Vitamine D en prévention des chutes et ostéoporose

Patrizia D'Amelio
Service de Gériatrie et Réadaptation Gériatrique
CHUV, Lausanne

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Agenda

- Vitamine D : de quoi parle-t-on ?
- Quels sont les taux de vitamine D dans la population ?
- Faut-il mesurer les taux de vitamine D ?
- La vitamine D dans la prévention de l'ostéoporose et des chutes, avons-nous des preuves ?
- Le traitement : Qui ? Comment ?
- Take home messages

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Métabolisme de la (des) vitamine(s) D : s'agit-il d'une vitamine ?

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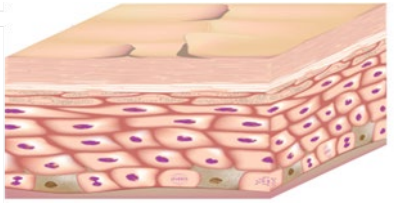
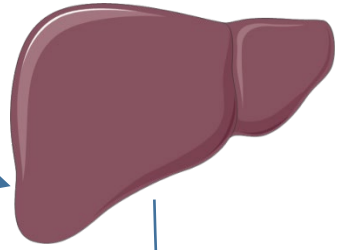
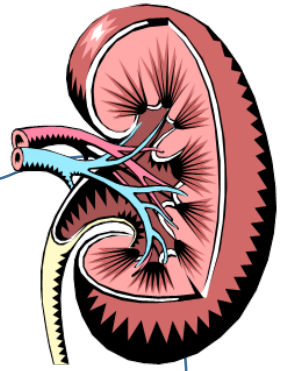


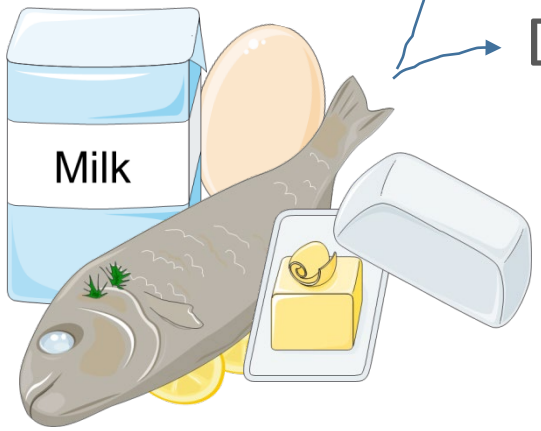
D_3



25 alpha hydroxylase



1 alpha hydroxylase



D_2

$25(OH)D$

24 alpha hydroxylase

$1,25(OH)_2D$

$24,25(OH)_2D$

La vitamine D contrôle l'homéostasie du calcium et du phosphate

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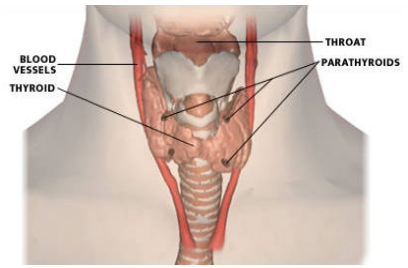
PTH



