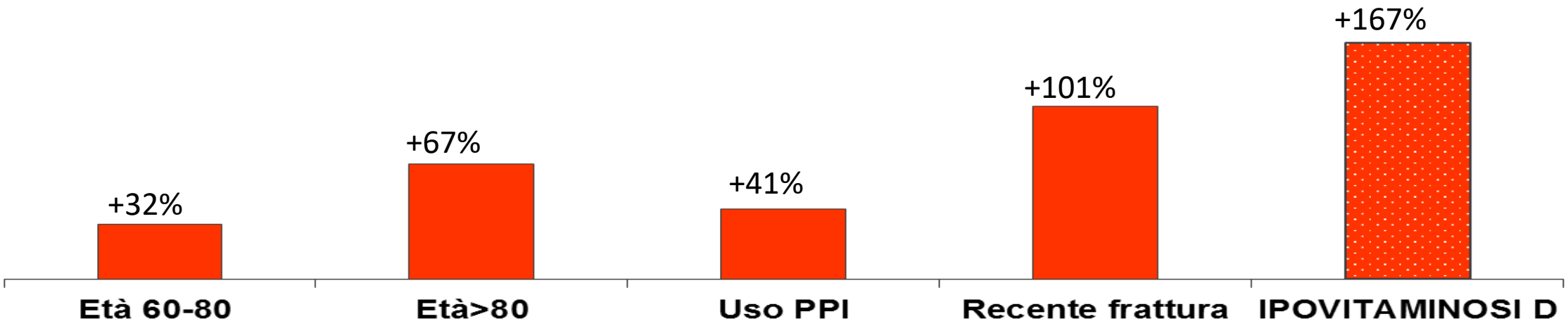
J Bone Miner Res 2014 Jan: 29 (1): 268-74

Predictors of Fracture While on Treatment With Oral Bisphosphonates: A Population-Based Cohort Study

Daniel Prieto-Alhambra,[1,2,3,4] Aina Pagès-Castellà,[3] Gemma Wallace,[2] M Kassim Javaid,[2,4] Andrew Judge,[2,4] Xavier Nogués,[1] Nigel K Arden,[2,4] Cyrus Cooper,[2,4] and Adolfo Diez-Perez[1]

FATTORI DI RISCHIO (significativi) PER FRATTURE MAGGIORI

AUMENTO DEL RISCHIO rispetto controlli di età < 60 anni, che non usano PPI , senza pregresse fratture e SENZA IPOVITAMINOSI D (valori > 20 ng/ml)