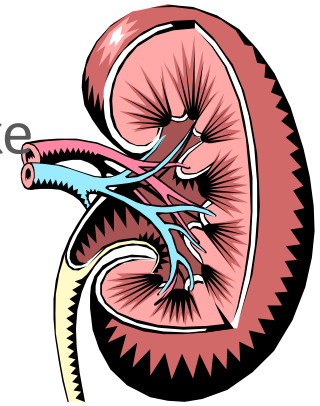
Ca^{++} and PO_4^{--}

Gut uptake

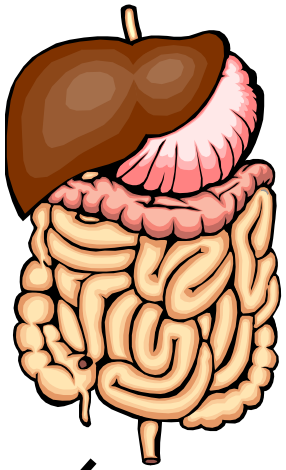
PTH

Ca++ release from bone

Ca++ reuptake



1,25 $(OH)_2 D_3$ syntesis

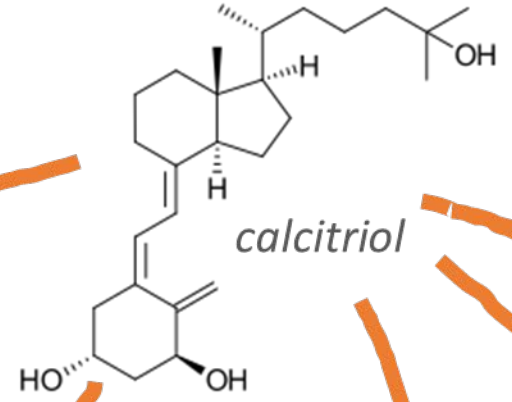


Serum calcium and phosphate homeostasis

Effets pléiotropiques de la vitamine D

Ca e P homeostasis

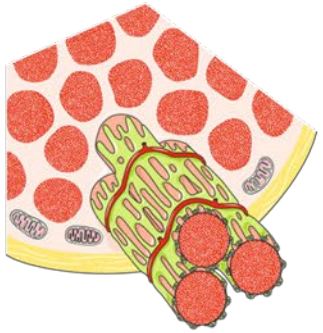
Bone health



calcitriol

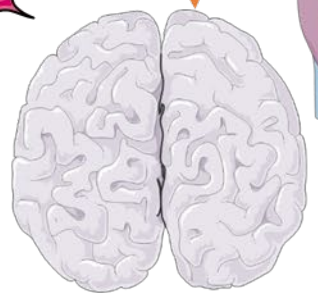
Anti-cancer effetct

Muscle mass
Muscle strenght
Better balance



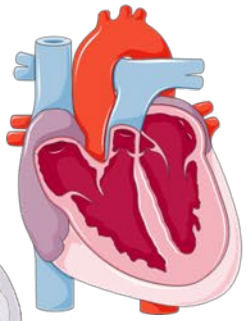
Muscle health

Immunomodulatory Effects



Cognitive performance

Cardiovascular health



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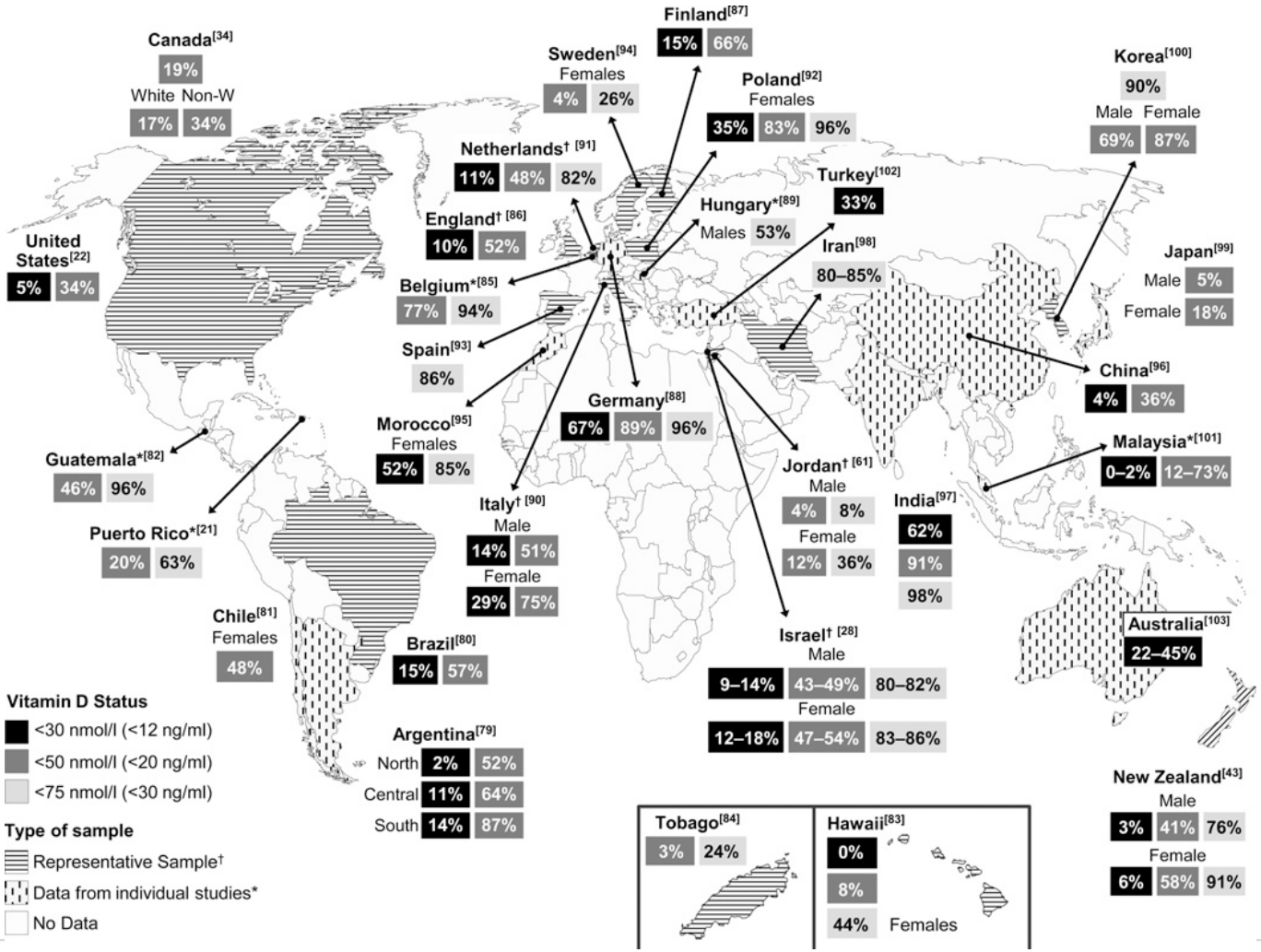
Épidémiologie de l'hypovitaminose D chez les personnes âgées



Palacios C & Gonzalez L. J Steroid Biochem Mol Biol. 2014

Normal or optimal values?

Source	Deficiency	Insufficiency	sufficiency
IOM (2010)	30 nMol/L	30-50 nMol/L	75-250 nMol/L
USA Endocrine Society (2011)	50 nMol/L	50-75 nMol/L	75-250 nMol/L
SIOMMS 2016	<25 nmol/l	25-50 nmol/l	50-80 nmol/l
AME (2018)			>75 nmol/L in patients at risk of bone disease

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Valeurs normales ou optimales ?

	Deficiency *	Insufficiency *	Optimal * Optimum *
GENERAL POPULATION	<10 ng/mL	<20 ng/mL	**20–50 ng/mL**
POPULATION AT RISK ** OR ON TREATMENT WITH *BONE MODIFYING AGENTS*	<10 ng/mL	<30 ng/mL	**30–50 ng/mL**

* Reported cut-off values should be considered with a margin of variability of +/−10%, considering the analytical variability of the 25(OH)D dosage. Moreover, due to the seasonal variability of 25(OH)D levels, a dosage performed at the end of winter/early spring should be particularly considered. A serum value of <10 ng/mL (25 nmol/L) is associated with rickets and osteomalacia, if long lasting. From ng/mL to nmol/L: ng/mL × 2.5.
** The population at risk of hypovitaminosis is shown in Table 2.

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Bertoldo F et al. Nutrients 2022

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Qui sont les sujets à risque d'hypovitaminose D ?

- Old people (≥75 years)
- Institutionalized subjects or conditions associated with inadequate solar exposure
- Obesity
- Pregnancy and breast-feeding
- Metabolic bone diseases and other skeletal disorders
- Vegan diet
- Anorexia nervosa
- Chronic renal failure
- Cancer (in particular breast, prostate, and colon)
- Type 2 diabetes mellitus
- Intestinal malabsorption and bariatric surgery
- Drugs that interfere with the absorption or hepatic metabolism of vitamin D (antiepileptics, glucocorticoids, antiviral AIDS, antifungal agents, cholestyramine)
- Cystic fibrosis

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Qu'en est-il des chuteurs ?

Characteristic	Placebo Without Exercise (n = 102)	Vitamin D Without Exercise (n = 102)	Placebo and Exercise (n = 103)	Vitamin D and Exercise (n = 102)
Age, y	73.8 (3.1)	74.1 (3.0)	74.8 (2.9)	74.1 (2.9)
Height, cm	160.7 (5.4)	159.2 (5.8)	159.4 (6.1)	159.7 (5.9)
Weight, kg	72.0 (12.4)	73.0 (13.1)	70.9 (10.6)	73.2 (10.5)
Fat, %	41.1 (6.7)	42.0 (7.2)	41.3 (6.4)	42.8 (5.3)
Calcium intake, mg/d	1040 (345)	1125 (420)	1119 (346)	1109 (385)
Vitamin D intake, µg/d	10.2 (4.1)	10.9 (4.2)	10.3 (3.6)	10.4 (3.9)
Serum 25-hydroxyvitamin D level, ng/mL	27.1 (7.5)	26.4 (6.9)	27.8 (7.2)	26.2 (7.0)

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Uusi-Rasi, K.; et al JAMA Intern. Med. 2015

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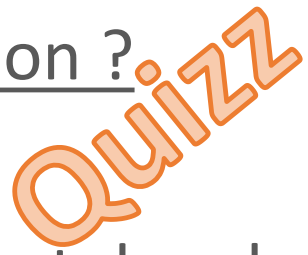

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Quand mesurer le taux de 25-OH vitamine D ?

A. Chez les personnes âgées de plus de 75 ans
B. Chez les patients atteints d'ostéoporose
C. Chez les patients souffrant de fractures
D. Chez les personnes qui tombent souvent

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L'évaluation biochimique des taux sériques de 25(OH)D doit-elle être effectuée dans la population générale ?

Benefits of Screening

Key Question 1a. Does screening for vitamin D deficiency improve health outcomes?

Key Question 1b. Does screening efficacy vary among patient subpopulations at higher risk for vitamin D deficiency (eg, persons residing in institutions, persons with obesity, persons with low levels of sun exposure, or older adults) or vary by race/ethnicity?

No studies were identified.

Harms of Screening

Key Question 2. What are the harms of screening for vitamin D deficiency?

No studies were identified.

Kahwati, LC et al. Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2021.

L'évaluation biochimique des taux sériques de 25(OH)D doit-elle être effectuée dans la population à risque d'hypovitaminose D ?

	Evidence Levels
It is suggested not to indiscriminately measure the levels of 25(OH)D in patients with conditions/pathologies at risk of hypovitaminosis D	⊕⊕
It is recommended the measurement of 25(OH)D levels only when it is deemed necessary for the clinical management of the patient (i.e., when osteomalacia is suspected)	⊕⊕

Bertoldo F et al. Nutrients 2022

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Quand mesurer le taux de 25-OH vitamine D ?