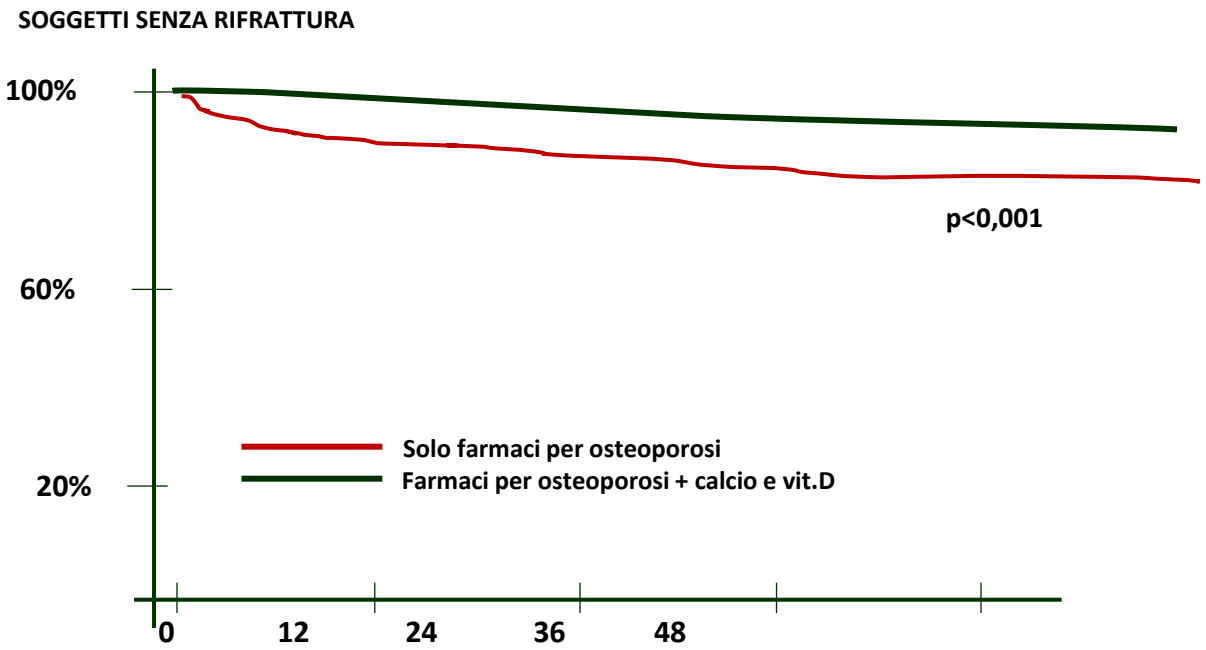


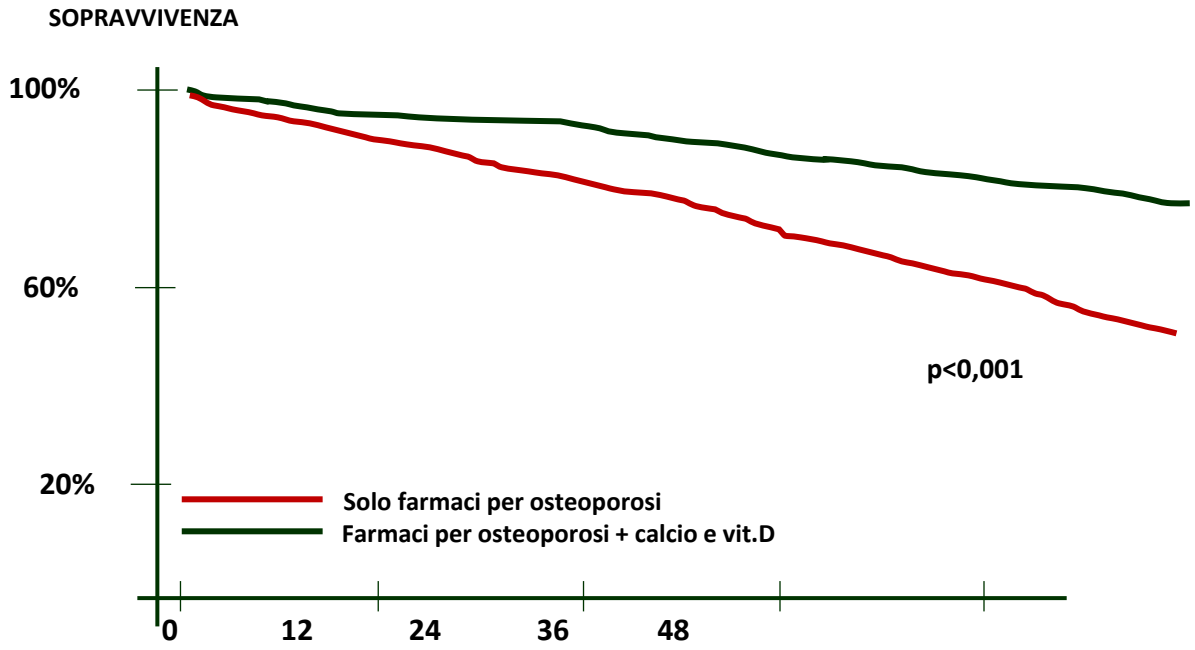
Modificato rispetto originale

Use of antiosteoporotic drugs and calcium/vitamin D in patients with fragility fractures: impact on re-fracture and mortality risk.

Endocrine. 2019 May;64(2):367-377

Degli Esposti L, Girardi A, Saragoni S, Sella S, Andretta M, Rossini M, Giannini S; on the behalf of the Study group





Modificato da Gatti D

Current Osteoporosis Reports (2020) 18:486–504

Vitamina D e DOLORE OSSEO

BONE AND JOINT PAIN (P MANTYH AND T SCHNITZER, SECTION EDITORS)

Do Bisphosphonates Alleviate Pain in Children? A Systematic Review

Mercedes Rodriguez Celin[1] · Jackeline C. Simon[1,2] · Joseph J. Krzak[1,3] · Alissa V. Fial[4] · Karen M. Kruger[1,2] · Peter A. Smith[1] · Gerald F. Harris[1,2]

Ipovitaminosi D

Aumentato Rischio
Alto turnover osseo

aumentato rischio
DOLORE OSSEO

Journal of Bone and Mineral Metabolism (2020) 38:806–818

ORIGINAL ARTICLE

High bone turnover state under osteoporotic changes induces pain-like behaviors in mild osteoarthritis model mice

Kenta Kiyomoto[1,2] · Kousuke Iba[1] · Megumi Hanaka[1] · Koji Ibe[1,3] · Hikaru Hayakawa[1] · Atsushi Teramoto[1] · Makoto Emori[1] · Toshihiko Yamashita[1]

Vitamina D e dolore da osteoporosi

Journal of Family Medicine and Primary Care
Published: 27-02-2021

Correlation between Vitamin D deficiency and nonspecific chronic low back pain: A retrospective observational study

Vinay Kanaujia[1], Raj Kumar Yadav[1], Shipra Verma[2], Sakshi Jain[3], Binayak Patra[1], Osama Neyaz[1]

Vitamina D e DOLORE

Vitamin D status in both groups

	Group 1	Group 2	*P*
Mean±std dev	14.11±5.14	37.11±7.1	<0.0001
Median	14	35	
Min - max	4.1 to 29	30.29-100.7	

30 ng/ml

VAS status in both groups

	Group 1	Group 2	*P*
Mean±std dev	5.71±0.97	4.88±1.23	<0.00001
Median	6	5	
Min - max	3 to 8	3 to 7	

376 patients of age 18 to 65 and either sex with nonspecific CLBP were included.