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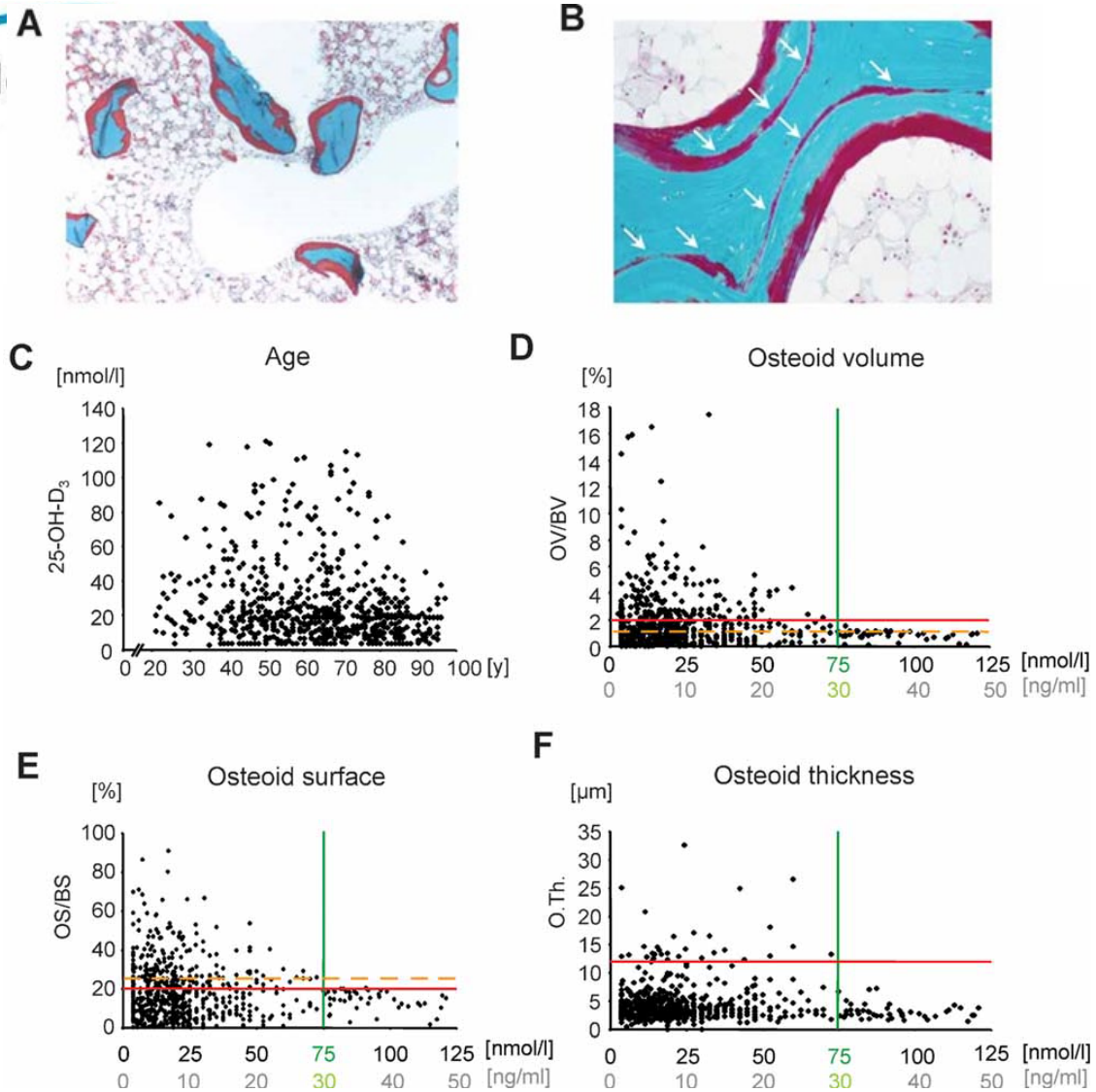
25(OH) vitamine D et ostéomalacie



675 patients

Priemel M., et al. J. Bone Min. Res. 2010

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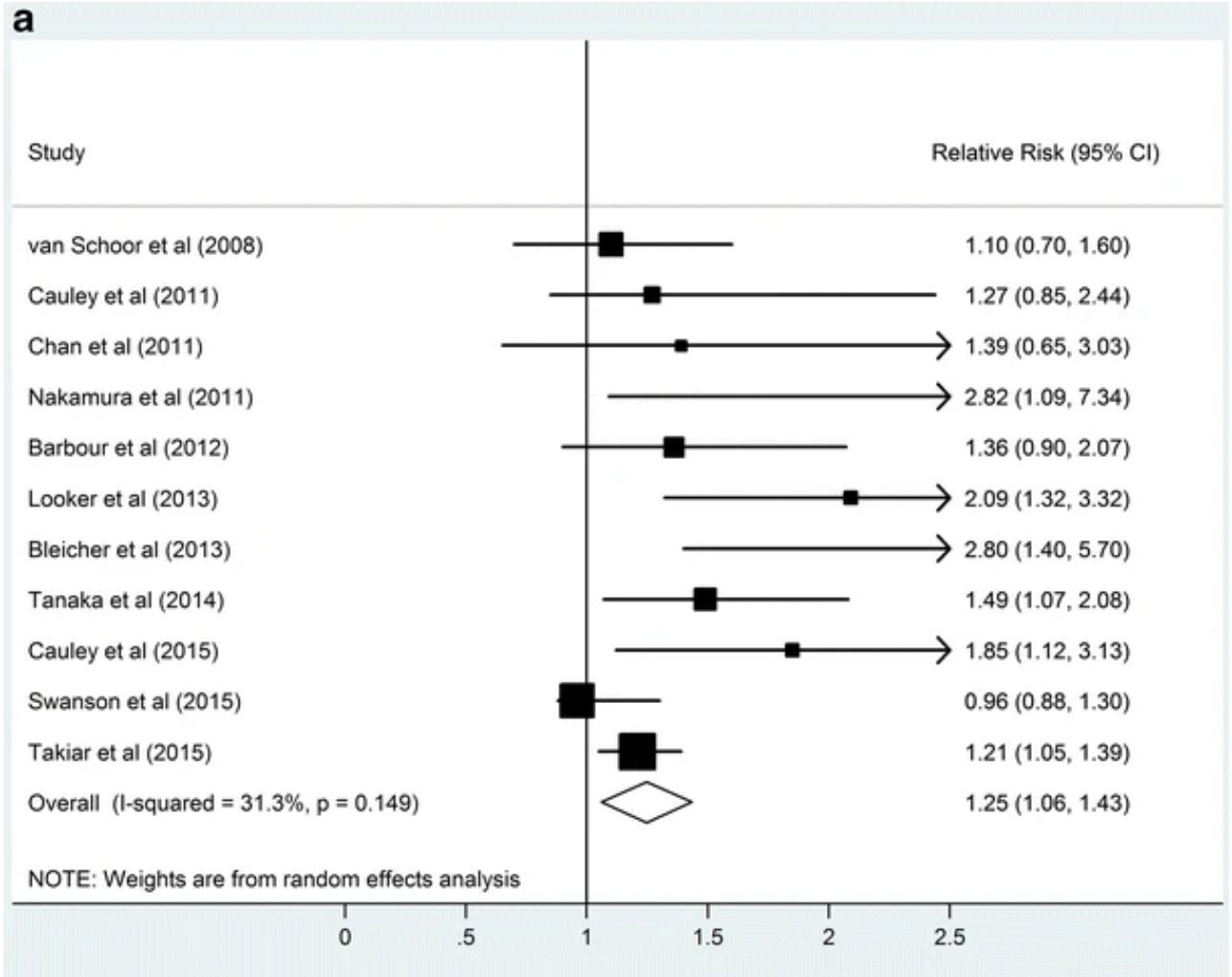
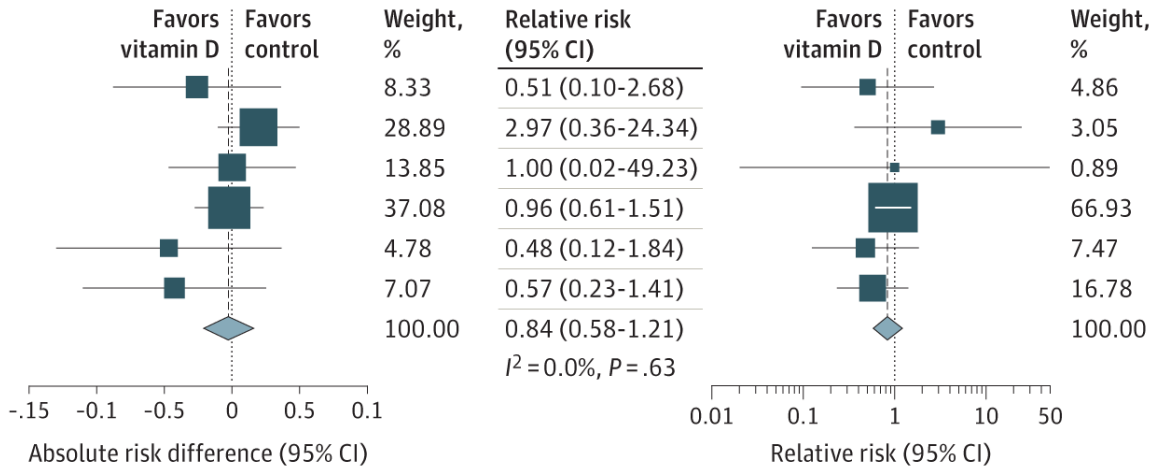
Des niveaux réduits de vitamine D sont associés à un risque accru de fracture du fémur



Feng, Y.; et al Osteoporos. Int. 2017

Le traitement à base de vitamine D réduit-il le risque de fracture ?

Source	Treatment duration	Fracture type	Calcium received	Vitamin D: No. with fracture	Vitamin D: No. without fracture	Control: No. with fracture	Control: No. without fracture	Absolute risk difference (95% CI)
Hansen et al,[26] 2015	52 wk	Undefined	None	2	73	4	72	-0.026 (-0.088 to 0.036)
Hin et al,[27] 2017	52 wk	Undefined	None	6	198	1	100	0.020 (-0.011 to 0.050)
Bislev et al,[17] 2019	12 wk	Undefined	None	0	40	0	41	-0.000 (-0.047 to 0.047)
Khaw et al,[54] 2017	3.3 y	Nonvertebral	None	34	578	38	620	-0.002 (-0.028 to 0.023)
Pfeifer et al,[52] 2000	1 y	Any	Both groups	3	67	6	61	-0.047 (-0.130 to 0.037)
Pfeifer et al,[51] 2009	1.75 y	Any	Both groups	7	115	12	108	-0.043 (-0.110 to 0.025)
Overall								-0.003 (-0.021 to 0.016)
								I^2 = 13.0%, P = .33



Kahwati, LC et al. Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2021.

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L'hypovitaminose D et les chutes

Une association modérée, mais cohérente, a été signalée entre de faibles niveaux de vitamine D et une diminution de la stabilité posturale, de mauvaises performances fonctionnelles et un risque accru de chutes.