Patients were divided into two:
- Vitamin D deficient (Group 1 =302)
- Normal (Group 2= 74)

The cut off Serum Vitamin D values was at 30 ng/mL.

BMC Research Notes | Pishgahi et al. BMC Res Notes (2019) 12:738 | Open Access

Lower serum 25-hydroxyvitamin D3 concentration is associated with higher pain and disability in subjects with low back pain: a case–control study

Alireza Pishgahi[1], Neda Dolatkhah[1*], Seyed Kazem Shakouri[1], Maryam Hashemian[2], Atefeh Amiri[3], Morteza Delkhosh Reihany[3] and Fatemeh Jahanjou[1]

Vitamina D e DOLORE

Table 1 Comparisons of demographic characteristics of participants in the case and control groups

Variables	Case group (N = 63)	Control group (N = 55)	p-value
Age, years	49.44 ± 12.77	50.02 ± 9.67	0.784
Sex			
Male	26 (41.26%)	29 (52.72%)	0.455
Female	37 (58.73%)	36 (65.45%)	
BMI (kg/m^2)	29.33 ± 5.05	28.10 ± 4.15	0.151
Waist circumference (cm)	93.821 ± 8.72	94.985	0.522
Hip circumference (cm)	108.11 ± 15.99	108.67 ± 10.61	0.819
Waist to hip ratio	0.97 ± 0.93	0.87 ± 0.07	0.395
Serum 25(OH) D (ng/ml)			
< 20	27 (42.85%)	8 (14.54%)	0.001
20 to 29.9	14 (22.22%)	15 (27.27%)	
≥ 30	22 (34.92%)	32 (58.18%)	

Values are mean ± SD OR number (%)

Multiple logistic regression analysis of LBP predictor

Variable	Case	Control	Crude OR (95% CI)	p-value
Serum 25(OH) D (ng/ml)				
≥ 30	21	32	2.593 (1.231 to 5.463)	0.012
< 30	42	23		

Variable	Case	Control	Adjusted OR (95% CI)[a]	p-value
Serum 25(OH) D (ng/ml)				
≥ 30	21	32	2.388 (1.114 to 5.119)	0.025
< 30	42	23		

[a] OR adjusted for physical activity

63 eligible patients with LBP and 55 healthy subjects enrolled in the study

Vitamina D e DOLORE

Systematic Review

Pain Physician 2017; 20:611-640 • ISSN 1533-3159

Mapping the Association between Vitamin D and Low Back Pain: A Systematic Review and Meta-Analysis of Observational Studies

Joshua Zadro, BAppSc[1], Debra Shirley, PhD[1], Manuela Ferreira, PhD[2], Ana Paula Carvalho-Silva, MSc[1], Sarah E. Lamb, PhD[3], Cyrus Cooper, PhD[3], and Paulo H. Ferreira, PhD[1]

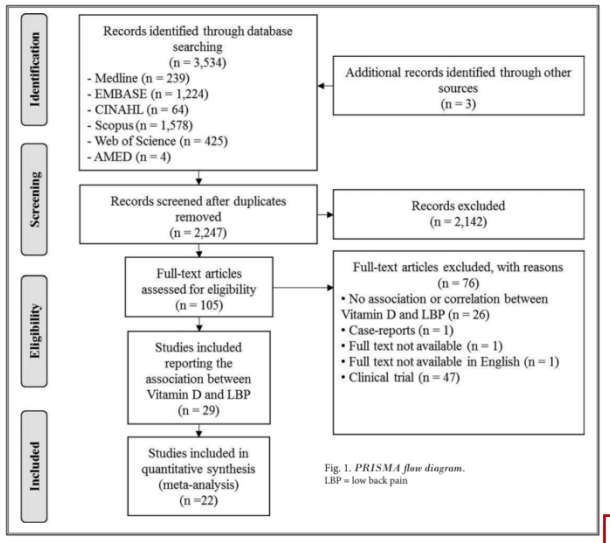
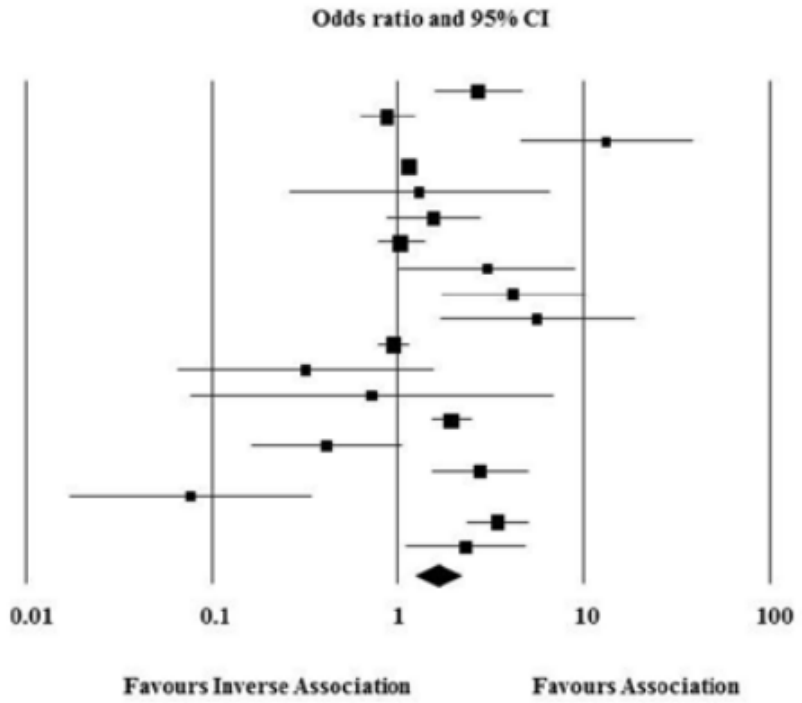