Latham NK, et al. J Am Geriatr Soc. 2003
Annweiler C, et al. J Nutr Health Aging. 2009
Bischoff-Ferrari HA, et al. BMJ. 2009
Bischoff-Ferrari HA, et al. Am J Clin Nutr. 2004
Pfeifer M, et al. J Bone Miner Res. 2000

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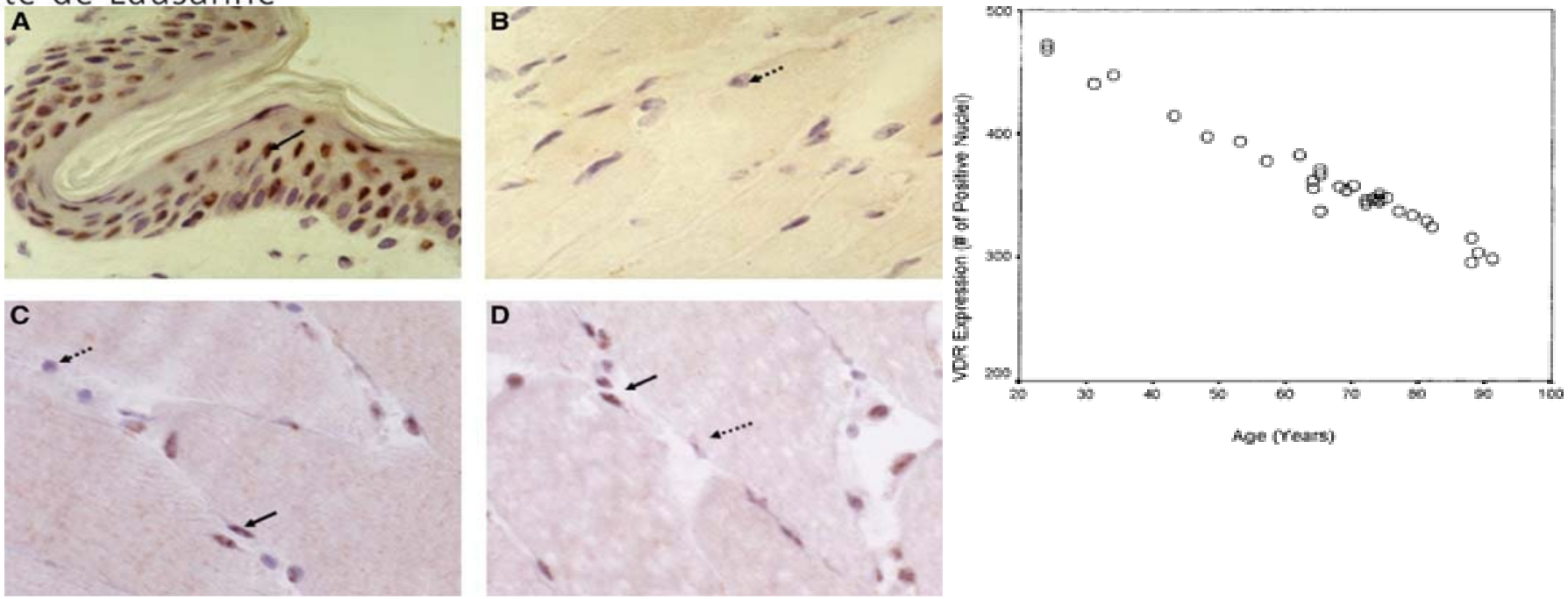
Les muscles squelettiques humains expriment le récepteur de la vitamine D

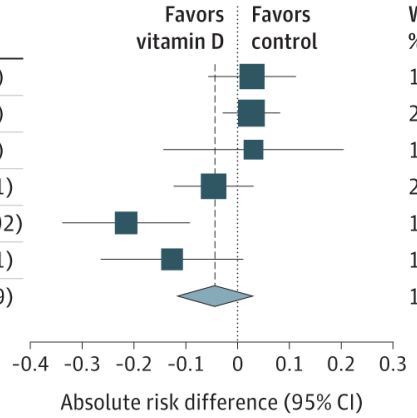


- Régulation du transport du calcium
- Absorption du phosphate inorganique pour la production de composés phosphatés riches en énergie composés phosphatés riches en énergie
- Synthèse des protéines

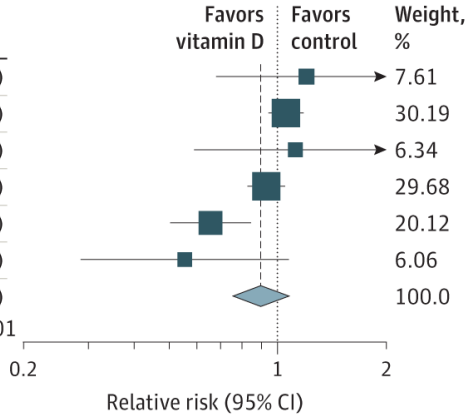
Pfeifer M, et al Osteoporosis Int 2012
Houston et al J Gerontol A Biol Sci Med Sci 2007

Le traitement à base de vitamine D réduit-il le risque de chute ?

Source	Treatment duration	Calcium received	Vitamin D: No. with event	Vitamin D: No. without event	Control: No. with event	Control: No. without event	Absolute risk difference (95% CI)
Hin et al,[27] 2017	1 y	None	34	170	14	87	0.028 (-0.057 to 0.113)
Khaw et al,[54] 2017	3.3 y	None	307	295	316	338	0.027 (-0.029 to 0.082)
Shea et al,[57] 2019	1 y	None	14	35	13	38	0.031 (-0.143 to 0.205)
Kärkkäinen et al,[39] 2010	3 y	Active intervention	179	108	205	101	-0.046 (-0.123 to 0.031)
Pfeifer et al,[51] 2009	1.75 y	Both groups	49	72	75	46	-0.215 (-0.338 to -0.092)
Pfeifer et al,[52] 2000	1 y	Both groups	11	59	19	48	-0.126 (-0.264 to 0.011)
Subtotal							-0.043 (-0.116 to 0.029)
							I^2 = 70.1%, P = .005

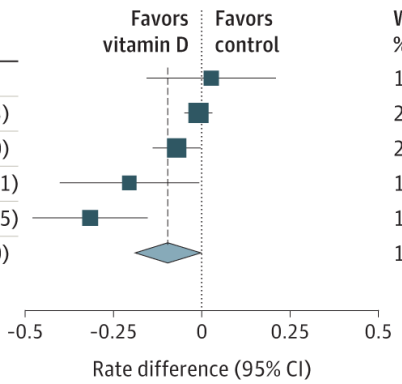


Weight, %	Relative risk (95% CI)
19.09	1.20 (0.68-2.14)
22.45	1.06 (0.94-1.18)
10.34	1.12 (0.59-2.14)
20.00	0.93 (0.83-1.05)
14.78	0.65 (0.51-0.84)
13.35	0.55 (0.29-1.08)
100.0	0.90 (0.75-1.08)
	I^2 = 66.8%, P = .01

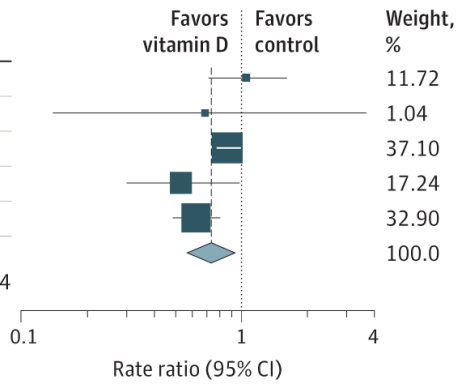


Weight, %
7.61
30.19
6.34
29.68
20.12
6.06
100.0

Source	Treatment duration	Vitamin D: No. of falls	Vitamin D: Person-years	Vitamin D: No. of falls per person-year	Control: No. of falls	Control: Person-years	Control: No. of falls per person-year	Rate difference (95% CI)
Hansen et al,[26] 2015	52 wk	71	154	.46	33	76	.43	0.03 (-0.16 to 0.21)
Wood et al,[58] 2012	52 wk	4	193	.02	3	100	.03	-0.01 (-0.05 to 0.03)
Kärkkäinen et al,[39] 2010	3 y	430	861	.50	524	918	.57	-0.07 (-0.14 to 0.00)
Pfeifer et al,[52] 2000	1 y	17	70	.24	30	67	.45	-0.20 (-0.40 to -0.01)
Pfeifer et al,[51] 2009	1.75 y	106	199.5	.53	169	199.5	.85	-0.32 (-0.48 to -0.15)
Subtotal								-0.10 (-0.19 to 0.00)
								I^2 = 76.9%, P = .002



Weight, %	Rate ratio (95% CI)
14.33	1.06 (0.71-1.62)
29.54	0.69 (0.14-3.70)
26.83	0.87 (0.77-0.99)
13.16	0.54 (0.30-0.98)
16.13	0.63 (0.49-0.80)
100.0	0.76 (0.57-0.94)
	I^2 = 59.9%, P = .04



Weight, %
11.72
1.04
37.10
17.24
32.90
100.0

Kahwati, LC et al. Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA 2021.

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La population générale doit-elle être supplémentée en vitamine D ?

	Evidence Levels
It is recommended not to administer vitamin D supplements in the general population, since there is no definite evidence of cost-effective benefits, either on mortality or on skeletal and extra-skeletal outcomes.	⊕⊕⊕

Bertoldo F et al. Nutrients 2022

Society	Vitamin D Supplementation
Institute of Medicine (2010)	600 IU/day, 18 years–70 years old 800 IU/day, over 70 years old
Endocrine Society Clinical Practice Guideline (2011)	1500 IU/day–2000 IU/day, over 19 years old
Osteoporosis Australia (2016)	At least 600 IU/day, under 70 years old At least 800 IU/day, over 70 years old Sun avoiders or people at risk of vitamin D deficiency: 1000 IU/day–2000 IU/day
National Osteoporosis Society Practical Guides (2013)	People aged 65 years and over, people who are not exposed to much sun, pregnant and breastfeeding women: 400 IU/day

In Subjects with Hypovitaminosis D, or Candidates for Bone Active Agents for Osteoporosis:	Evidence Levels
We suggest a dose of cholecalciferol supplementation between 800 IU/day and 2000 IU/day. There is no single, fixed dose for all subjects that needs to be supplemented.	⊕
We suggest a daily, weekly, monthly schedule based on the dose administered. In these settings, the maximum single daily dose to be administered should not exceed 100,000 IU. An adequate calcium intake (800–1000 mg/day) must always be ensured.	⊕
We recommend the use of an initial loading dose, followed by the maintenance dose in patients with symptomatic osteomalacia and/or serum 25(OH)D < 10 ng/mL, or in patients starting bone anti-resorptive therapy with intravenous bisphosphonates or denosumab with serum 25(OH)D < 20 ng/mL.	⊕⊕⊕
We recommend, as loading dose, cholecalciferol 3000–10,000 IU/day (average 5000 IU/day) for 1–2 months, or cholecalciferol in a single dose of 60,000 to 150,000 IU followed by the maintenance dose (2000 IU/day). Alternatively, we suggested calcifediol 20–40 mcg/day (4–8 gtt/day) for 20–30 days, before switching to maintenance dose *.	⊕⊕⊕

* With a limited recommendation for a faster normalization of serum levels of 25(OH)D only.