Fig. 1. *PRISMA flow diagram.*
LBP = low back pain

Author (year)	Odds ratio	Lower limit	Upper limit	p-Value	Vitamin D Deficient / Total LBP	Vitamin D Deficient / Total No LBP
Abdulmonem A (2014)	2.667	1.506	4.722	0.001	152 / 190	48 / 80
Alipour M (2015)	0.869	0.609	1.240	0.438	242 / 324	265 / 343
Baykara B (2014)	13.078	4.428	38.622	0.000	53 / 60	11 / 30
e Silva AV (2013)	1.138	1.027	1.261	0.014	1580 / 6284	682 / 2992
Haroon M (2011)	1.288	0.254	6.548	0.760	6 / 8	156 / 223
Heidari B (2010)	1.523	0.830	2.795	0.174	25 / 54	73 / 202
Hicks GE (2008)	1.029	0.748	1.414	0.862	83 / 350	123 / 530
Lotfi A (2007)	2.970	0.981	8.994	0.054	49 / 60	12 / 20
Madani M (2014)	4.140	1.666	10.285	0.002	138 / 148	40 / 52
Prakash S (2013)	5.536	1.611	19.019	0.007	31 / 35	21 / 36
Tanaka S (2013)	0.930	0.744	1.161	0.520	216 / 447	513 / 1023
Thörneby A (2016)	0.316	0.063	1.575	0.160	3 / 41	4 / 20
Ducher G (2011)	0.714	0.074	6.922	0.772	2 / 4	7 / 12
Lee KC (2014)	1.932	1.473	2.534	0.000	131 / 229	1281 / 3132
Santos F (2015)	0.409	0.158	1.059	0.066	7 / 20	141 / 248
Heidari B (Nov 2014)	2.729	1.473	5.056	0.001	57 / 81	47 / 101
Al-Jarallah K (2013)	0.076	0.017	0.345	0.001	12 / 18	79 / 82
Heidari B (2014)	3.402	2.285	5.064	0.000	117 / 163	160 / 374
Rkain H (2013)	2.291	1.067	4.919	0.034	83 / 105	28 / 45
Pooled effect	**1.595**	**1.202**	**2.115**	**0.001**		

I^2 = 84.9% random effects

OR 1,6 (1,2-2,1)



Conclusions:

Vitamin D deficiency is associated with LBP,
with stronger associations observed in younger women and those with severe levels of deficiency.

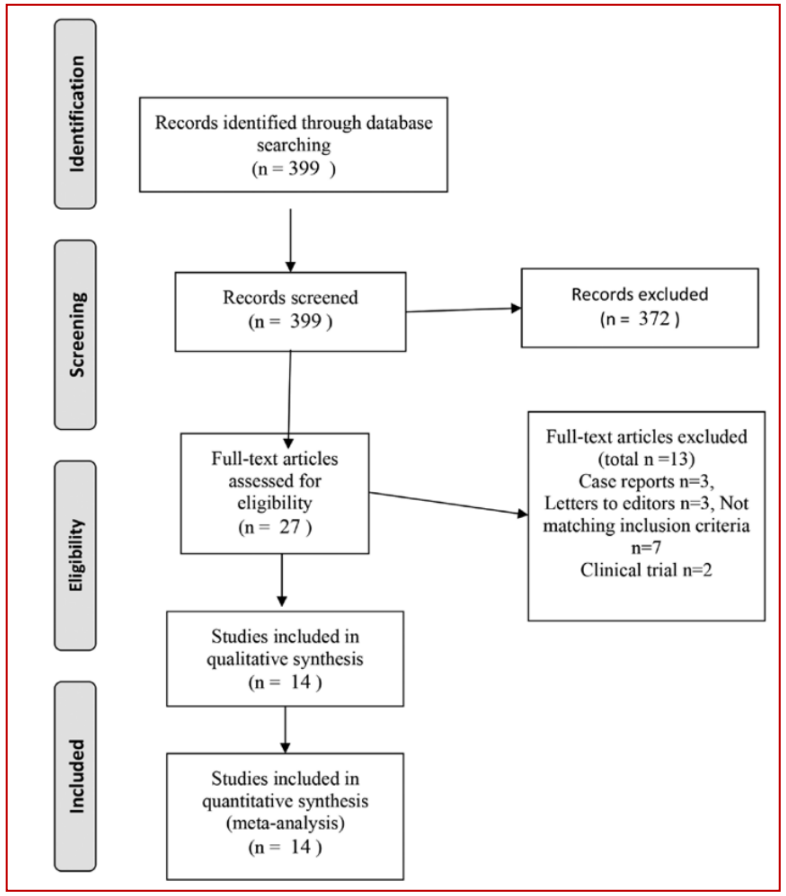
Vitamina D e DOLORE

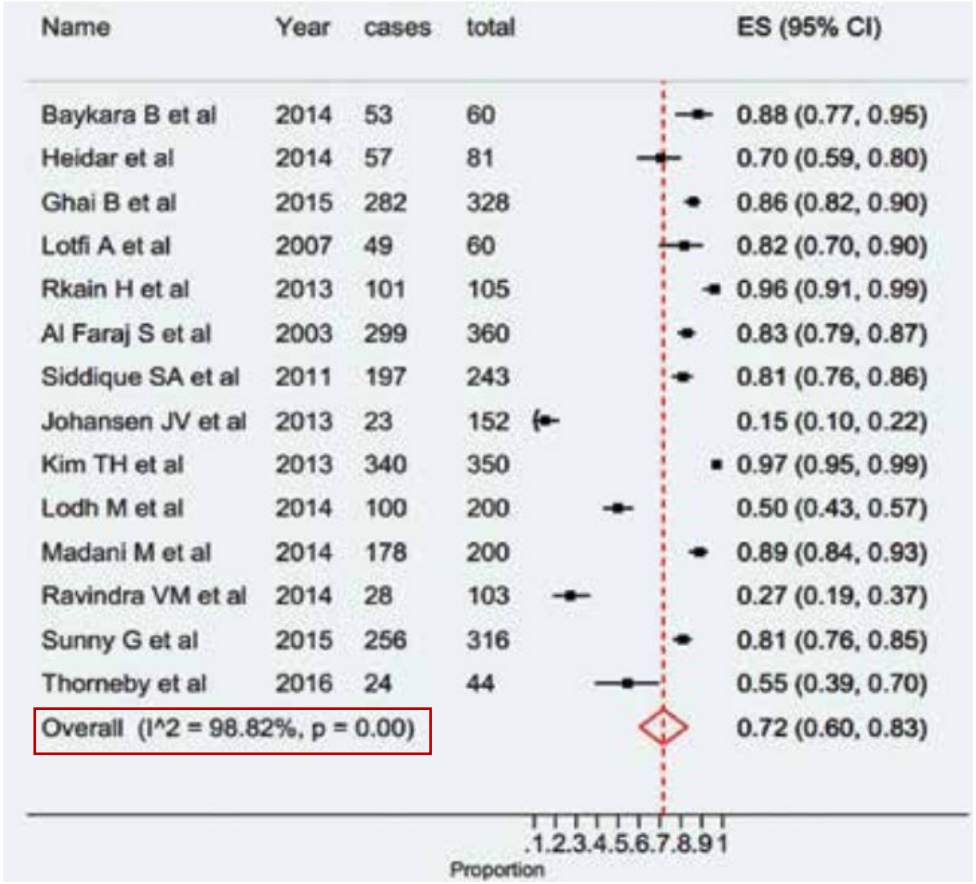
Meta-Analysis

Pain Physician 2018; 21:E389-E399• ISSN 2150-1149

High Prevalence of Hypovitaminosis D in Patients with Low Back Pain: Evidence from Meta-Analysis

Dipika Bansal, MD, DM[1], Chandra Sekhar Boya, MPharm, PhD[1], Rambabu Vatte, MPharm[1], and Babita Ghai, MD, DNB[2]





<u>CONCLUSIONS</u>:

We included 14 studies involving 2602 patients with LBP of whom 1987 (**<u>76.3%</u>**) had Hypovitaminosis D and the weighted pooled PR of hypovitaminosis D was **72%** (95% CI 60 - 83)

The present meta-analysis concludes a high prevalence of hypovitaminosis D was observed in patients with LBP. This provides a chance to screen the deficiency and correct it by supplementation, which can be therapeutic adjunct in the management of LBP patients

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Vitamina D e dolore da osteoporosi

Vitamina D e DOLORE

ORIGINAL STUDY *Menopause, Vol. 27, No. 5, 2020*

Does vitamin D status influence lumbar disc degeneration and low back pain in postmenopausal women? A retrospective single-center study

Hao-Wei Xu, MD, Yu-Yang Yi, MD, Shu-Bao Zhang, MD, Tao Hu, MD, PhD, Shan-Jin Wang, MD, PhD, Wei-Dong Zhao, MD, and De-Sheng Wu, MD, PhD

232 participants were retrospectively enrolled. Serum concentrations of bone turnover markers were measured using electrochemiluminescence assays. Disc degeneration was evaluated using the Pfirrmann grading system.