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Take home messages

- ✓ L'hypovitaminose D touche un grand nombre de patients dans le monde.
- ✓ Le niveau recommandé fait encore l'objet de débats, mais on s'accorde généralement à dire qu'il doit être supérieur à 20 ng/mL.
- ✓ La vitamine D a des effets prouvés sur la santé des os et des muscles.
- ✓ Aujourd'hui, il n'y a pas de consensus global sur l'efficacité du traitement.
- ✓ Les médecins doivent connaître ce problème, le reconnaître et traiter le bon patient avec le bon dosage.

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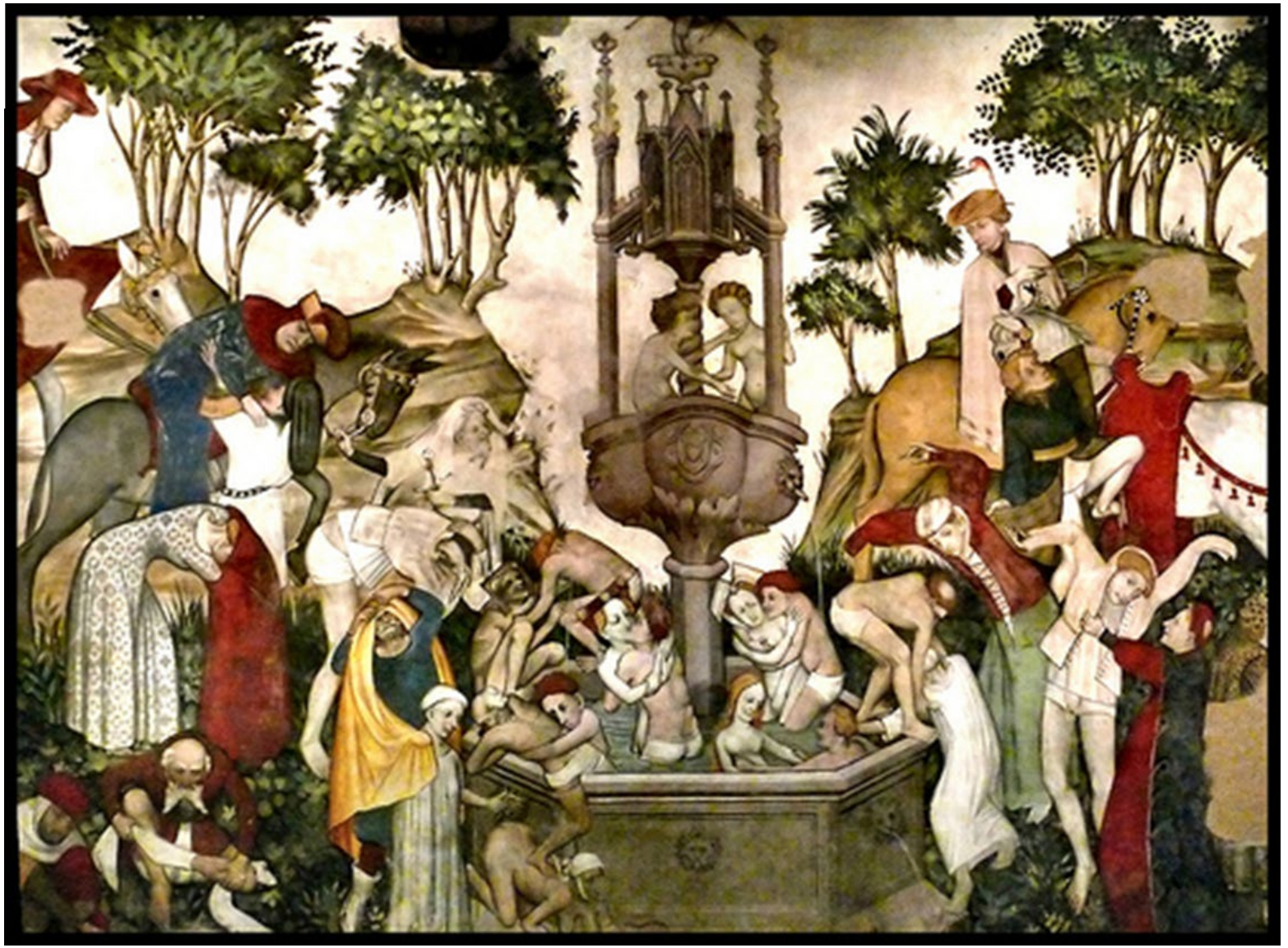
CHUV

Fontaine de jouvence



Maestro della Manta – 1420-Baronial Room - Manta Castle