The relationship between severity of disc degeneration and vitamin D levels in the postmenopausal women

Disc levels	Vitamin D serum levels (ng/mL)	Grade of disc degeneration	*F*	*P*
L4/L5	0-10	3.70 ± 0.84	3.973	0.02
	10-30	3.31 ± 0.72[a]		
	>30	3.28 ± 0.53[a]		
L1/S1	0-10	3.33 ± 0.72	3.277	0.04
	10-30	3.01 ± 0.64[a]		
	>30	2.99 ± 0.48[a]		

The sample size of different 25 (OH)D level was ≤10 ng/mL in 30 participants, 10-30 ng/mL in 173, and ≥30 ng/mL in 29.
All P values were calculated with the ANOVA analysis.
[a]Pairwise comparisons to group of vitamin D serum levels 0-10 (ng/mL), $P < 0.05$.

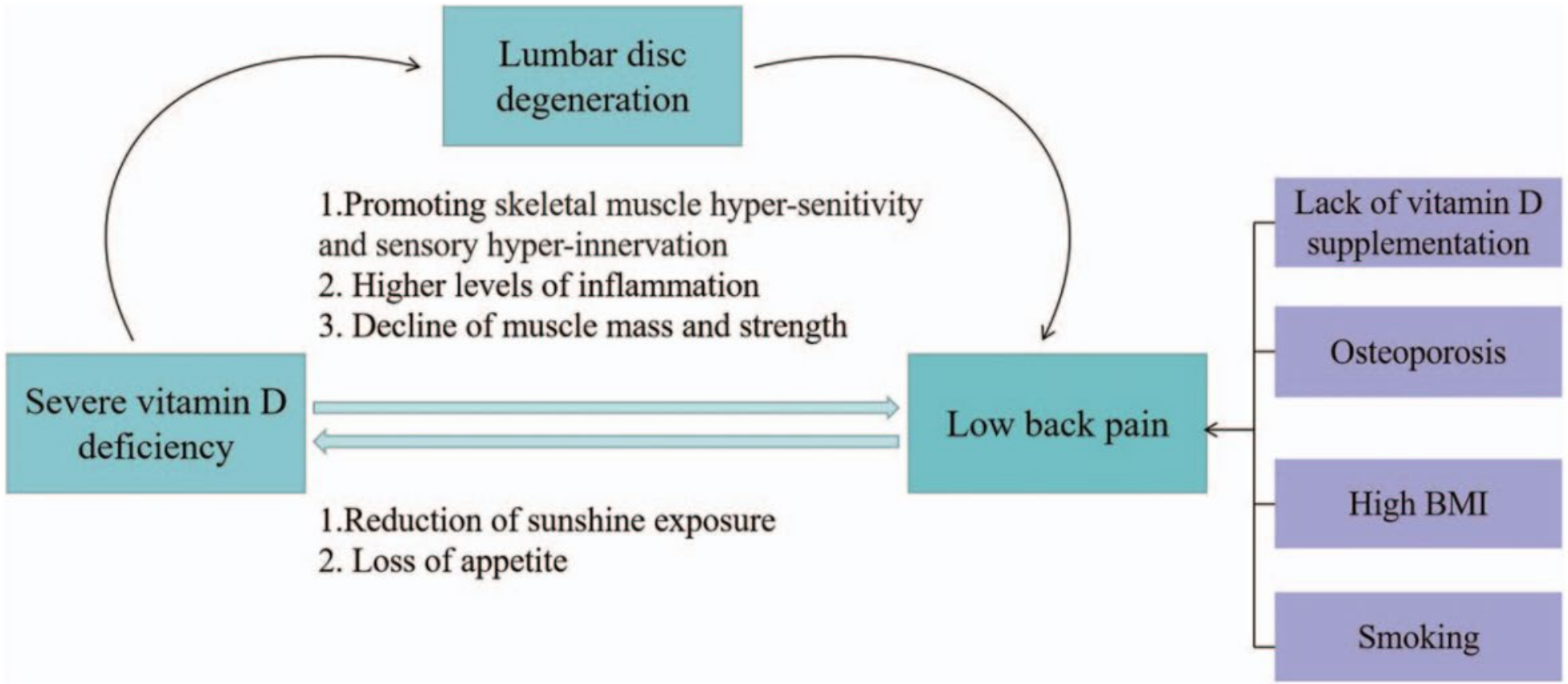
The severely deficient group (0-10) had:
- higher visual analog scale (VAS) scores for LBP ($p < 0.002$)
- lower bone mineral density T scores ($p < 0.004$)
than the other groups.

After adjustment for confounding factors:
-smoking,
-vitamin D deficiency,
-lack of vitamin D supplementation,
-high body mass index,
- low bone mineral density T score
were associated with higher incidence of moderate-to-severe pain in postmenopausal women ($p < 0.05$).

ORIGINAL STUDY *Menopause, Vol. 27, No. 5, 2020*

Does vitamin D status influence lumbar disc degeneration and low back pain in postmenopausal women? A retrospective single-center study

Hao-Wei Xu, MD, Yu-Yang Yi, MD, Shu-Bao Zhang, MD, Tao Hu, MD, PhD, Shan-Jin Wang, MD, PhD, Wei-Dong Zhao, MD, and De-Sheng Wu, MD, PhD



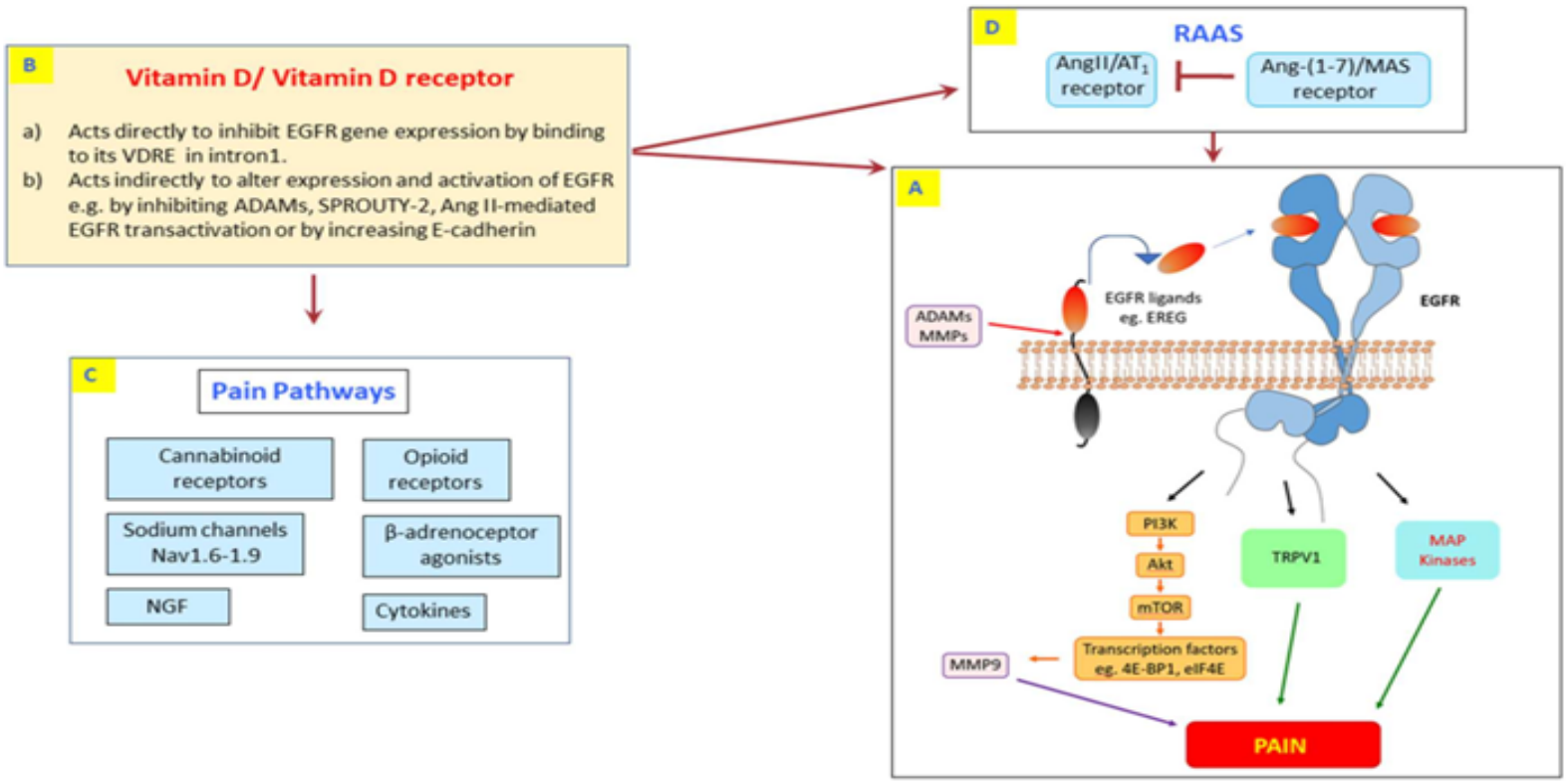
Vitamina D e DOLORE CRONICO

frontiers in Immunology

REVIEW
published: 28 May 2020
doi: 10.3389/fimmu.2020.00820

Vitamin D and Its Potential Interplay With Pain Signaling Pathways

Abdella M. Habib, Karim Nagi, Nagendra Babu Thillaiappan, VijayaKumar Sukumaran and Saghir Akhtar**



The epidermal growth factor receptor (EGFR) has been recently identified as novel signaling pathway involved in pain processing and their expression is also known to be regulated by the vitamin D pathway

About 50 million of the U.S. adult population suffer from chronic pain. It is a complex disease in its own right for which currently available analgesics have been deemed woefully inadequate since ~20% of the sufferers derive no benefit.

Vitamin D, known for its role in calcium homeostasis and bone metabolism,

is thought to be of clinical benefit in treating chronic pain without the side-effects of currently available analgesics

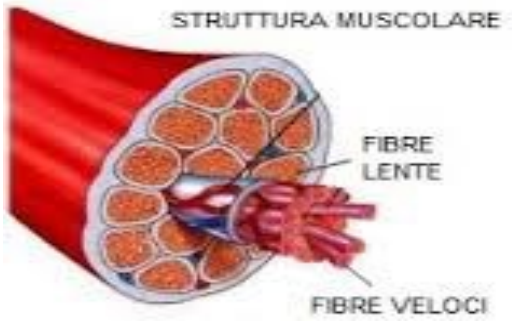
Calcif Tissue Int (2013) 92:151–162

Vitamina D e DOLORE CRONICO

ORIGINAL RESEARCH

Vitamin D and Its Role in Skeletal Muscle

Lisa Ceglia · Susan S. Harris



Vitamin D—Deficient Myopathy

Clinical Presentation

proximal myopathy
muscle weakness
diffuse skeletal or muscle pain
difficulty in climbing stairs
difficulty rising from a sitting

Muscle Histological Characteristics

enlarged interfibrillar spaces
fibrosis
infiltration of fat and glycogen
type II muscle fiber atrophy

Type II fibers:
- short bursts of speed and power
- quicker to fatigue
- the first to be recruited to prevent a fall

Nota 96 Persone con livelli sierici di 25OHD < 20 ng/mL e sintomi attribuibili a ipovitaminosi D

- disorientamento
- eccessivo ricorso a dosaggi inutili e costosi

Vitamina D e DOLORE CRONICO

- astenia,
- mialgie,
- dolori diffusi o localizzati,
- dolenza in sedi ossee,
- dolore lombosacrale, pelvico o agli arti inferiori,
- senso di impedimento fisico,
- debolezza muscolare con difficoltà ad alzarsi da seduto,
- andatura ondeggiante,
- propensione alle cadute immotivate

eccessive aspettative (sintomi) sulla supplementazione anche quando (più delle volte) non c'è alcuna associazione patogenetica

Journal of Steroid Biochemistry and Molecular Biology 196 (2020) 105488

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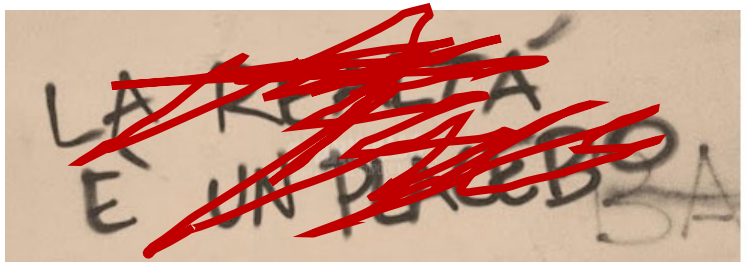
Vitamina D e DOLORE DIFFUSO



The effect of vitamin D replacement on spinal inhibitory pathways in women with chronic widespread pain

Ozge Kenis-Coskun*, Esra Giray, Osman Hakan Gunduz, Gulseren Akyuz

Patients received eight weeks of oral 50.000 IU/week of vitamin D3 replacement therapy and re-evaluated at the end of their treatment

The change of 25(OH)D levels, VAS and LANSS scores and CSP latency and durations before and after treatment.

Parameters	Before treatment	After treatment	
25(OH)D levels (ng/ml) mean ± SD	13.2 ± 4.3	33.3 ± 5.2	P < 0.001
VAS median	7	3	P < 0.001
CSP latency (ms) mean ± SD	74.2 ± 12.4	71.4 ± 10.6	P = 0.06
electrophysiologic CSP duration (ms) median	37.6	42.1	P = 0.12

A limitation of this study is that it did not have a placebo group

Definizione di sbrodolata…

Concluderei che…..

NEI PAZIENTI CON OSTEOPOROSI (ma anche negli altri) E’ MOLTO DIFFICILE CAPIRE DA QUALE PROBLEMA POSSA VENIRE IL DOLORE MUSCOLO-SCHELETRICO

E’ ASSOLUTAMENTE CREDIBILE PENSARE CHE ESSERE OSTEOPOROTICI IPOVITAMINOSICI D SIA UNO SVANTAGGIO IN TERMINI DI DOLORE osseo, muscolare, osteoarticolare , da ipersensibilizzazione, da….

IN OGNI CASO I PAZIENTI OSTEOPOROTICI NON DOVREBBERO **COMUNQUE** ESSERE IPOVITAMINOSICI D (PER UNA SERIA NOTEVOLE DI MOTIVI) **E MI SPIACEREBBE DAVVERO** FOSSE NECESSARIO UN PEGGIORAMENTO DEL DOLORE PER FAR SI’ CHE QUESTA CONDIZIONE (PURTROPPO ANCORA FREQUENTE) FOSSE CORRETTA.